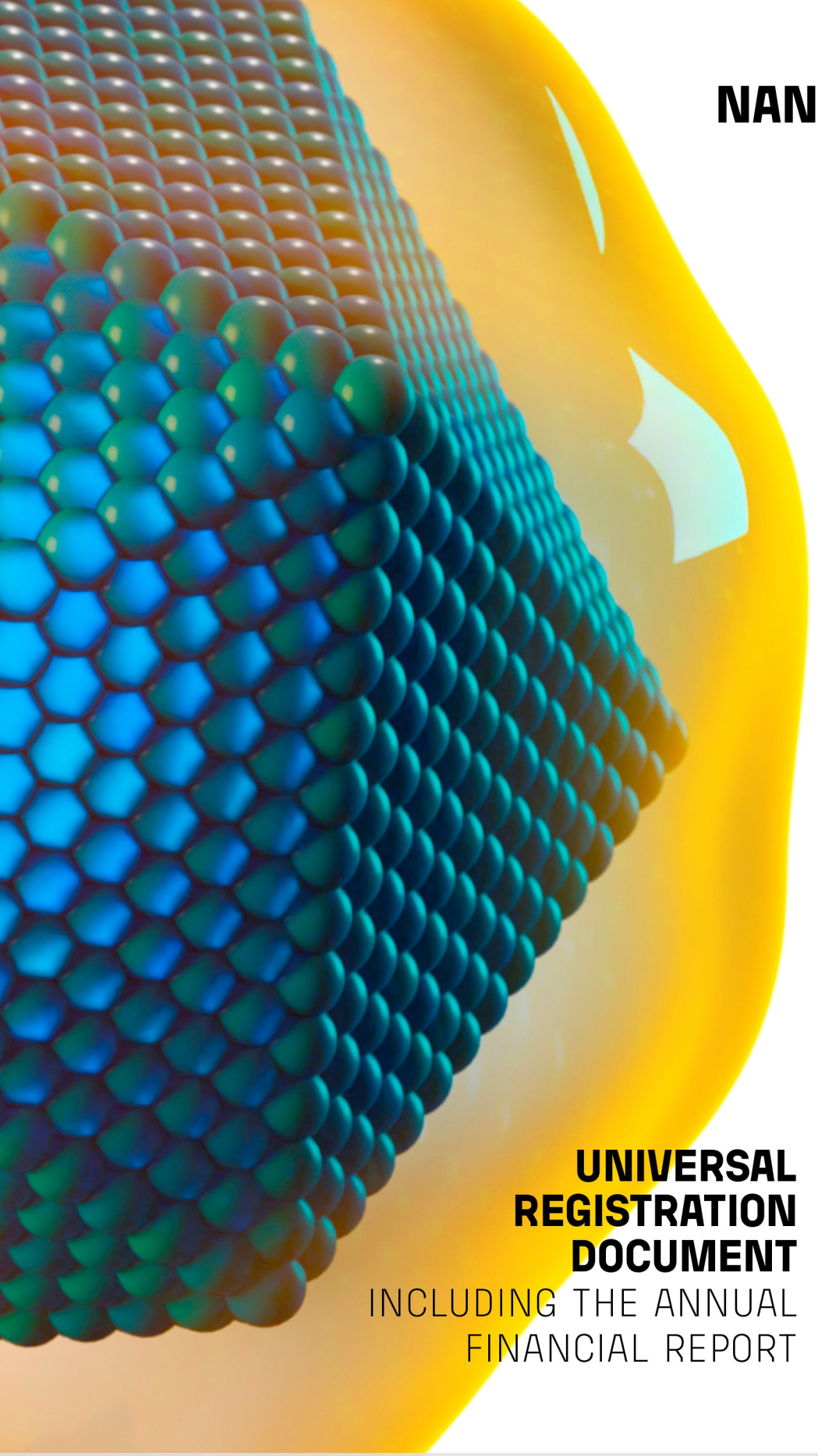
NANOBIOTIX

EXPANDING LIFE



2021

UNIVERSAL REGISTRATION DOCUMENT

INCLUDING THE ANNUAL FINANCIAL REPORT

AUTORITÉ DES MARCHÉS FINANCIERS

AMF

This universal registration document has been filed on April 08, 2022 with the French Financial market authority (Autorité des marchés financiers – AMF), as competent authority under Regulation (EU) 2017/1129, without prior approval in accordance with Article 9 of said Regulation.

The universal registration document may be used for the purposes of an offer to the public of securities or admission of securities to trading on a regulated market if completed by a securities note and, if applicable, its summary and amendment(s). The entity then formed is then approved by the AMF in accordance with the Regulation (EU) 2017/1129.

Copies of the universal registration document are available at no cost at the registered office of Nanobiotix, 60, rue de Wattignies, 75012 Paris – France. The universal registration document is also available on the website of Nanobiotix (www.nanobiotix.com) and on the website of the Autorité des marchés financiers (www.amf-france.org).

PROFILE

Nanobiotix is a late-stage clinical biotechnology company pioneering disruptive, nanophysics-based therapeutic approaches to revolutionize treatment outcomes for millions of patients with major diseases—starting with cancer. The company's vision is to expand possibilities for human life through the discovery and application of novel scientific ideas. Nanobiotix is supported by a passionate team of expert colleagues and strategic collaborators with a shared commitment to making a difference for humanity.

The Company's primary focus is the development and commercialization of lead product candidate NBTXR3. NBTXR3 is a novel, potentially first-in-class radioenhancer composed of modified, crystalline hafnium oxide nanoparticles that is administered via one-time intratumoral injection and activated by radiotherapy (RT). Once activated, the radioenhancer's physical mechanism of action is designed to induce significant tumor cell death in the target tumor, and to subsequently prime a systemic immune response.

Given the characteristics of NBTXR3, Nanobiotix believes that the radioenhancer could be broadly applicable across solid tumor indications and therapeutic combinations. As such, the product candidate's safety and efficacy potential was validated with the Company's positive results from a phase II/III study in soft tissue sarcoma (Act.in.Sarc). Nanobiotix is now targeting registration for NBTXR3 as a single-agent activated by radiotherapy in locally-advanced head and neck squamous cell carcinoma (LA-HNSCC), and evaluating as a combination agent with anti-PD-1 in an indication in advanced cancers. On a parallel path, the Company is working with collaborators to advance and expand development of the radioenhancer to additional tumor indications, therapeutic combinations, and patient populations for future registrational potential.

Currently, the Company-sponsored LA-HNSCC program includes a European phase I dose escalation/ dose expansion study (Study 102) that has completed recruitment, and a global phase III registration study (NANORAY-312) that is active and enrolling. The Company-sponsored combination program includes an ongoing phase I dose escalation / dose expansion study of NBTXR3 plus anti-PD-1 in the United States (US). Nanobiotix has also initiated engagement with US regulatory agencies on the design of a registration study for NBTXR3 plus anti-PD-1. The development expansion pathway, supported by our collaboration with The University of Texas MD Anderson Cancer Center, includes several active phase I and phase II studies evaluating NBTXR3 for the treatment of head and neck cancer, pancreatic cancer, esophageal cancer, and lung cancer. The Company expects to continue to expand the NBTXR3 pipeline with potential future collaboration as well.

The NBTXR3 development strategy consists of three (3) major components: (i) Demonstration of a tolerable safety profile and survival outcome superiority for NBTXR3 as a single-agent activated by radiotherapy in high risk, elderly patients with locally advanced head and neck squamous cell carcinoma (LA-HNSCC); (ii) Establishment of a pathway to registration for NBTXR3 as a combination agent with anti-PD-1; (iii) Proof-of-concept for NBTXR3 as both a single and combination agent in additional indications and patient populations.

Nanobiotix is dual-listed on the regulated market of Euronext in Paris (NANO) and the Nasdaq Global Select Market (NBTX). The company is headquartered in Paris, France and Cambridge, Massachusetts (US).

NOTES

Definitions

In the Universal Registration Document, and unless otherwise stated:

The terms “Company” or “Nanobiotix” refer to Nanobiotix, headquartered at 60, rue de Wattignies, 75012 Paris, registered in the Paris Trade and Corporate Register under number 447 521 600;

The term “Group” refers to the group of companies formed by the Company and its subsidiaries;

The term “we” refers to the Company or the Group, as appropriate.

A glossary defining certain terms used in the Universal Registration Document can be found in Section 6.6 of the Universal Registration Document.

The Universal Registration Document includes, among other things, the Company's financial statements prepared in accordance with accounting standards applicable in France for the year ended December 31, 2021, as well as a set of consolidated financial statements for the same year in accordance with IFRS accounting standards adopted by the European Union.

In accordance with Article 19 of the Regulation (EU) 2017/1129, the following information is incorporated by reference in the Universal Registration Document:

- the consolidated financial statements and the related statutory auditors’ report, as well as the management report for the year ended December 31, 2020, included in the 2020 universal registration document filed with the AMF on April 7, 2021, under number D.21-0272, and
- the consolidated financial statements and the related statutory auditors’ report, as well as the management report for the year ended December 31, 2019, included in the 2019 universal registration document approved by the AMF on May 12, 2020, under number R.20-010.

The 2019 universal registration document and the 2020 universal registration document are available on the Company's website.

Market and competition information

The Universal Registration Document includes, in particular in Section 1.3 "Description of activities," information relating to the Group's markets and its competitive position. This information comes in particular from studies carried out by external sources. Publicly available information, which the Company considers reliable, has not been verified by an independent expert, and the Company cannot guarantee that a third party using different methods to collect, analyze or calculate data on these markets would achieve the same results.

Forward-looking information

The Universal Registration Document contains information on the Group's prospects and development strategy. These indications are sometimes identified by the use of the future, conditional or forward-looking terms such as “consider,” “anticipate”, “think,” “aim,” “expect,” “intend,” “must,” “ambition,” “estimate,” “believe,” “wish,” “may” or, as the case may be, the negative form of those same terms, or any other similar variation or terminology. This information is not historical data and should not be construed as guarantees that the stated facts and data will occur. This information is based on data, assumptions and estimates considered to be reasonable by the Company. It is subject to change or modification due to uncertainties related in particular to the economic, financial, competitive or regulatory environment. This information is mentioned in various chapters of the Universal Registration Document and contains data on the Group's intentions, estimates and objectives concerning, in particular, the market in which it operates, its strategy, growth, results, financial position, cash flow and forecasts. The forward-looking information mentioned in the Universal Registration Document is given only as of the date of the Universal Registration Document. The Group operates in a competitive and ever-changing environment. It therefore cannot anticipate any risks, uncertainties or other factors that could affect its business, their potential impact on its business or the extent to which the materialization of a risk or combination of risks could have significantly different results from those mentioned in any forward-looking information, it being recalled that none of this forward-looking information constitutes a guarantee of actual results.

Risk factors

Investors are encouraged to carefully read the risk factors described in Section 1.5 “Risk Factors” in the Universal Registration Document before making any investment decision. The realization of some or all of these risks could have a significant adverse effect on the Group's business, financial situation, results or future prospects. In addition, other risks, not yet identified or considered insignificant by the Company as of the date of the Universal Registration Document, could also have a significant adverse effect.

We believe that expanding possibilities for human life starts with the eradication of serious illness. 2021, and consider that the milestones Nanobiotix achieved therein, would enable our company to move forward in our mission to revolutionize treatment outcomes for millions of patients with cancer and other major diseases. While COVID-19, and the systemic challenges presented by efforts to curtail its spread, are still with us, the patients we aim to serve are in urgent need of innovation. This need fuels our commitment to deliver on the promise of our pipeline and the continued advancement of our product candidates toward registration.

2021 showcased the potential of our development programs exploring the broad potential therapeutic benefit of our novel radioenhancer: NBTXR3. Both our single-agent and therapeutic combination development programs yielded new data suggesting radiotherapy-activated NBTXR3 may improve clinical outcomes for patients with either local or systemic disease. Additionally, our preclinical programs produced intriguing data on the NBTXR3 mechanism of action and combination potential with multiple immune checkpoint inhibitors that merit further investigation and could inform future development opportunities. We activated sites and initiated recruitment efforts for NANORAY-312, our global phase III registration study evaluating NBTXR3 for high risk, elderly patients with locally advanced head and neck cancer; enabling the randomization of our first patient in January 2022. In addition, our team worked closely with The University of Texas MD Anderson Cancer Center to continue recruitment for several active studies and to launch new studies. We also added a new strategic partner to advance and expand development of NBTXR3 in Asia. The team at Curadigm secured a collaboration agreement to investigate its proprietary Nanoprimer technology in combination with therapeutic candidates in Sanofi's gene therapy pipeline and continues to lay the groundwork for future clinical development. In parallel, in 2021 we strengthened our leadership team with the appointment of both a new supervisory board chairman and a new chief financial officer.

Under the leadership of our new CFO, we took measures in 2021 to increase operational efficiencies and optimize capital allocation. These measures effectively extended our operating runway while further strengthening our priority pathways in head and neck cancer and immunotherapy. Moving forward into 2022, we remain focused on executing our ongoing studies; capturing the opportunity to drive value by defining our registration strategy for NBTXR3 in combination with anti-PD-1; and expanding the solid tumor-agnostic, therapeutic combination-agnostic profile of NBTXR3 through our strategic collaborations.

First and foremost, our confidence is driven by the belief that our disruptive approach can make a real difference for patients in need. However, none of our efforts would be possible without the outstanding and continued support we receive from our team, collaborators, and shareholders. We offer our heartfelt appreciation for your commitment to walk with us in our journey to expand life.

Thank you,

Laurent Levy

Key events

Nanobiotix, founded in 2003, is a pioneering and leading nanomedicine company that has developed new approaches to local cancer treatment. Nanobiotix aims to become a major player in healthcare, providing new and innovative solutions for the benefit of patients, while creating sustainable value for its shareholders.

_2003
Nanobiotix was created in France from a spin-off of the State University of New York at Buffalo (USA).

_2007-2010
The Company developed the NanoXray research program, leading to the filing of several patent families and the launch of preclinical trials.

_2011
Nanobiotix received approval from the Affsaps (ex-Agence Nationale de Sécurité du Médicament et des produits de Santé, France) to start the first phase I/II clinical study in humans evaluating NBTXR3 for patients with locally advanced soft tissue sarcoma.

_2012
In August, the Company entered into a licensing agreement for the development and commercialization of NBTXR3 in the Asia-Pacific region with the Taiwanese company PharmaEngine. On October 29, 2012, Nanobiotix shares were listed on the regulated market of Euronext Paris.

_2013
Nanobiotix received approval by the ANSM to start a new phase I clinical trial in head and neck cancer.

_2014
In September, the Company's first U.S. subsidiary was established in Cambridge, Massachusetts. At the same time, the Company received authorization from the ANSM to start the phase II/III clinical study evaluating NBTXR3 for patients with locally advanced soft tissue sarcoma.

_2015
In July, the ANSM authorized the start of a phase I/II clinical study evaluating NBTXR3 for patients with primary and metastatic liver cancers. In late December, the Company received approval from the U.S. Food and Drug Administration (FDA) regarding the application for Investigational New Drug (IND) status to start the first clinical study in the United States (US) evaluating NBTXR3 in prostate cancer.

_2016
Nanobiotix launched a new immuno-oncology research program with NBTXR3 and the first application for market authorization (CE mark) for the product candidate.

_2017
The Company opened its own manufacturing site - at BioPark in Villejuif (France) - increasing its capacity to produce NBTXR3 to meet the growing future demand related to clinical trials and patient needs. Concurrently, the FDA provided approval of the IND application for the first immuno-oncology clinical study in the US evaluating NBTXR3 in combination with an anti-PD-1 antibody for patients with lung and head and neck cancers. This year also saw the creation of two new Nanobiotix subsidiaries - one in Germany and the other in Spain.

_2018
Nanobiotix reached agreement on a non-dilutive financial partnership with the European Investment Bank (EIB) to boost the Company’s research, development, and innovation activities, in the form of a

loan of up to €40 million until July 26, 2020, subject to the achievement of a set of agreed upon performance criteria. The Company also disclosed positive results from its phase II/III clinical study evaluating NBTXR3 in soft tissue sarcoma, which demonstrated significant superiority and clinical benefits over the standard of care. This randomized clinical study validated the mode of action of NBTXR3.

_2019

In January, the Company launched a new clinical collaboration with The University of Texas MD Anderson Cancer Center (MD Anderson)—one of the world's leading specialized hospitals for the treatment of cancer. The collaboration included, initially, nine new phase I and II clinical studies evaluating NBTXR3 for the treatment of six different types of cancer—head and neck, pancreatic, thoracic, ~~thoracic,~~ pulmonary, gastrointestinal and genitourinary cancers—involving approximately 340 patients.

A €14 million second tranche disbursement of loan financing from the EIB was received in March.

Also in March, following feedback from the FDA, the Company announced its clinical registration plan for NBTXR3 in head and neck cancer in the US.

In April, NBTXR3 received European market approval (CE mark), enabling the Company to commercialize NBTXR3, under the brand name Hensify®, for the treatment of locally advanced soft tissue sarcoma in 27 European Union countries. Concurrently, the Company raised €29.5 million through a private placement.

In December, the Company was awarded the French Prix Galien Award for most innovative MedTech.

_2020

In January, the Company articulated the plan for its global phase III registration study in head and neck cancer along with an overall update on its broad applicability of its development program.

In February,the FDA granted fast track designation to NBTXR3 for treatment of the head and neck cancer population in the planned global phase III study.

In May, the first phase I study in collaboration with MD Anderson evaluating NBTXR3 in pancreatic cancer received a 'Safe to Proceed' notification from the FDA.

In July, the Company raised €20 million in a placement of new ordinary shares with US and European investors.

In November, the Company presented positive first clinical data from its phase I immuno-oncology study showing a possible conversion of anti-PD-1 non-responders to responders with NBTXR3.

In November, two new studies in collaboration with MD Anderson evaluating NBTXR3 in combination with anti-PD-1 for head and neck cancer received 'Safe to Proceed' notifications from the FDA.

In December, Nanobiotix shares were listed, through ADS's, on the Nasdaq Global Select Market under the symbol "NBTX".

_2021

In January, Nanobiotix' subsidiary Curadigm secured a new collaboration agreement with Sanofi focused on gene therapy pipeline.

In May, the Company partnered with LianBio to develop and commercialize potential first-in-class radioenhancer NBTXR3 across tumor types and therapeutic combinations in China and other Asian markets.

In June, MD Anderson initiated the fifth clinical study under the clinical collaboration agreement with Nanobiotix evaluating NBTXR3 in lung cancer.

In October, Nanobiotix presented the first survival data from its priority head and neck cancer pathway among five presentations at the 2021 Annual Meeting of the American Society for Radiation Oncology.

In November, Nanobiotix announced new preclinical data highlighting NBTXR3 immune priming and checkpoint inhibitor combination.

_2022

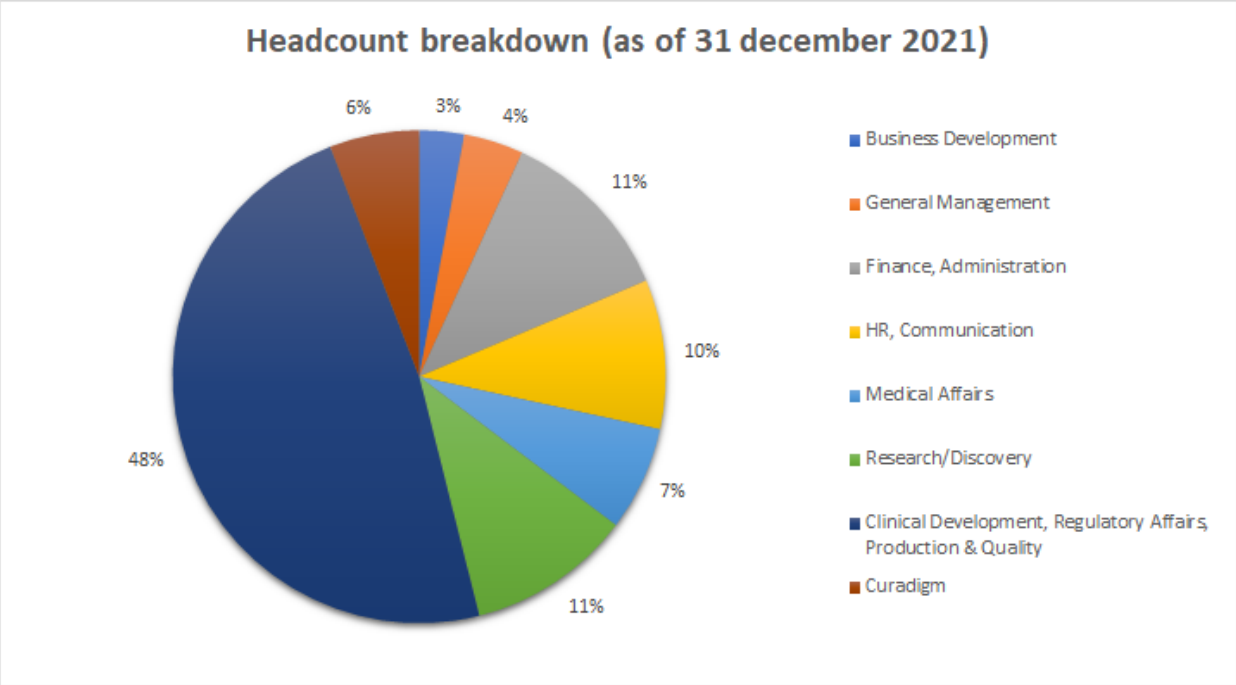
In January, first patient was enrolled in NANORAY-312 Global phase III study of NBTXR3 in head and neck cancer and Nanobiotix announced publication of new preclinical immunotherapy data showcasing the combination potential of NBTXR3 with anti-PD-1 and anti-CTLA-4.

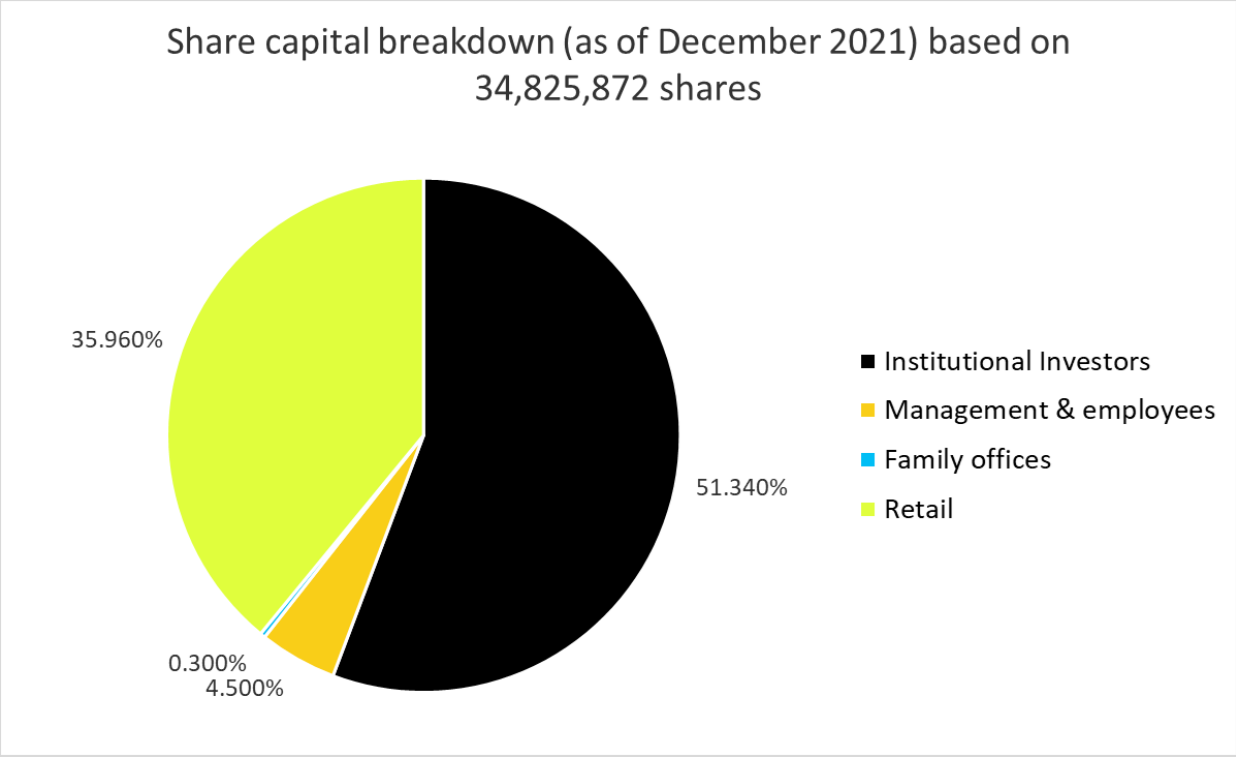
In February, a new clinical case study highlighting first patient experience of NBTXR3 treatment for pancreatic cancer was published.

NBTXR3 / Hensify® key figures

- First European market approval (CE mark) obtained, enabling the marketing of Hensify® for the treatment of locally advanced soft tissue sarcoma in 27 EU countries
- More than 13 clinical trials in several types of cancer
- Used alone or in combination with other cancer therapies, including chemotherapy and checkpoint inhibitors such as anti-PD-1 immunotherapy,
- Proof of concept in a randomized phase II/III in Soft Tissue Sarcoma (STS) featured in The Lancet Oncology
- 400+ patents issued or in process of being issued
- Fast track designation granted by U.S. FDA for investigation in head and neck cancer
- 75+ clinical sites activated worldwide
- 400+ physicians involved in clinical trials
- 250+ patients treated in the studies
- Countries where Nanobiotix runs or has run clinical trials: France, Belgium, Italy, Spain, Poland, Norway, Hungary, Romania, Hong Kong, Taiwan, Philippines, Germany, United States of America, South Africa, Australia

100 employees (excluding trainees), as of 31 December 2021
Headquarters in Paris, 5 wholly owned subsidiaries based in France, Cambridge, USA, Madrid, Spain and Munich, Germany, including Curadigm, a spin-off based in Paris, France and Boston, USA.

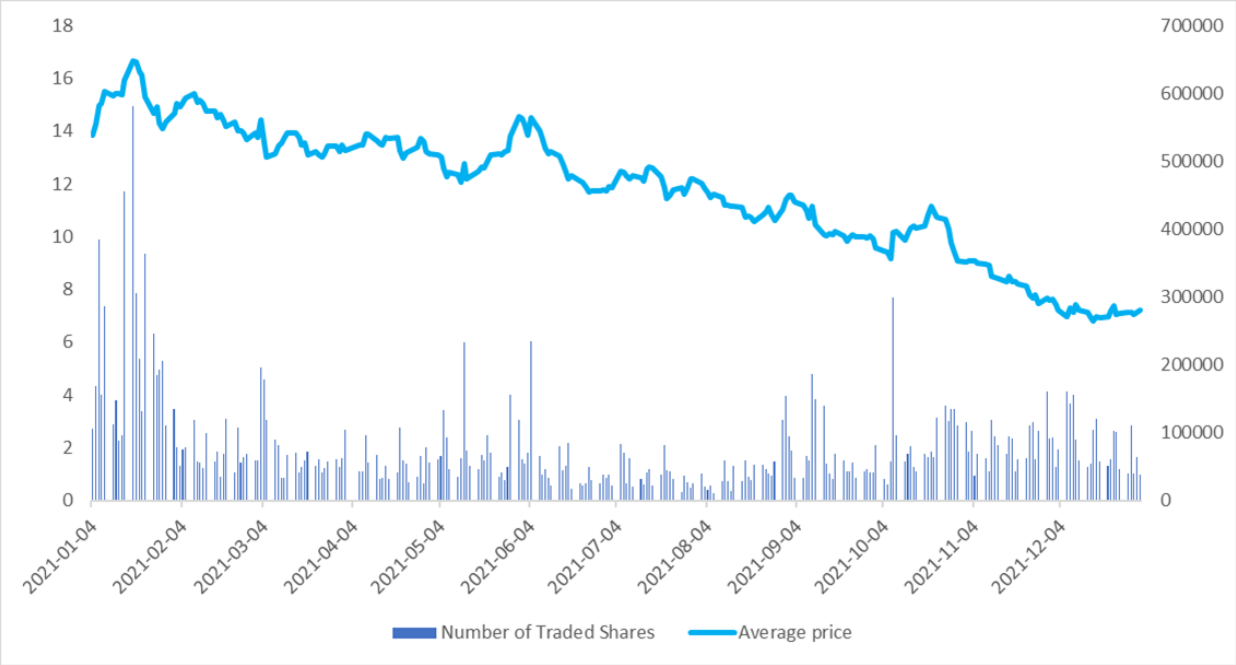




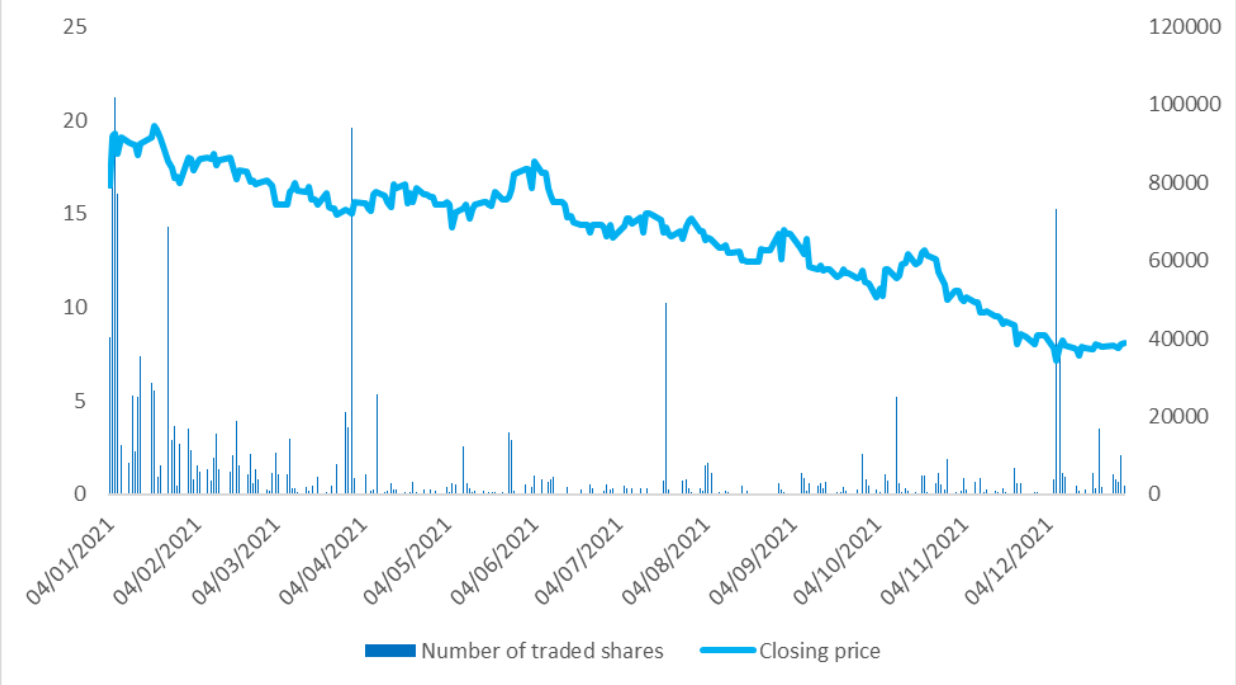
**To the Company's knowledge*

Stock market information

2021 share price & volume evolution on Euronext



2021 share price & volume evolution on Nasdaq



Stock market data

Share code
Name: Nanobiotix
Places of listing: regulated market of Euronext Paris, compartment B (ISIN code: FR0011341205, Mnemonic code: NANO) and Nasdaq Global Select Market (Mnemonic: NBTX)
Date of initial public offering on the regulated market of Euronext Paris: 29 October 2012
Date of initial public offering on the Nasdaq Global Select Market: 11 December 2020

Indices
CAC Health Care
CAC Mid & Small
CAC Pharma & Bio
CAC Small
CAC® PME
NEXT 150
NEXT BIOTECH
TECH 40
NASDAQ COMPOSITE

Additional information
Share eligible for SRD

Tickers
Reuters: NANO.PA
Bloomberg: NANO.FP

International analyst coverage
Nanobiotix has benefited from international analyst coverage since its initial public offering, mainly in France, the United States, the Netherlands and the United Kingdom:

JEFFERIES (UK)	Lucy Codrington
GILBERT DUPONT (FR)	Guillaume Cuvillier
KEMPEN (NL)	Ingrid Gafanhao
H.C. WAINWRIGHT & Co. (US)	Ramakanth Swayampakula
DEGROOF PETERCAM (BE)	David Seynnaeve
PORTZAMPARC (FR)	Clement Bassat
UBS (US)	Colin Bristow
Evercore ISI (US)	Jonathan Miller / Mike DiFiore

Financial publication calendar

March 30, 2022 – 2021 Full-Year Corporate and Financial Update

May 10, 2022 – First Quarter 2022 Corporate and Financial Update

June 21, 2022 – Annual General Meeting, Paris, France

September 7, 2022 – 2022 Half-Year Corporate and Financial Update

November 9, 2022 – Third Quarter 2022 Corporate and Financial Update

NBTXR3 pipeline

^ NANORAY-312, a global Phase III clinical trial for elderly patients with locally-advanced head and neck cancer who are ineligible for platinum-based (cisplatin) chemotherapy, will be activated in Europe and the United States initially as a Phase III trial. We expect to activate the first clinical site for NANORAY-312 in Europe in the fourth quarter of 2021, with the first patient to be randomized in early 2022. We expect U.S. site activation and enrollment to begin in 2022. For its evaluation of NANORAY-312, the FDA has accepted the available data from Study 102 Escalation. NBTXR3 for the treatment of locally advanced head and neck cancers received Fast Track designation from the FDA in February 2020.

† LianBio has been granted development and commercialization rights for NBTXR3 in key countries in Asia. In addition, certain NBTXR3 clinical trials conducted by our former collaborator, PharmaEngine, are currently being conducted in Asia and are in the process of being concluded or terminated. See "1.3.14.3. of the Universal Registration Document" for additional details.

* Phase I/II Study initiated by former partner, PharmaEngine. In conjunction with the termination of the license and collaboration agreement, PharmaEngine will implement the early termination and wind-down of this clinical trial in accordance with good clinical practice guidelines. The trial will be deemed completed when all enrolled patients have reached "end-of-study" and PharmaEngine issues a final study report.

Following proof-of-concept and European market approval for NBTXR3 in locally advanced soft tissue sarcoma of the extremities and trunk wall (Brand Name: Hensify®) in 2019, Nanobiotix will continue to prioritize its registration pathway in the US and EU for the treatment of head and neck cancers, while also working to advance the Nanobiotix immuno-oncology (I/O) program and evaluate NBTXR3 in other indications such as lung, pancreatic, esophageal, hepatocellular carcinoma (HCC), and rectal cancers.

To implement this plan, Nanobiotix will focus on head and neck cancers while its partner (i.e. The University of Texas MD Anderson Cancer Center (MD Anderson) in the US is working on other indications.

Development in head and neck cancers moving forward

There are approximately 700,000 new head and neck cancer patients worldwide each year—300,000 of these patients reside in the US and the European Union (EU)[1]. 70-80% of all head and neck cancer patients will receive radiation therapy, but significant unmet medical needs remain regarding either local control, systemic control, toxicity, or some combination of the three[2]. This is especially challenging for patients ineligible for platinum based chemotherapy (cisplatin).

In February 2020, the U.S. Food and Drug Administration reviewed the Company's request for Fast Track designation and concluded that investigation of NBTXR3 activated by radiation therapy, with or without cetuximab, for the treatment of patients with locally advanced head and neck squamous cell cancer who are not eligible for platinum-based chemotherapy meets the criteria for a Fast Track development program.

Nanobiotix recently initiated NANORAY-312 — an open-label, Phase III dual-arm, investigator's choice, randomized (1:1) global registration trial including approximately 500 elderly head and neck cancer patients who are ineligible for platinum-based concurrent chemoradiation (cisplatin). Patients in the control arm will receive radiation therapy with or without cetuximab (investigator's choice), and patients in the treatment arm will receive NBTXR3 activated by radiation therapy with or without cetuximab (investigator's choice). The primary endpoint of the study is progression-free survival (PFS) and the key secondary endpoint is overall survival (OS). The study is designed to demonstrate superiority if results show Hazard Ratios of at least 0.692 and 0.75 for PFS and OS, respectively, of NBTXR3 activated by radiation therapy over control with a statistical power of 89% on PFS and on OS with a statistical power of 80%. In addition, overall response rate, safety and quality of life will be evaluated as secondary endpoints. At final analysis, a median PFS of 9 months and median OS of 12 months are expected to be achieved in the control arm.

According to these assumptions, NANORAY-312 is expected to take approximately 48 months to be complete. It includes a futility analysis, expected approximately 18 months, and a pre-specified interim efficacy analysis after approximately 30 months after the first patient is randomized. To the fullest extent permitted by applicable regulations, the Company plans to submit an application for accelerated approval if results of the interim analysis are positive (≥ 6 months PFS difference).

First clinical sites were activated in Europe with first patient randomized in January 2022, we expect US site and Asia site (LianBio) activation in 2022.

Confirming efficacy with Phase I (Study 102) expansion

Nanobiotix has already reported promising early signs of efficacy for patients with head and neck cancer from Study 102 — a Phase I trial of NBTXR3 activated by intensity-modulated radiation therapy (IMRT) in advanced head and neck squamous cell carcinoma (HNSCC). The patient population for Study 102 includes elderly and frail patients who are ineligible for cisplatin or intolerant to cetuximab. As a result of this report, the Company launched an expansion cohort to strengthen preliminary efficacy data. Recruitment for the expansion cohort reached its target of 44 evaluable patients in the first quarter of 2022.

Additional development in head and neck with partners

To serve as many head and neck cancer patients as possible, Nanobiotix is engaged in ongoing clinical collaborations with MD Anderson in the US . The Company is collaborating with MD Anderson on several clinical trials across multiple indications, three (3) of which are expected to evaluate head and neck cancer in patient populations outside of the trials Nanobiotix is executing alone (e.g. borderline resectable, inoperable head and neck cancer (re-irradiation), etc.) The Company previously explored the safety and feasibility of NBTXR3 activated by radiation therapy in combination with cisplatin in a Phase I/II trial for patients with locally advanced cancer of the oral cavity and oropharynx with former regional partner in Asia, PharmaEngine.

Immuno-oncology program with NBTXR3

In addition to the main program evaluating the use of NBTXR3 as a single agent, Nanobiotix is running an I/O combination program in the United States. For the past decade, there has been excitement around the ability of I/O agents (immune checkpoint inhibitors or ICIs) to activate the immune system to attack tumor cells.

However, many tumors exhibit little or no response to these therapies and are considered "cold," due to a lack of immunogenicity. As a result, a small fraction of patients realizes the benefits of ICIs[3]. The Nanobiotix I/O combination program is comprised of Study 1100—a Phase I basket trial in the US—, and a large-scale collaboration with MD Anderson evaluating NBTXR3 activated by radiation therapy in combination with various immune checkpoint inhibitors (anti-PD-1, anti-PD-L1, anti-CTLA4, and LAG-3) across several preclinical and clinical trials. The program aims to evaluate the potential for NBTXR3 activated by radiation therapy in combination with immune checkpoint inhibitors to provide better local and systemic control; convert checkpoint inhibitor non-responders into responders; and increase survival.

Study 1100 is an ongoing Phase I study evaluating the safety, efficacy, and tolerability of NBTXR3 activated by radiotherapy in combination with an anti-PD-1 therapy in three cohorts of patients. The first cohort includes patients with locoregional recurrent (LRR) or recurrent and metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). The two remaining cohorts include patients with lung or liver metastases from any primary cancer eligible for anti-PD-1 therapy (e.g. metastatic melanoma, metastatic NSCLC, metastatic small cell lung cancer, metastatic HNSCC, metastatic cervical cancer, metastatic urothelial cancer, triple-negative breast cancer, hepatocellular carcinoma, renal-cell carcinoma, etc.).

Development across other indications

Study 103 - evaluating NBTXR3 activated by radiation therapy for the treatment of patients with HCC and liver metastasis - has finished recruitment and final results were presented in the first quarter of 2021. Furthermore, the Company is evaluating NBTXR3 activated by radiation therapy for patients with naïve esophageal cancer, and pancreatic cancer through the clinical collaboration with MD Anderson.

Next steps in soft tissue sarcoma

Given positive Phase II/III results and medical device market approval for NBTXR3 in Europe for the treatment of soft tissue sarcoma of the extremities and trunk wall, the Company is currently preparing a post-registrational trial that will continue evaluating safety and efficacy, and will provide patients with access to the product. Based on the expected timing of discussions with GMED regarding the planned protocol and current impact of the COVID-19 pandemic on clinical development timelines, the Company expects to launch Study 401 in Europe in the second half of 2022.

Upcoming milestones

Advance toward NBTXR3 global commercial registration through NANORAY-312, evaluating the product candidate as a single-agent activated by radiotherapy for high-risk elderly patients with locally advanced HNSCC following preliminary survival data from phase I dose expansion study (Study 102 Expansion) showing a potential benefit for elderly patients with a worse prognosis. Expected 2022 milestones include:

- Randomize First NANORAY-312 Patient in Europe – January 2022 (Achieved)
- Activate First NANORAY-312 US Site
- Activate First NANORAY-312 Asia Site (by Company's partner LianBio)

Establish a registrational pathway for NBTXR3 in combination with anti-PD-1 following initial feedback from Regulatory Agency received in March 2022 and data from the Company's ongoing phase I study (Study 1100) suggesting NBTXR3 may prime immune response, enhance response rates in anti-PD-1 naïve patients, and help overcome resistance to prior anti-PD-1 therapy in non-responders.

Expected 2022 milestones include:

- Establish Recommended Phase II Dose (RP2D) in all cohorts
- Start RP2D expansion cohorts
- Present Updated Study 1100 Data
- Announce Development Next Steps in Immuno-Oncology

Expand evaluation of NBTXR3 safety and feasibility to additional solid tumor indications and therapeutic combinations outside of Company-led pathways through collaborators. Expected 2022 milestones include:

- Establish Recommended Phase II Dose (RP2D) in Pancreatic Cancer
- Present Data from Phase I evaluation of NBTXR3 plus chemoradiation in HNSCC
- Present Data from Phase I/II evaluation of NBTXR3 plus chemoradiation in Rectal Cancer

About NBTXR3

NBTXR3 is a novel, potentially first-in-class radioenhancer composed of modified, crystalline hafnium oxide nanoparticles that is administered via one-time intratumoral injection and activated by radiotherapy (RT). Once activated, the radioenhancer's physical mechanism of action is designed to induce significant tumor cell death in the target tumor, and to subsequently prime a systemic immune response. Given the characteristics of NBTXR3, Nanobiotix believes that the radioenhancer could be broadly applicable across solid tumor indications and therapeutic combinations.

[1] *Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians, 68(6), 394-424.*

[2] *Delaney, G., Jacob, S., Featherstone, C., & Barton, M. (2005). The role of radiotherapy in cancer treatment: estimating optimal utilization from a review of evidence-based clinical guidelines. Cancer: Interdisciplinary International Journal of the American Cancer Society, 104(6), 1129-1137.*

[3] *Spigel, David R., et al. (2015): 8009-8009. ; Ferris, Robert L., et al. New England Journal of Medicine 375.19 (2016): 1856-1867. ; Borghaei, Hossein, et al. New England Journal of Medicine 373.17 (2015): 1627-1639. ; Garon, Edward B., et al. New England Journal of Medicine 372.21 (2015): 2018- 2028. ; Seiwert, Tanguy Y., et al. The lancet oncology 17.7 (2016): 956-965. ; Antonia, Scott J., et al. New England Journal of Medicine 377.20 (2017): 1919-1929*

Table of Contents

1. NANOBIOTIX AND ITS ACTIVITIES PRESENTATION

1.1. SELECTED FINANCIAL INFORMATION

The main financial information below is extracted from the consolidated financial statements of the Company and was prepared with IFRS standards as published by the IASB (International Accounting Standards Board) and approved by the European Union on the date of preparation of these financial statements.

1.1.1. Indicators and key figures

Simplified balance sheet

Based on consolidated accounts (€K)	Dec 31, 2021 Audited	Dec 31, 2020 Audited	Dec 31, 2019 Audited
Non current assets	**8,709**	**8,782**	**10,078**
Intangible assets	4	21	163
Property, plant and equipment	8,186	8,256	9,386
Financial assets	519	505	529
Current assets	**93,060**	**125,248**	**46,127**
Other current assets	9,139	6,097	11,033
Cash and cash equivalents	83,921	119,151	35,094
Total assets	**101,769**	**134,030**	**56,205**
Equity	**26,790**	**70,468**	**(1,908)**
Non-current liabilities	**38,134**	**44,522**	**43,766**
incl. financial liabilities – non-current	37,816	44,107	43,435
Current liabilities	**36,845**	**19,041**	**14,347**
incl. financial liabilities - current	8,204	4,872	1,091
Total equity and liabilities	**101,769**	**134,030**	**56,205**

Simplified income statement

Based on consolidated accounts (€K)	2021 12 months Audited	2020 12 months Audited	2019 12 months Audited
Total revenues and other income	**2,647**	**2,512**	**2,541**
incl. Revenues	10	50	68
Operating loss	**(52,579)**	**(36,428)**	**(46,779)**
Financial loss	**5,580**	**2,847**	**(4,133)**
Net loss for the period	**(47,003)**	**(33,590)**	**(50,915)**
Total comprehensive loss	**(46,915)**	**(33,469)**	**(50,863)**

Operating expenses are divided between research and development costs and selling, general & administrative costs. Details are presented below:

Research and development costs

(€K)	2021 12 months Audited	2020 12 months Audited	2019 12 months Audited
Purchases, sub-contracting and other expenses	(19,562)	(12,734)	(16,804)
Payroll costs (incl. Share-based payments)	(9,605)	(10,306)	(11,980)
Depreciation, amortization and provision expenses	(1,211)	(1,290)	(1,627)
Total research and development costs	**(30,378)**	**(24,330)**	**(30,411)**

Selling, general and administrative (SG&A) expenses

(€K)	2021 12 months Audited	2020 12 months Audited	2019 12 months Audited
Professional fees, rental and other expenses	(9,638)	(6,482)	(9,435)
Payroll costs (incl. Share-based payments)	(9,379)	(7,789)	(9,205)
Depreciation, amortization and provision expenses	(417)	(340)	(270)
Total selling, general and administrative expenses	**(19,434)**	**(14,611)**	**(18,909)**

Simplified cash flow

Based on consolidated accounts (€k)	2021 12 months Audited	2020 12 months Audited	2019 12 months Audited
Cash flows used in operations, before tax and changes in working capital	(41,412)	(33,300)	(39,647)
Changes in working capital	11,540	5,762	(1,522)
Cash flows used in operating activities	**(29,872)**	**(27,538)**	**(41,169)**
Cash flows used in investing activities	**(242)**	**(112)**	**(1,459)**
Cash flows from financing activities	**(5,180)**	**111,769**	**41,489**
Impact of exchange rates changes on cash	64	(63)	29
Net cash flow	**(35,230)**	**84,056**	**(1,109)**

1.1.2. Highlights of the financial year

2021 included several major developments for Nanobiotix in clinical, preclinical and financial areas, which make us consider that it was a pivotal year for the Group and its leading product candidate NBTXR3.

Clinical

Positive results in rectal cancer (PEP503-RC-10001)

As previously announced, NBTXR3 clinical trials conducted by PharmaEngine, Inc. ("PharmaEngine") in Asia, including the PEP503-RC-10001 open-label Phase I/II clinical trial with radiotherapy in combination with chemotherapy for patients with unresectable rectal cancer, are in the process of being concluded or terminated.

Primary and secondary endpoints of the PEP503-RC-10001 trial will assess the safety profile and determine the dose-limiting toxicity, evaluate the recommended dosage and assess the antitumor activity by evaluating the response rate of NBTXR3 administered by intratumoral injection and activated by external beam radiation, with concurrent chemotherapy treatment in patients with unresectable rectal cancer. The trial, which is being conducted at one site in Taiwan, was expected to treat up to 42 patients. PharmaEngine will implement the early termination and wind-down of this clinical trial in accordance with good clinical practice guidelines. The trial will be deemed completed when all enrolled patients have reached "end-of-study" and PharmaEngine issues a final study report in accordance with good clinical practice guidelines.

In January 2021, PharmaEngine presented first clinical results from this study at the 2021 American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO-GI 2021). Intratumoral injection of NBTXR3 with concurrent chemo-radiation (CCRT) was feasible and the product candidate was well tolerated at all dose levels, and no adverse events (AEs) or serious adverse events (SAEs) associated with NBTXR3 were observed in the study. One dose-limiting toxicity associated with the injection procedure was observed (urinary tract infection). The most frequently reported AEs were diarrhea (approximately 45%), leukopenia (approximately 40%), and dermatitis (approximately 25%), however all were grade one or grade two. More than 70% of patients in the study showed objective tumor response after CCRT. Around 90% of patients underwent total mesorectal excision (surgery) and 17.6% achieved pathological complete response (pCR). 50% of patients receiving surgery in the study had good tumor regression (tumor regression grade 0 or 1 according to modified Ryan scheme). The recommended phase 2 dose (RP2D) was established at 22% of tumor volume.

First patient injected with NBTXR3 in a patient with esophageal cancer (MD Anderson,study 2020-0122)

In January 2021, the first patient was injected in a phase I study evaluating NBTXR3 activated by radiation therapy with concurrent chemotherapy for adult patients (age > 18 years) with stage II-III adenocarcinoma of the esophagus that are treatment naïve and radiographically non-metastatic at screening. This trial is an open-label, single-arm, prospective phase I study consisting of two parts: (i) does-escalation to determine the RP2D of NBTXR3 activated by radiotherapy with concurrent chemotherapy, and (ii) expansion at RP2D with toxicity monitoring. The objectives of the study are the determination of dose-limiting toxicity, the maximum tolerated dose and RP2D.

Initiation of new clinical study in lung cancer (MD Anderson,study 2020-0123)

In June 2021, a new phase I study evaluating NBTXR3 activated by radiation therapy (RT) for patients with non-small cell lung cancer (NSCLC) amenable to re-irradiation was initiated.

This phase I study, led by Saumil Gandhi, Assistant Professor, Department of Radiation Oncology, Division of Radiation Oncology, MD Anderson, investigates the safety and optimal dose of NBTXR3 when activated by radiation therapy for the treatment of non-small cell lung cancer that cannot be treated by surgery (inoperable) and has come back (recurrent). The study has a two-cohort, open label design consisting of two parts: (i) RT safety lead-in cohort recruiting up to 10 patients and NBTXR3 activated by RT dose-finding cohort recruiting up to 12 patients; and (ii) expansion at the recommended phase II dose (RP2D) with toxicity monitoring recruiting 12 patients. The dose levels explored to be explored are 22% and 33% of baseline gross tumor volume. The planned enrollment period is up to three years. The patient population includes adults (age ≥ 18 years) with medically inoperable NSCLC with overlap between recurrent disease in need of treatment and prior RT. Given the design of the study, patients in the first cohort in part one will receive RT and be monitored for safety before the second cohort is opened where patients will receive injections of NBTXR3.

Pre-clinical collaboration results

New preclinical data presented at the first American Association of Cancer Research (AACR) virtual special conference on radiation science and medicine

In March 2021, researchers from MD Anderson presented preclinical data in a poster presentation at the American Association of Cancer Research (AACR) Virtual Special Conference on Radiation Science and Medicine. This study examined NBTXR3 activated by radiotherapy in combination with anti-PD-1 along with TIGIT and LAG3 inhibitors in an in vivo anti-PD-1 resistant mouse model (344SQR). The data showed that the combination therapy of NBTXR3, activated by radiotherapy, in combination with anti-PD-1, anti-LAG3 and anti-TIGIT (Combo therapy) significantly promoted the proliferation activity of CD8+ T cells, improved local and distant tumor control and increased survival rate.

The anti-tumor efficacy of the Combo therapy was heavily dependent on CD4+ and CD8+ T cells. The data showed that the cured mice maintained significantly higher percentages of memory CD4+ and CD8+ T cells, as well as stronger anti-tumor immune activities than control, and those from the groups treated with the Combo therapy were immune to re-injections of tumor cells. Further, in this preclinical study, the Combo therapy augmented antitumor response in both irradiated and unirradiated (abscopal) tumors.

Red Journal publication of preclinical data showing radioenhancer NBTXR3 may "reprogram" the tumor microenvironment to overcome anti-PD-1 resistance and evoke abscopal effect

In September 2021, Nanobiotix announced the publication of preclinical findings with The University of Texas MD Anderson Cancer Center (MD Anderson) in the International Journal of Radiation Oncology, Biology, Physics (Red Journal). These data support the further exploration of potential first-in-class, solid tumor-agnostic, therapeutic combination-agnostic radioenhancer NBTXR3 as a new therapeutic option seeking to induce significant tumor cell death when activated by radiotherapy, prime immune response, and overcome resistance to anti-PD-1.

New Preclinical Data to be presented at the 36th Annual Meeting of the Society for the Immunotherapy of Cancer (SITC) Highlighting NBTXR3 Immune Priming and Checkpoint Inhibitor Combination

In November 2021, new preclinical immunotherapy data for novel, potentially solid tumor- and therapeutic combination-agnostic radioenhancer NBTXR3 were presented at the 2021 Annual Meeting of the Society for the Immunotherapy of Cancer (SITC). Preclinical data presented at the meeting by Nanobiotix showed that radiotherapy-activated NBTXR3 increases CD8+ T cell infiltration and modulates the T cell receptor ("TCR") repertoire, as well as marked modulation of immunopeptidome in treated tumor cells in a mouse model. Taken together, these variations could indicate that radiotherapy-activated NBTXR3 triggers more robust immune priming than radiotherapy alone and merits further evaluation of CD8+ response and abscopal effect.

Local control as a single agent for patients with head and neck cancer (Study 102 Expansion)

Study 102 Expansion, a phase I dose expansion study evaluating NBTXR3 as a single agent activated by radiotherapy in cisplatin-ineligible locally advanced HNSCC, is evaluating a single dose of NBTXR3 at 22% of baseline tumor volume (the RP2D). Primary endpoints of the study are objective response rate (ORR) and complete response rate (CRR) of the primary tumor.

Updated data from Study 102 Expansion presented at ASTRO further support NBTXR3 administration, followed by activation with radiotherapy, as feasible and well-tolerated. Data showed a median Overall Survival (mOS) of 18.1 months and a median Progression Free survival of (mPFS) of 10.6 months in the evaluable population (n=41) from the dose expansion part of its phase I, multicenter, open-label, non-randomized dose escalation and dose expansion study evaluating NBTXR3 as a single-agent activated by radiotherapy in tough-to-treat elderly and frail LA-HNSCC patients ineligible for cisplatin and intolerant to cetuximab (Study 102 Expansion). In the full population (all evaluable and non-evaluable patients treated; n=54), data showed a 14.1-month mOS and a 9.4-month mPFS. The data suggest that lower mOS and mPFS observed in the full population versus the evaluable population in the study could be related to early death associated with high burden of comorbidity in the non-evaluable population.

Evaluability in Study 102 Expansion was determined based on the patient receiving at least 80% of the intended intratumoral dose of NBTXR3, at least 60 Gy of radiotherapy, and the required imaging to assess the target lesion at baseline and at least once post treatment.

Response rates remained consistent with previously reported results from the dose escalation and dose expansion study, showing a best observed target lesion objective response rate (ORR) of 85.4% and a best observed target lesion complete response rate (CRR) of 63.4% (including one patient assessed as Complete Response by principal investigator per eCRF).

Of the 21 evaluable patients with a best observed overall response of complete response (CR) with a mean follow-up of 16.1 months, 6 patients died for non-oncologic reasons and only one died from disease progression.

NBTXR3 administration was feasible and well-tolerated overall. A total of 8 Grade 3-4 NBTXR3-related adverse events (AEs) were observed in 8 patients, representing 1.3% of all observed AEs. Of these AEs related to NBTXR3, 5 serious adverse events (SAEs) were observed including dysphagia, sepsis, soft tissue necrosis, stomatitis, and tumor hemorrhage. Of the SAEs, one death from sepsis assessed by the investigator as possibly related to NBTXR3, radiotherapy, and cancer was observed.

Priming Immune Response and Immunotherapy Combination in Advanced Cancers (Study 1100)

Data presented by Nanobiotix during ASCO from its ongoing Study 1100, a phase I study of NBTXR3 activated by radiotherapy for patients with advanced cancers treated with an anti-PD-1 therapy showed that as of the data cut-off, NBTXR3 activated by radiotherapy and combined with anti-PD-1 induced local or distant tumor regression in 76.9% (10/13) of evaluable patients in the study, regardless of their prior exposure to anti-PD-1.

As of the data cut-off, the data showed that among anti-PD-1 naïve patients, 80% (4/5) had tumor regression and 60% (3/5) had investigator-assessed objective response, including one (1) complete response according to response evaluation criteria outlined in RECIST 1.1.

Results also show NBTXR3 plus radiotherapy could potentially stimulate immune response and convert anti-PD-1 non-responders into responders. In patients with prior primary or secondary resistance to anti-PD-1, 75% (6/8) had tumor regression and 50% (4/8) had investigator-assessed objective response. These included one (1) complete response and two (2) partial responses by RECIST 1.1, along with one (1) additional investigator-assessed pathological complete response. Some patients in the study showed delayed tumor response and/or abscopal effect, suggesting NBTXR3 may potentially prime an immune response.

NBTXR3 administration by intratumoral injection was feasible and well-tolerated. As of the data cut-off date, the overall adverse event (AE) profile did not differ from what is expected with radiotherapy or anti-PD-1 agents. Sixteen serious AEs were observed, of which four (4) were identified as NBTXR3 or injection related.

Finance

Nanobiotix and PharmaEngine mutually agree to terminate their collaboration

In March 2021, in light of disagreements over a number of issues with respect to the development of NBTXR3 in the Asia-Pacific region, Nanobiotix and PharmaEngine mutually agreed to terminate the licensing and collaboration agreement entered into in August 2012. Accordingly, on March 4, 2021, Nanobiotix and PharmaEngine entered into a termination and release agreement (the "Termination Agreement"). Under the Termination Agreement, Nanobiotix retained all rights to the development and commercialization of NBTXR3 in the Asia-Pacific region. Nanobiotix agreed to make total termination payments to PharmaEngine of up to $12.5 million in the aggregate as described below.

PharmaEngine was eligible for and received a $2.5 million payment following the announcement of Nanobiotix's collaboration with LianBio for the Asia-Pacific region. During the six months ended June 30, 2021, PharmaEngine also received $4.0 million in conjunction with the completion of various administrative steps in connection with the winding-up of the collaboration.

PharmaEngine will be eligible to receive an additional $1.0 million in administrative fees and a final payment of an additional $5.0 million upon a second regulatory approval of an NBTXR3-containing product in any jurisdiction of the world for any indication. PharmaEngine is entitled to receive a low-single digit tiered royalty based on net sales of NBTXR3 in the Asia-Pacific region for a 10-year period commencing on the corresponding first date of sales in the region. As of December 31, 2021, these future payments were not accrued because the triggering events have not occurred.

As part of the Termination Agreement, PharmaEngine re-assigned to Nanobiotix rights for the development, manufacture, commercialization and exploitation of NBTXR3 in the Asia-Pacific region, as well as all development data, regulatory materials, and all regulatory approvals that are in the name of PharmaEngine or its affiliates. Consequently, NBTXR3 clinical trials conducted by PharmaEngine in Asia are in the process of being concluded or terminated.

Nanobiotix and PharmaEngine also agreed to a mutual release of all claims against the other party and its respective affiliates.

Nanobiotix partners with LianBio for the development and commercialization of NBTXR3 in several oncology indications and in combination with several anti-cancer therapies, in China and other Asian markets

In May 2021, Nanobiotix entered into a partnership with LianBio, a biotechnology company dedicated to bringing paradigm-shifting medicines to patients in China and major Asian markets, to develop and commercialize Nanobiotix's lead product candidate, NBTXR3 into Greater China (mainland China, Hong Kong, Taiwan, and Macau), South Korea, Singapore and Thailand.

LianBio will collaborate in the development of NBTXR3 in Asia Pacific, and contribute to patient enrollment in five future global registrational studies across several tumor types and therapeutic combinations including immunotherapy. LianBio will also support the expansion of global phase III registrational study in head and neck cancer into Greater China with longer term strategic alignment across multiple tumor indications and therapeutic combinations.

Under the terms of the agreement, the Company received a $20 million upfront payment and is entitled to receive up to an aggregate of $220 million in potential contingent, development and commercialization milestone payments. The Company will also be eligible to receive tiered, low double-digit royalties based on net sales of NBTXR3 in the licensed territories. LianBio will fund all development and commercialization expenses in the collaboration territory, and the Company will continue to fund all development and commercialization expenses in all other geographies.

Nanobiotix announces the appointment of Dr. Gary Phillips as Chairman of the Supervisory Board

In May 2021, Dr. Gary Phillips was appointed Chairman of the Company's supervisory board of the Company ("the "Supervisory Board"). Dr Phillips succeeded Laurent Condomine, who retired from the Supervisory Board after 11 years of leadership.

Nanobiotix announces the appointment of Bart Van Rhijn as Chief Financial Officer and member of the executive board of the Company to support its international expansion

On June 1, 2021, the Company announced the appointment of Bart Van Rhijn, MBA, as Chief Financial Officer and member of the executive board of the Company (the "Executive Board"). Bart Van Rhijn brings proven capabilities in global financial management, business development and pharmaceutical commercialization as the Company launched of its second clinical registration study for NBTXR3 in head and neck cancer (NANORAY-312), continued development in immunotherapy, and planned expansion across solid tumor types and therapeutic combinations. He succeeded Philippe Mauberna, who stepped down from his roles as Chief Financial Officer and Executive Board member after 8 years of service to the Company.

1.1.3. Recent events

Research and development updates

In January 2022, the Company announced enrollment of the first patient in NANORAY-312 global phase III registration trial. The study builds on Study 102, a phase I trial evaluating safety and early signs of efficacy for radiotherapy-activated NBTXR3 in high-risk elderly locally advanced head and neck squamous cell carcinoma who are ineligible to chemotherapy and intolerant to cetuximab. Preliminary data presented at the 2021 Annual Meeting of the American Society for Radiation Oncology (ASTRO) showed that the treatment was feasible and well tolerated at all dose levels. Exploratory efficacy data showed a high target lesion objective response rate of 85.4% and a target lesion complete response rate of 63.4%, along with a median PFS of 10.6 months and median OS of 18.1 months in the evaluable patient population, which has a poorer prognosis than those patients eligible for the phase III study. The Company expects first clinical site activation in the US during the first semester of 2022 while first clinical site activation in Asia by LianBio is expected in 2022.

As per the plan, the Company's resources are focused on head and neck cancers, as these indications have a high incidence, unmet medical needs, and offer a prime opportunity to demonstrate medical and economic value for NBTXR3.The Company is also moving forward with its evaluation of NBTXR3 as a potential pillar of immuno-oncology, given positive data showing that the product may generate an immune response in patients on its own, and also increase the efficacy of immune checkpoint inhibitors in combination. In parallel, Nanobiotix collaborators will continue to develop NBTXR3 across several additional indications including lung, esophageal, pancreatic, and others.

As such, in January 2022, Nanobiotix also announced the publication of new preclinical immunotherapy data on the combination potential of NBXTR3 with anti-PD-1 and anti-CTLA-4 in the peer-reviewed Journal of Nanobiotechnology. Data in an anti-PD-1 resistant lung cancer model showed that adding NBTXR3 to a combination of radiotherapy, anti-PD-1, and anti-CTLA-4 produced significant antitumor effects against both primary and secondary tumors, improved the mouse survival rate from 0 to 50%, and induced long term antitumor memory and that potential immune priming effect of NBTXR3 may scale beyond anti-PD-1, and could merit further investigation in preclinical and clinical settings.

In February 2022, Nanobiotix announced the publication of a new clinical case study with preliminary data on the first-in-human administration of NBTXR3 in pancreatic cancer. The case study provides the first demonstration of local endoscopic delivery of NBTXR3 to a deep visceral tumor, and adds to a growing body of clinical data suggesting injection feasibility in pancreatic cancer, head and neck cancer, lung cancer, liver cancer, colorectal cancer, esophageal cancer, prostate cancer and soft tissue sarcoma. Review of data as of the date of this document from Expansion Study 102 (n=44) shows median overall survival (mOS) of 23 months in evaluable patients demonstrating continued improvement relative to the analysis presented at ASTRO 21 and consistent with data reported from the dose escalation phase of Study 102.

COVID-19 Pandemic

Developments around the COVID-19 pandemic since its emergence in early 2020 are being closely monitored by the Company and its management. However, given the great uncertainty regarding the evolution of COVID-19 pandemic, global confinement measures and a possible resulting economic downturn, the potential impact of the pandemic on the Group's activities and future results remains highly uncertain.

The Group's first priority is the safety of its employees, patients and partners. It is taking all possible measures to protect those working in countries impacted by this epidemic.

The Company will continue to regularly assess the impact of COVID-19 on its business and will communicate any significant evolution on the subject to the market.

1.2. PRESENTATION AND EVOLUTION OF THE COMPANY

1.2.1. General presentation of the Company's activities

Nanobiotix, a spin-off from the State University of New York at Buffalo (SUNY Buffalo), was created in 2003. The Company is a pioneering leader in biotechnology, specializing in the development of physics-based treatment solutions that aim to significantly improve benefits for patients by bringing nanophysics to the heart of the cell. Nanobiotix's philosophy is to design and deliver innovative, effective and scalable solutions to address important unmet medical needs with expanded therapeutic potential offer by physics-based technology.

First-in-class radioenhancer NBTXR3, for which Nanobiotix has patented protection as summarized in the section 1.3.13.4 of the Universal Registration Document, aims to expand the benefits of radiotherapy for millions of patients with cancer. In addition, the Company's immuno-oncology program has the potential to bring a new dimension to immunotherapies in oncology.

Nanobiotix has been listed on the regulated market of Euronext in Paris since 2012 and on the Nasdaq Global Select Market since late 2020. The Company's headquarters are located in Paris, France. The Company has a wholly owned subsidiary in Cambridge, United States as well as five wholly-owned subsidiaries located in France, Spain and Germany, including Curadigm, based in Paris, France and its own wholly owned subsidiary—Curadigm Corp., located Cambridge, Massachusetts, United States. The Company has also established a branch based at Geneva, Switzerland.

Milestones in the Company's recent development

_2019

- **January:**
  - Nanobiotix and the University of Texas MD Anderson Cancer Center signed a large-scale global clinical collaboration on NBTXR3. The 9 clinical trials will evaluate NBTXR3 in 6 different cancers involving approximately 340 patients. Nanobiotix will fund this collaboration for a minimum total amount of approximately $11 million;
- **March:**
  - Nanobiotix received a payment of €14 million under the second tranche of the loan granted by the European Investment Bank;
- **April:**
  - Hensify® (NBTXR3), first ever radioenhancer, obtained European market approval (CE mark) for the treatment of locally advanced soft tissue sarcoma;
  - Nanobiotix raised approximately €29.5 million in a placement of new ordinary shares with new investors and existing shareholders from the United States and Europe.
- **May:**
  - Launch of Curadigm SAS as a wholly owned subsidiary of Nanobiotix. The technology aims to prime the body to receive various therapeutics and could reshape the balance between efficacy and toxicity for patients.
- **July:**
  - New organizational structure as the Company enters its next stage after first European Market Approval;
  - Publication of Phase III Soft Tissue Sarcoma data for first-in-class NBTXR3 in *The Lancet Oncology*;
- **September:**
  - Phase I study results showed first-in-class NBTXR3 could present a valuable option for patients with hepatocellular carcinoma or liver metastasis.

- **December:**
  - Nanobiotix received the 2019 Prix Galien award for first-in-class Hensify® for the Most Innovative Medtech.

_2020

- **February:**
  - Fast track designation granted by U.S.FDA for investigation of first in class NBTXR3 in Head and Neck cancer.
- **May:**
  - First Phase I trial with NBTXR3 in pancreatic cancer deemed safe to proceed per US FDA.
  - Positive first results from phase I expansion in locally advanced head and neck cancer published at ASCO 2020.
- **June:**
  - Nanobiotix secures €10M in non-dilutive financing;
- **July:**
  - Nanobiotix successfully raised approximatively €20 million through the placement of ordinary new shares to US and European investors.
- **October:**
  - First patient injected with NBTXR3 in pancreatic cancer and safe to proceed notifications for two additional trials within the MD Anderson collaboration;
- **November:**
  - Positive first clinical data showing potential signal of immune priming: conversion of anti-PD-1 non responders to responders with radioenhancer NBTXR3;
  - Two new phase II trials evaluating NBTXR3 in combination with anti-PD-1 for the treatment of head and neck cancer within the MD Anderson collaboration;
- **December:**
  - Closing of the global offering and full exercise of underwriters' option to purchase additional ADSs, bringing gross proceeds of global offering to $113.3 million;

_2021

- **January:**
  - Positive first results for novel NBTXR3 in rectal cancer study published at ASCO GI 2021;
  - Curadigm secured new collaboration agreement with Sanofi focused on gene therapy pipeline;
  - First patient injected with NBTXR3 in esophageal cancer.

- **March:**
  - Agreement reached with PharmaEngine, Inc. to terminate the License and Collaboration agreement that the Company and PharmaEngine entered into in August 2012.

- **May:**
  - Partnership with LianBio signed to develop and commercialize potential first-in-class radioenhancer NBTXR3 across tumor types and therapeutic combinations in China and other Asian markets;

- **June:**
  - Bart Van Rhijn joined as Chief Financial Officer and member of the Executive Board to support global expansion;
  - New data published for potential first-in-class radioenhancer NBTXR3 in combination with anti-PD-1 showing local or distant tumor regression in 76.9% of evaluable patients regardless of prior anti-PD-1 exposure;
  - Initiation of new clinical study evaluating NBTXR3 in lung cancer within the MD Anderson collaboration.

- **September:**
  - Red Journal publication of preclinical data showing radioenhancer NBTXR3 may « reprogram » the tumor microenvironment to overcome anti-PD-1 resistance and evoke abscopal effect.

- **October:**
  - Publication of first survival data in head and neck cancer: 18.1 month median overall survival for 41 evaluable elderly and frail patients with HNSCC in phase I expansion evaluating NBTXR3 as a single agent activated by radiotherapy.

_2022

- **January:**
  - First patient enrolled in NANORAY-312 global phase III registrational study of NBTXR3 in head and neck cancer.

  - **February:**
  - Publication of new clinical case study highlighting first patient experience of NBTXR3 treatment for pancreatic cancer

1.2.2. Organizational chart

Nanobiotix headcount counts 100 employees (excluding trainees) at the end of the 2021 financial year, supervised by a team of complementary and highly experienced management as well as a Supervisory Board composed of experts in their respective fields.

1.2.2.1. Management

The management of the Company includes highly experienced professionals.

Executive Board (the "Executive Board")

Laurent Levy, Ph.D., Co-founder, Chairman of the Executive Board

Nationality: French

Age: 50

Corporate office renewal date: March 8, 2016

Term of corporate office: at the end of the general shareholders meeting which shall approve the accounts for the financial year ended December 31, 2023

Biography

Laurent Levy is the co-founder of Nanobiotix and has served as our Chairman of our executive board since March 2003. He was first appointed as Chairman of the Executive Board of the Company on May 27, 2004. He has extensive experience in sciences and techniques related to nanotechnologies. His research at the frontier of biotechnology and nanotechnologies has resulted in the development of a number of concrete applications such as NBTXR3, which could open a new method for cancer treatment.

Prior to joining Nanobiotix, from 2000 to 2003, he served as consultant for Altran Technologies and worked in the development of the application of nanotechnologies with companies such as Sanofi S.A., Guerbet S.A., and Rhodia S.A., as well as for early-stage biotechnology companies. He has served as president of the supervisory board of Valbiotis S.A. (Euronext Paris: ALVAL) since March 2017, as a founding member of the Nanomedicine Translation Advisory Board since June 2014 and as vice chairman of the executive board of the European Technology Platform on Nanomedicine since December 2012. He is the author of more than 35 international scientific publications and communications, has made several innovations that led to patent applications and patents granted, and regularly speaks on the topic of using nanoparticles to fight cancer, including at a TEDxParis event. He holds a Doctorate in Physical Chemistry, specializing in nanomaterials, from the Pierre and Marie Curie University (Université Paris VI Pierre et Marie Curie) in Paris and from the CEA (Commissariat à l'Énergie Atomique et aux Énergies Alternatives), and a DEA (advanced studies and diplomas) in Physics of condensed matter from the UPVI-ESPCI (Paris), followed by a post-doctoral fellowship at the Institute for Lasers, Photonics and Biophotonics, SUNY (State University of New York), Buffalo, USA.

Bart Van Rhijn, Chief financial Officer

Nationality: Dutch

Age: 49

Corporate office appointment date: May 31, 2021

Term of corporate office: at the end of the general shareholders meeting which shall approve the accounts for the financial year ended December 31, 2023

Biography

Bart Van Rhijn brings extensive experience in consultancy, technology, and life sciences industries and joins Nanobiotix after nearly 3 years as chief financial officer at Servier Pharmaceuticals, LLC (Servier US). Prior to Servier US, he held leadership roles in prominent organizations in Europe and North America, including PricewaterhouseCoopers, Philips and Galderma in Head of Tax, Senior Director of Mergers and Acquisitions, and Head of Finance positions. Bart Van Rhijn's track record reflects a relentless commitment to streamlining business operations, driving growth, and unlocking value. His varied experiences include the successful reorganization of a healthcare technology-enabled services business, coordination of strategic financing transactions, and the efficient scaling of commercial businesses. Bart Van Rhijn Van Rhijn has a strong commitment to organizational health and empowers his teams to embrace innovation, challenge the status quo, and drive optimal results while putting patients and customers first. In addition, Bart Van Rhijn Van Rhijn is on the Advisory Board of a Boston-based healthcare start-up, is a venture partner at an emerging technology fund and co-founder of a podcast hosting and production start-up.

Bart Van Rhijn Van Rhijn received master's degrees in Civil Law and Tax Law at Leiden University, The Netherlands, obtained his MBA with honors from Babson's Olin School of Management, and his Certified Management Accountant (CMA) certification from the Institute of Management Accounts.

Anne-Juliette Hermant, Chief People Officer

Nationality: French

Age: 48

Corporate office renewal date: March 13, 2020

Term of corporate office: at the end of the general shareholders meeting which shall approve the accounts for the financial year ended December 31, 2023

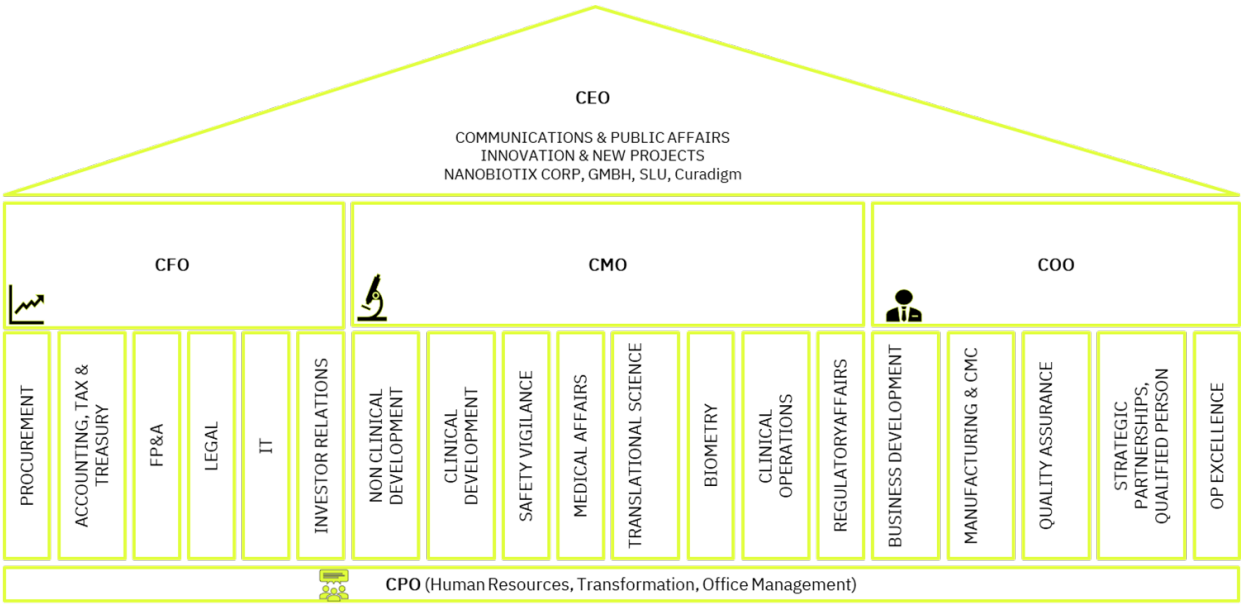
Biography

Anne-Juliette Hermant brings over 14 years in talent management and development acquired in different entities at AXA. She worked at AXA Partners for 3 years as Global Head of Talent, Development, Culture and Corporate Responsibility. Before AXA Partners, Anne-Juliette served as Chief Learning Officer of the AXA Group and was the Founder and Head of the AXA Research Fund, a €100 million fund created by the AXA Group to support frontier science in all fields related to an understanding of the risks faced by human society.

Anne-Juliette was born in Strasbourg, France and grew up between Guyane and the French Caribbean islands of Martinique and Guadeloupe. She relocated to Paris to pursue her studies and has remained in the city throughout her career.

Anne-Juliette holds a Ph. D in French literature from the Ecole Normale Supérieure and studied Politics at Sciences Po Paris.

1.2.2.2. Operational chart



1.2.2.2.1. Innovation and new projects

Nanobiotix's philosophy is rooted in the concept of pushing past the boundaries of what is known to expand possibilities for human life. The innovation and new projects team is dedicated to finding innovative therapeutic solutions to expand life of patients.

The project teams manage the Company's innovative projects autonomously, efficiently and reactively. To carry out their work and when necessary, research teams use subcontractors with state-of-the-art technologies.

The research team proactively acts in each Phase of the product development cycle and supports the development of new technologies and projects.

1.2.2.2.2. Clinical and non-clinical development

Nanobiotix is dedicated to the development of innovative treatments in the field of oncology for patients with significant unmet medical needs. This team ensures the integrity of research and the application of the highest ethical standards at all levels of clinical development organization and safety vigilance. It is also the guarantor of the application of national and international regulations.

In addition, the introduction of safe and effective therapies for cancer patients is the essential mission of clinical development and the safety-vigilance team. In particular, the Safety Vigilance team is responsible for training personnel in device vigilance and has been able to expand and improve the Nanobiotix program, which encompasses the legislative and regulatory context of device vigilance and the Company's preparation for the management of potential incidents and crisis situations. The

development team works closely with the research team to ensure a safe transition from animal to human for its innovative products, when they have reached their development phase. The operational model of Nanobiotix's development is designed around obtaining "proof of concept," which requires close interaction between different specialities and rapid decision-making.

With a model based on innovation and value creation, the Company designs and directs its clinical development programs and study protocols in close collaboration with its advisory committee. Further, their implementation is carried out in partnership with specialized providers approved by national and international regulatory agencies according to the specifics of the activities.

1.2.2.2.3. Regulatory affairs department

The management of regulatory affairs is a strategic function for the Company: internally, it is the link between the clinical research development, quality assurance department, safety-vigilance including supports device vigilance/pharmacovigilance, manufacturing and market access functions, therefore working in close collaboration with these departments. Outside the Company, it is the key contact with the regulatory authorities. All around the world, it liaises with the competent authority: the Agence Nationale de Sécurité du Médicament et des Produits de Santé (National Agency for the Safety of Medicines and Health Products or ANSM), the French medical device agency (GMED) in France, the *Food and Drug Administration* (FDA) in the US, etc.

The Regulatory Affairs department is responsible for regulatory oversight and compliance with all regulations and standards. The Regulatory Affairs department has been involved in the strategy of new health products since the launch of their development. It plays an important operational role, anticipating regulatory constraints and requirements, weighing the best registration procedures to follow, managing communication and negotiations with the authorities, preparing and submitting relevant regulatory applications to health authorities, and obtaining their approvals. It is responsible for maintaining marketing authorizations or CE markings (including labelling, notice and packaging), and is involved in managing a product's lifecycle.

1.2.2.2.4. Clinical operations

The Clinical operations department is made up of several teams including the clinical development team. The ultimate goal of human research is to improve the management and treatment of patients at all stages of the disease. Clinical trials assess the efficacy, safety and tolerability of new treatments before they can be offered to patients.

The department's missions and objectives include setting the clinical research strategy, the management of projects including the implementation of relevant risk management plans, the management of complex study budgets and associated resources (organization, administration, management, control, technical-regulatory support of clinical trials).
Fundamental operational objectives can be summed up as follows:

- Ensuring the quality of clinical trials conducted in health facilities;
- Accelerating patient recruitment in clinical trials;
- Ensuring the safety of patients included in clinical trials; and
- Optimizing the resources dedicated to clinical research.

To achieve these goals, the department relies on multidisciplinary collaborators:

- Tasked with filings with regulatory authorities, logistics, and monitoring of national, European or international clinical trials conducted by Nanobiotix;
- Who devote part of their activities to the design of the trial methodology, data management, analysis and publication of the results.

Nanobiotix outsources the following operations:

- Clinical monitoring and part of its management to a specialized organization with extensive oncology registration experience;
- Data management including electronic data storage and part of its data management;
- Statistical analysis and management of Independent Data Monitoring Committee (external trial committees, responsible for assessing patient safety); and
- Pharmacovigilance, storage and internal management in accordance with the recommendations of the EMA and the FDA.

The subcontractors selected by the Company have a Quality Assurance system and some have the Research Tax Credit (CIR) certification issued by the French Ministry of Research. These collaborations are mostly carried out within the framework of service agreements (provision of technology, scientific expertise, pharmacovigilance logistics, etc.). Usually, in addition to the payment of the sums owed under the agreements, Nanobiotix must, in some cases, add the partner's name with the Company's scientific publications, including publications on oncology medicine.

In all cases, clinical studies have been granted regulatory approval from health authorities, follow rigorous scientific protocols, and respect, in accordance with the principles of ethics, the interests of those subject to medical research.

1.2.2.2.5. Quality assurance department

The quality assurance department determines key processes, guides objectives, corrects potential malfunctions, and improves existing products or services for the whole of the Company’s quality system. It aims to mobilize all staff around the "quality" objectives. Quality improvement is also sought by an improvement in processes carried out step by step. The approach is iterative and aims for successive and continuous improvements. The quality assurance Department uses a methodical approach to problem solving and the treatment of any dysfunctions (deviation processing system). The processing of changes is based on the appropriate use, as a group, of quality methods and tools (change control system), as well as information meetings or training sessions on various types of topics.

In addition, the quality assurance department promotes quality research through improvement in the technical competence of Nanobiotix staff. Specialization has increased within the Company and the number of well trained and competent professionals needed for the control of manufacturing processes, analytical results and/or rendering of a service, has greatly increased.

Finally, the quality policy is also part of the regulatory certifications and CE-marking approval procedures, coordinated by the department of regulatory affairs. Together with the marketing These procedures are necessary for the marketing of products in Europe in particular.

Nanobiotix is ISO certified against ISO 13 4885 (2016) and within the CE mark according to 93/42/MDD Directive Annex II.3.

1.2.2.2.6. Medical affairs department

Nanobiotix has been building a strong Global Medical Affairs Department to support its move from a development organization to a late state clinical development company.

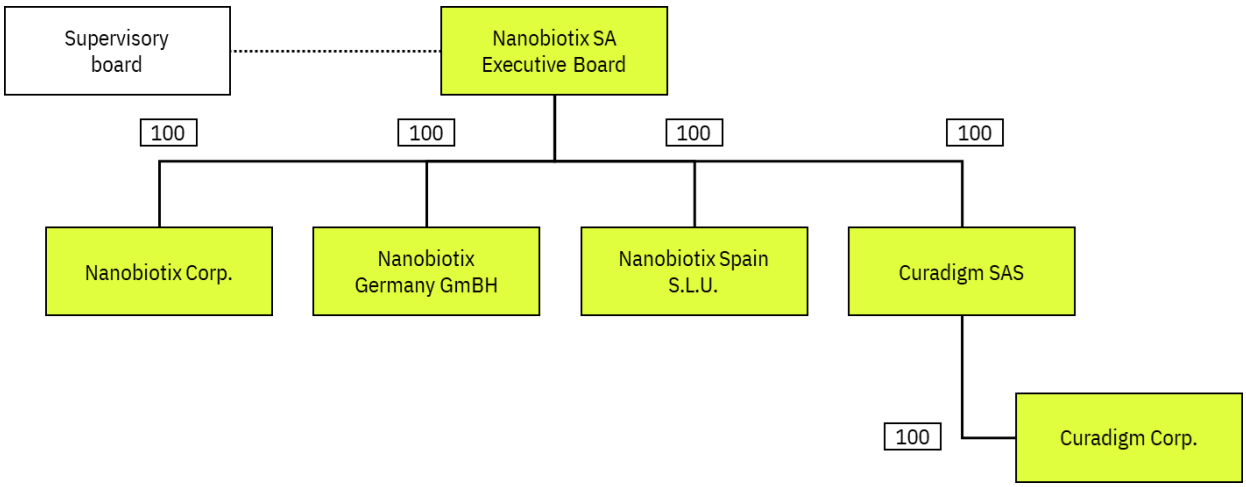
As such, the expansion of the Medical Affairs department will build on capabilities to support scientific communication and research on NBTXR3 by expanding the international team of medical science managers and experienced medical writers. The medical science managers and medical writers are Doctors of Medicine, Doctors of Pharmacy, or Doctors of Science, scientific experts in the health industry and more specifically in oncology.

The core business objectives of this team are to:

- Providing scientific and medical information in response to the requests of health professionals;
- Providing appropriate scientific and medical information (clinical, development, publications, etc.) based on the needs of health experts or professionals, through individual interviews or scientific meetings, and to write medical information materials, respond, as needed, to specific and medical questions, during medical commissions of hospitals in charge of the proper use of the product;
- Developing scientific partnerships to advance our scientific program
- Implement the medical strategy at the regional, national, European and American levels;
- Contribute to the coordination of clinical studies;
- Ensure the communication of clinical study results to Scientific conferences;
- Writing scientific publications and communication of results
- Providing scientific oversight.

The Global Medical Affairs Department relies on the CMO entity and works closely with the clinical development team and the department responsible for market access.

1.2.2.3. Legal Group chart



1.2.2.3.1. List of subsidiaries, branches, and secondary establishments

The Company holds a 100% interest in four subsidiaries: Nanobiotix Corp., a Delaware state law firm, Nanobiotix Spain S.L.U., a Spanish company, Nanobiotix Germany GmbH, a German company, and Curadigm SAS, a company incorporated under the laws of France. Curadigm SAS has itself a wholly owned subsidiary located in Cambridge, United States

For more information on these subsidiaries, see section 5.5 of the Universal Registration Document.

Nanobiotix also has a Swiss branch (succursale) as well as a secondary establishment located at 1, Mail of Professor Georges Mathé, 94 800 Villejuif, where its manufacturing site is located.

1.2.2.3.2. Main intragroup transactions

In the course of business, the Company has set up agreements relating to the organization of financial and other services within the Group according to the following structure:

- Cash agreement: entered into between the Company and its U.S. subsidiary in 2015, where advances made by any of the Group's entities, up to a maximum of €5 million, are paid for at the legal rate in France;
- Service agreements: service agreements have been entered into between the Company and its U.S., Spanish, and German subsidiaries in 2018, and its subsidiary Curadigm SAS in 2019, allowing subsidiaries to be remunerated for activities carried out for the benefit of the parent company;
- An agreement is also in place since 2019 with Curadigm SAS, for the purpose of re-invoice the overheads related to the space occupied by the subsidiary at the Company's headquarters in Paris.

Further details can be found in the Company's annual financial statements set forth in the notes to the income statement in the statutory accounts' appendices in section 4.3 of the Universal Registration Document.

1.2.3. Property, plants and equipment

The Company does not own any real estate. It leases its headquarters in Paris and, since 2017, the premises in the BioPark in Villejuif, near Paris, for production activities currently in the testing and testing phases. The lease that was renewed in 2021 has a term of 9 years, ending June 30, 2030. It also leases workspaces in the United States, in Cambridge, Massachusetts, for its US subsidiary, and in New York on a monthly basis. The Group's European subsidiaries do not rent premises, as employees are itinerant. The Company owns equipment for its research, development and manufacturing activities. This equipment was valued at €443 thousand (after depreciation) as of December 31, 2021 compared to €595 thousand at December 31, 2020.

Curadigm does not have any lease contracts in France or the United States but has a service agreement with Nanobiotix to get access to office space and laboratories in Nanobiotix' headquarters.

Information about lease agreements

For its head office, the Company rents space in two buildings at 60 rue de Wattignies in the 12th arrondissement of Paris. In 2017, the Company consolidated its leases where its head office is located. The single lease for the space leased at head office has a term of ten years, ending June 30, 2027, and the Company may give leave at the end of each three-year period. On January 24, 2019, in addition to the original lease agreement, an amendment was signed for an additional annual rent of €225 thousand, effective and retroactive to January 1, 2019. As a result, the overall annual rent will be increased to €686 thousand. The Company benefited from a rent-free period of 8 months from January to August 2019 to allow the Company to convert the newly leased space. No other material expenditures are expected in the short term, as of the date of the Universal Registration Document.

Since 1 January 2019, following the application of IFRS 16 – *Leases*, the Company recognizes all of its lease contracts in its consolidated balance sheet (see chapter 4.1. of the Universal Registration Document for further details.

Below is a list of the main running lease agreements the Company has entered into.

Information on leases

	INFORMATION RELATED TO LEASE AGREEMENTS (€k)								
	UTILISATION	Contractual status as of December 31, 2021				Contractual status as of December 31, 2020			
		SURFACES (m^2)	DEPOSIT OR GUARANTEE	QUATERLY RENT	END OF TERM	SURFACES (m^2)	DEPOSIT OR GUARANTEE	QUATERLY RENT	END OF TERM
Head office	Offices, laboratory, archives and parking	2,622	170	172	30/06/2027	2,622	170	172	30/06/2027
Manufacturing site	Manufacturing and development activities	1,195	63	94	29/06/2030	1,195	176	87	30/06/2026
US offices	Administration	36	16	34	Renewal clause	36	16	34	Renewal clause

Payments due per period at December 31, 2021

Contractual obligations (€k)	Payments due per period			
	At 1 year the most	At more than 1 year and up to 5 years	Over 5 years	Total
Simple leases	1,064	4,256	1,660	**6,980**

1.2.4. Investments

For the reporting period, the main net investments related to the Company's business were as follows:

Nanobiotix's net investments

Based on consolidated accounts (€K)	Dec 31, 2021 Audited	Dec 31, 2020 Audited	Dec 31, 2019 Audited
Intangible assets	4	21	163
Property, plant and equipment	8,186	8,256	9,386
Financial assets	519	505	529
Total	**8,709**	**8,782**	**10,078**

The main property, plant and equipment held by the Company consist mainly of fixtures and fittings and equipment in premises leased by the Company, technical equipment for research, development and production, as well as office and computer equipment. These fixed assets are shown in Note 6 to the consolidated financial statements for the year ended December 31, 2021, prepared under IFRS in section 4.1 of the Universal Registration Document.

Investments underway

As of the date of the Universal Registration Document, the majority of investments are made in France, given the location of its head office and manufacturing facilities as well as the majority of its employees.

The Company does not have any short or long-term investments planned.

1.3. DESCRIPTION OF ACTIVITIES

1.3.1. Overview

We are a clinical stage biotechnology company focused on developing first-in-class product candidates that use our proprietary nanotechnology to transform cancer treatment by increasing the efficacy of radiotherapy.

Our lead product candidate, NBTXR3, is an aqueous suspension of functionalized, crystalline hafnium oxide nanoparticles designed for injection directly into a malignant tumor and is activated by radiotherapy (RT). When exposed to ionizing radiation, NBTXR3 amplifies the localized intratumor killing effect of that radiation and may also prime adaptive immune response and create long-term anti-cancer memory. NBTXR3 is designed to enhance the overall efficacy of radiotherapy without resulting in additional side effects on the surrounding healthy tissues. Given the physical mechanism of action, we believe that NBTXR3 could be developed as a tumor-agnostic treatment targeting all solid tumors that are treated with radiotherapy and across therapeutic combinations, including immune checkpoints inhibitors.

Radiotherapy, also called radiation therapy, involves the use of X-rays or other high-energy particles or rays to kill cancer cells in tumors. It is among the most common cancer treatments, both as a standalone therapy and in combination with surgery, chemotherapy or biological therapies. In developed countries with access to radiotherapy, approximately 60% of all cancer patients will receive radiotherapy at least once, either alone or as a part of a more complex treatment protocol. Nevertheless, many of these patients still die from the progression of their cancer because, among other reasons, they are not able to receive a high enough radiation dose to completely destroy their tumor without resulting in an unacceptable level of damage to surrounding healthy tissues. We believe that by mitigating these limitations, NBTXR3 may improve the survival rate and quality of life for cancer patients.

Our pioneering approach uses nanophysics to bring a physical mode of action to destroy cancer cells. Unlike traditional chemotherapies or biologics, NBTXR3 has a broadly applicable mechanism of action that we believe to have the potential to be used in the treatment of all solid tumor types in conjunction with radiotherapy. The nanoparticles have a high electron density, which allows a tumor that contains NBTXR3 to absorb more energy than could otherwise be absorbed by the cancer cells alone. This controlled concentration of energy leads to greater localized cancer cell destruction. When exposure to radiation ceases, the nanoparticles return to their inactive, inert state. However, the subsequent effect of improved physical cell destruction may allow for a greater exposition of tumor antigens in the microenvironment. Preclinical data and early data from our ongoing clinical studies both suggest that NBTXR3 activated by radiation therapy may allow for the priming of the immune system. This priming effect, if validated through further clinical testing, may be due to the activation of complex causal mechanisms, referred to as pleiotropic biological pathways, and increased exposition of antigens resulting in the activation of a patient's own immune cells to destroy cancer cells in the body. We believe that NBTXR3's novel mechanism of action and effect, when activated, on the tumor microenvironment could enable better local control of tumors and may potentially enhance systemic control of tumors.

We believe that NBTXR3's mode of action could improve outcomes for patient populations across all solid tumors that may be treated with radiotherapy alone or in combination with other therapeutic agents. These patient populations represent a significant market opportunity for NBTXR3. Moreover, we believe NBTXR3 could bring new opportunities to patients with cancers that cannot currently be treated with radiotherapy because of the radiosensitivity, or other characteristics, of the tissues near the tumor. The three most advanced indications for which we have announced positive clinical trial results are locally advanced STS (for which we can already legally commercialize NBTXR3 in the EU),

locally advanced head and neck cancers (for which the FDA has granted Fast Track designation for the treatment of elderly patients ineligible for platinum-based chemotherapies, the patient population for our global Phase III clinical trial) and liver cancers.

We achieved a major proof-of-concept milestone for NBTXR3 with the completion of our randomized, controlled Phase II/III clinical trial in the EU for the treatment of patients with locally advanced STS of the extremities and trunk wall. Our Phase II/III clinical trial achieved its primary endpoint showing approximately twice as many STS patients who received NBTXR3 plus radiotherapy achieved a pathological complete response, which is defined as less than 5% residual viable cancer cells in the tumor, compared to patients who received radiotherapy alone. This difference was statistically significant and served as the basis to obtain the right to legally commercialize the product in the EU. In April 2019, we completed the regulatory process for the CE mark of NBTXR3, thereby allowing the product to be commercialized in the 27 EU countries for the treatment of locally advanced STS of the extremity and chest wall. We are currently preparing to conduct Study 401 (MS01_1), a post-registrational trial that will continue evaluating the safety and efficacy of NBTXR3, now approved for commercial sale for the treatment of locally advanced STS in the EU under the brand name, Hensify®, and provide patients with access to the product.

We are currently prioritizing the development of NBTXR3 in the United States and the EU for the treatment of patients with locally advanced head and neck cancers ineligible for chemotherapy, which we believe presents a significant opportunity for NBTXR3 because of the high incidence of these cancers and the significant unmet medical need for such patients. More than half of locally advanced head and neck cancers include large primary tumors which may invade underlying structures, spread to regional nodes or both. Moreover, approximately 50% of patients with locally advanced head and neck cancer who are unable to receive chemotherapy succumb to their cancer within 12 months from the start of radiotherapy. Further, because treatment of locally advanced forms of head and neck cancer ordinarily requires aggressive, concerted measures, the subpopulation of elderly patients generally suffers from limited therapeutic options. Accordingly, we believe NBTXR3 could represent a significant benefit for this patient population with the potential to extend survival and improve quality of life.

In 2018, we concluded an initial dose escalation phase of Study 102 Escalation, our Phase I clinical trial in elderly patients with locally advanced head and neck cancers who are ineligible for chemotherapy or intolerant to cetuximab, a patient population that is typically treated with radiotherapy alone. In Study 102 Escalation, nine out of the 16 evaluable patients who received NBTXR3 plus radiotherapy achieved a complete response according to RECIST 1.1, the response evaluation criteria in solid tumors, a set of published rules that define whether tumors in cancer patients have improved, stayed the same or worsened during treatment. Of the seven patients who received radiation plus the two highest doses of NBTXR3 and who were alive at the 12- month cut-off date, five of seven patients were still alive at 24 months following treatment. Patients who received NBTXR3 in this trial also have not experienced any serious adverse events associated with treatment. Based on these encouraging results, we commenced Study 102 Expansion, a Phase I expansion study to obtain additional preliminary efficacy data.

We presented updated clinical results from Study 102 Expansion at the 2021 Annual Meeting of the American Society for Radiation Oncology (“ASTRO”) in October 2021 showing a median Overall Survival (“mOS”) of 18.1 months and a median Progression Free Survival of (“mPFS”) of 10.6 months in the evaluable population (n=41), with a cut-off date of September 3, 2021. Investigator-assessed response rates remained consistent with previously reported results from the dose escalation and dose expansion study, showing a best observed target (injected) lesion ORR of 85.4%, and a best observed target lesion CRR of 63.4% at a median follow up of 9.5 months. These best observed target lesion response rates include one patient recorded by the principal investigator of the study as an unconfirmed complete response. NBTXR3 administration remained feasible and well-tolerated. A total of eight Grade 3-4 NBTXR3-related AEs were observed in eight patients, representing 1.3% of all AEs. Of these AEs related to NBTXR3, five SAEs were observed including dysphagia, sepsis, soft tissue necrosis,

stomatitis, and tumor hemorrhage. One death from sepsis occurred, which the investigator assessed as possibly related to NBTXR3, radiotherapy, and cancer. See "1.3.6.2. of the Universal Registration Document." A review of data as of the February 22, 2022 cut off date from Expansion Study 102 shows median overall survival (mOS) of 23 months in evaluable patients (n=44) demonstrating continued improvement relative to the analysis presented at ASTRO 21 and consistent with data reported from the dose escalation phase of Study 102.

We are conducting NANORAY-312, a global Phase III clinical trial for elderly patients with squamous cell carcinoma who are ineligible for platinum-based chemotherapy. The first clinical sites for NANORAY-312 were activated in Europe during the fourth quarter of 2021, with the first patient being randomized in January 2022. We expect activation and enrollment at U.S.sites and Asian sites, through our collaboration partner LianBio, to begin in 2022.

Alongside our core NBTXR3 development program, we are also pursuing a robust development program to study the use of radiotherapy-activated NBTXR3 in combination with immune checkpoint inhibitors across several solid tumor indications. In recent years, significant attention has been focused on the potential of immuno-oncology treatments, and in particular, checkpoint inhibitors. Checkpoint inhibitors are a type of immunotherapy that function to block proteins that stop the immune system from attacking cancer cells. In doing so, they enable the patient's T cells to recognize cancer cells that would otherwise be invisible to immune attack. However, many tumors exhibit little or no response to checkpoint inhibition (these tumors are referred to as "cold" tumors). Our preclinical and early clinical results suggest that NBTXR3 plus radiotherapy may prime the immune response, thereby rendering otherwise cold tumors more prone to recognition by the patient's immune system (making them "hot tumors") and therefore potentially more responsive to I-O treatments such as checkpoint inhibitors.

As part of our checkpoint inhibitor combination development program, we are conducting Study 1100, a Phase I basket trial for NBTXR3 in combination with the anti-PD-1 checkpoint inhibitors nivolumab (Opdivo) or pembrolizumab (Keytruda) in patients with LRR or R/M HNSCC or with lung or liver metastases from any primary cancer that is eligible for anti-PD-1 therapy. We presented updated clinical results from Study 1100 at ASTRO's Annual Meeting in October 2021. We believe that these early results suggest that NBTXR3 has the potential to increase the proportion of patients that respond to immune checkpoint inhibitors, and we have commenced initial discussions with regulatory authorities regarding the potential registration pathway, for this immunotherapy combination. In early 2022, we amended the Study 1100 protocol to add an expansion phase in three cohorts, including two cohorts focused on R/M HNSCC patients that are either naïve to anti-PD-(L)-1 therapy or resistant to prior anti-PD-(L)-1 therapy and combining other eligible patients with lung and/or liver metastasis from anti-PD-(L)-1 resistant advanced cancers into a third cohort. See "1.3.6.3. of the Universal Registration Document" for additional detail. As part of our clinical collaboration with MD Anderson, we plan to evaluate NBTXR3 in combination with various checkpoint inhibitors (anti-PD-1, anti-PD-L1 and anti-CTLA-4) in patients across several indications, including inoperable, locally advanced head and neck cancer, R/M HNSCC, advanced solid tumors, and metastatic lung or liver cancer.

As of December 31, 2021, NBTXR3 has been administered to approximately 300 patients. Given Nanobiotix's focus areas, and balanced against the scalable potential of NBTXR3, we have engaged in a strategic collaboration strategy with large and reputable partners to expand development of the product candidate in parallel with our priority development pathways, as discussed under the caption "—NBTXR3 Development Pipeline" below. In 2018 we entered into a broad, comprehensive clinical research collaboration with MD Anderson to sponsor several Phase I and Phase II studies in the United States to evaluate NBTXR3 across tumor types and therapeutic combinations, with a total of approximately 340 patients expected to be enrolled across these clinical trials. Five clinical trials under this collaboration—a Phase I study in patients with locally advanced or borderline resectable pancreatic cancer, a Phase I study in patients with esophageal cancer, a Phase I study in patients with non-small cell lung cancer and two Phase II studies in patients with head and neck cancer in combination with

anti-PD-1—have commenced enrollment. In May 2021, we entered into a collaboration agreement with LianBio to develop and commercialize NBTXR3 in key countries in Asia, including Mainland China, Taiwan and South Korea, pursuant to which LianBio has undertaken to contribute to enrollment in up to five global registrational studies for NBTXR3.

We were founded as a spin-off from the State University of New York, Buffalo in 2003. Team members at Nanobiotix, including our founder, Laurent Levy, have nearly two decades of experience developing Nanobiotix's technology and we believe Nanobiotix to be a pioneer and leader in the field of nanomedicine. We have built an integrated, multidisciplinary team that combines expertise in physics, biology and medicine. We believe that its unique expertise in nanotechnology will provide its stakeholders with opportunities to expand its product pipeline and to advance the development of its product candidates, either on its own or in collaboration with third parties. Our corporate headquarters and manufacturing facilities are located in Paris, France, with U.S. operations in New York City, New York and Cambridge, Massachusetts.

NBTXR3 Development Pipeline

As a result of nearly two decades of experience developing our technology, and our broad collaboration with MD Anderson, we have a robust development pipeline. The chart below highlights ongoing and planned clinical trials portfolio, including those that are under Nanobiotix's collaboration with MD Anderson. Nanobiotix is currently in discussions with MD Anderson to determine the indications for the remaining trials. Additional detail regarding Nanobiotix's most advanced clinical trials is provided under the section "Business—Our Clinical Programs."

^ NANORAY-312, a global Phase III clinical trial for elderly patients with locally-advanced head and neck cancer who are ineligible for platinum-based (cisplatin) chemotherapy, is being activated in Europe and the United States initially as a Phase III trial. We activated the first clinical sites for NANORAY-312 in Europe in the fourth quarter of 2021, with the first patient randomized in January 2022. We expect U.S. activation and enrollment at U.S. sites and Asian sites (through LianBio) to begin in 2022. We expect U.S. site activation and enrollment to begin in 2022. For its evaluation of NANORAY-312, the FDA has accepted the available data from Study 102 Escalation. NBTXR3 for the treatment of locally advanced head and neck cancers received Fast Track designation from the FDA in February 2020.

† LianBio has been granted development and commercialization rights for NBTXR3 in key countries in Asia. In addition, certain NBTXR3 clinical trials conducted by our former collaborator, PharmaEngine, are currently being conducted in Asia and are in the process of being concluded or terminated. See "1.3.14.3. of the Universal Registration Document" for additional details.

* Phase I/II Study initiated by former partner, PharmaEngine. In conjunction with the termination of the license and collaboration agreement, PharmaEngine will implement the early termination and wind-down of this clinical trial in accordance with good clinical practice guidelines. The trial will be deemed completed when all enrolled patients have reached "end-of-study" and PharmaEngine issues a final study report.

The anticipated clinical milestones discussed in the pipeline chart above, and in the Universal Registration Document generally, are subject to the potential impact of the COVID-19 pandemic on Nanobiotix's business and may be delayed as a result. The COVID-19 pandemic has caused some delays in the review of data and enrollment in studies. Despite these delays, Nanobiotix's overall development plan continues, prioritizing head and neck cancer and immuno-oncology. The COVID-19 pandemic has not negatively impacted our liquidity and/or funding sources. For more information about the ways in which we have been, and may be, impacted by COVID-19, please the section titled "Risk Factors".

Strategy of Nanobiotix

The goal of Nanobiotix is to become a leader in the biotechnology industry, based on the systematic combination of NBTXR3 and radiotherapy, either alone or in further combination with immuno-therapies or chemotherapies, in the treatment of solid tumors. The key elements of this strategy include the following:

- **Complete the development of, and satisfy applicable EU and U.S. regulatory requirements for NBTXR3 for the treatment of locally advanced head and neck cancers.** Based on encouraging results from Study 102 Escalation, Nanobiotix is conducting Study 102 Expansion to collect additional preliminary efficacy data. Updated clinical results from Study 102 Expansion were presented at ASTRO's Annual Meeting in October 2021 showing a mOS of 18.1 months and a mPFS of 10.6 months in the evaluable population (n=41). As of the September 3, 2021 data cut-off, there were 41 evaluable patients in the Study 102 Expansion. Investigator-assessed, response rates remained consistent with previously reported results from the dose escalation and dose expansion study, showing a best observed target (injected) lesion ORR of 85.4%, and a best observed target lesion CRR of 63.4% at a median follow up of 9.5 months. These best observed target lesion response rates include one patient recorded by the principal investigator of the study as an unconfirmed complete response. NBTXR3 administration remained feasible and well-tolerated. A total of eight Grade 3-4 NBTXR3-related AEs were observed in eight patients, representing 1.3% of all AEs. Of these AEs related to NBTXR3, five SAEs were observed including dysphagia, sepsis, soft tissue necrosis, stomatitis and tumor hemorrhage. Of the SAEs, one death from sepsis occurred, which the investigator assessed as possibly related to NBTXR3, radiotherapy, and cancer. See "1.3.6.2. of the Universal Registration Document." A review of data as of the February 22, 2022 cut off date from Expansion Study 102 shows median overall survival (mOS) of 23 months in evaluable patients (n=44) demonstrating continued improvement relative to the analysis presented at ASTRO 21 and consistent with data reported from the dose escalation phase of Study 102. We commenced NANORAY-312, a global Phase III clinical trial for elderly patients with locally advanced head and neck squamous cell carcinoma who are ineligible for platinum-based chemotherapy, randomizing the first patient in January 2022. In the United States, NBTXR3, classified as a drug, was granted Fast Track designation from the FDA in February 2020 for the treatment of locally advanced head and neck cancers, which Nanobiotix believes could allow for expedited clinical development. Nanobiotix expects approximately 500 patients to be enrolled in this global Phase III trial, including up to 100 patients to be enrolled by LianBio. The initial readout will be based on event-driven progression-free survival ("PFS"), and the final readout will be based on overall survival ("OS"). A futility analysis is expected approximately 18 months after the first patient is randomized, and the interim analysis for PFS superiority is expected approximately 30 months after first patient randomization. The final analysis will report on PFS and OS.

- **Establish NBTXR3 as a complementary product to immune checkpoint inhibitors.** Nanobiotix is conducting, and continues to further develop a global I-O development program to explore the use of NBTXR3 as a complement to immune checkpoint inhibitors across several solid tumor indications. In preclinical studies, NBTXR3 activated by radiation therapy in combination with immune checkpoint inhibitors demonstrated potential to convert checkpoint inhibitor non-

responders into responders, provide better local and systemic control and increase survival. Nanobiotix is conducting Study 1100, a Phase I basket trial of NBTXR3 in combination with anti-PD-1 checkpoint inhibitors in patients with LRR or R/M HNSCC or with lung or liver metastases from any primary cancer eligible for anti-PD-1 therapy. Updated clinical results were presented from ongoing Study 1100 at ASTRO's Annual Meeting in October 2021. Nanobiotix believes that these updated results suggest that NBTXR3 could benefit this patient population with the potential to increase the proportion of patients that respond to immune checkpoint inhibitors, and discussions have been initiated with regulatory authorities regarding the potential registration pathway for this immunotherapy combination. In early 2022, we amended the Study 1100 protocol to add an expansion phase in three cohorts, including two cohorts focused on R/M HNSCC patients that are either naïve to anti-PD-(L)-1 therapy or resistant to prior anti-PD-(L)-1 therapy and combining other eligible patients with lung and/or liver metastasis from anti-PD-(L)-1 resistant advanced cancers into a third cohort. See "1.3.6.4. of the Universal Registration Document" for additional detail. In addition, pursuant to its collaboration with MD Anderson, Nanobiotix is planning to evaluate NBTXR3 in combination with various checkpoint inhibitors (anti-PD-1, anti-PD-L1, and anti-CTLA-4) across several cancer indications.

- **Expand the opportunity for NBTXR3 as a treatment for solid tumor indications.** Nanobiotix believes that NBTXR3's physical mode of action could make it broadly applicable across a multitude of solid tumor indications. In addition to head and neck cancers and STS, Nanobiotix intends to continue to develop and pursue NBTXR3 for other indications, and has already gathered data from clinical trials in liver cancers in the EU, prostate cancer in the United States, and rectal cancer in Taiwan. In December 2018 Nanobiotix entered into a collaboration with MD Anderson as part of which Nanobiotix intends to conduct multiple clinical trials in the United States to evaluate NBTXR3 plus radiotherapy, either alone or in further combination with immuno-therapies or chemotherapies, across several cancer types. If Nanobiotix is able to demonstrate the applicability of NBTXR3 to solid tumor cancers in its current and planned clinical trials, Nanobiotix believes it would to be able to increase the addressable patient population of NBTXR3 to encompass a significant portion of the patients who receive radiotherapy as part of their solid tumor cancer treatment.

- **Complete post-approval trials for NBTXR3 for the treatment of locally advanced STS in the EU.** Following positive results from our Phase II/III clinical trial in April 2019, NBTXR3 became the first ever radioenhancer to have a CE mark, allowing it to be commercialized for the treatment of locally advanced STS under the brand name Hensify®. Nanobiotix is currently preparing a post-marketing Study, (MS01_01 - also referred as Study 401) to continue evaluating acute and long-term safety, feasibility and efficacy in this population.

- **Build an effective clinical development program and establish a global commercial infrastructure for NBTXR3.** Nanobiotix has conducted clinical trials involving multiple therapeutic areas throughout the United States and the EU, in which more than 400 physicians have been involved. In addition, Nanobiotix's global medical science liaison team has consulted closely with a number of physicians, hospitals, clinics, and cancer treatment centers in the United States and key European markets to better understand their needs as clinicians and institutions and to tailor NBTXR3 accordingly. Nanobiotix plans to focus our commercialization and marketing efforts for NBTXR3 in Europe and the United States, subject to the grant of any marketing authorization by, among others, health regulatory agencies. Nanobiotix has entered into an agreement with LianBio for the development and potential commercialization of NBTXR3 in key countries in Asia. Nanobiotix retains development and commercialization rights to NBTXR3 in all other geographies, and may develop and commercialize NBTXR3 in other specific regions, independently or through collaboration agreements.

1.3.2. Current cancer treatment options and limitations

In general, there are four commonly used cancer treatment methods: surgery, radiotherapy, chemotherapy and targeted therapies, in which drugs target specific molecules of the tumor tissue. These treatments may be used individually or in combination with one another.

Surgery remains the primary method for the eradication of solid cancers that are discovered at an early stage. Surgery aims to remove not only the tumor from the body, but also a ring of surrounding healthy tissues (referred to as the surgical margin), to try to ensure that all cancer cells are removed. Surgery may not be a viable option based on a patient's health or the characteristics of the patient's cancer. For example, when a patient's cancer has spread, or metastasized, surgery alone may not be adequate to remove the cancer. When surgery is an option, it is often combined with radiotherapy or chemotherapy either before the surgery, in an effort to try to reduce the size of the tumor so that it is easier to remove with clean margins, or after the surgery, in an effort to eliminate residual cancer cells.

Radiotherapy is the administration of ionizing radiation, which are high-energy particles or rays such as X-rays, gamma rays, electron beams or protons, to destroy or damage cancer cells by blocking their ability to grow, divide and multiply. Radiotherapy is delivered over a period of several days to several weeks at a specific dose. Typically, patients receive a fraction of the dose per day. The duration and dosage of radiotherapy are based on the standard of care specific to the cancer indication.

Radiotherapy is typically measured in grays (''Gy''), a unit of ionizing radiation dose with one Gy representing the absorption of one joule of energy per kilogram. In developed countries with access to radiotherapy, approximately 60% of all cancer patients will receive radiotherapy at least once, either alone or as a part of the more complex treatment protocol.

The primary growth drivers for the radiotherapy market globally are technological advancements and the associated growing adoption of radiotherapy devices and procedures. Improving the accuracy and precision of the delivery of radiation enhances the efficacy of radiotherapy and reduces the side effects and damage to surrounding healthy tissues, which has led to greater adoption of these techniques by the medical community and more widespread use among cancer patients. Because high-dose radiotherapy can be delivered in a more precise way, it can be used to target tumors that were previously inaccessible, such as brain tumors, thereby opening the radiotherapy market to additional patient populations. In addition, new technologies that require lower doses of radiation to destroy cancer cells can now be used in patients who may previously have been considered too fragile for higher-dose radiation.

Despite these technological advancements and the increasing use of radiotherapy in treating cancer, there remain significant limitations to its use. Although radiotherapy is a local approach, it often causes damage to surrounding healthy tissues, and may not be an effective treatment for cancers that have spread, or metastasized. As a result, physicians may decide to withhold radiotherapy, because a high enough dose to kill the tumor cells would create unacceptable damage to surrounding healthy tissues and cause other toxic side effects.

In addition, the I-O treatment approach has emerged as an option for cancer treatment. The I-O treatment approach is a relatively new approach to fighting cancer that does not directly target the tumor, but instead aims to stimulate and activate the patient's own immune system, allowing it to recognize cancer cells and destroy them. I-O treatments have demonstrated efficacy broadly in the treatment of many types of cancer, including among others leukemia, melanoma, lung cancer, prostate cancer, skin cancer, cancer of the digestive system, gynecological cancer and renal cancer. However, not all patients may benefit from I-O therapy. I-O therapy may be ineffective when a patient's tumor is "cold", meaning that the cancer either has not been recognized or has not provoked a strong enough

response by the patient's immune system. The challenge remains to find new ways to turn a cold tumor into a hot tumor—one that will be responsive to I-O treatment approaches.

1.3.3. NBTXR3: Addressing the challenges of radiotherapy and immuno-oncology

We have designed NBTXR3 to address limitations inherent in radiotherapy, either alone or in combination with other treatment approaches:

- By amplifying the intratumor killing effect of the radiation dose within cancer cells, NBTXR3 is designed to give a radiation dose greater efficacy.
- By localizing the radiation dose within the tumor, NBTXR3 is designed to enhance the efficacy of radiotherapy without resulting in additional toxicities on the surrounding healthy tissues.

With respect to I-O treatment approaches to fighting cancer, our preclinical and early clinical results suggest that NBTXR3 plus radiotherapy may prime the immune response, thereby rendering otherwise cold tumors more prone to recognition by the patient's immune system and therefore potentially more responsive to I-O treatments such as checkpoint inhibitors.

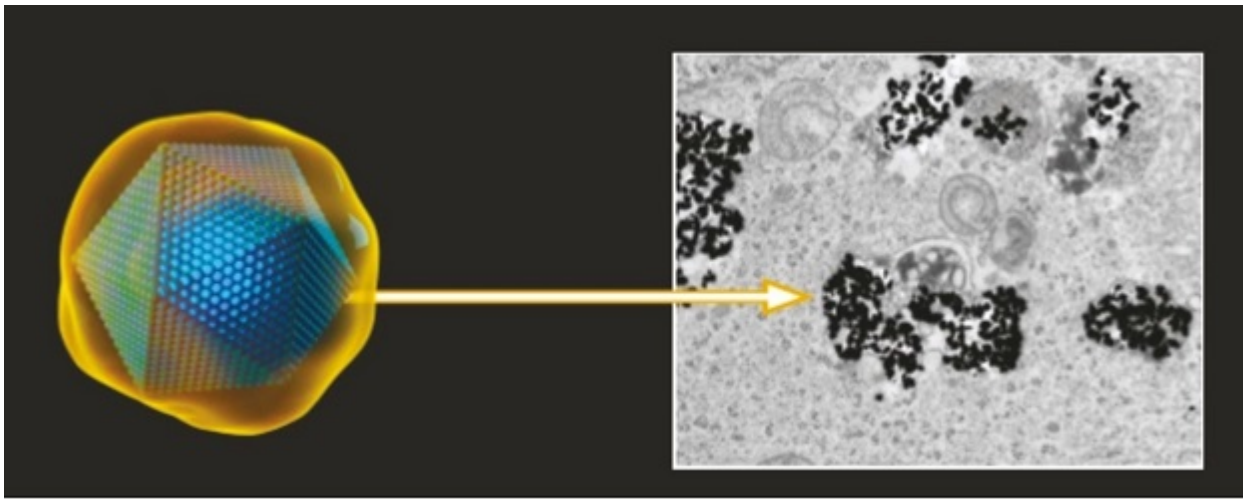
1.3.4. Our NBTXR3 technology

We are exploring the potential for nanotechnologies to provide solutions to unmet therapeutic needs in oncology. Our pioneering approach uses nanophysics to bring a physical mode of action to destroy cancer cells from within. When used in conjunction with radiotherapy, our NBTXR3 nanoparticles increase the absorption of the administered radiation, thereby magnifying and focusing the dose locally within a malignant tumor, but without causing incremental damage to surrounding healthy tissues. In magnifying the effect of the radiation, we believe our NBTXR3 technology improves the benefit-risk ratio of radiotherapy for patients.

The amount of energy that can be deposited in a cell through radiotherapy is a function of the cell's ability to absorb the radiation, which depends on the amount and form of energy used and the electron density of the receiving molecules. A cell is primarily composed of water, which has a very low electron density. At an average size of approximately 50 nanometers in diameter, our nanoparticles are directly injected into a malignant tumor prior to standard radiotherapy and can be internalized into the cell through endocytosis to function as radioenhancers. The inert nanoparticles have an inorganic core of crystallized hafnium oxide, which has a high electron density. When exposed to radiation, the high electron density of the nanoparticles allows the cancer cells to absorb more energy than would otherwise be absorbed by the water molecules in the tumor. The high electron density of the nanoparticles is essential for their effective interaction with radiation, while their physical and chemical properties do not cause incremental damage to surrounding healthy tissues.

The following image is a transmission electron micrograph of a cross-section slice of a tumor with nanoparticles after injection.

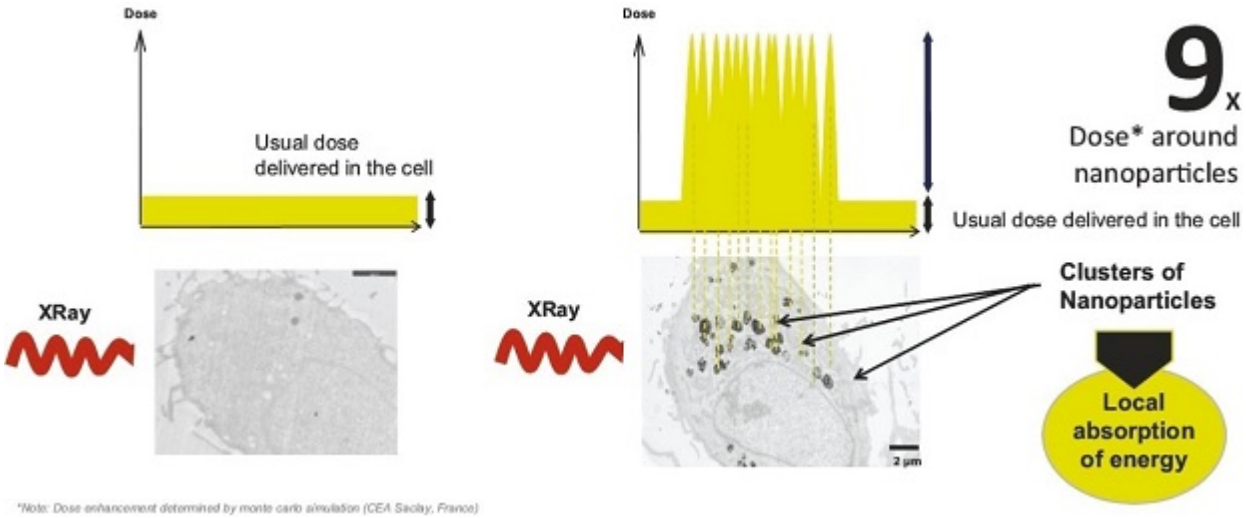
Clustered 50 nm Nanoparticles in cytoplasm



NBTXR3 is a novel approach to the local treatment of cancer that we believe provides a solution to the basic limitation of radiotherapy - an inability to deliver sufficient amounts of radiation to eradicate the tumor because of the low radiation tolerance of the surrounding healthy tissues.

The following illustration shows a representative increase in the radiation dose absorbed around the NBTXR3 nanoparticles administered into cancer cells.

NBTXR3 Nanoparticles Amplifying the Effect of Radiation



Mode of action of NBTXR3 nanoparticles

During radiotherapy, the interaction between the radiation and the targeted cell molecules ionizes atoms, freeing electrons from the orbit of the atoms. These electrons dissipate their energy in multiple interactions with surrounding molecules, producing free radicals, which are highly reactive ionized molecules in the cell. These free radicals are primarily responsible for the effectiveness of radiotherapy in causing DNA damage, ultimately leading to cell death.

The mode of action of NBTXR3 nanoparticles can be described in four stages:

Stage 1: Activity/Inactivity Principle

Our nanoparticles are inert, meaning that they produce no effect without ionizing radiation. When activated by radiation, a number of phenomena occur. First, the radiation is absorbed by the hafnium oxide core of the nanoparticles. Because the core of the nanoparticle has a significantly higher electron density than water, it can absorb significantly more energy than a tumor cell could without the cluster of nanoparticles. Greater energy absorption generates more electrons, and ultimately more free radicals.

Stage 2: Cell Damage

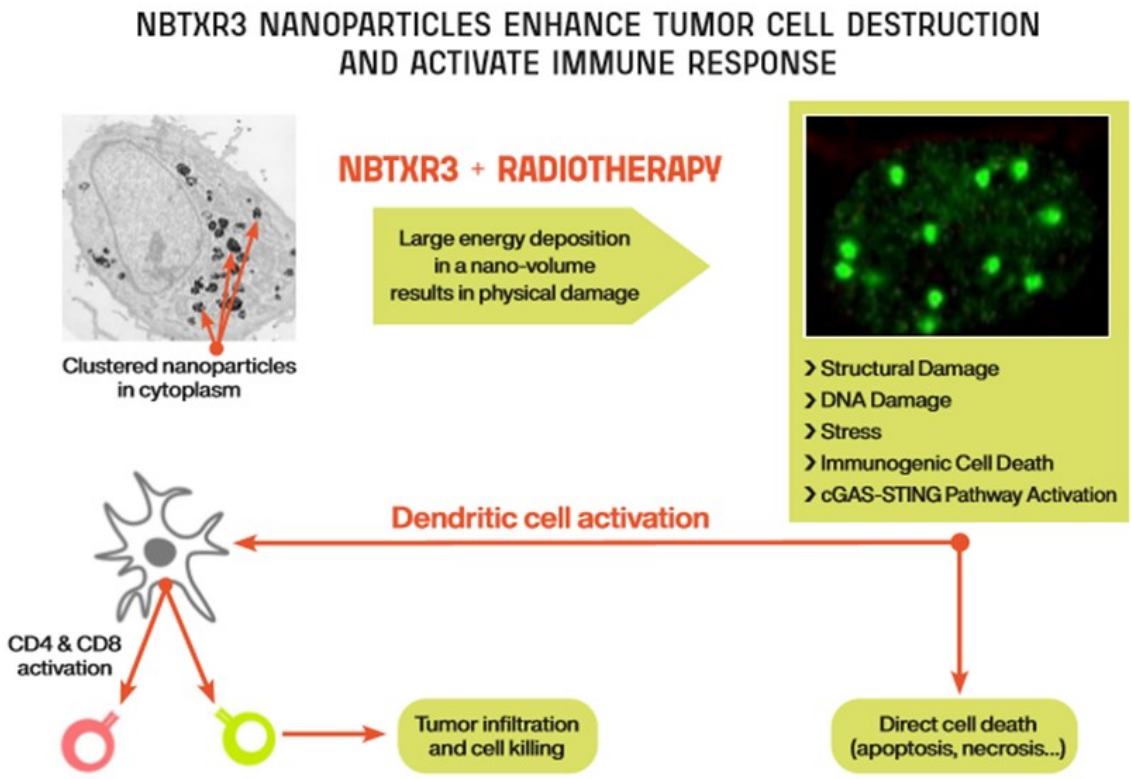
The electrons generated in the energy absorption disperse through the cancer cells and dissipate their energy in multiple interactions with surrounding molecules, creating free radicals. The free radicals are highly reactive and tend to destroy the covalent links of the molecules they interact with, such as DNA, RNA and proteins. Specifically, they cause severe and irreparable DNA damage mainly responsible for the lethal effect of ionizing radiation on cells. The free radicals therefore increase the localized cancer cell destruction.

Stage 3: Subsequent Action in the Cells

The destructive effect of free radicals is amplified and localized by the radiation-activated nanoparticles, which generate a controlled concentration of energy within the tumor. Ionizing radiation can be applied to the nanoparticles repeatedly because they return to their inactive, inert state after each exposure to radiation. Multiple courses of radiotherapy can be administered to a tumor that has received a single injection of our nanoparticles.

Stage 4: Immune Activation

In our preclinical studies and our early clinical data, the treatment using radiation-activated nanoparticles has also been observed to trigger destruction of metastatic cells due to immunogenic cell death from the activation of the immune system. Based on these observations we believe that our nanoparticles may prime the body's immune response, rendering tumors more prone to recognition by a patient's immune system. In the illustration below, clusters of NBTXR3 nanoparticles are injected into the cell and, when activated by radiotherapy, cause destruction of cancer cells due to the high energy absorption. This destruction may include structural damage, DNA damage, stress to the cells, immunogenic cell death (a specific form of cell death related to the immune system) and cGAS-STING pathway activation (an immune sensing mechanism). This results in both direct cell death and activation of dendritic cells. Once activated, the dendritic cells trigger additional immune system activation, including the activation of lymphocytes, or white blood cells in the immune system, including T cells such as CD4 (regulatory T cells) and CD8 (cytotoxic T cells). This activation of lymphocytes has the effect of "priming" the immune system to be able to better recognize and kill cancer cells.



1.3.5. Overview of NBTXR3

NBTXR3, a sterile aqueous suspension of crystalline hafnium oxide nanoparticles, is administered through a single image-guided local injection directly into the tumor prior to radiotherapy. In our clinical trials, the dosage of injected NBTXR3 is based on a percentage of the baseline tumor volume and is determined during the initial phase of the respective clinical trial for different indications. NBTXR3 nanoparticles have a negative-charge surface coating, which allows them to interact with the surface of the tumor and accumulate inside the tumor cells. NBTXR3 is designed to render the targeted tumor more operable or help destroy it completely.

NBTXR3 can easily be incorporated into the current standard of care in radiotherapy. Hospitals and medical facilities where radiotherapy is delivered do not need any new equipment or to otherwise make significant capital investments in new technology in order to treat patients with NBTXR3.

We are currently prioritizing the development of NBTXR3 in the United States and the EU for the treatment of head and neck cancers, although we are also studying, or have studied, NBTXR3 across a broad range of indications, including locally advanced soft tissue sarcoma, primary and secondary liver cancers, prostate cancer, pancreatic cancer, esophageal cancer and non-small cell lung cancer. We believe NBTXR3 has the potential to treat all solid tumors where radiotherapy can be used. We have also observed that NBTXR3 activated by radiotherapy could modulate the antitumor immune response, supporting the rationale for its use as an in situ cancer vaccine, potentially in combination with I-O treatments. With respect to our I-O development program, the initial cancer indications for NBTXR3 in combination with immuno-oncology therapies - and, in particular, checkpoint inhibitor combinations - are head and neck cancers (including recurrent / metastatic head and neck squamous cell carcinoma) as well as lung and liver metastases from any primary cancer eligible for anti-PD-1 therapy.

For certain cancer indications, NBTXR3 can be combined with a gel to create a new formulation, which we refer to as NBTXR3-gel, for direct application in the tumor cavity following surgical removal of the tumor. Potential cancer indications for NBTXR3-gel include certain types of breast cancer, operable lung cancers, vertebral metastases and retroperitoneal STS.

1.3.6. Our clinical programs

NBTXR3 has been, and is currently being evaluated in several clinical trials worldwide in various cancer patient populations.

In December 2018, we entered into a large-scale comprehensive NBTXR3 clinical collaboration with MD Anderson. The collaboration is expected to support multiple clinical trials with NBTXR3 for use in treating several cancer types—including head and neck, pancreatic, lung, esophageal cancers—and is expected to involve approximately 340 patients. The first clinical trial under our collaboration with MD Anderson in patients with locally advanced or borderline resectable pancreatic cancer dosed its first patient in September 2020 while the second clinical trial in patients with esophageal cancer dosed its first patient in January 2021. The third clinical trial under this collaboration for non-small cell lung cancer amenable to re-irradiation was activated in February 2021. The fourth and fifth clinical trials for inoperable LRR HNSCC (I-O program) and R/M HNSCC (I-O program) were activated in March 2021 and April 2021, respectively. The R/M HNSCC clinical trial dosed its first patient in July 2021. Each of these five clinical trials is open and enrolling patients, although two of the trials have experienced slower recruitment and enrollment than planned as a result of the COVID-19 pandemic. The sixth planned clinical trial, in advanced solid tumors with lung or liver metastasis, is in the early stages of the regulatory review process, and the co-development with MD Anderson of additional clinical trials is ongoing. See “1.3.14.1. of the Universal Registration Document” for further detail regarding the terms of the collaboration.

In May 2021, we entered into an exclusive license and collaboration agreement with LianBio for the development and commercialization of NBTXR3 in key parts of Asia—Mainland China, Macau, Hong Kong, Thailand, Taiwan, South Korea and Singapore. LianBio has committed to enrolling patients in the Territory in NANORAY-312 as well as four additional registrational studies that we intend to conduct across indications and therapeutic combinations.

In August 2012, we entered into an exclusive license and collaboration agreement with PharmaEngine for the development and commercialization of NBTXR3 in the Asia Pacific region. In March 2021, we and PharmaEngine mutually agreed to terminate the agreement. Three NBTXR3 clinical trials conducted by PharmaEngine were conducted in Asia and we expect data to be available during 2022.
See “1.3.14.3. of the Universal Registration Document” for additional details.

Refer to the paragraph titled “**NBTXR3 Development Pipeline**” above for our ongoing and planned clinical trials, including those being undertaken and contemplated by MD Anderson, our principal collaboration partner.

1.3.6.1. Locally advanced soft tissue sarcoma

Background and opportunity

Soft tissue sarcomas ("STS") are rare cancers that develop in different types of soft tissues, including muscles, joint structures, fat, nerves and blood vessels. Although STS can develop at any anatomic site, it occurs in the extremities (arms and legs) in approximately 60% of cases. The American Cancer Society estimates that in 2020 in the United States, approximately 13,130 patients were diagnosed with STS, and approximately 5,350 STS patients died from this cancer. In the EU, over 23,000 patients are diagnosed with STS each year. The National Cancer Institute estimates that the five-year survival rate for STS patients is approximately 65%. Median overall survival for patients with advanced, metastatic STS is estimated to be 18–19 months. Radiotherapy followed by surgery is part of the typical treatment regimen for patients with non-metastatic advanced, resectable STS of the extremities in Europe.

Achieving local control of the tumor is critical to improving survival rates and reducing the need for limb amputations. Patients with locally advanced STS are high-risk patients and have few therapeutic options capable of achieving local control. Consequently, innovative treatments to improve cancer cell destruction and the feasibility of surgical resection are needed. NBTXR3, when activated by radiotherapy, is designed to enhance the efficacy of radiation both by destroying more tumor cells and rendering the tumor more susceptible to surgical resection, thereby improving patient outcomes.

Phase II/III Trial design

Following the positive results of our Phase I trial described below, we commenced a Phase II/III trial for EU registration (Study 301), which we also refer to as the Act.In.Sarc trial, to measure the anti-tumor activity of preoperative NBTXR3 activated by radiotherapy, as compared to radiotherapy alone, in patients with locally advanced STS. The Act.In.Sarc trial was conducted at more than 30 sites worldwide, including 23 sites in Europe and seven sites in the Asia-Pacific region. The Phase II/III clinical trial was completed outside of Asia in 2018, and the Phase III trial in the Asia-Pacific region was completed by PharmaEngine in the first half of 2021.

Through the course of the Act.In.Sarc trial, a total of 180 adult patients with locally advanced STS of the extremity or trunk wall were randomized, at a 1:1 ratio, to treatment under one of two arms: (i) single intratumoral injection of NBTXR3 at the recommended dose (10% of the tumor volume), followed by five weeks of radiotherapy (the "**NBTXR3 arm**"), or (ii) five weeks of radiotherapy alone (the "**control arm**"). In both cases, the radiotherapy was followed by surgical resection of the tumor. Of the 180 patients recruited for the trial, 176 were analyzed for the primary endpoint in the intended-to-treat full analysis; three patients were incorrectly diagnosed with STS and one patient was found to be ineligible for pre-operative radiotherapy.

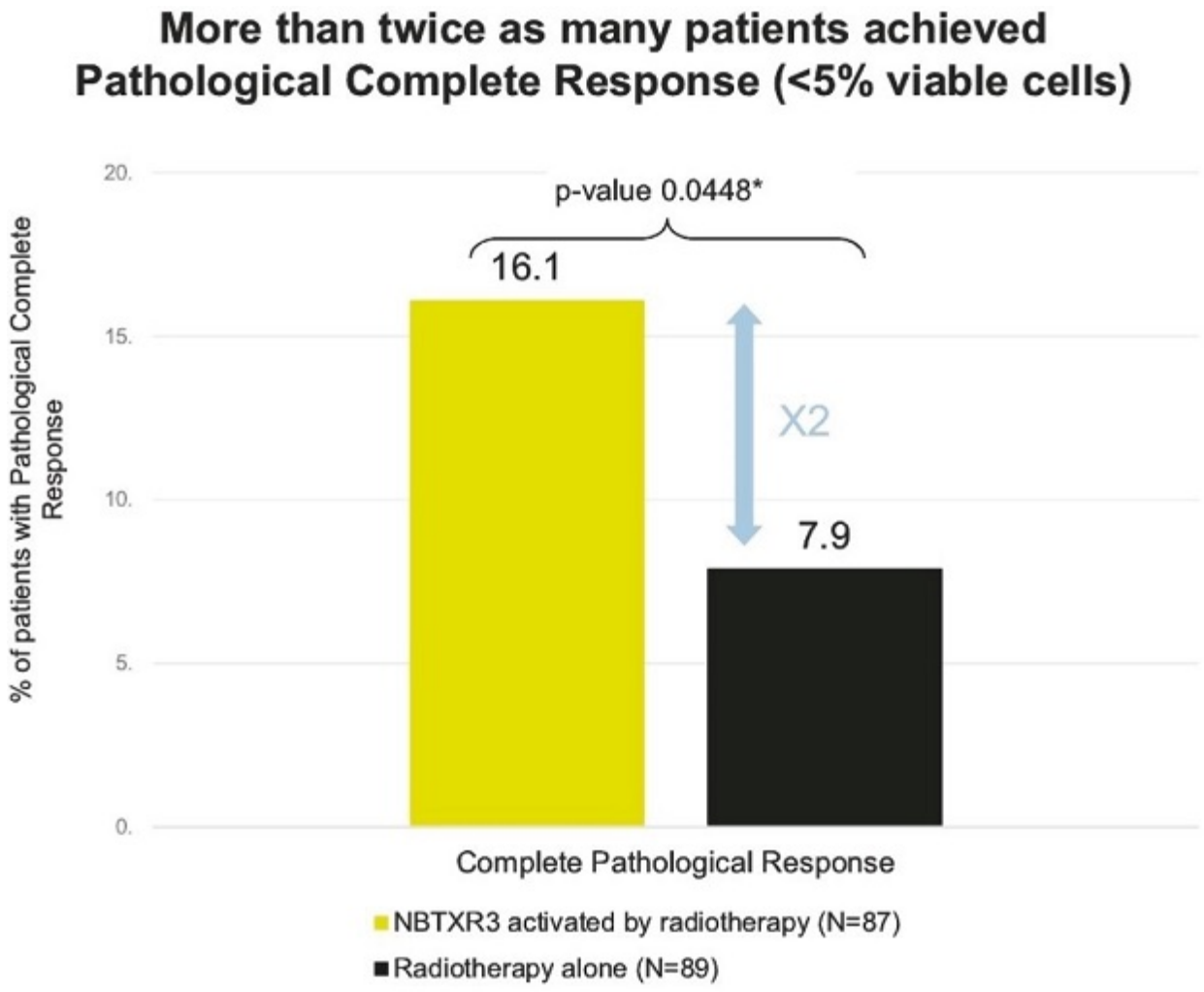
The primary endpoint of the Phase II/III trial was an increase in the pathological complete response rate of intratumoral injection of NBTXR3 activated by external beam radiation therapy ("**EBRT**"), as compared against EBRT alone. The primary endpoint was evaluated, in accordance with European Organisation for Research and Treatment of Cancer guidelines, by a centralized group of pathologists who were blinded to the arm of treatment. The secondary endpoints were to evaluate the safety profile of NBTXR3 activated by radiotherapy and compare the rate of tumor surgery with R0 margins (meaning no remaining cancer cells could be seen microscopically within a widely accepted margin after resection), the percentage of tumor necrosis/infarction, limb amputation rates and tumor response as measured by RECIST 1.1.

Results

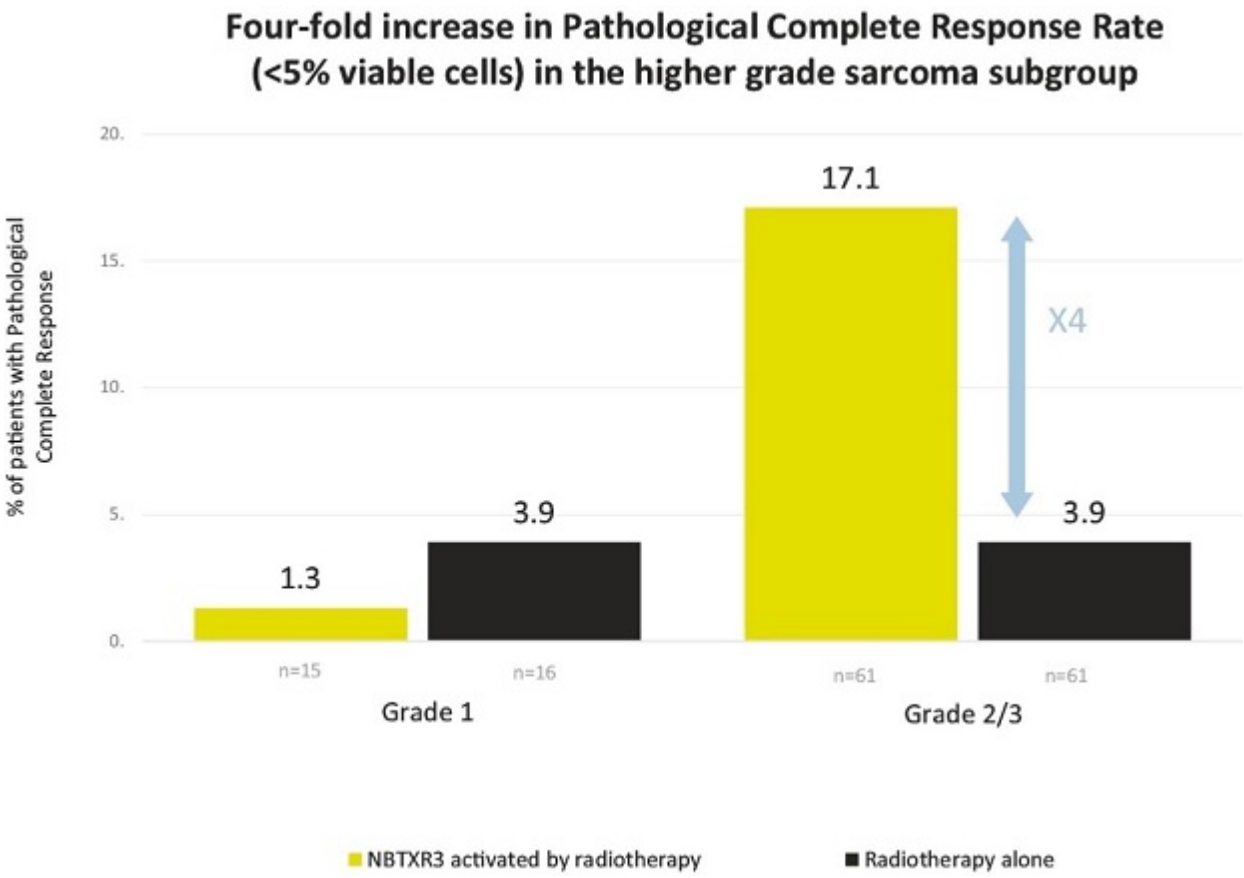
Pathological complete response rate

The trial achieved its primary endpoint, with 16.1% of patients in the NBTXR3 arm having a pathological complete response (defined as less than 5% of residual viable cancer cells in the tumor) compared to 7.9% of patients in the control arm. The difference was statistically significant, with a p-value of 0.0448. A p-value, or probability value, cited in figures in the Universal Registration Document as "p", is the likelihood of finding the observed, or more extreme, outcome (e.g., a significant difference in terms of response for patients receiving NBTXR3 plus radiotherapy relative to patients receiving radiotherapy alone) when a baseline outcome is assumed to be true (e.g., patients receiving NBTXR3 plus radiotherapy and patients receiving radiotherapy alone both having an equal response). A p-value of less than or equal to 0.05 is generally considered to demonstrate statistical significance, meaning that one would accept the observed outcome as reasonable evidence to not accept the baseline outcome.

In addition, in the subgroup of patients with a higher histology grade (i.e., a more aggressive disease), which represented the majority of patients in the trial, pathological complete response was achieved in four times as many patients in the NBTXR3 arm (17.1%) compared to patients in the control arm (3.9%). The following graph shows the percentage of patients in each arm based on whether they were considered to have Grade 1 or Grade 2/3 tumors. The remaining patients in each arm of the trial had tumors of unknown grade.



**ITT FAS = Intention To Treat Full Analysis Set; statistically significant at a threshold of 0.04575*



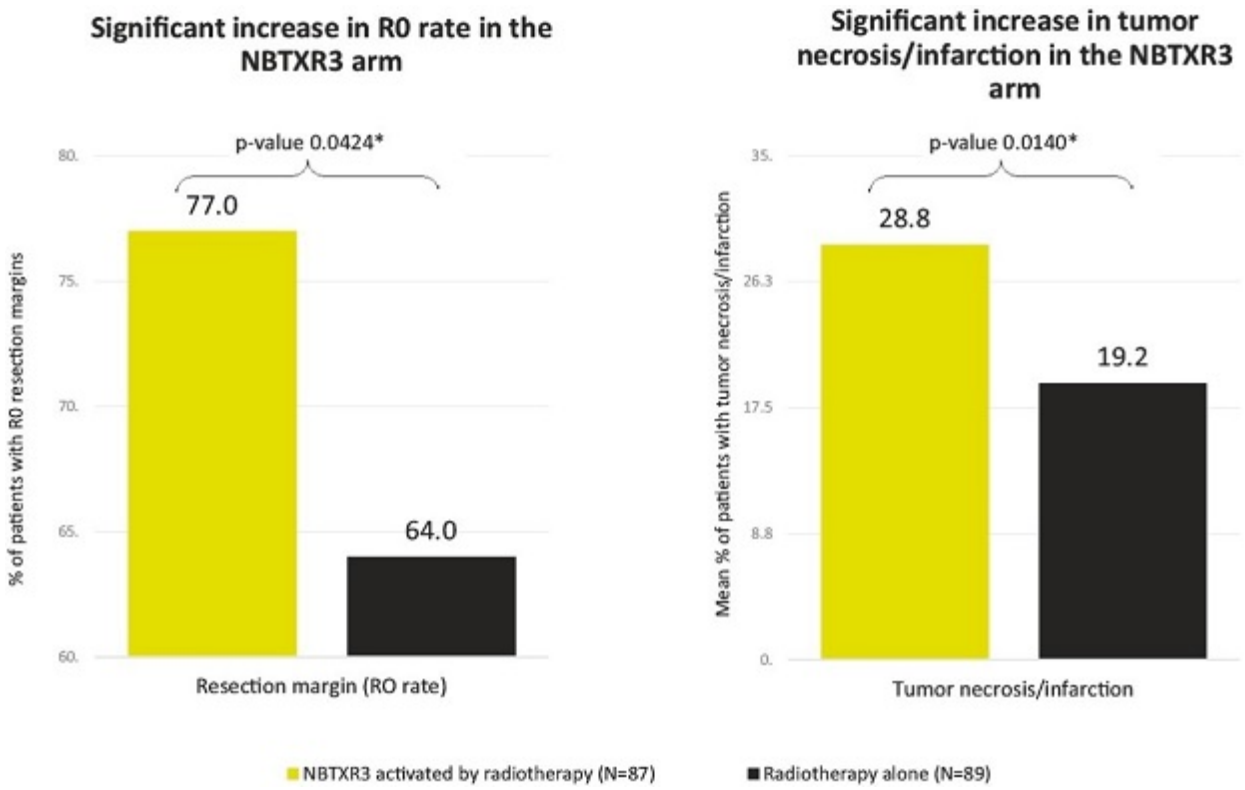
Patients in the NBTXR3 arm were more likely to have a pathological response (not limited to a complete response). The portion of patients with pathological "nearly" complete response (defined as less than 7% of residual viable cancer cells in the tumor) and pathological response with 10% or less of residual viable cancer cells were 24.7% and 34.6%, respectively, in patients in the NBTXR3 arm as compared to 14.8% and 19.8%, respectively, in patients in the control arm.

R0 resection margin

The main secondary endpoint of the trial, the rate of tumor surgery with R0 margins, was also met. R0 resection margin was observed in 77% of the patients in the NBTXR3 arm, compared to 64% of patients in the control arm. This difference was statistically significant, with a p-value of 0.0424.

Tumor necrosis/infarction

Based on histologic analysis, we observed that the mean percentage of tumor necrosis/infarction achieved was 28.8% for patients in the NBTXR3 arm, compared to 19.2% for patients in the control arm, a difference that was also statistically significant, with a p-value of 0.014.



Safety profile similarity between NBTXR3 and control arms

Similar safety profiles were observed in the NBTXR3 arm and the control arm, including the rate of postsurgical wound complications. NBTXR3 did not impair the patients' ability to receive the planned dose of radiotherapy ("RT" in the table below). In the NBTXR3 arm, 7.9% of patients experienced grade 3-4 acute immune reactions, which were manageable and of short duration. Further, NBTXR3 showed a good local tolerance in patients and did not have any impact on the severity or incidence of radiotherapy-related AEs. The tables below summarize selected contemporaneous safety information gathered as part of the trial, which is the date that was submitted in connection with the regulatory process for the CE mark of NBTXR3.

Safety Data – Phase II/III in STS	Arm A NBTXR3 activated by RT (N=89)	Arm B RT alone (N=90)
Patients with any TEAE[a]	**87 (97.8%)**	**87 (96.7%)**
Patients with any NBTXR3 related TEAE	31 (34.8%)	NA
Patients with any TEAE leading to death (death regardless of the causality assessment)	0	2 (2.2%)
Patients with any serious TEAE	**28 (31.5%)**	**14 (15.6%)**
Patients with any serious NBTXR3 related TEAE	9 (10.1%)	NA
Patients with any serious TEAE related to radiation therapy	5 (5.6%)	5 (5.6%)
Patients with any serious AE[b]	**35 (39.3%)***	**27 (30.0%)**
Patients withdrawn from study treatment due to TEAE	1 (1.1%)	0

[a] Treatment Emergent AEs are AE observed during the on-treatment period.
[b] Serious AEs are adverse events reported during the whole study period (i.e. on-treatment and follow-up periods).
NA, not applicable
*Includes 21 treatment-related serious adverse events which include (1) twelve serious adverse events of injection site pain, anaphylactic shock, cytokine release syndrome, hypersensitivity, postoperative wound complication, post-procedural complication, post-procedural infection, apnea, panniculitis and hypotension deemed to be related to NBTXR3 and (2) nine serious adverse events of injection site pain, hypotension, presyncope, injection site extravasation, cytoikine release syndrome, aplea and pulmonary embolism deemed to be injection related. Also includes serious adverse events deemed to be unrelated to treatment, such as events deemed to be related solely to underlying disease.

The trial results were presented in October 2018 at the European Society for Medical Oncology ("**ESMO**") 2018 Congress and the American Society for Radiation Oncology 60th Annual Meeting and subsequently published online in the peer-reviewed journal The Lancet Oncology in July 2019.

Based on these trial results, in April 2019, we completed the regulatory process for the CE mark of NBTXR3, thereby allowing the product to be commercialized for the treatment of locally advanced STS of the extremities and trunk wall under the brand name Hensify® in the 27 EU countries.

Long-term patient follow-up is currently ongoing to evaluate the time-to-local / distant recurrence and local / distant recurrence rates at 12 and 24 months. At the 2021 Annual Meeting of ASCO, we reported on long-term safety of NBTXR3 in patients treated in the Act.In.Sarc trial. As evaluated by several patient- and physician-reported methods, the long-term safety evaluation did not identify any negative impact on patient quality of life or long-term morbidity from NBTXR3.

In light of our current development priorities, we do not presently intend to pursue commercialization for NBTXR3 for the treatment of locally advanced STS of the extremities and trunk wall in additional jurisdictions. We are currently preparing a post-registrational trial (Study 401 (MS01_1)) that will continue evaluating the safety and efficacy of Hensify® and still provide patients with access to the product. Based on the expected timing of discussions with regulatory authorities regarding the planned protocol and impact of the COVID-19 pandemic on clinical development timelines, launch of Study 401 (MS01_1) in Europe is expected in 2023.

The Act.in.Sarc trial followed positive results of our initial Phase I trial, which we conducted to evaluate the tolerance and feasibility of increasing doses of NBTXR3 by intratumoral injection, activated by external radiotherapy, in patients with locally advanced STS of the extremity. Through the course of this dose escalation study, we analyzed 22 patients at two sites in France with a single intratumoral injection of NBTXR3 prior to the first radiotherapy session.

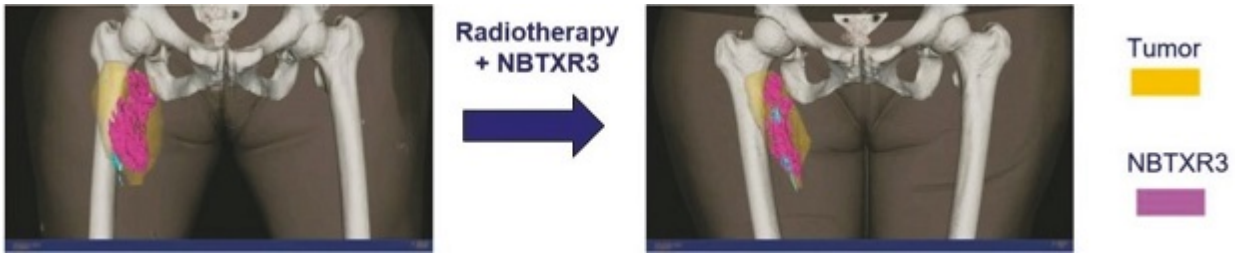
Phase I Trial Design

The primary endpoints of the Phase I trial were to evaluate the feasibility of NBTXR3 intratumoral injection and early dose-limiting toxicities and tolerance of NBTXR3. The secondary endpoints were to evaluate the tumor response to NBTXR3 activated by radiotherapy, measured in terms of the destruction of malignant cells, evaluate the response rate to NBTXR3 activated by radiotherapy by medical imaging and characterize the distribution of NBTXR3 in the body over time.

Results

Initial data from the Phase I trial confirmed NBTXR3's long-term intratumoral bioavailability and an absence of leakage to surrounding healthy tissues. We observed persistence of the nanoparticles in the tumor mass throughout five weeks of radiotherapy, confirming the feasibility of local injection of NBTXR3 and the clinical relevance of a single injection. A single injection was sufficient to achieve long-term intratumoral residence in all histological types and sizes for the sarcomas. No grade three or four adverse events were observed at the recommended dose of 10%. The initial data established feasibility for our NBTXR3 therapeutic approach. As a result, we broadened the target patient population for the trial, amending the research protocol in 2013 to include patients with sarcoma of the trunk wall.

The final Phase I trial results were positive—on average, we observed 40% shrinkage in treated tumor size and an average pathological response of 73% in tumors known to be treatment-resistant across different sarcoma subtypes, including undifferentiated sarcoma, rhabdomyosarcoma, and synovial sarcoma. Four serious adverse events of pyrexia, abdominal pain, injection-site reaction and post-operative wound complication were deemed to be related to NBTXR3 and two serious adverse events of injection site pain and hypoaesthesia were deemed to be injection related. All patients that participated in the trial underwent complete extended surgical resection of the tumor, which was the therapeutic aim. Complete tumor resection is optimal because it impacts the local recurrence rate and improves prognosis and survival rates. The following graphic depicts shrinkage of the tumor in a representative patient in the trial after five weeks of treatment.



1.3.6.2. Locally advanced head and neck cancers

Background and opportunity

Squamous cell carcinoma of the head and neck cancers constitute more than 95% of head and neck cancers and include cancers of the oral cavity, tongue and oropharynx, a part of the throat, larynx and hypopharynx. These structures play a critical role in a human's ability to swallow, eat, breathe and speak. The American Cancer Society estimates that in 2020 in the United States, approximately 53,260 patients will be diagnosed with oral or oropharyngeal cancer and approximately 10,750 patients will die from the cancer. According to 2018 estimates by the Global Cancer Observatory, part of the World Health Organization's International Agency for Research on Cancer, around 890,000 patients are diagnosed globally each year with head and neck cancer. The five-year survival rate for patients with oral and oropharyngeal cancer is approximately 65%. These cancers represent a major public health concern.

Cisplatin-based chemotherapy in combination with concomitant definitive radiation is the standard treatment for locally advanced head and neck cancers in both the United States and the EU which cannot be resected or for patients who refuse surgery. However, it is often not an option for elderly or frail patients who are unable to endure the physical strain inherent in chemoradiation treatment. The alternative treatment to chemoradiation is cetuximab in combination with radiotherapy, but its efficacy is less well established in elderly patients. These patients are estimated to account for approximately 25% of patients with head and neck cancers. In data presented at the Multidisciplinary Head and Neck Cancers Symposium 2020, elderly patients treated with radiotherapy alone or radiotherapy in combination with cetuximab had a median PFS of 7.3 months. Elderly patients with locally advanced tumors who receive radiation only also generally have limited OS expectancy (median of 12 months following diagnosis, based on our review and sub-group analysis of scientific literature relating to head and neck cancers) and typically experience poor quality of life, as they have limited therapeutic options and a high unmet medical need and are largely underrepresented in existing clinical trials.

The following table summarizes data from certain published scientific literature relating to head and neck clinical trials evaluating radiotherapy combined with the identified chemotherapies:

Patient Population / %		**Best Observed Response (Overall Response)**	**Best Observed Response (Complete Response)**	**Best Observed Response (Partial Response)**	**Best Observed Response (Stable Disease)**	**Best Observed Response (Progressive Disease)**
Patients receiving radiotherapy alone *Bonner et al. 2006*		64%	Not available	Not available	Not available	Not available
Median age (years)	58					
KPS (Performance Score)						
90-100	66					
60-80	33					
Unknown	1					
Tumor Stage						
T1-T3	72					
T4	28					

Patients receiving radiotherapy and cetuximab *Bonner et al. 2006*		74%	Not available	Not available	Not available	Not available
Median age (years)	56					
KPS (Performance Score)						
90-100	70					
60-80	30					
Unknown	1					
Tumor Stage						
T1-T3	70					
T4	29					
TX	<1					
HPV negative patients with oropharyngeal HNSCC receiving radiotherapy and cisplatin *Harrington et al. 2013 (evaluable patients)*		58%	31%	27%	0%	42%
Median age (years)	57					
ECOG (%)						
0 (KPS 100)	52					
1 (KPS 80-90)	48					
2 (KPS 60-70)	0					
Stage (%)						
III	21					
IVA/B	79					
Primary tumor site (%)						
Oral cavity	9					
Oropharynx	61					
Hypopharynx	21					
Larynx	9					
HPV status OPSCC (%)						
HPV+	13					
HPV-	87					

Patient Population / %		**Best Observed Response (Overall Response)**	**Best Observed Response (Complete Response)**	**Best Observed Response (Partial Response)**	**Best Observed Response (Stable Disease)**	**Best Observed Response (Progressive Disease)**
HPV positive patients with oropharyngeal HNSCC who received induction chemotherapy, radiotherapy and cetuximab *Marur et al. 2017 (evaluable patients)*		95%	49%	46%	1%	0%
Median age (years)	57					
ECOG						
0 (KPS 100)	91					
1 (KPS 80-90)	9					
0 (KPS 60-70)	—					
Stage (%)						
III	15					
IVA/B	85					
Primary tumor site (%)						
Oral cavity	—					
Oropharynx	100					
HPV status OPSCC (%)						
HPV+	100					
HPV-	—					

Abbreviations: HPV (human papillomavirus); OPSCC (oropharyngeal squamous cell carcinoma); ECOG (a standardized measure–ranging from 5 to 0–of a patient's level of functioning in terms of his/her ability to care for him/herself, carry out daily activity and engage in physical ability; a lower score means the patient is better able to function); KPS (a standardized measure–ranging from 0 to 100–of a patient's level of functioning in terms of his/her ability to care for himself/herself, carry out daily activity and engage in physical ability; a higher score means the patient is better able to function).

This historical literature is presented solely to illustrate the current market opportunity arising from existing application of the standard treatment—chemotherapies in combination with concomitant radiation—for patients with locally advanced head and neck cancers. Because of the unique design of such studies applied to specific patient populations, no comparison with any of our clinical trials is possible and none should be inferred from this background data.

Phase III Registration Trial Design ("**NANORAY-312**")

In February 2020, we submitted to the FDA for review the NANORAY-312 protocol for a global Phase III clinical trial in elderly patients with locally-advanced head and neck cancer who are ineligible for platinum-based (cisplatin) chemotherapy. The study is ongoing. First clinical sites for NANORAY-312 were activated in Europe during the fourth quarter of 2021, with the first patient being randomized in January 2022. We expect U.S. sites and Asian sites (through LianBio's activities) activation and enrollment to begin in 2022.

The clinical trial will be a controlled randomized (1:1) two-arm global registration trial including elderly head and neck cancer patients who are ineligible for platinum-based (cisplatin) chemoradiotherapy. Patients in the control arm will receive definitive radiation therapy versus patients in the treatment arm, who will receive NBTXR3 activated by definitive radiation therapy. In both arms cetuximab addition would be allowed as per investigator's choice. The trial is expected to be conducted at more than 150 sites worldwide and approximately 500 patients will be randomized.

The primary endpoint of the study is the PFS and the key secondary endpoint is the OS. The study is designed to demonstrate a superiority of NBTXR3 activated by radiation therapy over control on PFS with a statistical power of 89% and on OS with a statistical power of 80% (hazard ratio of at least 0.692 and 0.75 for PFS and OS, respectively). An interim analysis aiming to demonstrate superiority of NBTXR3-containing arm over control on PFS and on OS is planned. In addition, overall response rate, safety and quality of life will be evaluated as secondary endpoints.

A futility analysis is expected at approximately 18 months after the first patient is randomized, the interim analysis for PFS superiority is expected at approximately 30 months after first patient randomization, and the final analysis at approximately 48 months. In the event of clinically meaningful PFS improvement in the planned interim analysis with no detrimental OS effect having been observed, a submission requesting accelerated approval of NBTXR3 in the United States for this indication will follow (≥ 6 months PFS difference). A median PFS of 9 months and median OS of 12 months is expected in the control arm with an expected positive Hazard Ratio (NBTXR3/control) of 0.75 for NBTXR3 arm. The Hazard Ratio is a measure of the risk of a particular event occurrence in one group compared to another group, over time. For example, a Hazard Ratio of 0.75 indicates that risk of death is reduced by one fourth in the treatment arm as compared to the control arm.

NANORAY-312 will utilize four stratification factors: (i) Investigator's choice (cetuximab addition or not), (ii) HPV status (HPV-positive oropharynx versus other), (iii) modified Charlson Comorbidity Index, or mCCI score at screening (2 to 3 versus ≥ 4) and (iv) region (North America & Western Europe versus Rest of World).

The Charlson Comorbidity Index (CCI) measures the burden of disease and predicts mortality in various diseases. The CCI encompasses 19 medical conditions, each weighted according to its impact on mortality. The mCCI further integrates the patient's age as an additional scoring information to the CCI.

In February 2020, we received Fast Track designation from the FDA for NBTXR3 in this patient population. Fast Track designation is a process designed to facilitate the development and accelerate the review of treatments for serious conditions and that have the potential to address unmet medical needs.

Phase I ("**Study 102 Escalation**") and Phase I Expansion ("**Study 102 Expansion**") Trial Design

We are conducting a Phase I clinical trial of NBTXR3 activated by intensity-modulated radiation therapy in patients with locally advanced squamous cell carcinoma of the oral cavity or oropharynx who are ineligible for cisplatin (the frontline chemotherapy drug for advanced head and neck cancers) or intolerant to cetuximab (a monoclonal antibody used as part of targeted cancer therapy in head and neck cancers). Recommended Phase 2 Dose ("RP2D") has been determined in the Study 102 Escalation. We are in the process of conducting the dose expansion part of the trial at the RP2D. The Study 102 Expansion is being conducted at 20 sites in Europe. In Study 102 Escalation, the administered dosage was escalated, with 19 patients receiving an injection of NBTXR3, followed by intensity-modulated radiation therapy (70Gy in total, or 2Gy per day, five days a week for seven weeks), in accordance with standard medical practice, commencing one to five days after NBTXR3 injection.

The primary endpoint of Study 102 Escalation was to evaluate the safety of NBTXR3 and determine the recommended Phase II dose of NBTXR3 activated by radiotherapy and the primary endpoints of the Study 102 Expansion are to confirm that the recommended dose is safe and to obtain preliminary evidence of efficacy by observing the objective response rate and complete response rate of the primary tumor by imaging according to RECIST 1.1.

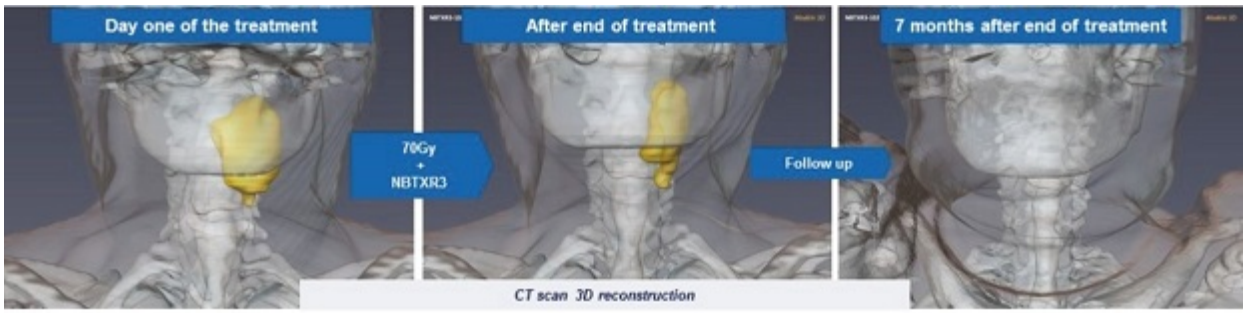
The secondary endpoints of both phases were to evaluate the safety and tolerability of NBTXR3, to evaluate the overall response rate and the complete response rate (based on the RECIST 1.1) of NBTXR3, to evaluate the local and general PFS, assess the feasibility of local administration by intratumoral injection of NBTXR3, and characterize the body kinetics of NBTXR3 administered by intratumoral injection.

Under the RECIST 1.1 criteria, (i) complete response, or CR, refers to the disappearance of all target lesions, (ii) partial response, or PR, refers to a decrease of at least 30% of target lesions, (iii) overall response, or OR, refers to CR and PR, taken together, (iv) progressive disease, or PD, refers to an increase of at least 20% of target lesions or the appearance of one or more new lesions, (v) stable disease, or SD, refers to a lack of sufficient shrinkage to qualify for PR, but also a lack of sufficient increase to qualify for PD, and (vi) unconfirmed response refers to target lesions that still require a confirmatory scan at a subsequent time point.

Dose Escalation Results

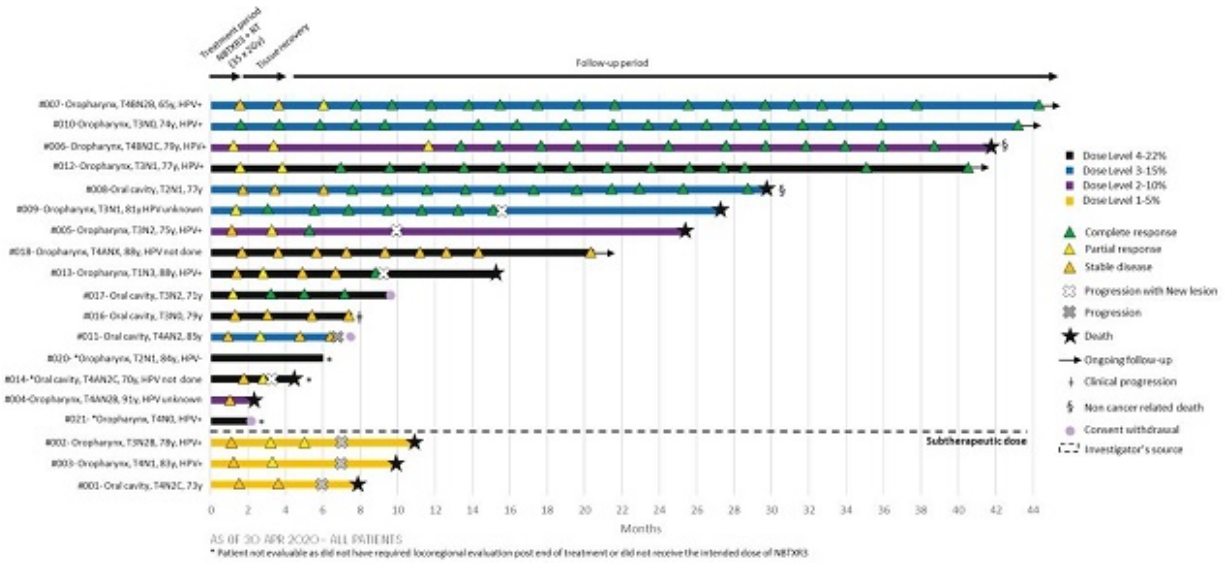
Phase I Escalation. We initially presented preliminary efficacy and safety results from Study 102 Escalation in February 2020 at the Multidisciplinary Head and Neck Cancers Symposium. Additional patient follow-up has been conducted through April 2020. NBTXR3 was well tolerated in the trial and the recommended dose was established as equivalent to 22% of tumor volume. Preliminary results included no observed serious side effects or serious adverse events related to NBTXR3 observed, and feasibility of injection at all dose levels (5%, 10%, 15% and 22%) with no leakage to surrounding healthy tissues.

The following graphic depicts shrinkage of the tumor in a representative patient in the trial over time following treatment. The tumor continued to shrink after the end of treatment, with the patient achieving a complete response at seven months.



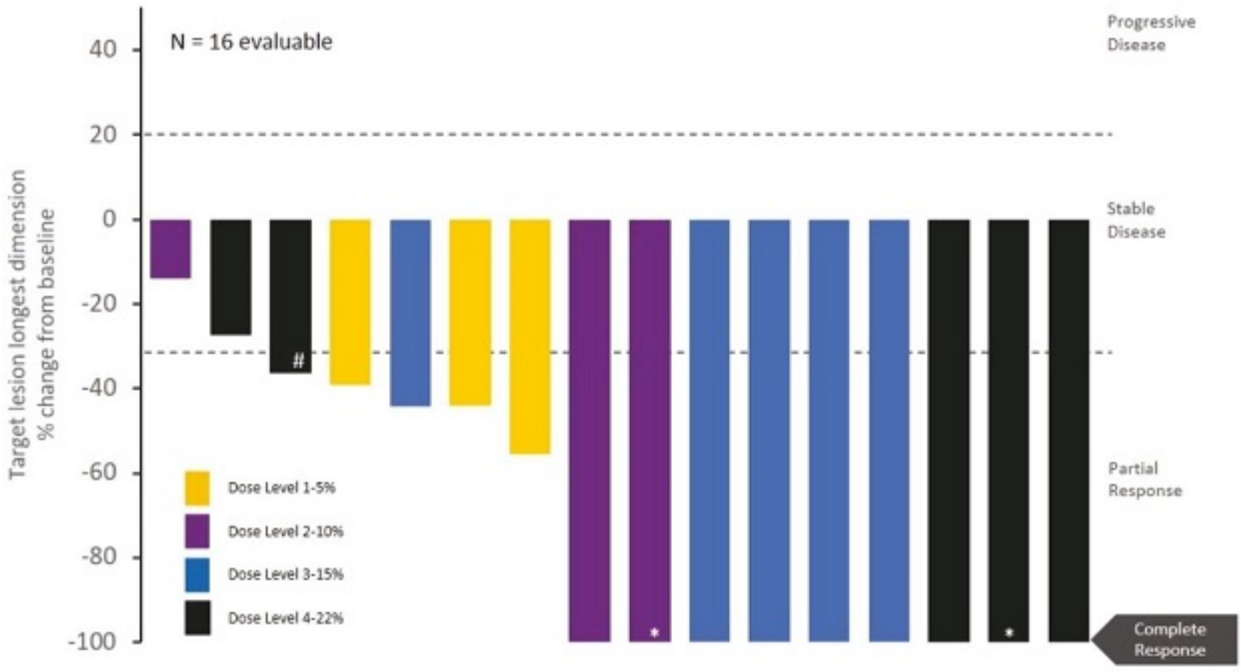
As of April 2020, nine out of the 16, or 56%, evaluable patients who received the intended dose of NBTXR3 and radiotherapy had achieved a complete response of the injected lesion, according to the RECIST 1.1., as assessed by the investigator. Overall complete response (including non-injected lesions) was observed in five of the 16 patients, or 31%, and objective response rate was observed, as per Investigator's assessment, in 11 of the 16 patients, or 68%. Of the seven patients who received the two highest doses of NBTXR3 plus radiotherapy and were alive at the 12-month cut-off date, five patients were still alive at 24 months following treatment. Of the 13 evaluable patients receiving the highest dose levels (therapeutic doses 10%, 15%, and 22%), nine patients, or 69%, achieved a complete response of the injected lesion. Follow up of treated patients remains ongoing. We are encouraged by the preliminary results, and we believe NBTXR3 has the potential to extend survival and improve quality of life in this advanced cancer patient population. The following chart shows follow-up data of the 19 treated patients at the various NBTXR3 dose levels as of the end of April 2020, including the type of cancer, tumor grade, age and human papilloma virus status for each patient.

Patient Follow-up in Study 102 Escalation Locally Advanced Head and Neck Cancers Trial



The following chart shows the best observed response by investigator's assessment from baseline of each of the 16 evaluable patients.

Patients' Investigator's assessed Best Response in Study 102 Escalation Locally Advanced Head and Neck



Best primary lesion response per investigator assessment; n=16 evaluable; *Unconfirmed CR; # Patient still evaluated for best response.
Note: 3 Patients at level 22% are not evaluated as they did not receive the intended dose of NBTXR3 or did not have the require locoregional assessment post end of treatment.
Cut-off date: 30 APR 2020

Dose Expansion Results

Phase I Expansion.

As of January 2022, 56 patients were treated in the expansion cohort of which 44 were confirmed to be evaluable, one additional patient is ongoing but is not yet evaluable. Therefore, patient accrual was completed and recruitment is closed. Ongoing patients on the study will be followed up for safety, response, PFS and OS for a minimum of 12 months after treatment completion.

The most recent updated efficacy and safety results from the ongoing Study 102 Expansion were presented at the Annual Meeting of ASTRO in October 2021. As of the September 3, 2021 cut-off date, 54 patients had received NBTXR3 and 41 patients were evaluable for objective tumor response. The expansion cohort utilizes the highest dose level (22%) from Study 102 Escalation in order to potentially strengthen preliminary efficacy data from that initial escalation phase. Evaluability in Study 102 Expansion was determined based on the patient receiving at least 80% of the intended intratumoral dose of NBTXR3, at least 60 Gy of radiotherapy, and the required imaging to assess the target lesion at baseline and at least once post treatment. In the evaluable patient population, the median overall survival was 18.1 months, and the median progression free survival was 10.6 months. Among the 21 patients with best observed overall response of complete response, six patients died for non-oncologic reasons and only one died from disease progression. The median overall survival was not reached at the cut-off date (mean follow up of 16.1 months). Investigator-assessed response rates remained consistent with previously reported results from the dose escalation and dose expansion study, showing the primary tumor objective response rate according to RECIST 1.1, as per investigator assessment, was 85.4% (35 out of 41 patients), consisting of 26 patients with primary tumor complete response (63.4%) and 9 patients with primary tumor partial response (22.0%). The other six patients were considered to have primary tumor stable disease. One patient, identified in the chart below as having stable disease (as noted with a double asterisk), was recorded by the principal investigator on

the electronic case report form ("eCRF") as having achieved an unconfirmed complete response of the injected lesion, and we have included this patient in the 63.4% primary tumor complete response rate and the 85.4% primary tumor objective response rate. Because many of the patients are early in their follow-up, there is potential for the rate of complete response to improve with the passage of time, as seen in the dose escalation part. Median follow up as of September 3, 2021 was 9.5 months since administration of NBTXR3.

Based on an assessment under the mCCI, the patient population in the Study 102 Expansion is at higher risk of early death than the global elderly head and neck cancer population.

In head and neck cancer, an mCCI ≥ 4 is correlated with higher risk of death relative to the broader population.

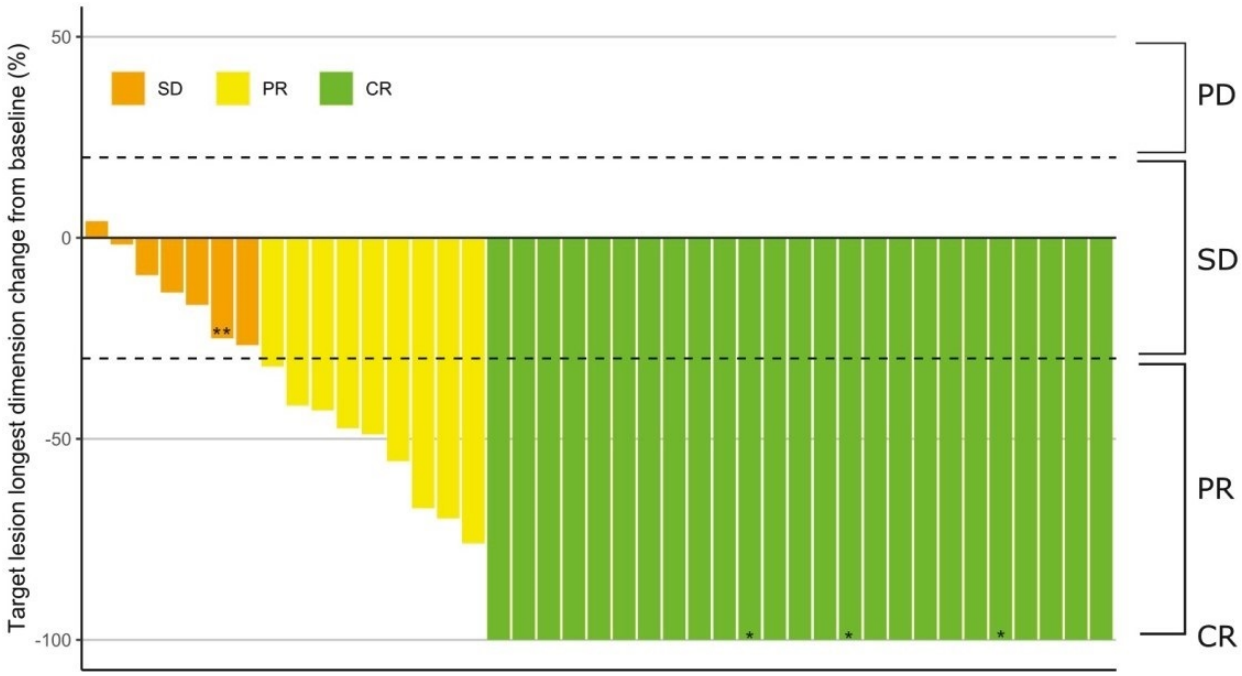
In the Study 102 Expansion "all patients treated" population (54 patients, including 13 non-evaluable patients), mOS was 14.1 months, and median PFS was 9.4 months. Among the "all patients treated" population, 63% of all patients, and nine out of the 13 non-evaluable patients included in the survival analysis, had an mCCI of four or more — an mCCI score associated with a risk of early death (defined as death within 180 days after initiation of treatment), which is two to three times the prevalence of high mCCI in the overall LA-HNSCC population that has been reported in the literature (Zumsteg ZS, et al. Cancer 2017; 123: 1345-53). Of the 13 non-evaluable patients, two were still pending evaluability assessment and of the 11 remaining, seven had early occurring death (within 180 days after initiation of treatment). In contrast, in evaluable patients the mOS that was reached was 18.1 months as of the September 3, 2021 cut-off, suggesting the observed mOS in all treated patients could be related to the high number of non-evaluable patients and a higher mCCI score observed in this subgroup which may reflect a higher risk for early death as compared to lower mCCI scores.

Among evaluable patients with oropharyngeal head and neck cancer with negative HPV status, objective response rate of the target lesion was 100% (12 out of 12 patients), consisting of eight patients with complete response (66.7%) and four patients with partial response (33.3%). In the subgroup composed of oropharyngeal head and neck cancer patients with positive HPV status, objective response rate, as per investigator's assessment, of the target lesion was 100% (10 out of 10 patients) consisting of nine patients with complete response (90%) and one patient with partial response.

Final results might differ from what has been reported at ASTRO's Annual Meeting in October 2021.

The following chart shows the best observed target lesion response from baseline of each of the 41 evaluable patients as of September 3, 2021.

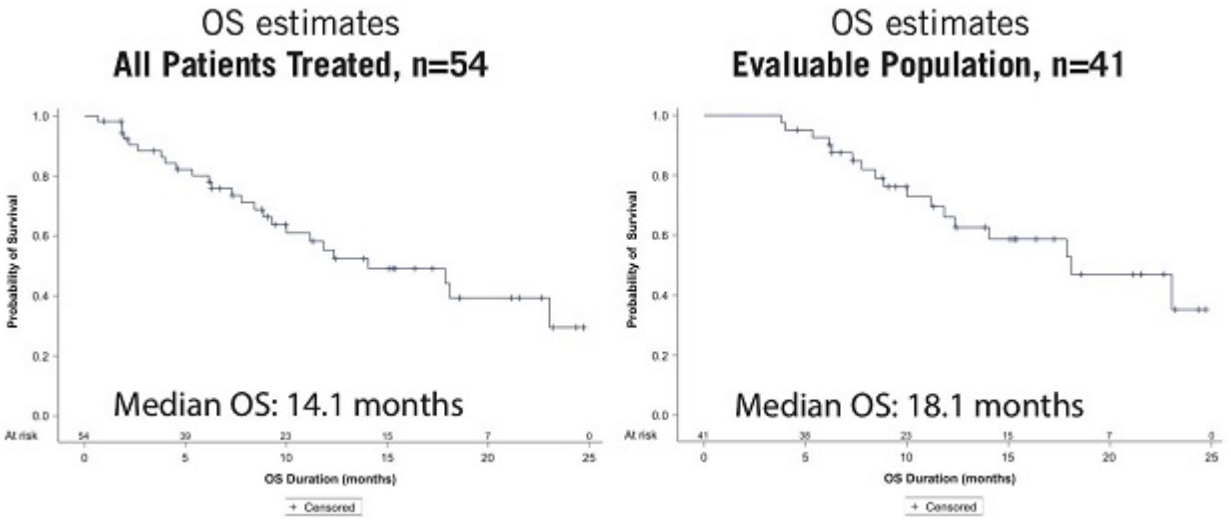
Patients' Best Observed Target Lesion Response by RECIST 1.1 as per Investigator Assessment in Study 102 Expansion Locally Advanced Head and Neck Cancers Trial (Evaluable Population: N=41)



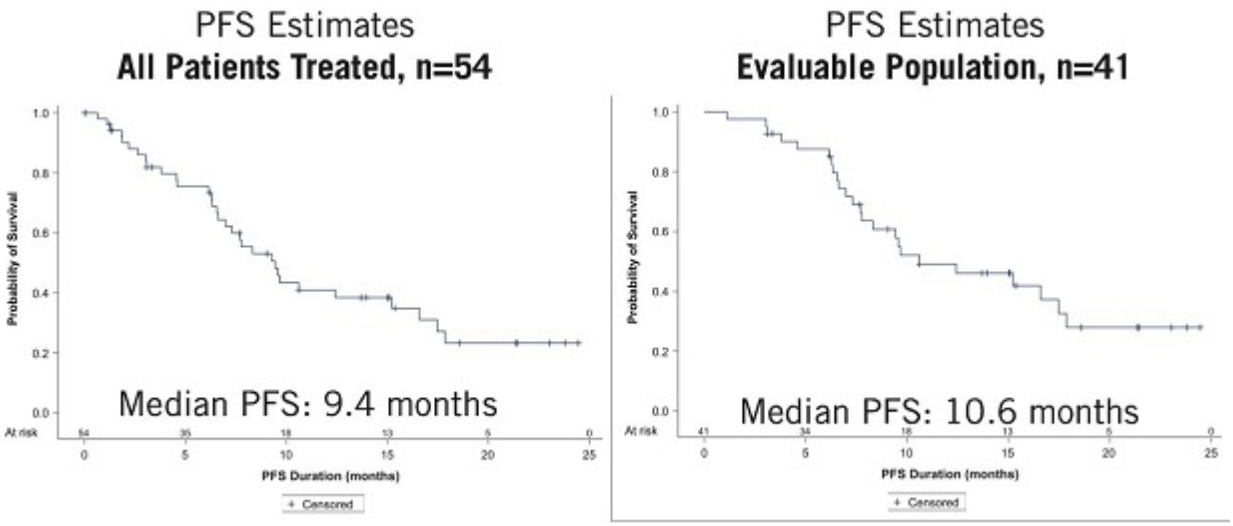
* unconfirmed complete response
** CR as per investigator

he following charts show the survival of the 41 evaluable patients and the 54 patients in the "all patients treated" population as of September 3, 2021.

Kaplan Meier Curve of Survival in Study 102 Expansion Locally Advanced Head and Neck Cancers Trial

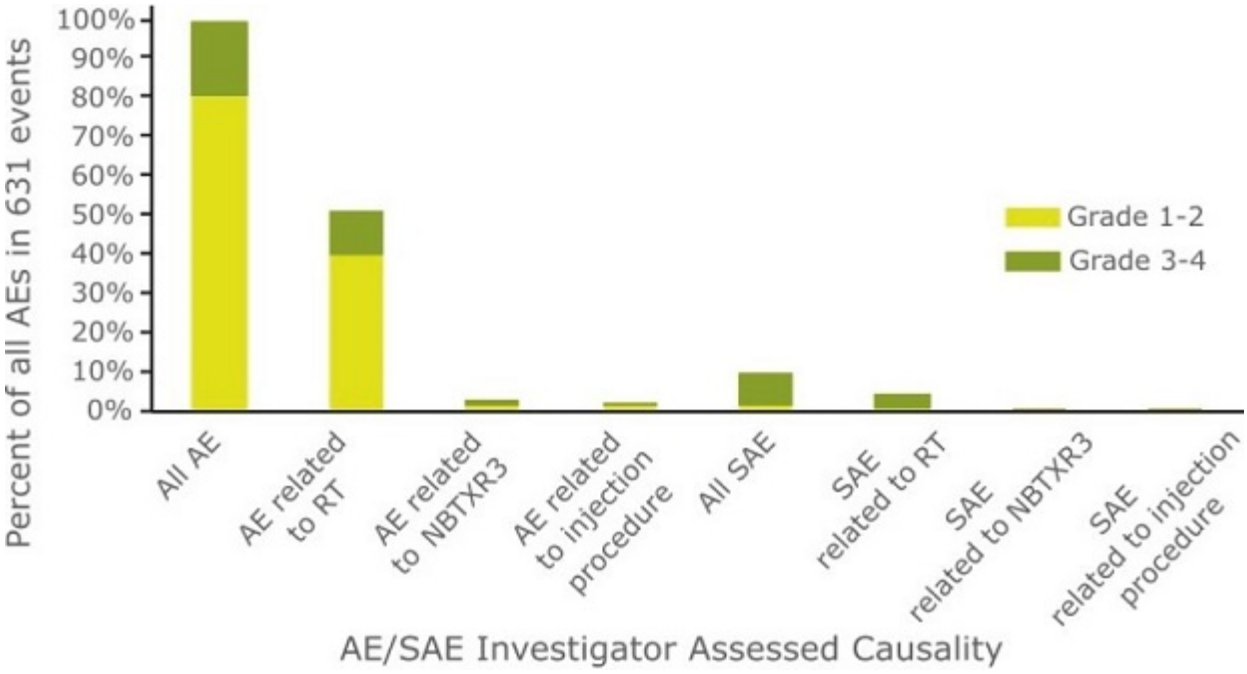


Kaplan Meier Curve of Progression Free Survival in Study 102 Expansion Locally Advanced Head and Neck Cancers Trial



NBTXR3 has continued to be well tolerated in Study 102 Expansion. Five SAEs related to NBTXR3 were observed across five patients: one Grade 4 tumor hemorrhage (also related to radiotherapy), one Grade 3 stomatitis (also related to radiotherapy), one Grade 3 soft tissue necrosis (also related to radiotherapy), one Grade 4 dysphagia (also related to radiotherapy) and one Grade 4 sepsis (also related to radiotherapy and disease). Of the SAEs, one death from sepsis occurred, which the investigator assessed as possibly related to NBTXR3, radiotherapy, and cancer.

The AEs and SAEs are set forth in the graph below.



A review of data as of the February 22, 2022 cut off date from Expansion Study 102 shows an ongoing median overall survival (mOS) of 23 months in evaluable patients (n=44) demonstrating continued improvement relative to the analysis presented at ASTRO 21 and consistent with data reported from the dose escalation phase of Study 102.

1.3.6.3. Immuno-Oncology ("I-O") Program Trials

Background and opportunity

In recent years, significant attention has been focused on the potential of I-O treatments to treat cancer patients, and in particular, with the approval of first checkpoint inhibitors anti-CTLA4 (ipilimumab) and anti-PD(L)1 (such as pembrolizumab, nivolumab, durvalumab, or atezolizumab). Checkpoint inhibitors are a type of immunotherapy that function to block proteins that stop the immune system from attacking cancer cells. In doing so, they enable the T cells to recognize cancer cells that would otherwise be invisible to immune attack. However, many cancers, which are often referred to as "cold" tumors, exhibit little or no response to checkpoint inhibition.

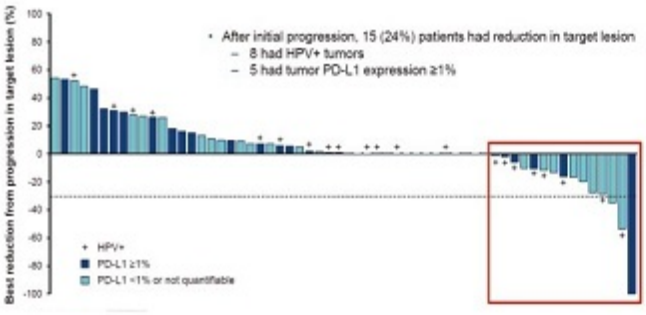
Cancer immunotherapy is becoming a major treatment paradigm for a variety of cancers. Although immunotherapy, especially the use of immune checkpoint inhibitors, has achieved clinical success, most cancer patients present resistance to I-O treatments. In fact, published scientific data shows that only 15%-20% of non-small cell lung cancer patients and 13%-22% of head and neck squamous cell carcinoma patients respond to immune checkpoint inhibitors.

Recently, significant interest has been focused on the possibility of achieving improved response rate across cancers using various therapies in combination with I-O. The figures below show data from a non-exhaustive selection of published scientific literature relating to clinical trials evaluating I-O treatments in combination or alone for the treatment of head and neck cancer in I-O naïve and I-O non-responder patients.

Outlook of Best Percentage Change from Baseline in HNSCC Trials
(Literature Data)

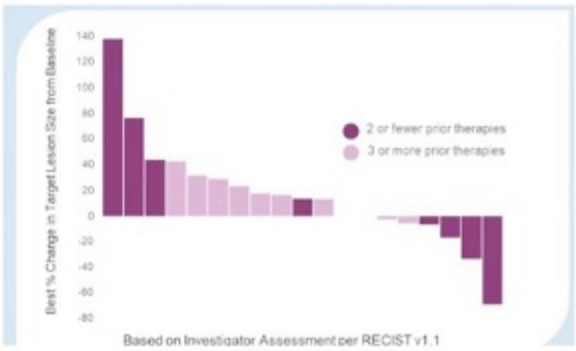
PD-1 Non-Responders ("NR") Trials

Nivolumab
CHECKMATE 141 – Anti-PD-1 NR



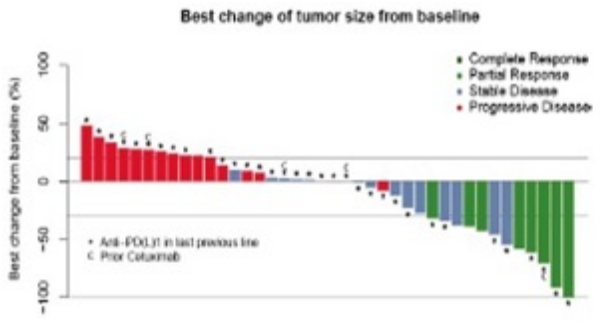
Source: Haddad R, et al., "Treatment Beyond Progression With Nivolumab in Patients With Recurrent or Metastatic (R/M) Squamous Cell Carcinoma of the Head and Neck (SCCHN) in the Phase 3 Checkmate 141 Study: A Biomarker Analysis and Updated Clinical Outcomes." European Society for Medical Oncology, September 11, 2017.

Eganelisib + Nivo
MARIO 1 – CPI NR



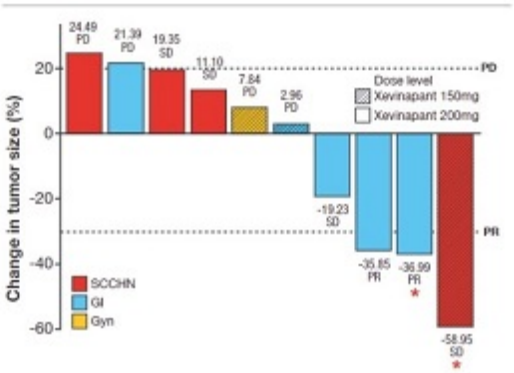
Source: Cohen E, Postow M, Sullivan R, et al., "352 Updated clinical data from the squamous cell carcinoma of the head and neck (SCCHN) expansion cohort of an ongoing Ph1/1b Study of eganelisib (formerly IPI-549) in combination with nivolumab." Journal for ImmunoTherapy of Cancer, December 10, 2020.

Monalizumab + Cetux
previous Anti-PD-1



Source: Fayette J, et al., "Monalizumab in combination with cetuximab post platinum and anti-PD-(L)1 in patients with recurrent/metastatic squamous cell carcinoma of the head and neck (R/M SCCHN): Updated results from a phase II trial." European Society for Medical Oncology, December 9, 2020.

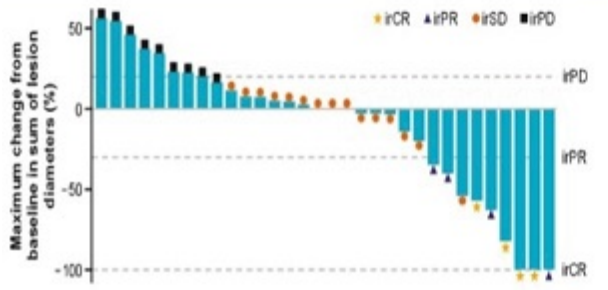
Debio + Anti-PD-1
previous Anti-PD-1



Source: Azaro-Pedrazzoli A, et al. "Safety and efficacy of Xevinapant (Debio 1143), an antagonist of inhibitor of apoptosis proteins (IAPs), in combination with nivolumab in a Phase Ib/II trial in patients failing prior PD-1/PD-L1 treatment." European Society for Medical Oncology, September 17, 2020.

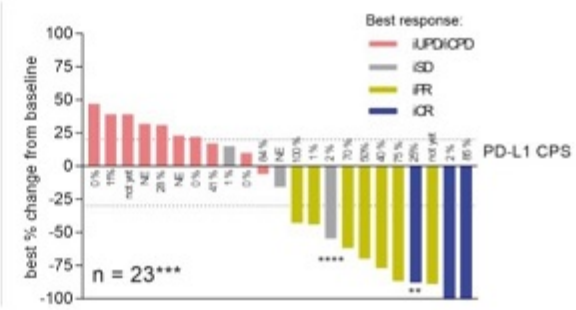
PD-1 Naïve Trials

Feladilimab + Pembro
INDUCE 1 – Anti-PD-1 Naïve



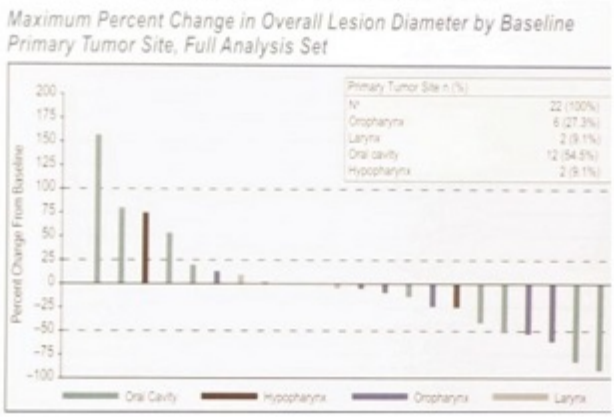
Source: Angevin E, et al. "Updated analysis of the inducible T-cell co-stimulatory receptor (ICOS) agonist, GSK3359609 (GSK609), combination with pembrolizumab (PE) in patients (pts) with anti-PD-1/L1 treatment-naive head and neck squamous cell carcinoma (HNSCC)." Journal of Clinical Oncology, May 25, 2020

Eftilagimod + Pembro
TACTI-002 – Anti-PD-1 Naïve



Source: Krebs M, et al., "790 A phase II study (TACTI-002) of eftilagimod alpha (a soluble LAG-3 protein) with pembrolizumab in PD-L1 unselected patients with metastatic non-small cell lung(NSCLC) or head and neck carcinoma(HNSCC)." Journal for ImmunoTherapy of Cancer, December 10, 2020.

T VEC + Pembro
MASTERKEY-232 – 2L Naïve



Source: Harrington K, et al. "Safety and preliminary efficacy of talimogene laherparepvec (T-VEC) in combination (combo) with pembrobrolizumab (Pembro) in patients (pts) with recurrent or metastatic squamous cell carcinoma of the head and neck (R/M HNSCC): A multicenter, phase 1b study (MASTERKEY-232)." Journal of Clinical Oncology, June 1, 2018.

This foregoing historical data survey is presented solely to illustrate the current market opportunity arising from existing application of available I-O treatments—in combination or alone—for head and neck cancer patients that are either naïve or non-responder patients. Because of the unique design of such studies applied to specific patient populations, no comparison with any of our clinical trials is possible and none should be inferred from this background data.

Supporting Rationale for I-O Treatment Approach

We believe that NBTXR3 activated by radiotherapy in combination with immune checkpoint inhibitors has the potential to unlock the potential of I-O treatments by converting checkpoint inhibitor non-responders into responders and is being explored in multiple settings.

Our preclinical and early clinical trial results suggest that NBTXR3-enhanced radiotherapy may prime the immune response, thereby rendering otherwise cold tumors more prone to recognition by the

patient's immune system and therefore more responsive to I-O treatments such as checkpoint inhibitors. This effect is also referred to as causing a "cold" tumor to become "hot."
In preclinical experiments, we observed NBTXR3 activated by radiotherapy kill more cancer cells in vitro than radiotherapy alone, leading to the release of a greater number of tumor-associated antigens. In addition, in in vitro experiments performed on different human cancer cell lines, we observed NBTXR3 activated by radiotherapy enhance the expression of markers of immunogenic cell death, as well as activation of the cGAS-STING pathway (a component of the immune system that detects tumor-derived DNA and generates intrinsic anti-tumor immunity). These results suggest that NBTXR3 activated by radiotherapy could modulate the immunogenicity of the cancer cells.

We also observed NBTXR3 activated by radiotherapy in vivo generate an abscopal effect, which is a reduction of metastases burden outside the irradiated area. This abscopal effect depends on the increase of CD8+ T cell lymphocyte infiltrates (T lymphocytes that work to kill malignant tumor cells) in both treated and untreated tumors, induced by NBTXR3 activated by the radiotherapy.

In our Phase II/III locally advanced STS clinical trial, based on immunohistochemistry analyses, we observed that NBTXR3 activated by radiotherapy increased the density of CD8+ T cell lymphocytes and also decreased FOXP3+ (Treg) (regulatory T cells that work to suppress immune response) compared to radiotherapy alone in the tumors, while macrophage number remained relatively constant.

In March 2021, researchers from our collaborator, MD Anderson, shared preclinical data in a poster presentation at the American Association of Cancer Research (AACR) Virtual Special Conference on Radiation Science and Medicine. This study examined NBTXR3 activated by radiotherapy in combination with anti-PD-1 along with TIGIT and LAG3 inhibitors in an in vivo anti-PD-1 resistant mouse model (344SQR). The data showed that the combination therapy of NBTXR3 + radiotherapy + anti-PD-1 + anti-LAG3 + anti-TIGIT (Combo therapy) significantly promoted the proliferation activity of CD8+ T cells, improved local and distant tumor control, and increased survival rate. The anti-tumor efficacy of this Combo therapy was heavily dependent on CD4+ and CD8+ T cells. The data showed that the cured mice maintained significantly higher percentages of memory CD4+ and CD8+ T cells, as well as stronger anti-tumor immune activities than control, and the cured mice from the groups treated with the Combo therapy were immune to reinjections of tumor cells. Further, in this preclinical study, the Combo therapy augmented anti-tumor response in both irradiated and unirradiated (abscopal) tumors.

Together, these data suggest that NBTXR3 activated by radiotherapy could be able to modulate the anti-tumor immune response and transform the tumor into an in situ vaccine, which prompted the initial development of our I-O program.

Development in I-O

We are conducting, and continue to further develop, a global I-O development program to explore the use of NBTXR3 as a complement to immune checkpoint inhibitors across several solid tumor indications.

The Study 1100, a Phase I basket trial of NBTXR3 activated by SBRT and followed by an anti-PD-1 checkpoint inhibitor in patients with R/M HNSCC or with lung or liver metastases from selected solid tumors prior resistant to anti-PD-1 therapy, is ongoing. A clinical study protocol amendment was submitted to the FDA at the start of 2022, to include three expansion cohorts of up to 35 patients each, in order to evaluate the safety and efficacy of the combination in patients with either R/M HNSCC which failed a prior PD-(L)1 treatment (cohort 1), or in R/M HNSCC patients that are PD-1 naive (who have never received I-O treatment before) (cohort 2) or in patients with selected solid tumors (non-HNSCC cohort 3) resistant to prior PD-(L)1 treatment.

In addition, pursuant to our collaboration with MD Anderson, we are planning to evaluate NBTXR3 in combination with various other checkpoint inhibitors (anti-PD-1, or anti-PD-L1) across several cancer indications. There are currently three clinical trials contemplated as part of our I-O program under the MD Anderson collaboration. The first two trials are currently enrolling patients, a Phase II trial in the reirradiation setting of NBTXR3 combined with pembrolizumab for inoperable, locoregionally recurrent or second primary HNSCC, and a Phase II trial for NBTXR3 for recurrent/metastatic HNSCC patients with limited PD-L1 expression or refractory to PD-1 blockade on combination with pembrolizumab. The third, a randomized Phase I/II trial for NBTXR3 combined with an anti-PD-1 or PD-L1 +/- RadScopal™ in patients with advanced solid tumors and lung or liver metastases, is in the protocol development stage. We are conducting, and continue to further develop, a global I-O development program to explore the use of NBTXR3 as a complement to immune checkpoint inhibitors across several solid tumor indications.

1.3.6.4. I-O Program—HNSCC, Lung Metastasis or Liver Metastasis

Phase I Basket Trial Design ("**Study 1100**")

We initiated a Phase I prospective, multi-center, open-label, non-randomized clinical trial evaluating the safety and efficacy of NBTXR3 activated by radiation therapy combined with anti-PD-1 checkpoint inhibitors (nivolumab or pembrolizumab). The trial is being conducted in two consecutive phases: dose escalation followed by dose expansion. The Dose Escalation part of the trial includes three patient populations:

- patients with locoregional recurrent (LRR) or recurrent and metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) amenable to irradiation of the head and neck (HN) field that are anti-PD-1 therapy naïve or non-responsive to an anti-PD-1 therapy ("HNSCC Cohort"),

- lung metastases from any primary cancer eligible for anti-PD-1 therapy ("Lung Cohort") or

- liver metastases from any primary cancer eligible for anti-PD-1 therapy.

The Dose Expansion part of the trial has the following treatment cohorts, which were introduced through a protocol amendment in early 2022:

- Locoregional recurrent and/or metastatic HNSCC and that are resistant to a prior anti-PD-1/L1 therapy with at least one lesion located in either HN region, lungs or liver, amenable for intratumoral injection and irradiation.

- Locoregional recurrent and/or metastatic HNSCC naïve to anti-PD-1/L1 therapy and eligible for an anti-PD-1 therapy with at least one lesion located in either HN region, lungs or liver amenable for intratumoral injection and irradiation.

- Lung or liver or soft tissue metastases of primary tumor originating from either NSCLC, malignant melanoma, HCC, RCC, urothelial cancer, cervical cancer or TNBC that are resistant to a prior anti-PD-1/L1 therapy and eligible for anti-PD-1 therapy with at least one lesion located in either soft tissue, lungs or liver that could be injected intratumorally and irradiated.

The trial's main objective is to determine the recommended Phase II dose of NBTXR3 activated by radiotherapy in combination with an anti-PD-1. The trial is ongoing and is being conducted at up to 20 sites in the United States; we intend to enroll a total of approximately 141 evaluable patients in the trial.

The dose escalation phase is based on a classical 3+3 design, meaning that at least three patients will be treated at the initial dose level, with treatment escalated to the next level in the absence of any dose-limiting toxicity occurrences, in order to identify the appropriate dose of NBTXR3 to be injected into the tumor. NBTXR3 doses will be escalated, but the anti-PD-1 antibody dose will remain constant.
Primary and secondary endpoints will determine the recommended Phase II dose of NBTXR3 activated by radiotherapy and evaluate safety and efficacy, while exploratory endpoints will further characterize the treatment-induced gene expression, including enriched cytokine activity and markers of adaptive immune response and T-cell receptor signalling pathways.

Results

We presented updated clinical results from ongoing Study 1100 at the 2021 ASTRO Annual Meeting in October 2021. As of the September 3, 2021 cut-off date, 21 patients received NBTXR3 and/or radiotherapy, with 16 patients evaluable for tumor response. Five patients were unevaluable (two patients died with no post-treatment scans, one patient had no post-baseline scan and two patients did not receive at least 80% of NBTXR3).

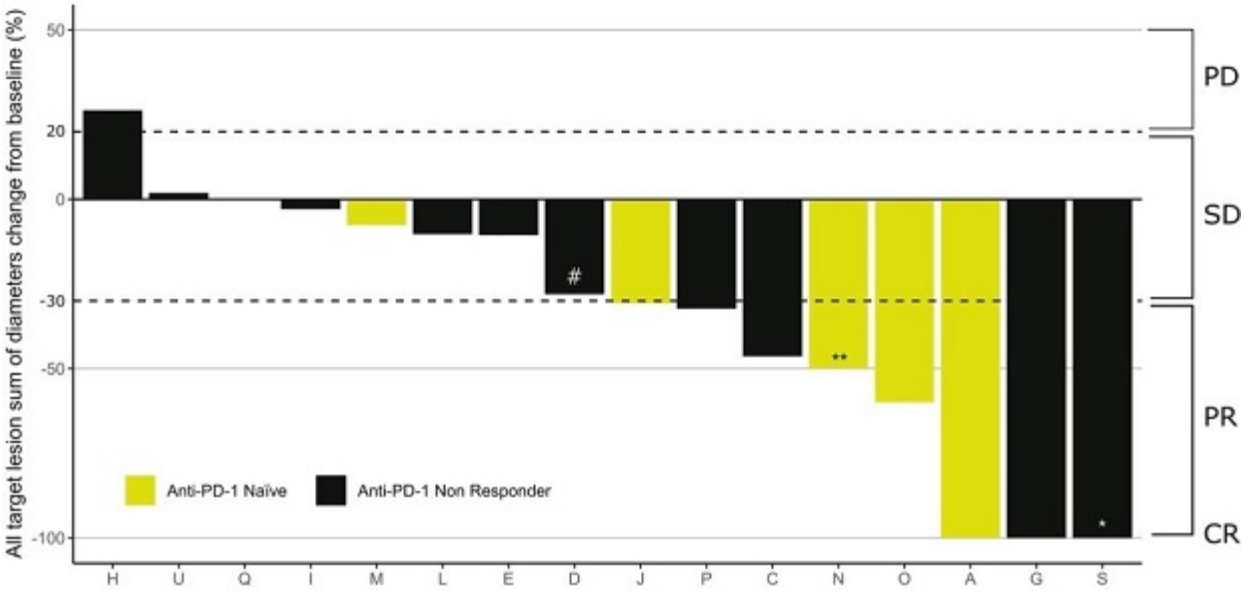
The updated results suggest that NBTXR3 administration has been feasible and well-tolerated in all patients currently enrolled in Study 1100. Through the cut-off date, six SAEs were observed which were identified as related to NBTXR3 or the injection procedure in 4 patients, and which included facial paresis, lymphocyte count decrease, weight decrease, hyperglycemia, pneumonitis and soft tissue necrosis. No injection and/or NBTXR3 related AEs of grade 3 or more were reported in the lung metastasis cohort and no injection and/or NBTXR3 related AEs of grade 3 or more were reported at dose level 33%. No injection and/or NBTXR3 related SAE nor death was observed in the lung metastasis and the liver metastasis cohorts. One patient in the HNSCC Cohort died from pneumonitis, approximately 2 months post-NBTXR3 injection, related to anti-PD-1 and possibly related to NBTXR3.

Injection and/or NBTXR3 related adverse events (AEs) grade ≥ 3

All Patients Treated	Cohort 1 - HNSCC Level 1 (22%) nPt=7		Cohort 3 - Liver Mets Level 1 (22%) nPt=3		Overall nPt=21	
Preferred Term	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Facial Paresis	1	1	0	0	1	1
Hyperglycaemia	1	1	0	0	1	1
Lymphocyte Count Decreased	0	0	1	1	1	1
Pneumonitis	1	1	0	0	1	1
Soft Tissue Necrosis	1	1	0	0	1	1
Weight Decreased	1	1	0	0	1	1
Total number of AEs	**5**	**5**	**1**	**1**	**6**	**6**

Regardless of prior anti-PD-1 exposure (i.e., I-O Naïve and I-O non-responders), in target lesion (injected and non-injected), best objective response rate was 56% and best disease control rate (patients with CR, PR, or SD) was 94%. Best objective overall response rate was 50% and best overall disease control rate was 81%. This preliminary data suggests a correlation between the local and systemic response in both anti-PD-1-naïve and post-anti-PD-1-failure patients irrespective to the tumor origin in patients receiving NBTXR3 in combination with radiation therapy and anti-PD-1. Details for best observed responses for the 16 evaluable patients currently enrolled in Study 1100 are set forth in the following charts:

Best Observed Target Lesion Response as per Investigator Assessment based on RECIST 1.1



Patient D: pCR based on biopsy sample located in the target lesion
* Patient S: Patient with unconfirmed complete response
** Patient N: Lymph node size is 8mm; complete response as per RECIST 1.1

Note: Patient B, that has been previously included in the efficacy population, is now excluded due to a change of evaluability definition. This patient, despite being treated with a lower dose of NBTXR3, had a best objective response of partial response in both all target lesions and overall assessed by RECIST 1.1.

Response as per Investigator Assessment based on RECIST 1.1 (Evaluable Population: n=16)

Best Observed Target Lesion Response (Injected and Non-Injected Lesion/s)	Naive	NR	All
CR	2**	3#,*	31%
PR	2	2	25%
SD	1	5	38%
PD		1	6%
Best Objective Response (Target Lesions) (CR + PR)	80%	45%	56%
Best Disease Control Rate (CR + PR + SD)	100%	91%	94%

Best Observed Overall Response	Naive	NR	All
CR	1	2#	19%
PR	3	2	31%
SD	1	4	31%
PD		3	19%
Best Objective Response (Overall) (CR + PR)	80%	36%	50%
Best Disease Control Rate (CR + PR + SD)	100%	73%	81%

#Patient D: pCR based on biopsy sample located in the target lesion
*Patient S: Patient recorded as unconfirmed CR by PI as per eCRF
**Patient N: Lymph node size is 8mm; CR per RECIST 1.1

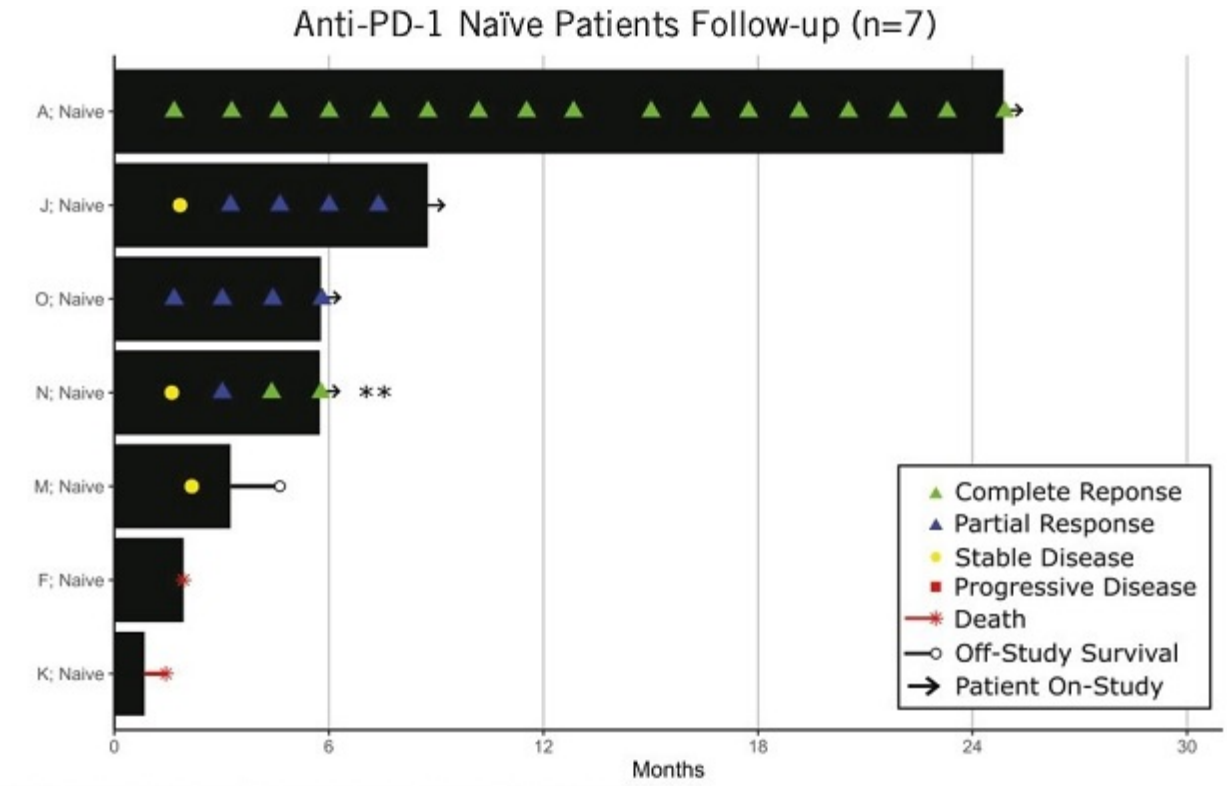
In addition, for three patients who exhibited prior resistance to anti-PD-1, a potential abscopal effect was observed. Specifically, improved control of the disease was observed in two patients (I and L) with highly progressive disease (PD on anti-PD-1 within six months of therapy), where both patients achieved best observed response of stable disease on a non-target, non-irradiated lesion. Reversed resistance was observed in one patient (C) where the patient achieved best observed response of complete response in non-target, non-irradiated lesion. Furthermore, one patient (G) with a liver metastasis from a Stage IV HNSCC with prior secondary resistance, showed a delayed and confirmed response that has deepened over time with a best observed response of complete response, suggesting a potential long term immune response.

While the observations with respect to these three patients (I, L and C) may indicate the potential of NBTXR3 in combination with anti-PD-1 checkpoint inhibitors to induce an abscopal effect or, in the case of patient G, a systemic immune response, and support further evaluation of such potential responses, in light of the small number of enrolled patients and because certain local lesions in both the I-O naïve

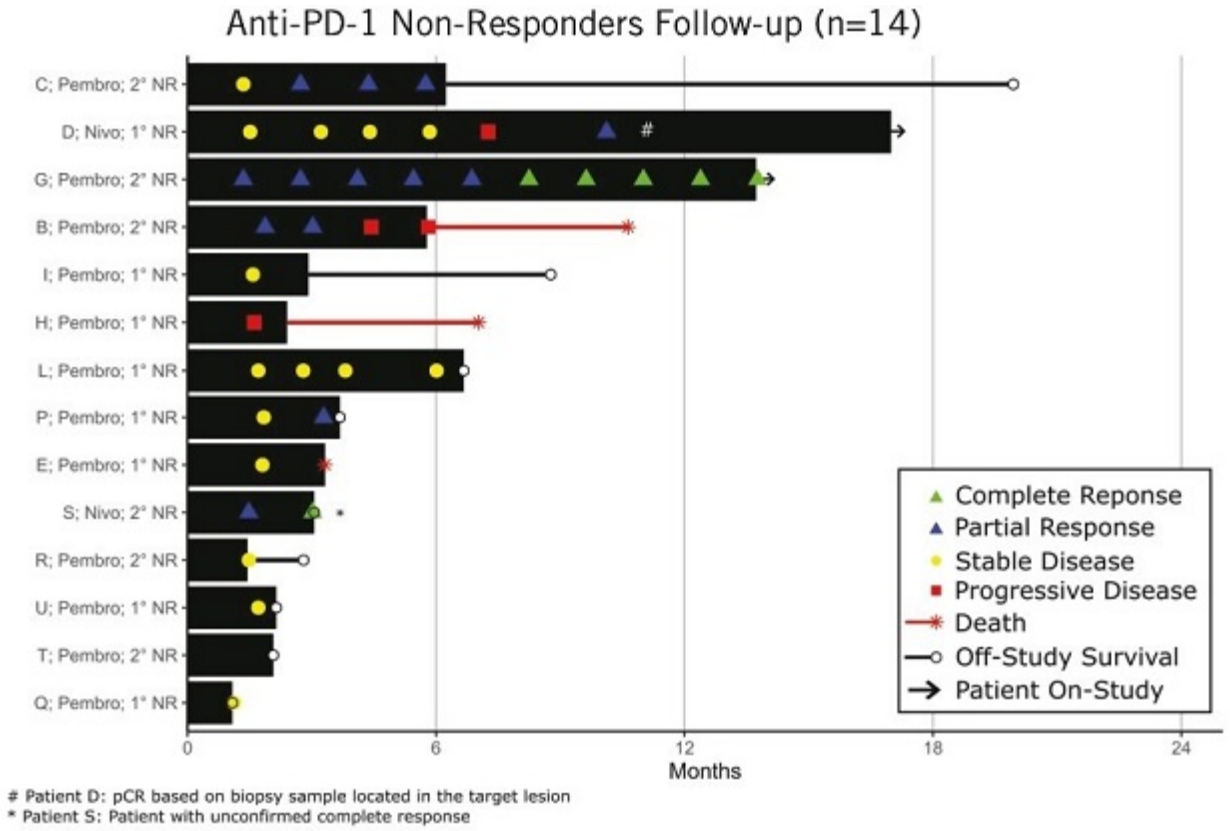
and I-O non-responder patients potentially received low-dose radiation due to their vicinity to target treatment areas, such data should not be interpreted as statistically significant evidence of any result.

The charts below present preliminary response data for Study 1100 in the "all patients treated" population, which comprises 21 patients, including 5 non-evaluable patients.

All Target Lesions Response per Investigator Assessment Based on RECIST 1.1
(All Patients Treated: n=21)

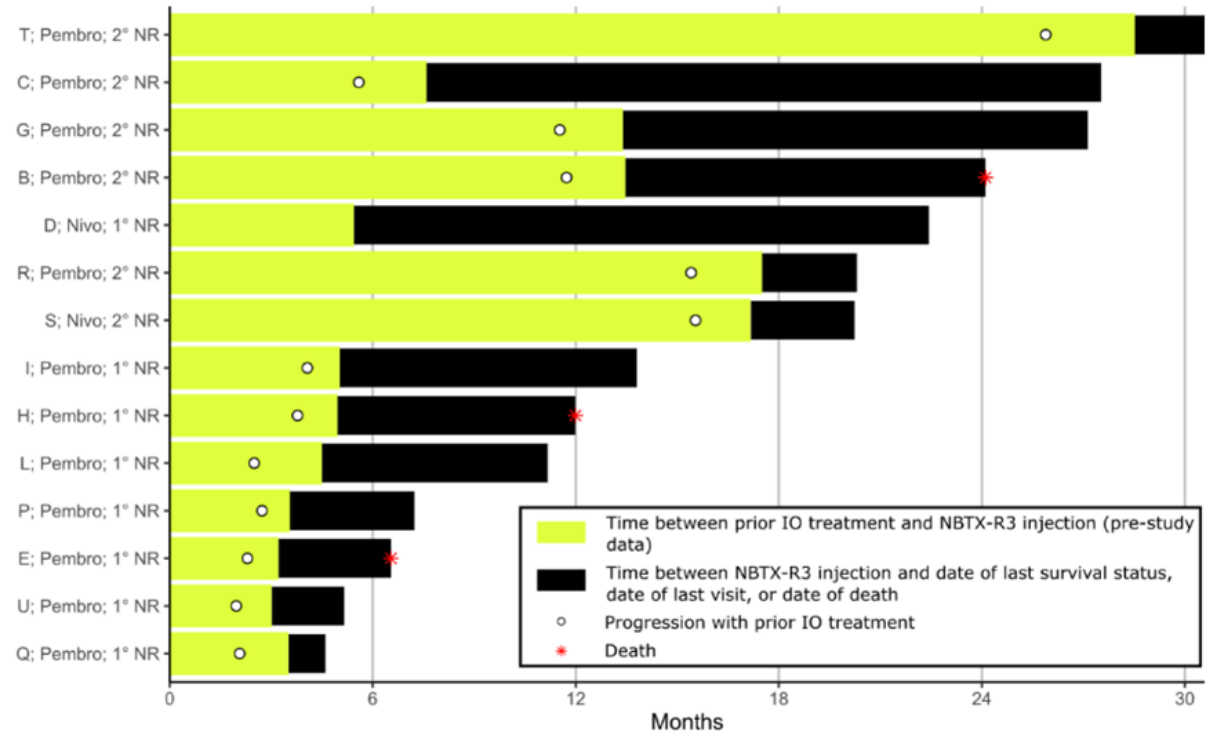


** Patient N: Lymph node size is 8mm; complete response as per RECIST 1.1



Although Study 1100 data is preliminary and based on a small patient population, we believe these results suggest potential for NBTXR3 activated by radiation therapy to improve treatment outcomes for patients by increasing the proportion of patients that respond to immune checkpoint inhibitors. Recruitment in Study 1100 remains ongoing.

With respect to the 14 anti-PD-1 non-responders included in the “all patients treated” population, the following chart provides additional information regarding (i) the time elapsed between prior anti-PD-1 IO treatment and injection with NBTXR3 and (ii) the time elapsed between the NBTXR3 injection and the last survival status, date of last visit, or date of death, as applicable:



For this non-responder population, which includes both patients with primary resistance and secondary resistance to anti-PD-1, median time alive, including pre-Study 1100 anti-PD-1 administration and subsequent to enrollment in Study 1100 was 17.02 months.

1.3.6.5. Liver cancers

Background and opportunity

According to the World Health Organization, liver cancer is currently the fourth most common cause of cancer death in the world and is estimated to have caused over 830,180 deaths in 2020. The American Cancer Society estimated that in 2021 in the United States, 42,230 people would be diagnosed with liver cancer and 30,230 patients would die of the disease. In Europe, an estimated 47,000 patients die of liver cancer each year. The five-year survival rate for patients with localized liver cancer is approximately 31%; once the cancer has spread to other organs or tissues, this survival rate drops to approximately 3%.

Two types of liver cancer are hepatocellular carcinoma (“HCC”), the most common type of liver cancer, and secondary liver cancer, or liver metastasis, which occurs when cancer from another part of the body spreads to the liver. Surgical resection is often not an option for patients with either HCC or liver metastasis. Moreover, because patients suffering from HCC or liver metastases typically have underlying liver dysfunction and concomitant malignancies, local and systemic treatment options are few in number, with significant limitations. Stereotactic body radiation therapy (“SBRT”)—a high-precision radiation therapy, delivered as high-energy dose fractions—is a prevalent alternative therapy that has been shown to improve outcomes for these patients, as third-party clinical trials have observed a direct correlation between higher doses of radiation and increased survival rates. However, SBRT dosage is limited due to potential toxicity to surrounding tissues and the need to preserve liver function. Our clinical trial described below evaluated NBTXR3 in patients with liver cancers in need of an alternative treatment, when standard care protocols either could not be used or did not exist. By increasing the absorption of the administered SBRT dose within the tumor itself, without causing

additional damage to surrounding healthy tissues, and causing more effective tumor destruction, we believe NBTXR3 can improve prognoses for this patient population.

Phase I/II trial design ("**Study 103**")

We completed Phase I of a Phase I/II clinical trial to evaluate the use of NBTXR3 activated by SBRT in liver cancers. The Phase I trial was conducted at six sites in the EU. For this dose escalation phase of the clinical trial, we recruited 23 patients, divided in two subgroups: patients with primary liver cancer (HCC) and patients with secondary liver cancer (liver metastases).

The endpoint of the Phase I part of the trial was to determine the recommended dose of NBTXR3 and to assess early signs of anti-tumor activity. In this portion of the trial, patients received a single intra-lesional injection of NBTXR3, at increasing dose levels, in each case activated by SBRT.

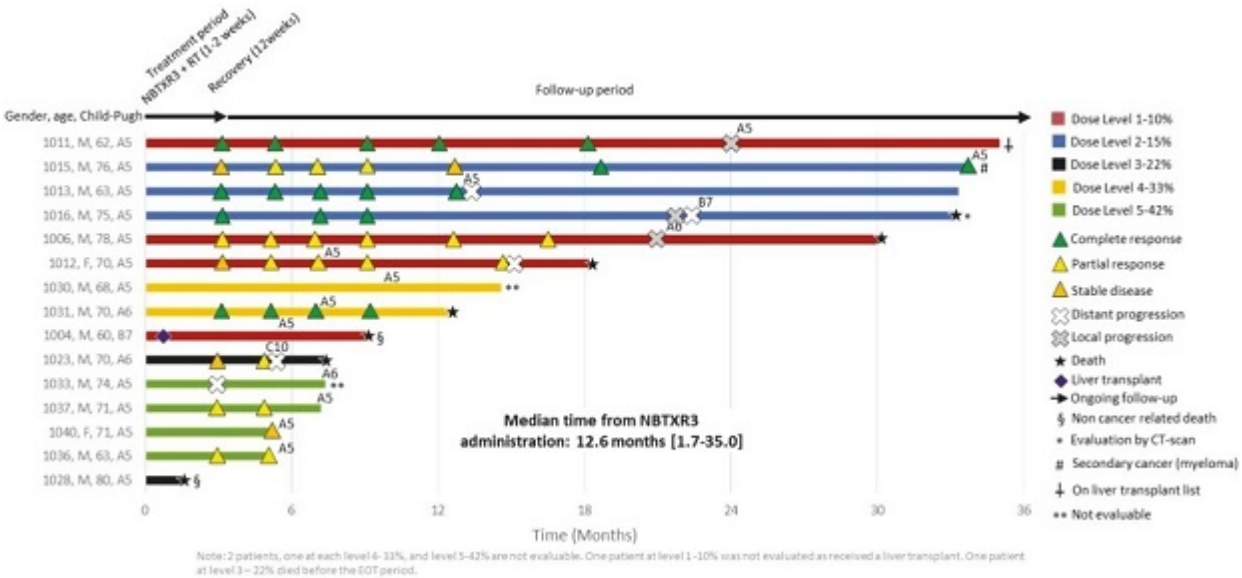
Results

Final data with respect to the Phase I part of Study 103 was presented in October 2020 at the annual meeting of the American Society for Radiation Oncology (ASTRO) and in January 2021 at the annual meeting of the Gastrointestinal Cancers Symposium (ASCO-GI).

Results from the Phase I part of Study 103 showed feasibility of injection at each of the five tested dose levels (10%, 15%, 22%, 33% and 42%) with no leakage to surrounding healthy tissues. One SAE of bile duct stenosis was deemed to be related to NBTXR3 and no dose-limiting toxicities were observed. The recommended Phase II dose (RP2D) has been set at 42%. In 11 patients evaluable for efficacy, early data showed a target lesion objective response rate of 90.9% in evaluable HCC patients and a target lesion objective response rate of 71.4% in evaluable patients with liver metastasis.

For HCC patients, preliminary results showed that out of eleven evaluable patients, ten responded at least partially and five of the eleven patients (45.5%) reached complete response.

Details for the 11 total HCC patients enrolled in Study 103 are set forth in the following chart:



In the metastatic setting, out of the seven patients evaluated for efficacy, five patients presented a partial response and two patients presented stable disease.

We believe these results suggest meaningful potential to address an unmet medical need in an indication with typically extremely poor prognosis. Although this data is preliminary, it further supports the potential transferability of NBTXR3 across multiple solid tumor indications.

The further development in this indication, including the next steps following Study 103, will be evaluated following the launch of NANORAY-312.

1.3.6.6. Pancreatic cancer (MD Anderson acting as sponsor of this Trial)

Background and opportunity

Pancreatic cancer is a rare, deadly disease. Worldwide, there were 495,773 new cases in 2020. Given that surgery with R0 resection (i.e., macroscopically complete tumor removal with negative microscopic surgical margins) remains the only hope for long-term survival, clinical trials have investigated various neoadjuvant strategies—wherein patients receive anti-cancer drugs or radiation prior to surgery—to increase the surgery-eligible population while also increasing the R0 resection rate. According to the American Cancer Society, for all stages of pancreatic cancer combined, the five-year relative survival rate is 10%.

In support of the rationale for neoadjuvant therapy, a retrospective analysis demonstrated a near doubling in OS in pancreatic ductal adenocarcinoma ("PDAC") patients who underwent surgery, which was attributed, at least in part, to the increased proportion of borderline resectable pancreatic cancer ("BRPC") patients who became eligible for surgery as a result of neoadjuvant intervention. Importantly, there are also select cases of locally advanced pancreatic cancer ("LAPC") patients being considered for surgical resection based on their response to therapy. Given the poor prognosis of PDAC, therapeutic regimens able to increase the proportion of BRPC and LAPC patients eligible for surgery could improve survival outcomes in this population with unmet need.

Phase I Trial Design

The trial is an open-label, single-arm, prospective Phase I study consisting of two parts: (i) dose-escalation to determine the RP2D and (ii) expansion at RP2D.

The patient population will include adults (age ≥ 18 years) with BRPC or LAPC that are radiographically non-metastatic at screening, having received between two to six months of chemotherapy prior to trial enrollment and that have not previously received radiation therapy or surgery for pancreatic cancer. The number of participants enrolled will be determined based on the maximum number required to establish the RP2D. Up to 24 subjects will be enrolled, including a maximum of twelve subjects with LAPC for the dose-finding part. Twelve additional subjects with either LAPC or BRPC will be enrolled for the RP2D expansion. The first patient was dosed in this trial in September 2020. The objectives of the study are the determination of the incidence of dose-limiting toxicity, the maximum tolerated dose and will lead to finding the RP2D.

1.3.6.7. Lung cancer (MD Anderson acting as sponsor of this Trial)

Background and opportunity

According to the World Health Organization, lung cancer is currently the most common cause of cancer death in the world and is estimated to have caused over 1.7 million deaths in 2020. According to the American Cancer Society, in 2021 it is estimated that there will be approximately 235,760 new cases of lung cancer diagnosed in the United States. It is estimated that in the United States there will be approximately 131,880 deaths from lung cancer in 2021. Non-small cell lung cancer ("NSCLC") is the most common type of lung cancer, accounting for 84% of all lung cancer diagnoses. The five-year relative survival rate for NSCLC at all stages was 25%.

Phase I Trial Design ("**Study 2020-0123**")

The trial is an open-label, two-cohort, prospective Phase I study consisting of two parts: (i) a radiation therapy safety lead-in, and NBTXR3 activated by radiation therapy dose-finding to determine the RP2D, and (ii) expansion at RP2D with toxicity monitoring.

The patient population will include adults (age ≥ 18) with inoperable LRR NSCLC stage IA to IIIC that are radiographically non-metastatic at screening and have previously received definitive radiation therapy. The number of participants enrolled will be determined based on the maximum number required to establish the RP2D. Cohort 1 will evaluate the safety of intensity-modulated radiation therapy ("IMRT") monotherapy in 10 patients using an approach similar to a 3+3 design. If 45 Gy in 15 fractions is deemed safe, cohort 2 will test that regimen with NBTXR3 activated by IMRT. Alternatively, if 45 Gy in 15 fractions is deemed to have excessive toxicity, a 30 Gy in 10 fractions regimen will be used in combination with NBTXR3 in cohort 2. Up to 24 subjects will be enrolled in cohort 2, including a maximum of 12 subjects for the dose-finding part. Twelve additional subjects will be enrolled for the NBTXR3 RP2D expansion.

Enrollment for our Phase I clinical trial of NBTXR3 with MD Anderson for patients with lung cancer receiving re-irradiation has commenced. The planned enrollment period is up to three years. The dose levels to be explored are 22% and 33% of baseline gross tumor volume.

1.3.6.8. Esophageal cancer (MD Anderson acting as sponsor of this Trial)

Background and opportunity

According to the World Health Organization, esophageal cancer is currently the sixth most common cause of cancer death in the world and is estimated to have caused 544,076 deaths in 2020. The American Cancer Society estimates that in 2021 in the United States, there will be approximately 19,260 new esophageal cancer cases diagnosed, and approximately 15,530 deaths due to esophageal cancer. Approximately 20% of patients survive esophageal cancer at least five years after diagnoses.

Phase I Trial Design ("**Study 2020-0122**")

This trial is an open-label, single-arm, prospective Phase I study consisting of two parts: (i) does-escalation to determine the RP2D of NBTXR3 activated by radiotherapy with concurrent chemotherapy, and (ii) expansion at RP2D with toxicity monitoring.

The patient population will include adults (age > 18 years) with stage II-III adenocarcinoma of the esophagus that are treatment naïve and radiographically non-metastatic at screening. The number of participants enrolled will be determined based on the maximum number required to establish the RP2D of NBTXR3 activated by radiation therapy. Up to 24 subjects will be enrolled, including a maximum of 12 subjects for the dose-finding part. Twelve additional subjects will be enrolled for the RP2D expansion.

Enrollment has commenced, and the planned enrollment period is 24 months. The first patient was dosed in this trial in January 2021. The objectives of the study are the determination of dose-limiting toxicity, the maximum tolerated dose and RP2D.

1.3.6.9. Prostate cancer

Background and opportunity

Prostate cancer is the second leading cause of death from cancer and the second-most common form of cancer in the United States in men. The American Cancer Society estimates that in 2021 in the United States, approximately 248,530 people will be diagnosed with prostate cancer and approximately 34,130 patients will die from the disease. Worldwide, there were approximately 1.4 million new cases in 2020. Patient prognosis is good for local and regionalized prostate cancer, but for prostate cancer that has spread to other parts of the body, the five-year survival rate is approximately 31%.

Achieving local control is key for treatment of prostate cancer to prevent relapse and subsequent spreading of the disease. Prostate cancer patients typically receive one of two forms of radiotherapy—EBRT or brachytherapy combined with EBRT. Third-party clinical data has shown that radiotherapy, and specifically the increasing of the radiation dose delivered, significantly improves local control of prostate tumors and reduces recurrence and metastasis.

Phase I/II Trial Design ("**Study 104**")

We initiated a Phase I/II clinical trial of NBTXR3 to evaluate the safety and efficacy of NBTXR3 for the treatment of tumors resulting from prostate cancer. Study 104 enrolled patients with intermediate and high-risk prostate cancer who were eligible to receive one of two radiotherapy standards of care at one site in the United States. One group evaluated NBTXR3 in conjunction with EBRT delivered as intensity-modulated radiation therapy. The second group evaluated NBTXR3 in combination with brachytherapy and EBRT.

The trial administered NBTXR3 to five patients in Phase I. No SAEs were reported by these patients.

The primary endpoints of the Phase I dose escalation trial were to determine the safety and the recommended doses and early dose-limiting toxicities of NBTXR3 activated by EBRT or by brachytherapy plus EBRT and to assess early signs of anti-tumor activity. The secondary endpoints were to evaluate the dose toxicity and tolerance of NBTXR3, evaluate the complete response rate of NBTXR3, evaluate the local and general PFS time and the OS rate, assess the feasibility of local NBTXR3 administration by intratumoral injection, and evaluate the biochemical failure before activation by intensity-modulated radiation therapy.

We have decided to stop this trial as we focus primarily on advancing the development of NBTXR3 for the treatment of locally advanced head and neck cancers. However, we continue to evaluate prostate cancer within the context of our overall development program for NBTXR3 in the treatment of solid tumors.

1.3.7. PharmaEngine trials

In August 2012, we entered into an exclusive license and collaboration agreement with PharmaEngine for the development and commercialization of NBTXR3 in the Asia-Pacific region. In March 2021, in light of disagreements over a number of issues with respect to the development of NBTXR3 in the Asia-Pacific region, we and PharmaEngine mutually agreed to terminate the agreement. Three NBTXR3 clinical trials (including certain Asia-Pacific sites for the Act.in.Sarc trial) conducted by PharmaEngine in Asia were concluded or terminated, and we retain all rights to the development and commercialization

of NBTXR3 in the Asia-Pacific region, pursuant to the terms of a Termination and Release Agreement that we entered into with PharmaEngine in March 2021 (see "1.3.14.3. of the Universal Registration Document" below for additional information).

1.3.7.1. Head and Neck Cancers Treated with Radiotherapy plus Chemotherapy

Trial Design ("**PEP503-HN-1002**")

In addition to our contemplated Phase III and ongoing Phase I clinical trials of NBTXR3 in head and neck cancers, PharmaEngine has been conducting a Phase I/II clinical trial of NBTXR3 for patients with head and neck cancers to be treated by radiotherapy plus cisplatin. The primary endpoints of the study were to determine the optimal NBTXR3 dose and to assess the preliminary safety and efficacy of NBTXR3 administered by intratumoral injection in combination with radiotherapy plus chemotherapy. The trial, which is being conducted in Taiwan and was recruiting patients in the Phase I dose escalation part, was expected to treat up to 42 patients. PharmaEngine has implemented the early termination and wind-down of this clinical trial, which will conclude with the issuance of a final study report in accordance with good clinical practice guidelines.

1.3.7.2. Rectal Cancer

Trial Design ("**PEP503-RC-1001**")

PharmaEngine has been conducting an open-label Phase I/II clinical trial of NBTXR3 with radiotherapy in combination with chemotherapy for patients with unresectable rectal cancer. Primary and secondary endpoints were to assess the safety profile and determine the dose-limiting toxicity, evaluate the recommended dosage and assess the anti-tumor activity by evaluating the response rate of NBTXR3 administered by intratumoral injection and activated by external beam radiation, with concurrent chemotherapy treatment in patients with unresectable rectal cancer. The trial, which is being conducted at one site in Taiwan, was expected to treat up to 42 patients. PharmaEngine will implement the early termination and wind-down of this clinical trial, and the trial will be deemed completed when all enrolled patients have reached "end-of-study" and PharmaEngine issues a final study report in accordance with good clinical practice guidelines.

Results

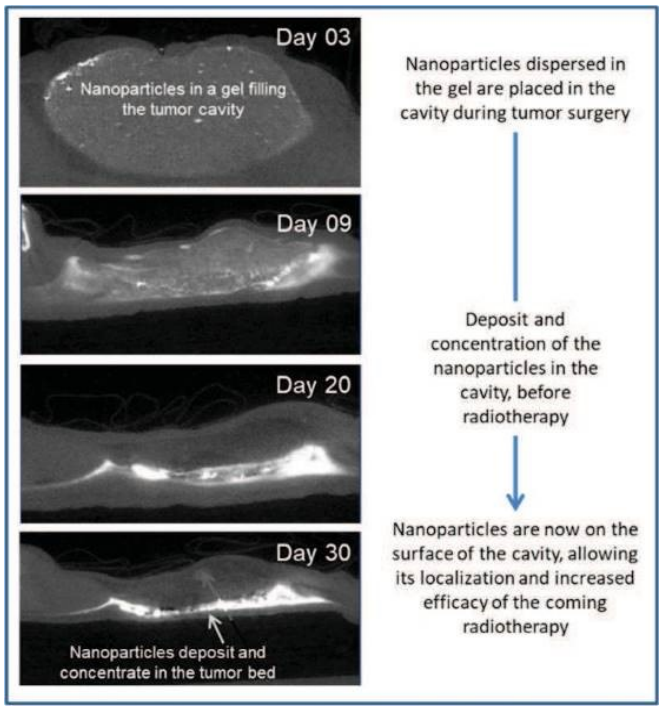
PharmaEngine presented first clinical results from Study PEP503-RC-1001 at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium in January 2021. Intratumoral injection of NBTXR3 with CCRT was feasible and the product candidate was well tolerated at all dose levels, and no AEs or SAEs associated with NBTXR3 were observed in the study. One dose-limiting toxicity associated with the injection procedure was observed (urinary tract infection with sepsis). The most frequently reported AEs were diarrhea (approximately 45%), leukopenia (approximately 40%), and dermatitis (approximately 25%); however, all were grade one or grade two.

More than 70% of patients in the study showed objective tumor response after CCRT. Approximately 90% of patients underwent a total mesorectal excision (surgery)and 17.6% achieved pathological complete response (pCR). 50% of patients receiving surgery in the study had good tumor regression (tumor regression grade 0 or 1 according to modified Ryan scheme). The RP2D was established for the ongoing Phase II part of the trial at 22% of tumor volume.

1.3.8. Our pre-clinical program on NBTXR3-gel

We are developing NBTXR3-gel, NBTXR3 in a gel formulation, for direct application in the tumor cavity following tumor ablation or resection surgery, before wound closure. As illustrated below, NBTXR3-gel is designed to prepare the surgical site for postoperative radiotherapy (adjuvant treatment) in order to destroy residual cancer cells not removed during surgery.

Application of NBTXR3-gel in tumor cavity



This unique product candidate has a dual aim: effective destruction of cancer cells remaining after surgery and enhancement of tumor cavity radiation by localizing the radiation.

The initial cancer indications we are exploring for NBTXR3-gel are certain types of breast cancer, operable lung cancers, vertebral metastases and retroperitoneal STS.

Pre-clinical data publication

In July 2021, Nanobiotix and MD Anderson published in the International Journal of Radiation Oncology, Biology, Physics (Red Journal) preclinical findings of a mouse model study examining the triple combination of NBTXR3 plus radiotherapy plus anti-PD-1. This preclinical data, which showed that the triple combination significantly delayed the growth of both irradiated and unirradiated tumors in both anti-PD1-sensitive and anti-PD1-resistant lunch cancer models, supports the further exploration of NBTXR3 as a therapeutic option for the treatment of bother primary and metastatic lung cancer and the potential for transforming irradiated tumors into “self-vaccines.”

In November 2021, we presented preclinical data at the 2021 Annual Meeting of the Society for the Immunotherapy of Cancer (SITC) that showed that in the studies mouse model radiotherapy-activated NBTXR3 increased CD8+ T cell infiltration and modulated the T cell receptor (“TCR”) repertoire, as well as marked modulation of immunopeptidome in treated tumor cells. Taken together, these variations support further evaluation of radiotherapy-activated NBTXR3’s potential to trigger more robust immune priming than radiotherapy alone and further evaluation of CD8+ response and potential abscopal effect.

1.3.9. The Curadigm Platform

Beyond NBTXR3, Nanobiotix is also evaluating several additional potential development programs in nanomedicine.

In July 2019, Nanobiotix formed a wholly-owned subsidiary — Curadigm SAS — with the mission of leveraging Nanobiotix's expertise and know-how beyond oncology to expand treatment benefits across multiple therapeutic classes by increasing drug bioavailability while decreasing unintended off-target effects, specifically liver toxicity.

For most therapeutics today, only a small portion of the medicine administered is effective. After injection, the dose moves through the patient's circulatory system within the blood. While a small portion reaches the targeted tissue, the remainder is either cleared from the body or accumulates—potentially with toxic effect—in organs such as the liver or spleen.

Leveraging our deep expertise in nanotechnology, Curadigm is developing a nanoparticle, called Nanoprimer, that primes the body for therapeutic treatment. Nanoprimer is based on proprietary technology invented at Nanobiotix and transferred to Curadigm for development and potential commercialization. Injected intravenously prior to a recommended therapeutic, the Nanoprimer has been designed with specific physico-chemical properties that allow it to transiently occupy the liver cells responsible for therapeutic clearance and is intended to prevent rapid clearance, thereby increasing blood bioavailability and subsequent accumulation of therapeutics in the targeted tissues. As a result, a greater portion of the therapeutic treatment remains available for accrual in the target tissue, thereby increasing therapeutic action.

Nanobiotix believes that the Curadigm technology could have broad implications across the healthcare system by increasing the efficacy of therapeutics at their current dose or lowering the necessary dose in order to decrease toxicity and cost and allowing for novel therapeutic approaches and new approaches to drug design. Preclinical in vivo data evaluating Curadigm's concept has been generated combining the Nanoprimer with different therapeutic agent families such as small molecules and nucleic acids and has been published in scientific journals.

As the Nanoprimer is a combination product candidate that does not alter or modify the therapies it is paired with, we expect that Curadigm will continue to seek partnerships across drug classes-particularly with nucleic acid-based therapies. To support the development of its platform, Curadigm may pursue various funding opportunities, including, without limitation, partnership and collaboration arrangements, licensing opportunities and/or sales of Curadigm securities to third-party investors from time to time.

Curadigm Collaboration with Sanofi

In January 2021, a research project involving Curadigm's Nanoprimer technology was selected for the Sanofi iTech Awards Program for its potential to significantly improve gene therapy development. Curadigm entered into a collaboration agreement with Sanofi that is expected to include direct funding and scientific exchanges. The goal of the project is to establish proof-of-concept for the Nanoprimer as a combination product that could improve treatment outcomes for Sanofi's gene therapy product candidates. Such research period has been extended to remain in effect until the submission of a final report by Curadigm to Sanofi.

1.3.10. Manufacturing

We contract the production of NBTXR3 to high-precision manufacturing partners. Our contracts with these contract manufacturing organizations generally provide that the manufacturing partner may not transfer its rights or sub-contract any of the services covered. The manufacturing partners are required to perform their obligations in accordance with international professional standards, including the Good Manufacturing Practices guidelines issued by the International Council for Harmonization.

In November 2017, we opened a facility to expand our manufacturing capabilities, increase production capacity of NBTXR3 for our clinical trial needs and prepare for potential commercialization. This facility is located in the Villejuif BioPark, a scientific research and innovation center just outside of Paris, France. We expect that the facility will in due course expand our production capacity with the aim to produce NBTXR3 for our ongoing clinical trials and our initial commercial phase. Additionally, we have designed our manufacturing process to implement in a timely manner further set-up of in-house additional production lines.

1.3.11. Commercialization

We have not yet developed commercial infrastructure in either the United States or the EU, and we are in the process of defining our commercialization strategy. We intend to establish a global commercial infrastructure outside the countries in which LianBio will commercialize NBTXR3 by building our own commercial capabilities as well as evaluating partnering opportunities.

We believe that our commercial infrastructure, if and when established, will target the community of physicians who are the key specialists in diagnosing and treating the patient populations for which NBTXR3 is being developed. We may enter into additional development and commercialization agreements with third parties in select geographic territories for any of our product candidates that successfully complete applicable pre-marketing regulatory requirements in order to optimize sales.

1.3.12. Competition

The development of treatments for cancer is subject to rapid technological change. Many companies, academic research institutions, governmental agencies and public and private research institutions are pursuing the development of medicinal products, devices and other therapies that target the same conditions that we are targeting, including in some cases in the same patient populations that we are targeting.

Approximately 60% of all cancer patients undergo radiotherapy at some point during their course of treatment. Current research in radiotherapy focuses primarily on (1) methods to increase sensitivity of tumors to radiation and (2) methods to protect healthy tissues from radiation. In addition, many researchers believe that radiotherapy can enhance the body’s immune response, thereby making a previously unsusceptible tumor susceptible to vaccines.

Companies that are developing treatments to increase sensitivities of tumors to radiation and other sources of energy include MagForce AG, Merck & Co., NH TherAguix, Nanospectra Biosciences, Inc., RiMO Therapeutics and Coordination Pharmaceuticals, Inc. Like us, these companies are pursuing various technologies that involve the delivery of a substance to a tumor that works to destroy the tumor cells without causing additional damage to surrounding healthy tissues. Any product candidates that we or they develop and commercialize may compete with existing therapies, as well as new therapies that may become available in the future, including therapies with a mode of action similar to that of NBTXR3.

Many of our competitors, either alone or with their collaboration partners, may have significantly greater financial resources and expertise in research and development, preclinical testing, clinical trials, manufacturing, and marketing than we do. Future collaborations and mergers and acquisitions may result in further resource concentration among a smaller number of competitors. These competitors also compete with us in recruiting and retaining qualified research and development and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with more established companies.

The key competitive factors affecting the success of NBTXR3 and any other product candidates that we develop, if approved, are likely to be their efficacy, safety, convenience, price and the availability of reimbursement from government and other third-party payors. We must also protect our proprietary technology used in the development of our product candidates. Our commercial opportunity could be reduced if our competitors develop and commercialize products that are more effective or demonstrate a more favorable safety profile than any products that we may develop. Our competitors may also successfully complete applicable pre-marketing regulatory requirements for their products more rapidly than we do.

1.3.13. Research & Development and patents

1.3.13.1. Research & Development

Since the Company's creation, most of the resources have been devoted to research and development activities. These activities are described in detail in paragraph 1.3.1. for research and development (research, preclinical, clinical, medical and regulatory) and production activities. In order to carry out their work, the research and development teams use subcontractors with state-of-the-art technologies and/or the necessary expertise. In the 2021 workforce, 37 employees hold a doctorate in medicine, pharmacy or science. The research and development function remains largely dominant, accounting for 73% of employees.

1.3.13.2. Innovation policy

Nanobiotix has implemented an innovation policy to promote and transform new ideas into products for human health. Since its creation, most of the Company's resources have been devoted to the development of the "NBTXR3" patent portfolio, enabling Nanobiotix to offer an unprecedented approach to cancer treatment. The Company is also developing exploratory research programs for new nanoparticles for new applications in nanomedicine.

1.3.13.3. Publications

Nanomedicine is a very innovative field of research. A pioneer and major player in this sector, Nanobiotix has developed technologies recognized by the international scientific and medical communities. The major work of our researchers and the results of our clinical trials are regularly published and presented at international scientific events (non-exhaustive list):

- A new radio-enhancer, PEP503 (NBTXR3), in combination with concurrent chemoradiation in locally advanced or unresectable rectal cancer: The dose-finding part of a phase I/II trial. Wang J-Y, Huang C-W, Huang M-Y, Hu H-M, Hsu W-H, Shih H-Y, et al. Journal of Clinical Oncology. 2021;39(3_suppl):66-.
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1.3.13.4. Intellectual property

We are innovators in oncology-related nanotechnology. We rely on a combination of patent, trademark, copyright, and trade secret laws in the United States and other jurisdictions to protect our intellectual property rights. No single patent or trademark is material to our business as a whole.

We seek to protect and enhance our proprietary technology, product candidates, inventions and improvements that are commercially important to the development of our business by seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We will also seek to rely on regulatory protection afforded through orphan drug designation, data exclusivity, market exclusivity and patent term extensions where available.

To achieve this objective, we maintain a strategic focus on identifying and licensing key patents that provide protection and serve as an optimal platform to enhance our intellectual property and technology base. Our technologies and product candidates are protected by more than 400 issued or pending patents and patent applications in over 23 patent families across the world. We hold key

patents and patent applications with respect to the concepts, products and uses of nanoparticles activated by ionizing radiation through NBTXR3 technology and for new applications in nanomedicine.

Summarized below are our material patents and patent applications in our own name:

Technology	Number of patent families	Expiration date for each patent family	Countries in which patents are issued
NanoXray Technology [(1)]	13	2025	Australia, Brazil, Canada, China, Eurasia (1 country), Europe (7 countries), Israel, India, Japan, South Korea, Mexico, South Africa, Hong Kong
		2031	United States (U.S. continuation granted)
†		2029	Australia, Brazil, Canada, China, Algeria, Eurasia (9 countries), Europe (34 countries), Indonesia, Israel, India, Japan, South Korea, Morocco, Mexico, New Zealand, South Africa, Macau, Hong Kong, Singapore
		2031	United States, **
		2030	Australia, Canada, China, Eurasia (1 country), Europe (22 countries), Indonesia, Israel, India, Japan, South Korea, Mexico, New Zealand, United States, Singapore, South Africa, Hong Kong, Brazil,**
		2032	China, Europe (7 countries), Japan
		2035	United States
		2032	Australia, Canada, China, Eurasia (1 country), Europe (13 countries), Indonesia, Israel, India, Japan, South Korea, Mexico, New Zealand, Singapore, Ukraine, South Africa, **
		2035	United States
††		2034	Australia, China, Europe (36 countries), Indonesia, Japan, Mexico, New Zealand, Israel, Ukraine, United States, Eurasia (1 country), Hong Kong, South Africa, Singapore, South Korea **
		2034	Australia, Canada, China, Europe (25 countries), Indonesia, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, Hong Kong, South Korea, Eurasia (1 country), Ukraine **
		2034	Japan, United States, Europe (Validated in 7 countries)
		2034	United States, Japan, **
†††		2036	Israel, Australia, United States, Ukraine, **
		2041	**
		2041	**
Other technologies	10	2034 2035	Australia, Canada, Eurasia (validation in process), Israel, India, Indonesia, Mexico, South Korea, Japan, New Zealand, Ukraine, Singapore, South Africa, **, # United States
		2035 2036	Europe (23 countries), Japan, United States, #
		2035	Japan, Europe (Validated in 23 countries), **, #
		2035	Japan, United States, **, #
		2035	Australia, India, Japan, Mexico, New Zealand, Ukraine, United States, Singapore, About to be granted in Israel, **, #
		2037	United States, **, divisional application filed U.S.

Technology	Number of patent families	Expiration date for each patent family	Countries in which patents are issued
		2037	United States, **
		2037	United States, Eurasia (1 country), **
		2038	**
		2038	**
		2041	**

(1) The NanoXray technology covers, among other things, three product candidates, each of which is based on the same hafnium oxide core. The goal of each of these three product candidates is to help patients receiving radiotherapy by enhancing the effect of radiotherapy within tumor cells, without increasing the dose to surrounding healthy tissues. The three product candidates differ in the composition of the nanoparticle coating or formulation, which have been developed for three different modes of administration to cover most oncology applications. The most advanced product candidate in the NanoXray portfolio, and our current focus for development and commercialization, is injectable NBTXR3.

 # Patent family owned by Curadigm.

** This expiration year does not take into account supplementary patent protection that could be obtained for some of our patents in the United States, Europe and other countries. Expiration dates for U.S. patents not yet granted may be subject to patent term adjustment.*

*** Patent application pending in at least one country/jurisdiction.*

† Patent family covering the specific composition utilized in NBTXR3 (i.e., composition of matter). This patent family covers the injectable use of metal oxide nanoparticles with a specific density for killing tumor cells, including cancer cells. The injectable use of an efficient dose of NBTXR3 in oncology is covered by this patent family.

†† Patent family covering the specific composition utilized in injectable NBTXR3 (i.e., composition of matter). This patent family covers the injectable use of metal oxide nanoparticles with a specific density for killing tumor cells and shrinking tumors where a certain number of electrons are delivered to the targeted tumor. The injectable use of an efficient dose of NBTXR3 in oncology is covered by this patent family.

††† Patent family covering the specific composition utilized in NBTXR3 (i.e., composition of matter). This patent family covers the injectable use of NBTXR3 as a therapeutic vaccine used to induce an immune response, including its use in immuno-oncology and its combination with other checkpoint inhibitors.

In addition to patent protection, we have trademark protection in many countries for our “Nanobiotix” name and Nanobiotix logo. We own over 300 trademark registrations and applications related to our products, product candidates, processes and technology worldwide. Trademark registrations are generally granted for a period of ten years and are renewable. We anticipate we will apply for additional patents and trademark registrations in the future as we develop new products, product candidates, processes and technologies.

We also rely on trade secrets to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We seek to protect our proprietary technologies, in part, through confidentiality agreements with our employees, consultants, scientific advisors, contractors and others with access to our proprietary information. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by our competitors.

1.3.14. Our Major Contracts

We have entered into collaboration agreements in order to enable us to optimize our resources, expedite product development, potentially generate revenue and maintain limited risk exposure outside of Europe.

1.3.14.1. M.D. Anderson Cancer Center of the University of Texas

On December 21, 2018, the Company entered into a clinical research collaboration agreement with the MD Anderson Cancer Center of the University of Texas ("MD Anderson") in the field of nanoparticles in order to improve the efficiency of radiotherapy treatment for certain types of cancer. The agreement was amended and restated in January 2020 and subsequently amended in June 2021.

Obligations of the Parties

Under the terms of the collaboration agreement, MD Anderson undertakes to lead several Phase I/II clinical trials for NBTXR3 in various indications (head and neck, pancreatic, thoracic, lung, etc.), according to a timetable and predefined recruitment thresholds. The Company expects to enroll approximately 340 patients across several clinical trials. For this purpose, MD Anderson provides the staff, equipment and the premises required for each test. As no exclusivity has been granted under the collaboration agreement, MD Anderson can conduct similar clinical trials with third parties, simultaneously if need be. For more information on the clinical trials conducted within the MD Anderson collaboration, see the paragraph titled "NBTXR3 Development Pipeline" in Section 1.3.1 of the Universal Registration Document.

The Company provides the required doses of NBTXR3 for each clinical trial and funds the clinical trials. The Company thus commits to pay a minimum amount of approximately US $11 million for the conduct of the trials until the end of the collaboration. Approximately US $1 million was paid upon entering into the agreement and $1 million was paid on February 3, 2020. Additional payments will be paid semi-annually during the collaboration on the basis of patients enrolled during the relevant period, with the balance payable upon enrollment of the final patients for all studies. The Company is also required to make an additional one-time milestone payment upon (i) a first regulatory approval obtained from the FDA for NBTXR3 and (ii) the enrollment of a certain number of patients in the United States. The amount of this one-time milestone payment by the Company will increase significantly each year depending on the date on which the prerequisite conditions are met : between $2.2 million (if they are met in 2020) and $16.4 million (if they are met in 2030). Further details can be found in the notes to the Group's consolidated accounts in section 4.1. of the Universal Registration Document, specifically in sections 4.1.6.1.2, 4.1.6.4.3 and 4.1.6.23.

The protocol, schedule, monitoring, termination and replacement of each trial will be determined by mutual agreement between MD Anderson and the Company.

MD Anderson has made a number of representations for the benefit of the Company and has granted the Company audit and information rights in connection with these clinical trials, in particular with respect to pharmacovigilance.

Intellectual Property

Each party retains ownership of its pre-existing or property rights generated outside the scope of the collaboration agreement, it being specified that the Company licenses NBTXR3 to MD Anderson for use in clinical trials.

The Company is the exclusive owner of any right, title or other interest in any invention or discovery made in a clinical trial that incorporates NBTXR3 or any formulation relating to NBTXR3 (the "NBTXR3 Inventions"). As such, MD Anderson agrees to transfer any rights it may have in the NBTX3 Inventions.

The Company grants MD Anderson a non-exclusive, perpetual and irrevocable license, free of charge, for non-profit academic or research purposes to use the NBTXR3 Inventions.

Any inventions and discoveries, other than a NBTXR3 Invention, made in the course of a clinical trial (the "Other Inventions") are the property of their inventor(s), MD Anderson and/or the Company, as the case may be.

MD Anderson grants the Company a non-exclusive license, free of charge, to any Other Invention it may own as well as an exclusive option to negotiate an exclusive, remunerated license on this Other Invention (the "Option"). If the Company does not exercise the Option or if the parties are unable to reach an agreement on the terms of the license, in each case within a specified period of time, MD Anderson would then be free to license the Other Invention to any third party.

Finally, MD Anderson and the Company are co-owners of the data and clinical results generated in the conduct of the trials performed within the collaboration agreement, it being specified that MD Anderson may use these data for academic or non-profit research purposes. For each clinical trial, MD Anderson and the principal investigator decide on the date, content and authors of the first publication of the clinical data and results, it being specified that the Company has a right of review of such publications. Any unpublished data is considered confidential and may not be transferred by one party to a third party without the written consent of the other party.

Responsibility

The Company shall be liable to MD Anderson, each principal investigator and their affiliates for any damages resulting from NBTXR3 (whether due to the manufacture, design or use by a patient of the product candidate or to the negligence of the Company in the performance of its obligations under the collaboration agreement), subject to any gross negligence or willful misconduct of the indemnified party. In addition, the Company shall be liable for medical costs reasonably incurred by a patient for any treatment resulting directly from the administration of NBTXR3. Accordingly, the Company is required to maintain an insurance policy covering its liability for clinical trials conducted by MD Anderson.
MD Anderson is liable to the Company and its affiliates for any damages resulting from (i) injury to a patient that is directly caused by the failure of MD Anderson or its personnel to comply with the trial protocol or (ii) gross negligence or willful misconduct by MD Anderson in the conduct of the trial, subject to any gross negligence or willful misconduct of the indemnified party.

Term and Termination

The collaboration agreement between MD Anderson and the Company is entered into for the duration of the clinical trials, with a term of no less than 5 years.

The agreement may be terminated by either party in the event of a serious breach of the other party's obligations under the agreement which is not remedied within 30 days of the first party's notification of the breach to that party. Termination of the contract shall not affect the conduct of ongoing clinical trials, which shall be conducted in accordance with their original terms.

Either party may terminate a clinical trial (i) in the event of a serious breach of the other party's obligations (including those under the trial protocols) which has not been remedied within 30 days of notification of the breach sent to that party by the former party, (ii) due to health and safety issues related to NBTXR3 or the procedures applicable to that clinical trial, or (iii) if the parties are unable to agree on the identity of the principal investigator to conduct the trial or if the principal investigator does not agree to the terms of the collaboration agreement or trial protocol. In addition, a clinical trial is automatically terminated in the event of withdrawal or rejection of the regulatory approvals required to conduct the trial.

Pursuant to this agreement, the collaboration is implemented under the supervision of a steering committee, comprising three representatives of each party, and provides a process for dispute resolution by a Senior Vice President of MD Anderson and the chairman of the Company's executive board.

For each clinical trial, the Company must pay any costs reasonably incurred in the conduct of the trial in question that would be due at the end date of the trial or at the date of termination of the collaboration agreement.

1.3.14.2. LianBio

On May 11, 2021, the Company entered into a strategic License, Development and Commercialization Agreement (the "LianBio Agreement") with LianBio Oncology Limited, a Hong Kong company, for the development and commercialization of NBTXR3, as a product activated by radiotherapy in the field of oncology, in key parts of Asia—the People's Republic of China, Macau, Hong Kong, Thailand, Taiwan, South Korea and Singapore (collectively, the "Territory"). The Company has granted LianBio an exclusive, royalty-bearing license which includes, subject to certain conditions, the right for LianBio to grant sublicenses to its affiliates and/or third-party subcontractors involved in the development of NBTXR3.

Obligations of the Parties

Under the LianBio Agreement, LianBio is exclusively responsible for the development and commercialization of NBTXR3 throughout the Territory, except for specified ongoing trials that the Company will conclude. The Company is responsible for the manufacturing of NBTXR3 and will be the exclusive supplier of NBTXR3 to LianBio.

Pursuant to the LianBio Agreement, LianBio will have to enroll a specified percentage of the worldwide total number of patients in the Company's global Phase III registrational study evaluating NBTXR3 for patients with locally advanced head and neck squamous cell carcinoma (NANORAY-312) and each of four other specified global registrational trials across indications and therapeutic combinations. For NANORAY-312, LianBio is expected to enroll approximately 100 patients based on the Company's current worldwide enrollment expectations. In the event that LianBio does not meet its enrollment undertaking for these trials, LianBio will be responsible for covering certain incremental costs incurred by the Company as a result. Otherwise, LianBio will fund all development and commercialization expenses in the Territory, and the Company will fund all development and commercialization expenses in all other geographies.

For all non-registrational trials (i.e., Phase I or Phase II trials) undertaken to support the development and approval of NBTXR3, the Company and LianBio have agreed to provide each other with rights to access all clinical efficacy and safety data. For additional registrational trials, the Company and LianBio have agreed to provide each other with rights to access all clinical safety data and to provide an opportunity to license and right of reference to efficacy data, subject to certain cost-sharing and/or enrollment undertakings.

Pursuant to the LianBio Agreement, LianBio has sole control over commercialization in the Territory and is responsible for all costs and expenses of such commercialization. LianBio, or its affiliates and/or sublicensees, is solely responsible for all communications, filings with, as well as approvals sought from regulatory authorities to obtain all marketing authorizations in relation to NBTXR3 in the Territory.
As consideration for entering into the LianBio Agreement, the Company received a non-refundable upfront payment from LianBio of $20.0 million in June 2021.

The Company is also eligible to receive up to an aggregate of $220 million in potential contingent, development and commercialization milestone payments. The Company will also be eligible to receive tiered, low double-digit royalties based on net sales of NBTXR3 in the Territory, subject to downward adjustment based on enrollment incentives and customary country-by-country competition- and intellectual property-related triggers. Royalties will be payable on a product-by-product and country-by-country basis until the latest of (i) the expiration of the last-to-expire valid claim of a licensed patent covering NBTXR3, (ii) the expiration of regulatory exclusivity of NBTXR3, or (iii) the ten-year anniversary of the first commercial sale of NBTXR3. Upon the expiration of the royalty term in a given country, LianBio shall be granted a perpetual, royalty-free, sublicensable license in such country.

Responsibility

Pursuant to the LianBio Agreement, the collaboration is implemented under the supervision of a joint steering committee, which will include an equal number of representatives of each party, including one member of senior leadership of each of LianBio and the Company, and will meet on a regular basis to provide oversight and facilitate information sharing between LianBio and the Company. In the event of a dispute among representatives at the joint steering committee, the matters shall be escalated to appropriate senior officers of LianBio and the Company. In the event such senior officers cannot reach an agreement on the matters at hand within a set timeframe, LianBio and the Company have agreed that one of the parties shall have the final decision-making authority on certain specific matters, without prejudice to any contractual obligations set out under the LianBio Agreement.

Pursuant to the LianBio Agreement, LianBio's Territory-specific development and regulatory plan and commercialization in the Territory will be conducted pursuant to LianBio's Territory-specific plans, which will be subject to periodic updates and joint steering committee review.

The Company retains the first right to prosecute, maintain and defend, at its expense, all of its licensed patents in the Territory. In the event that the Company elects not to prosecute or maintain any such patent in the Territory or not to defend a patent in the Territory, the Company has agreed to notify LianBio, and LianBio shall have the right, but not the obligation, to assume such prosecution, maintenance or defense at its own expense. LianBio shall have the first right to enforce, at its expense, the Company's intellectual property against infringement in the Territory, except where the Company is enforcing such intellectual property both within and outside the Territory against such infringement. In the event that LianBio elects not to enforce the Company's intellectual property against infringement in the Territory, it has agreed to notify the Company, and the Company will have the right to enforce such intellectual property at its expense.

The Company and LianBio have agreed to customary confidentiality obligations with respect to trade secrets and confidential or proprietary information disclosed in connection with their respective performance under the LianBio Agreement, subject to customary exceptions. The Company and LianBio have agreed to provide customary indemnification to one another for claims relating to their respective obligations under the LianBio Agreement. LianBio has agreed to maintain a customary liability insurance policy during the term of the LianBio Agreement.

LianBio has undertaken to conduct and ensure that all of its affiliates, sublicensees and subcontractors conduct their business under the LianBio Agreement in accordance with applicable laws and, to the extent applicable with respect to certain development activities, FDA and EU medical device requirements.

Dispute Resolution

The LianBio Agreement provides a dispute resolution mechanism with respect to interpretation of rights or obligations and any alleged breaches under the LianBio Agreement. The dispute resolution mechanism provides for the escalation of such matters to the joint steering committee and, if unresolved following such escalation, further escalation to the respective chief executive officers of the Company and LianBio to negotiate in good faith. If such matter is unable to be resolved, the LianBio Agreement provides for arbitration, except that certain disputes relating to intellectual property matters are not subject to such an arbitration requirement and may be brought in courts of competent jurisdiction.

Intellectual Property

The Company and LianBio retain ownership of their respective pre-existing intellectual property. Other inventions and discoveries relating to NBTXR3 made in the course of performing obligations under the LianBio Agreement made solely by the Company or LianBio, as the case may be, will be owned by the respective inventors. To the extent an invention or discovery relating to NBTXR3 is made by LianBio and the Company together, such invention and any related patents will be jointly owned by LianBio and the Company. The rights to file, prosecute and enforce such jointly-owned patents will be determined by mutual agreement through the joint steering committee.

Termination

Unless terminated earlier, the LianBio Agreement will remain in effect for so long as royalties are payable under the LianBio Agreement. The LianBio Agreement may be terminated earlier by either party if the other party commits an uncured material breach. In any event where LianBio has a termination right based on a material breach by the Company, LianBio may elect in lieu of termination to continue the LianBio Agreement, subject to a downward percentage reduction in all milestone and royalty payments.

Either party may also terminate the agreement in the connection with the occurrence of certain insolvency or bankruptcy events with respect to the other party. LianBio may terminate the agreement following a change in control of the Company, subject to a specified notice period. The Company may terminate the agreement under certain circumstances in connection with a change of control of LianBio. The Company may also terminate the LianBio Agreement in the event that LianBio or its affiliates bring or join any challenge to the validity or enforceability of the Company's patents, subject to certain limited exceptions.

Termination of the LianBio Agreement will terminate all rights, licenses and sublicenses under the agreement, subject to the Company's agreement, in certain cases, to negotiate in good faith with sublicensees regarding a potential direct license.

1.3.14.3. PharmaEngine

In August 2012, the Company entered into a license and collaboration agreement with PharmaEngine, a Taiwan-based company, for the development and commercialization of NBTXR3 (under the code name PEP503) in several countries in the Asia-Pacific region. Under this agreement, PharmaEngine was responsible for the development (non-clinical and clinical research) and marketing of NBTXR3 across the Asia-Pacific region. In return, PharmaEngine was required to make payments to the Company based on the achievement of development and commercialization milestones for NBTXR3. The Company received an upfront payment of $1 million upon signing the agreement and, through December 31, 2020, received $2 million in two interim payments.

In March 2021, in light of disagreements over a number of issues with respect to the development of NBTXR3 in the Asia-Pacific region, the Company and PharmaEngine mutually agreed to terminate the agreement. Accordingly, on March 4, 2021, the Company and PharmaEngine entered into a Termination and Release Agreement. Under the termination agreement the Company will retain all rights to the development and commercialization of NBTXR3 in the Asia Pacific region. The Company has agreed to make total termination payments to PharmaEngine of up to $12.5 million in the aggregate. PharmaEngine was eligible for, and received, a $2.5 million payment from the Company following the announcement of its collaboration with LianBio for the Asia-Pacific region. During the six months ended June 30, 2021, PharmaEngine also received $4.0 million from the Company in conjunction with the completion of various administrative steps in connection with the winding-up of the collaboration.

PharmaEngine will be eligible to receive from the Company an additional $1.0 million in administrative fees and a final payment of an additional $5 million upon a second regulatory approval of an NBTXR3-containing product in any jurisdiction of the world for any indication. PharmaEngine is entitled to receive from the Company a low-single digit percentage tiered royalty based on net sales of NBTXR3 in the Asia-Pacific region for a 10-year period commencing on the corresponding first date of sales in the region.

As part of the termination agreement, PharmaEngine has re-assigned to the Company rights for the development, manufacture, commercialization and exploitation of NBTXR3 in the Asia-Pacific region, as well as all development data, regulatory materials, and all regulatory approvals that are in the name of PharmaEngine or its affiliates. Consequently, NBTXR3 clinical trials conducted by PharmaEngine in Asia are in the process of being concluded or terminated.

The Company and PharmaEngine also agreed to a mutual release of all claims against the other party and its respective affiliates.

1.3.14.4. EIB Finance Contract and Royalty Agreement

In July 2018, the Company and the European Investment Bank (“EIB”) entered into a Finance Contract and a Royalty Agreement. The EIB loan is comprised of three potential disbursement tranches, each of which may be drawn in the absence of an event of default or prepayment event, subject to the Company achieving specified documentary and/or performance criteria and making customary representations and warranties.

In October 2018, upon satisfying the requisite documentary criteria, the Company drew the initial tranche of €16.0 million (repayable in a single installment at maturity).

In March 2019, upon achieving the requisite performance criteria (the positive evaluation of the Phase III clinical benefit/risk ratio of NBTXR3 for the treatment of STS by the French notified body covering medical devices, GMED, and the successful identification of the recommended NBTXR3 dosage in its locally advanced head and neck cancers clinical trial), the Company drew the second tranche of €14.0 million (repayable in semi-annual installments of principal and interest after a two-year grace period).

In addition to the initial tranche and the second tranche, the terms of the EIB loan provide for a final €10.0 million third tranche if it satisfies the applicable performance criteria prior to July 26, 2021. The disbursement of the third tranche is dependent on two conditions: (i) obtaining the CE mark for NBTXR3 and achieving the primary endpoint of the pivotal Phase III clinical trial for NBTXR3 in the treatment of locally advanced head and neck cancers and (ii) the Company raising of new equity financing, which was achieved with its April 2019 capital increase. The deadline for the satisfaction of the requisite performance criteria, which was initially July 26, 2020, was extended to provide an additional year to satisfy the performance conditions and draw the third tranche. If drawn, the third tranche would be repayable in semi-annual installments after a one-year grace period, through the date that is five years after disbursement.

As of December 31, 2021, the outstanding balance of the EIB loan was €26.4 million (see "4.1.6.12.2. of the Universal Registration Document" for additional details).

Prior to repayment at maturity (or earlier prepayment), interest on the first tranche shall accrue at the rate of 6% annually, with such interest being capitalized and added to the outstanding principal. Together with the requisite installment of principal, interest on the second tranche (at a 5% fixed rate) and, if disbursed, the third tranche (at a 4% fixed rate) is payable, following the applicable grace period, semi-annually in arrears. The final repayment with respect to each tranche is due five years from the date of its disbursement. Interest on any overdue amounts accrues at an annual rate equal to the higher of the applicable rate plus 2% or EURIBOR plus 2%.

The Company may repay, in whole or in part, any tranche, together with accrued interest upon 30 days prior notice, subject to the payment of a customary prepayment fee. EIB may require the Company to prepay all outstanding amounts under the EIB loan in connection with certain events, including a substantial reduction in the anticipated cost of the Company's NBTXR3 development program, a prepayment of certain non-EIB financing, certain change of control events, Dr. Laurent Levy ceasing to be the Chairman of the Company's executive board or ceasing hold a specified number of shares, or certain dispositions of assets related to the Company's NBTXR3 development program, in each case, subject to the payment of a customary prepayment fee.

EIB may also require immediate repayment, together with accrued interest and a customary prepayment fee, in connection with the occurrence of any event of default with respect to the Company or its subsidiaries, including failure to pay any amounts due under the EIB loan, a determination of a material defect in any previously made representation or warranty, any cross-default involving the acceleration or cancellation of an amount equal to at least €100,000 or pursuant to any other loan from EIB, certain bankruptcy or insolvency events, the occurrence of any material adverse change, or any failure to comply with any other provision under the Finance Contract that remains uncured for 20 business days.

Prepayment fees, if required, are calculated as a percentage of the amount prepaid, which percentage decreases over time.

The terms of the EIB loan impose restrictions on the Company and its subsidiaries that may impact the operation of the Group's business, including, among others, restrictions on (i) the disposition of any part of the Group's business or assets outside of arm's length ordinary-course transactions, (ii) restructuring or making any substantial change to the nature of the Group's business, (iii) entering into certain merger or consolidation transactions, (iv) the disposition of the Company's shareholdings in its material subsidiaries, (v) pursuing acquisitions or investments, (vi) incurring any indebtedness in excess of €1.0 million in the aggregate, (vii) providing guarantees in respect of liabilities or other obligations, (viii) engaging in certain hedging activities, (ix) granting security over Group assets, (x) paying dividends or repurchasing Company shares, or (xi) impairing Group intellectual property rights. Pursuant to these

restrictions, we obtained the EIB's consent to the PGE Loans, which represented an aggregate indebtedness of €10 million.

Any of the Company's subsidiaries whose gross revenues, total assets or EBITDA represents at least 5% of the Group's consolidated gross revenues, total assets or EBITDA is required to guarantee the Company's borrowings under the EIB loan.

Pursuant to the Royalty Agreement, the Company also committed to pay royalties to EIB on an annual basis for a period of six years beginning on January 1, 2021 and payable with respect to the preceding year on each June 30 during the period from 2022 through 2027. The amount of royalties payable is calculated based on a low single-digit royalty rates which vary according to the number of tranches that have been drawn, and indexed on the Group's annual sales turnover.

In the event that the Company elects to prepay a tranche of the EIB loan, EIB requires prepayment of the EIB loan in connection with an event of default or other prepayment event under the Finance Contract, or a change of control event occurs following the maturity of the EIB loan, EIB is entitled to request payment of an amount equal to the highest of (i) the net present value of all future royalties, as determined by an independent expert, (ii) the amount required for EIB to realize an internal rate of return of 20% on the EIB loan, and (iii) €35.0 million. Interest on any overdue amounts accrues at an annual rate equal to 2%.

1.3.14.5. State-guaranteed loans

On June 5, 2020, the Company received initial approval from each of HSBC France and Bpifrance for two State-guaranteed loans (prêts garanti par l'Etat) of €5.0 million each, representing a total amount of €10 million. Accordingly, the Company entered into two agreements with HSBC France and Bpifrance Financement respectively, each providing for a €5 million State guaranteed loan.

Extension of reimbursement both BPI and HSBC

Agreement entered into with HSBC France

On June 22, 2020, the Company entered into a State-guaranteed loan agreement (prêt garanti par l'Etat) with HSBC France ("**HSBC**") to be applied to the Company's general business needs (the "**HSBC PGE Loan**"). The €5 million loan is 90% guaranteed by the French State. The loan has an initial maturity of 12 months and no interest for this initial 12-month period. No amount is required to be paid during this initial 12-month period.

The Company was required to pay to a "guarantee fee" equal to 0.25% of the €5 million principal amount, which amount was payable on the initial maturity date.

The Company had the option to decide, at the end of the first year, whether to repay the loan amount or to amortize the loan over an additional period of one, two, three, four or five years. Prior to giving effect to an election to extend the amortization period, HSBC notified the Company of the interest rate applicable to the amortization period. The Company elected to amortize the principal amount of the loan over a period of five years, during which the HSBC PGE Loan will bear interest at a fixed rate of 0.310% to which shall be added a guarantee fee of 0.50% per annum for the first two years of amortization and 1% per annum for the third, fourth and fifth year of amortization (payable over 90% of the loan outstanding amount). The loan is prepayable, at the Company's option, upon three months' prior notice.

HSBC may declare the loan repayable upon eight days' prior notice as a result of the occurrence of certain events, which remain unremediated by the Company, including (i) the Company's failure to pay any amounts due under the HSBC loan, (ii) a merger or demerger with, or the winding-up of, the Company, (iii) the disposition of a Company, (iv) a significant decrease in the value of Company's assets or an event likely to alter the Company's financial capacity to meet its obligations under the HSBC loan, and (v) the default by the Company in the payment of an amount due under any other loan agreement to which the Company is a party, or (vi) the acceleration of any of any amount due under any other loan pursuant to any other HSBC or third-party loan agreement.

The loan will become immediately repayable upon the occurrence of certain other events of default, including the use of the loaned funds for a purpose not authorized by the HSBC loan, any breach of international sanctions regulations and the occurrence of certain bankruptcy or insolvency events.

Agreement entered into with Bpifrance Financement

On July 10, 2020, the Company entered into a State-guaranteed loan agreement (prêt garanti par l'Etat) with Bpifrance Financement to be applied to the Company's cash flow needs. The €5 million loan has a six-year term and is 90% guaranteed by the French State. The loan bore no interest for the first 12 month period but, following such 12 month period and for the subsequent five years, bears an interest rate of 2.25% per annum, inclusive of an annual State guarantee fee of 1.61% per annum. The principal and interest of the Bpifrance PGE Loan will be repaid in 20 quarterly installments from October 31, 2021 until July 26, 2026.

The loan is prepayable, at the Company's option, upon one month's prior notice. Any early repayment of the loan, be it voluntary or involuntary, shall be subject to a lump-sum indemnity equal to 5% of the prepaid principal amount during the first year and reduced to 3% after this period. Bpifrance Financement's acceptance of the early repayment is subject to the payment of the indemnity.

Bpifrance Financement may declare the loan repayable upon eight days' prior notice as a result of the occurrence of certain events, including (i) use of the loaned funds for a purpose not authorized by the Bpifrance Financement loan, (ii) the Company's failure to pay any amounts due under the Bpifrance Financement loan, (ii) the transfer or pledging by Company of all or part of the shares or voting rights of the Company or one of its subsidiaries without Bpifrance Financement's prior approval, (iv) a merger, demerger or partial asset contribution with, or the winding-up of, the Company, (v) the suspension of or change in the Company's business activities, (vi) a breach of the provisions of the Bpifrance Financement loan and (vii) misrepresentation under the Bpifrance Financement loan agreement.

The loan will become immediately repayable upon the occurrence of certain other events, including (i) a share capital reduction of the Company that is not motivated by losses, the distribution of reserves outstanding on the date of execution of the Bpifrance Financement loan or the reimbursement of a shareholders' loan without the prior approval of Bpifrance Financement, (ii) the seizure of Company assets or the transfer of Company business undertakings and (iii) the occurrence of a material event of a legal or financial nature with significant consequences regarding the Company's business or profitability.

1.3.15. Our research agreements

We have established strategic collaborations with a number of hospitals, clinics and cancer treatment centers in France and abroad. These agreements provide that we may negotiate certain commercial rights with such collaborators with respect to joint inventions or inventions made by our collaborators that arise from the results of the collaboration.

Under the preclinical research agreements for these collaborations, we retain exclusive ownership over any inventions made solely by us. Any invention made solely by a research institution would be owned by the relevant research institution, but would be subject to option to obtain an exclusive license, which would be free for research purposes and royalty-bearing for commercial activities. Inventions made jointly by us and a research institution would be jointly owned. As of December 31, 2021, no inventions under these programs have been made solely by a research institution or jointly by us and a research institution.

We have entered into an agreement with Institut Gustave Roussy, one of the world's leading cancer-research institutes and the largest cancer center in France, for radiobiology research and preclinical development of NBTXR3. Pursuant to the agreement, we conduct studies at Institut Gustave Roussy's radiobiology lab to evaluate the antitumor activity of nanoparticles activated by ionizing radiation. We maintain all rights to the products of our studies; however, Institut Gustave Roussy may use the results without charge solely for the purposes of its own academic research.

We have also partnered with The University of Texas MD Anderson Cancer Center in Houston, Texas to conduct immunotherapeutic preclinical research in lung cancer, combining NBTXR3 and immune checkpoint inhibitors. This research collaboration is distinct from our clinical trial collaboration with MD Anderson and is intended to enable us to generate preclinical data using NBTXR3 activated by radiotherapy plus anti-PD-1 nivolumab (murine version of Opdivo) or other immune checkpoint inhibitors, such as anti-CTLA-4, anti-TIGIT and anti-LAG3.

1.3.16. Trademarks, trademark applications and domain names

We own various trademark registrations and applications, and unregistered trademarks and service marks. ''Nanobiotix,'' ''NBTXR3,'' the Nanobiotix logo and other trademarks or service marks of Nanobiotix S.A. appearing in the Universal Registration Document are the property of Nanobiotix or its subsidiaries. Solely for convenience, the trademarks, service marks and trade names referred to in the Universal Registration Document are listed without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. All other trademarks, trade names and service marks appearing in the Universal Registration Document are the property of their respective owners. We do not intend to use or display other companies' trademarks and trade names to imply any relationship with, or endorsement or sponsorship of us by, any other companies.

The Company, in its trademark filing strategy, registers them domestically or internationally. Trademark registrations are generally granted for a period of ten years and are renewable indefinitely. Some pay proof of use for the maintenance of fees. In other countries, registrations remain valid unless a level is interested in suing forfeiture for failure to use the mark. The Company holds various brands that are the main and most important:

Nanobiotix

The Company holds a number of domain names and different extensions, the main and most important of which are:

www.nanobiotix.com ; .fr .net ; .org ; .eu ; .biz ; www.actinsarc.com ; www.hensify.com

1.3.17. Government regulation, product approval and certification

Government authorities in the United States, at the federal, state and local level, in the European Union and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. NBTXR3 and any other therapeutic candidates that we develop must be approved by the FDA before they may be legally marketed in the United States and must complete the conformity assessment procedure with the Notified Body before they may be legally marketed in the EU. In addition, in the European Union, the Group is subject to data protection rules. Finally, the Group's activities may be qualified as sensitive activities and thus enter into the scope of the foreign investment control regime in France.

1.3.17.1 Regulation in the United States

United States Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act and implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and subsequent compliance with appropriate federal, state and local statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post approval may subject an applicant to administrative and/or judicial sanctions. FDA sanctions may include, among other actions, refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies in accordance with applicable regulations, including good laboratory practice ("GLP") regulations;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable regulations, including current good clinical practice ("GCP") regulations to establish the safety and efficacy of the drug candidate for its proposed indication;
- Submission to the FDA of a new drug application ("NDA") for a new drug product;
- A determination by the FDA within 60 days of its receipt of an NDA to accept the submitted NDA for filing and thereafter begin a substantive review of the application;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with cGMP regulations to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;

- Potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Before testing any compounds with potential therapeutic value in humans, the drug candidate goes through a preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the drug candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs. The data sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocols for human studies. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period or issues an earlier notice that the clinical trial may proceed. In the case of a clinical hold, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose a clinical hold on a drug candidate at any time before or during clinical trials due to safety concerns or noncompliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that cause us or FDA to suspend or terminate such trial.

Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board ("**IRB**"), at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers issues such as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase I.* The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion, the side effects associated with increasing doses, and if possible, to gain early evidence of effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase II.* The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases or conditions and to determine dosage tolerance, optimal dosage and dosing schedule.
- *Phase III.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall benefit/risk ratio of the product and provide an adequate basis for product approval. Generally, two adequate and well-controlled Phase III clinical trials are required by the FDA for approval of an NDA. Phase III clinical trials usually involve several hundred to several thousand participants.

Post-approval studies, or Phase IV clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase IV studies.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase I, Phase II and Phase III clinical trials may fail to be completed successfully within any specified period, if at all. The FDA, the IRB or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated checkpoints based on access to certain data from the study. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must include developed methods for testing the identity, strength, quality and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

FDA Review and Approval Process

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The application must include negative or ambiguous results of preclinical and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product to the satisfaction of the FDA. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act ("PREA"), an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s).

The FDA reviews the completeness of each NDA submitted before accepting it for filing and may request additional information rather than accepting the NDA for filing. The FDA must make a decision on accepting an NDA for filing or refusing to file within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under the Prescription Drug User Free Act ("PDUFA"), the FDA has ten months from the

60-day filing date in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the 60-day filing date for a priority NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

The FDA reviews each NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. For novel drug products or drug products which present difficult questions of safety or efficacy, FDA may decide to hold an advisory committee, typically a panel that includes clinicians and other experts, to provide independent advice that will contribute to the quality of the agency's regulatory decision-making and lend credibility to the product review process, including a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical sites to assure compliance with GCP requirements.

After the FDA evaluates the application, manufacturing process and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase III clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases, patient populations and dosages, or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. For example, the FDA may require Phase IV testing which involves clinical trials designed to further assess a drug's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also determine that a risk evaluation and mitigation strategy ("REMS") is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS, and the FDA will not approve the NDA without an approved REMS. Depending on FDA's evaluation of a drug's risks, a REMS may include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution requirements, patient registries and other risk minimization tools. Following approval of an NDA with a REMS, the sponsor is responsible for marketing the drug in compliance with the REMS and must submit periodic REMS assessments to the FDA.

Post-Approval Requirements

Any drug products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, and complying with FDA promotion and advertising requirements, which include, among other requirements, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry sponsored scientific and educational activities, and requirements for promotional activities involving the Internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including, among other things, recall or withdrawal of the product from the market. In addition, changes to the manufacturing process are strictly regulated, and depending on the significance of the change, may require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

The FDA also may require Phase IV testing and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures, such as a REMS. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Coverage and Reimbursement

A pharmaceutical manufacturer's ability to commercialize any approved drug product successfully depends in part on the extent to which coverage and adequate reimbursement for such drug product and related treatments will be available from third-party payors, including government health administration authorities, private health insurers, health maintenance organizations and other organizations. Third-party payors determine which drug products and treatments they will cover and establish reimbursement levels. Assuming coverage is obtained for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use a drug product, or agree to treatment using a drug product, unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of the drug product and associated treatment. Therefore, coverage and adequate reimbursement is critical to new drug product acceptance. Coverage decisions may depend

upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

Third-party payors are developing increasingly sophisticated methods of controlling healthcare costs, such as by limiting coverage and the amount of reimbursement for drug products and related treatments. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Further, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors in the United States.

Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor and product to product. As a result, the coverage determination process is often a time-consuming and costly process that requires pharmaceutical manufacturers to provide scientific and clinical support for the use of its drug products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Healthcare Laws

Healthcare providers, physicians and others will play a primary role in the recommendation, and the incorporation into treatment regimes, of drug products, if approved. A pharmaceutical manufacturer's business operations in the United States and its arrangements with clinical investigators, healthcare providers, consultants, third-party payors and patients expose it to broadly applicable federal and state fraud and abuse and other healthcare laws. These laws may impact, among other things, research, proposed sales, marketing and education programs for product candidates that obtain marketing approval. Restrictions under applicable U.S. federal and state and foreign healthcare laws and regulations include, particularly in the EU, but are not limited to, the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing compensation, including any kickback, bribe or rebate, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any item, good, facility or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- U.S. federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which can be enforced by individuals through civil whistleblower or qui tam actions, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;
- HIPAA, which created additional federal criminal statutes which prohibit, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or knowingly and willingly falsifying, concealing or covering up a material fact or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, which impose certain requirements on covered entities, including certain healthcare providers, health plans and healthcare clearinghouses, and their business associates, individuals and entities that perform functions or activities that involve individually identifiable health information on behalf of covered entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- U.S. federal transparency requirements under the Physician Payments Sunshine Act, enacted as part of the ACA, that require applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to track and annually report to CMS

payments and other transfers of value provided to physicians and teaching hospitals, and certain ownership and investment interests held by physicians or their immediate family members; and

- analogous state or foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements, state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA, thus complicating compliance efforts.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is costly. It is possible that governmental authorities will conclude that business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If a pharmaceutical manufacturer's operations are found to be in violation of any of these laws or any other governmental regulations that may apply to it, it may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of operations.

Healthcare Reform

In the United States, the ACA is significantly impacting the provision of, and payment for, healthcare. Various provisions of the ACA were designed to expand Medicaid eligibility, subsidize insurance premiums, provide incentives for businesses to provide healthcare benefits, prohibit denials of coverage due to pre-existing conditions, establish health insurance exchanges, and provide additional support for medical research. With regard to therapeutic products specifically, the ACA, among other things, expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare prescription drug benefit.

Since its enactment there have been judicial and legislative challenges to certain aspects of the ACA, as well as executive branch efforts to repeal or replace certain aspects of the ACA. Most recently, the executive branch has sought to bolster the ACA through executive order.

While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act included a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." The Further Consolidated Appropriations Act, 2020, signed into law on December 19, 2019, repealed certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the medical device excise tax, and, effective for 2021, the annual fee imposed on certain health insurance providers based on market share. The BBA, among other things, amended the ACA, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment.

In addition, both the Budget Control Act of 2011 and the ATRA have instituted, among other things, mandatory reductions in Medicare payments to certain providers.

We cannot predict the ultimate content, timing or effect of any changes to the ACA or other federal and state reform efforts, and there can be no assurance that any such health care reforms will not adversely affect our future business and financial results.

Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Additionally, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

1.3.17.2. Regulation in the EU

In the EU, health products qualify typically as medicinal products or as medical devices. The pre-market requirements applicable to each of these types of products vary significantly.

The demarcation between the definitions of “medical device” and “medicinal product” can sometimes be blurred, or difficult to draw, for some products referred to as “borderline products.” In order to determine whether a product constitutes a medical device or a medicinal product, a number of factors must be taken into account, including the claims regarding the function of the product, the mode of action on the human body and the primary intended purpose of the product. Classification decisions are taken at a national level about individual products. Although these decisions are based on a number of principles that are harmonized across the aiming at a uniform approach to product classification across EU Member States, it is possible that these principles are interpreted differently on a case-by-case basis and that, as a result, a product may be classified as a medicinal product in one Member State and as a medical device in another. The classification of our product, NBTXR3 as a medical device is supported by the conformity assessment procedure applied by the relevant EC Notified Body, which led to the drawing up of the EU Declaration of Conformity, as well as by the opinions released in 2009 and in 2011 by the national competent authorities of Ireland and Spain, respectively. Should national authorities in other EU Member States disagree with such classification, and instead classify our products as medicinal products, our products would be subject to a different regulatory framework, including in particular stringent pre-market authorization requirements that differ significantly from the conformity assessment procedures that are applicable to medical devices.

An Evolving Regulatory Framework

On May 26, 2021, after four year transition period, the Medical Devices Regulation (Regulation (EU) 2017/745, the “MDR”) became fully applicable and introduced substantial changes to the previous regulatory regime applicable to medical devices (including in particular Directive 93/42/EEC, the “MDD”).

Under the transitional provisions of the MDR, until May 26, 2021, the certification procedures underlying the CE marking of medical devices could be carried out, at the manufacturer’s choice, either

in accordance with the MDR or in accordance with the MDD. Where a manufacturer elected to perform certification under the MDD - as we did in connection with our NBTXR3 product for the treatment of STS - the related certificates remain valid until May 25, 2024 (for certificates issued prior to May 25, 2017) or May 26, 2024 (for certificates issued on or after May 25, 2017). The medical devices to which these certificates apply may only be sold in the EEA if they continue to comply with the MDD and provided that no significant changes are brought to these devices' design or intended purpose. Moreover, the manufacturers of those devices that are certified under the MDD have to comply with a number of requirements of the MDR, e.g., those relating to post-market surveillance and vigilance, and they are able to sell such devices only up until May 26, 2025 at the latest. After that date, all devices sold in the EEA will have to be fully compliant with the MDR.

Under the MDR, all devices incorporating or consisting of nanomaterials are classified as Class III if they present a high or medium potential for internal exposure. The MDR introduced higher clinical data requirements for such Class III devices. In particular, manufacturers are generally required to conduct new clinical investigations, subject to certain exceptions. We cannot guarantee that our ongoing trials for our product candidates, including our lead product candidate NBTXR3, will be considered as "sufficient" under the MDR.

The MDR also introduced increased scrutiny of conformity assessments by Notified Bodies for implantable Class III devices. For such devices, the MDR requires that, as part of the conformity assessment procedure, the clinical evaluation assessment report of the concerned Notified Body be submitted to the European Commission for review by an expert panel. The conformity assessment of such devices is further subject to a scrutiny mechanism potentially involving the competent authorities of the EEA, the European Commission, and the Medical Device Coordination Group. Nevertheless, Article 54(2) of the MDR lays out certain exceptions to the need to carry out a clinical evaluation consultation procedure.

In addition, under the MDR, manufacturers of Class III devices are subject to a new annual safety reporting requirement called the Periodic Safety Update Report ("PSUR"), aimed at capturing the results and conclusions of the analyses of the post-market surveillance data gathered as a result of the manufacturer's post market surveillance plan..

Additional guidance and legislation further specifying the applicable requirements and obligations under the MDR is expected. We are in the process of assessing the impact of the MDR and associated acts and guidance on our business. Due to these new regulatory requirements, conformity assessment procedures in the EU may experience delays.

CE Marking Requirements

As manufacturers of medical devices, in the EU we are required under the MDR to affix a CE mark to our products in order to sell our products in Member States of the EU. The CE mark is a symbol that indicates conformity with the applicable regulatory requirements.

Medical Devices in the EU are classified in four different classes (I, IIa, IIb and III) depending on their inherent risk. The MDR includes specific rules on classification of medical devices.

EU Development Process

For Class III devices, such as NBTXR3, and for implantable devices, it is necessary, save for exceptions, to carry out a clinical investigation to demonstrate that the product complies with the applicable regulatory requirements, including as regards safety and performance.

Any clinical investigation must comply with all relevant legal, ethical and regulatory requirements.

Clinical investigations must take into account scientific principles underlying the collection of clinical data and be conducted in accordance with the principles of good clinical practice. This means that, for example, all research subjects must have provided their prior informed consent for participation in any clinical investigation.

A clinical investigation can be carried out only if the relevant competent national authorities have approved it and the relevant ethics committee(s) have not issued a negative opinion in relation to it.

The MDR specifically requires that, subject to certain conditions, serious adverse events, device deficiencies and related updates be recorded and notified to all competent authorities of the EU Member States in which the clinical investigation is being performed. Termination of a clinical investigation must also be notified to such authorities and be followed by a clinical investigation report, irrespective of the outcome of the investigation.

The MDR specifies conditions required for the collection of data from clinical investigations relating to medical devices.

These requirements include rules on informed consent and the protection of vulnerable persons (e.g., persons under 18 years of age, pregnant women and disabled persons).

The conduct of a clinical investigation is subject to EU Member State national laws. For instance, in France, there are specific rules governing the protection of patients (including, for example, regarding consent and insurance).

Tracking

The MDR introduced a system for the registration of devices and their manufacturers, importers and authorized representatives, and allows EU Member States to also maintain or introduce registration obligations for distributors if they so wish. Moreover, in order to allow identification and to ensure the traceability of devices throughout the supply chain, the MDR requires the establishment of a Unique Device Identification (UDI) system

Notified Bodies and Conformity Assessment Procedures

To demonstrate compliance with the applicable regulatory requirements, manufacturers of medical devices must follow a conformity assessment procedure which varies according to the type of medical device and its risk classification. Except for certain Class I devices, a conformity assessment procedure typically requires the intervention of an independent organization accredited to conduct conformity assessments, known as a “Notified Body.” Under the conformity assessment procedure we have elected to follow for our products, the Notified Body audits and examines the technical file and the quality system applied to the design, manufacture and final inspection of our products. If we successfully complete the applicable procedure, the Notified Body issues a certificate of conformity. This certificate entitles a manufacturer to affix the CE mark to its medical devices after having also prepared and signed a “EU declaration of conformity” indicating that the product meets the applicable regulatory requirements. The certificate of conformity is valid for a maximum of five years, and may be extended on application for a further period not exceeding five years. While we have successfully completed the applicable regulatory procedures for our NBTXR3 product for the treatment of STS, we cannot guarantee that all our product candidates will be equally successful.

If we modify substantively our devices we may need to broaden, or re-perform, the certification underlying the CE mark of the modified product. The certificate of conformity can be suspended or withdrawn, e.g., where a Notified Body finds that pertinent regulatory requirements are not met and the manufacturer has not implemented appropriate corrective measures within the time limit set by the Notified Body. The same may be true for any new products that we may develop in the future.

The MDR strengthened the rules on the designation, organization and surveillance of Notified Bodies. These must meet the same high quality standards throughout the EU and have permanent availability of sufficient administrative, technical and scientific personnel as is necessary to carry out their tasks. Notified Bodies must carry out inspections of manufacturers' premises, some of which are unannounced. For certain devices, including Class III implantable devices, Notified Bodies must submit their clinical evaluation assessment report to the European Commission which in turns must submit it to an independent expert panel except for the products which are exempted according to Article 54(2) of the MDR.

Post-Market Vigilance

Once CE-marked and placed on the EEA market, medical devices are subject to vigilance requirements. In accordance with these requirements, manufacturers must report incidents to the competent authorities and are required to take appropriate “field safety corrective actions” to prevent or reduce the risk of serious incidents associated with devices made available on the market. Such actions must also be communicated to users through field safety notices. Manufacturers must equally report statistically significant increases in the frequency of certain incidents by means of trend reports.

In addition to reporting obligations for manufacturers regarding serious incidents and incident trends, the MDR introduced an obligation for EU Member States to encourage and enable healthcare professionals, users and patients to report suspicious incidents at national level.

Pricing and Reimbursement

Sales of our products in the EEA will be largely influenced by the outcome of our pricing and reimbursement negotiations with the national authorities of each of the EEA Member States, such as government social security funds. These third-party payors are increasingly limiting coverage and reimbursement for medical products and services. In addition, EEA governments have continued implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution with cheaper products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our products or a negative outcome of our reimbursement negotiations could reduce physician usage of our products once approved and have a material adverse effect on our sales, results of operations and financial condition.

Marketing, Advertising and Transparency

In the EU, the marketing and advertising of medical devices is subject to both legal and voluntary self-regulatory rules at EU and national level including as regards the strict prohibition of misleading and unfair advertising of medical devices. Moreover, under EU-wide voluntary self-regulatory rules, interactions between medical device manufacturers and healthcare professionals and healthcare organizations – including in particular any transfers of value that (a) such interactions cannot be misused to influence purchasing decisions through undue or improper advantages and (b) cannot be contingent upon sales transactions, use or recommendation of any specific products. Additional requirements may apply depending on the specific jurisdiction concerned.

Finally, increasing transparency requirements are mandated under national legislation and/or self-regulatory codes of conduct. Under these requirements, manufacturers of health products can be required to publicly disclose any transfers of value (whether in kind or in cash) they provide to, e.g., healthcare professionals and healthcare organizations.

As a result of the above requirements, manufacturers of medical devices are subject to increased monitoring of their promotional activities as well as of their other interactions with healthcare professionals and organizations. Any breach of the applicable rules can result in serious sanctions, including criminal, civil or administrative sanctions depending on the affected jurisdiction.

Data Protection Rules

The Regulation 2016/679, known as the General Data Protection Regulation, or GDPR, as well as EU Member State national legislations, apply to the collection and processing of personal data, including health-related information, by companies located in the EU, or in certain circumstances, by companies located outside of the EU and processing personal information of individuals located in the EU.

These laws impose strict obligations on the processing of personal data, including health-related information, in particular in relation to their collection, use, disclosure and transfer.

Also, in certain countries, in particular France, the conduct of clinical trials is subject to compliance with specific provisions of the Act No.78-17 of 6 January 1978 on Information Technology, Data Files and Civil Liberties, as amended, and in particular Chapter IX relating to the processing of personal data in the health sector. These provisions require, among others, the filing of compliance undertakings with "standard methodologies" adopted by the French Data Protection Authority (the "CNIL"), or, if not complying, obtaining a specific authorization from the CNIL.

The most common standard methodologies are the following:

- Decision No. 2018-154 of May 3, 2018 concerning the approval of a standard methodology for processing personal data in the context of research in the field of health, which does not require the express consent of the person involved (methodology MR-003);
- Decision No. 2018-153 of May 3, 2018 concerning the approval of a standard methodology for the processing of personal data carried out within the context of research in the field of clinical trials, which requires the express consent of the person involved (standard methodology MR-001);

In certain specific cases, entities processing health personal data may have to comply with article L1111-8 of the French Public Health Code which imposes certain certifications for the hosting service providers.

Foreign investment control regime in France

Over the past few years, the French government has strengthened its foreign investment control regime. Thus, as at the date of the Universal Registration Document, any investment:

i. by (a) any non-French citizen, (b) any French citizen not fiscally residing in France, (c) any non-French entity or (d) any French entity controlled by one of the aforementioned persons or entities;
ii. that will result in the relevant investor (a) acquiring control of an entity registered in France, (b) acquiring all or part of a business line of an entity registered in France, or (c) for non-EU or non-EEA investors crossing, directly or indirectly, alone or in concert, a 25% threshold of voting rights in an entity registered in France; and

iii. where this entity registered in France is developing activities in certain strategic industries (sensitive sectors or sensitive activities) related to (a) activity likely to prejudice national defense interests, participating in the exercise of official authority or are likely to prejudice public policy and public security (including weapons, double-use items, IT systems, cryptology, date capturing devices, gambling, toxic agents or storage of data), (b) activities relating to essential infrastructure, goods or services (including energy, water, transportation, space, telecom, public health, farm products or media), and (c) research and development activity related to critical technologies (including biotechnology, cybersecurity, artificial intelligence, robotics, additive manufacturing, semiconductors, quantum technologies or energy storage…) or dual-use items, is subject to the prior authorization of the French Ministry of Economy, which authorization may be conditioned on certain undertakings.

Additionally, in the context of the ongoing COVID-19 pandemic, the Decree (décret) n°2020 892 dated July 22, 2020, as amended by the Decree (décret) n°2020-1729 dated December 28, 2020 and by the Decree (décret) n°2021-1758 dated December 22, 2021, has created a new 10% threshold of the voting rights applicable until December 31, 2022 for the non-European investments (i) in an entity governed by French law and (ii) whose shares are admitted to trading on a regulated market, replacing the 25% above-mentioned threshold for certain activities.

On November 5, 2020, the French Ministry of Economy informed us that our activities are subject to the foreign investment control regime described above. Therefore, investments in our Company meeting the above criteria are subject to prior authorization by the French Ministry of Economy.

A fast-track procedure shall apply for any non-European investor exceeding this 10% threshold who will have to notify the Minister of Economy who will then have 10 days to decide whether or not the transaction should be subject to further examination.

If an investment requiring the prior authorization of the French Minister of Economy is completed without such authorization having been granted, the French Minister of Economy might direct the relevant investor to nonetheless (i) submit a request for authorization, (ii) have the previous situation restored at its own expense or (iii) amend the investment.

In the absence of such authorization, the relevant investment shall be deemed null and void. The relevant investor may be found criminally liable and may be sanctioned with a fine not to exceed the greater of the following amounts: (i) twice the amount of the relevant investment, (ii) 10% of the annual turnover before tax of the target company or (iii) €5 million (for a company) or €1 million (for a natural person).

1.3.17.3. Regulation in Asia

We possess the rights to develop and commercialize NBTXR3 in the Asia-Pacific region. We anticipate that the development and commercialization, if any, of NBTXR3 in the Asia-Pacific region would initially target Taiwan, China and Japan.

Taiwan

In Taiwan, NBTXR3 has been tentatively classified as a drug for regulatory purposes.

Taiwan Drug Development Process

Under the Pharmaceutical Affairs Act (the "PAA"), the competent authority at central government level is the Taiwan Ministry of Health and Welfare ("MOHW"). The Taiwan Food and Drug Administration ("TFDA") under the MOHW is in charge of the administration, inspection and testing of pharmaceutical

products (including drugs and medical devices). Companies that plan to import drugs into or manufacture drugs in Taiwan must receive a prior drug permit license from MOHW and comply with other applicable laws and regulations in Taiwan. Sale of drugs in Taiwan is also subject to applicable laws and regulations. The drug development and marketing process in Taiwan mainly involves preclinical tests, clinical trials, manufacturing and post-market monitoring. The said process is subject to scrutiny and/or approval by the TFDA, such as IND, approval (which must be approved by the TFDA before human clinical trials may begin) and NDA approval. Additionally, according to the PAA, unless otherwise announced by the MOHW, for purposes of pharmaceutical products manufacture, the factory facilities, equipment, organization and personnel, production, quality control, storage, logistics, handling of customer complaints, and other matters requiring compliance shall comply with the Pharmaceutical Good Manufacturing Practice Regulations; the manufacture may only begin after the MOHW has completed its inspection and granted approval and the pharmaceutical products manufacture license has been obtained. After marketing, the pharmaceutical products are still subject to applicable and regulations For instance, with respect to the post-marketing monitoring, a manufacturer or an importer of a new drug defined under the PAA shall collect safety information on drug use available both domestically and abroad during the safety monitoring period; in addition to making report following the Regulations Governing the Reporting of Severe Adverse Reactions of Medicines, such manufacturer or an importer shall also file periodic safety update report to MOHW within the specified time period.

People's Republic of China

In the People's Republic of China (excluding Hong Kong, Macau and Taiwan), no determination has yet been made as to whether NBTXR3 will be classified as a drug or medical device for regulatory purposes.

If NBTXR3 is classified a drug, a market approval is required for its development and commercialization. Extensive data derived from preclinical laboratory tests and studies meeting the requirements of Chinese law are required to support the granting of approval by the National Medical Product Administration ("NMPA") for a new drug product to proceed with clinical trials. If clinical trials sufficiently establish that the product is safe and effective, the NMPA will issue approval for the product to be marketed. Similar to the United States and the EU, the process for obtaining such marketing approval is lengthy, although the Chinese government has recently made efforts to reduce the time required and to streamline the process. After obtaining marketing approval, the marketing approval holder must conduct post-marketing approval studies to closely monitor the use of the product for purposes of reporting its demonstrated safety and efficacy to the NMPA. Further, the marketing approval holder must closely monitor any adverse events or product quality issues, and disclose any such events or issues to the NMPA, as well as potentially to other government agencies and the public. An overseas entity must appoint a domestic agent in assisting it to apply for market approval in China, and the approval holder and its domestic agent will be jointly liable for the aforementioned obligations.

If NBTXR3 is classified a medical device, clinical evaluation is required to prove its safety and effectiveness for proceeding with recordation or registration. The clinical evaluation could be clinical trials or analysis on clinical literatures and materials, depending on the product features, clinical risks, existing clinical data and other information. If it is further classified as a Class I medical device (with low risk level), recordation with the NMPA would suffice and no approval is required. If it is classified as a Class II or III medical device (with moderate or high risk level), registration with the NMPA will be required. Prioritized examination and approval would likely to be granted to an innovative medical device to shorten the timeframe for getting market approval. For overseas recordation/registration holder to import its product into China, it must appoint a domestic agent in assisting it to apply for device recordation/registration in China, and the holder and the domestic agent will be jointly liable for the safety and effectiveness during whole life cycle of a medical device including on quality management, post marketing research and risks management, adverse event monitoring and re-evaluation, product recall systems and other obligations as provided by the Chinese law.

Japan

In Japan, NBTXR3 is classified as a drug.

The Ministry of Health, Labour and Welfare (the "MHLW") regulates drugs and medical devices under the Pharmaceuticals and Medical Devices Act (the "PMD Act") and its implementing regulations. The MHLW delegates part of the oversight to the Pharmaceuticals and Medical Devices Agency (the "PMDA"), an independent administrative institution. In order to market a drug or a highly-controlled medical device in Japan, marketing authorization must be obtained in advance. Foreign companies that plan to import drugs or medical devices into Japan must be registered with the MHLW through a separate process. The process for obtaining marketing authorization includes preclinical tests, clinical trials and compliance review of the application for marketing authorization by the PMDA. After marketing authorization is obtained, drugs and medical devices are subject to continuing regulations under the PMD Act. For example, a new drug is subject to periodic reexamination by the MHLW and the marketing authorization holder must continue to collect clinical data during such specified reexamination period. In addition, the marketing authorization holder must report to the MHLW when it learns of new information regarding the efficacy and safety of its product, including occurrences of adverse events.

1.4. ANALYSIS AND COMMENTS ON THE GROUP'S FINANCIAL RESULTS

Readers are invited to read the following information on the Group's financial position and results in conjunction with the consolidated accounts established in IFRS standards for the years ended December 31, 2019, 2020 and 2021, (i) in Chapter 4 of the Universal Registration Document on May 13, 2020 under number R. 20-010, (ii) in Chapter 4 of the Universal Registration Document on April 7, 2021 under number D. 21-0272 and (iii) in Chapter 4 of the Universal Registration Document.

1.4.1. Income statement analysis

1.4.1.1. Revenues and other income from activity

The Company's ordinary activities revenues were as follows:

(€K)	2021	2020	2019
Services	5	50	40
Other sales	5	—	28
Licenses	—	—	—
Total revenues	**10**	**50**	**68**
Research tax credit	2,490	1,927	2,437
Subsidies	126	526	20
Other	21	10	17
Total other income	**2,638**	**2,462**	**2,473**
Total revenues and other income	**2,647**	**2,512**	**2,541**

The Company's revenue of €10 thousand in 2021, €50 thousand in 2020 and €68 thousand in 2019 were derived mainly from the charging-back of shared external clinical research organization costs in connection with the development support provided by the Company to PharmaEngine as part of the 2014 amendment to the Company's License and Collaboration Agreement.

Research tax credit increased from €1,927 thousand in 2020 to €2,490 thousand in 2021 due mainly to an increase of research and development expenses.

1.4.1.2. Other income

Subsidies

Since its creation, the Company has received a certain number of grants or subsidies from the State or public authorities to finance its operations or specific recruitments, due to its innovative nature. Grants are recognized as income as the related expenses are incurred, independently of cash inflows.

Research tax credit

Research tax credits are granted to companies by the French state in order to encourage them to carry out technical and scientific research. Companies that can prove that their expenditure meets the required criteria (research expenditure located in France or, since 1 January 2005, within the European Union or in another State party to the Agreement on the European Economic Area that has entered into a tax treaty with France containing an administrative assistance clause) benefit from a tax credit that may be used to pay the corporate tax due for the year in which the expenditure is incurred and the three following years or, where appropriate, be refunded for its excess portion.

The Company has benefited from the research tax credit since its creation.

The research tax credit recorded for the year ended 31 December 2021 is €2,490 thousand. In November 2021, the Company received the refund for the 2020 research tax credit for €1,927 thousand. The Company has requested its reimbursement under the Community SME scheme in accordance with existing legislation.

These financings are recorded as "Other Revenues" in the year that recorded the corresponding expenses or costs. The share of financing related to activated expenses is deducted from the balance sheet of capitalized expenses and the income statement from the amortization expenses of those costs.

1.4.1.3. Operating expenses

1.4.1.3.1. Research and development costs

These costs include:

- Research and development payroll costs;
- Clinical, non-clinical and development costs related to the on-going studies;
- The costs of manufacturing prototypes of equipment and of certain tested products;
- Some intellectual property expenses ;
- Expenses related to regulatory affairs;
- Expenses related to the development of the quality system;
- And travel costs.

All of these research and development expenses (R&D) incurred to date have been recorded as expenses, with the Company considering that the technical feasibility of its development projects will not be demonstrated until the issuance of the approvals necessary for the marketing of its products, which is also the time at which substantially all of the development costs will have been incurred.

The breakdown of research and development costs is as follows:

(€K)	2021 12 months Audited	2020 12 months Audited	2019 12 months Audited
Purchases, sub-contracting and other expenses	(19,562)	(12,734)	(16,804)
Payroll costs (incl. Share-based payments)	(9,605)	(10,306)	(11,980)
Depreciation, amortization and provision expenses	(1,211)	(1,290)	(1,627)
Total R&D costs	**(30,378)**	**(24,330)**	**(30,411)**

The total amount of expenses incurred with respect to research and development activities increased by €6.0 million, or 24.9%, from €24.3 million for the year ended December 31, 2020 to €30.4 million for the year ended December 31, 2021. This net increase was mainly due to:

- Purchases, sub-contracting and other expenses increased by €6.8 million, or 54% for the year ended December 31, 2021 as compared with the same period in 2020. This reflects the increase of the clinical development activities, especially our clinical trial NANORAY-312;

- a decrease of €700 thousand or 6.8%, in payroll costs, which was mainly due to a change in the mix and in the location of research and development staff. As of December 31, 2021, our workforce included 75 research and development staff as compared with a total of 66 as of December 31, 2020; and

- a decrease of €79 thousand in depreciation, amortization and provision expenses primarily mainly due to the application of the IFRS 16 standard.

The total amount of expenses incurred with respect to research and development activities decreased by €6.1 million, or 20.0%, from €30.4 million for the year ended December 31, 2019 to €24.3 million for the year ended December 31, 2020. This net decrease was mainly due to:

- Purchases, sub-contracting and other expenses decreased by €4.1 million, or 24% for the year ended December 31, 2020 as compared with the same period in 2019. This reflects the Company's endeavor to decrease costs while maintaining clinical trials development during the COVID-19 pandemic.

- a decrease of €1.7 million, or 14.4%, in payroll costs, which was mainly due to a decrease of 15 research and development staff for the year ended December 31, 2020 as compared with the same period in 2019. As of December 31, 2020, our workforce included 66 research and development staff as compared with a total of 81 as of December 31, 2019 ; and

- a decrease of €337 thousand in depreciation, amortization and provision expenses primarily mainly due to a €145 thousand payment related to a provision for disputes for the year ended December 31, 2020, which amount was €164 thousand for the same period in 2019.

1.4.1.3.2. Selling, general and administrative (SG&A) expenses

General and selling expenses mainly include administrative staff costs, organizational costs related to the head office in Paris, external expenses such as accounting, legal, human resources, communication and strategic marketing expenses. Their total amount was as follows during the reported period:

(€K)	2021 12 months Audited	2020 12 months Audited	2019 12 months Audited
Professional fees, rental and other expenses	(9,638)	(6,482)	(9,435)
Payroll costs (incl. Share-based payments)	(9,379)	(7,789)	(9,205)
Depreciation, amortization and provision expenses	(417)	(340)	(270)
Total SG&A costs	**(19,434)**	**(14,611)**	**(18,909)**

Our SG&A expenses increased by €4.8 million, or 33.0%, from €14.6 million for the year ended December 31, 2020 to €19.4 million for the year ended December 31, 2021. This was primarily due to:

- an increase in purchases, fees and other expenses of €3.1 million or 48.7%. This variation reflects two main impacts, first the legal expenses relating to partnership agreements as well as consulting fees, legal and compliance expenses as a result of being a US public company. The second main impact relates to recruitment expenses; and

- an increase of €1.6 million or 20.4% in payroll costs due to a change in the mix and location of our SG&A staff (more US based employees). At December 31, 2021 we employed 25 SG&A staff as compared with 24 as of December 31, 2020.

Depreciation, amortization and provision expenses increased from €340 thousand in 2020 to €417 thousand in 2021, primarily due to the to the extension of Villejuif leases.

Our SG&A expenses decreased by €4.3 million, or 22.7%, from €18.9 million for the year ended December 31, 2019 to €14.6 million for the year ended December 31, 2020. This was primarily due to:

- a decrease in purchases, fees and other expenses of €3.0 million or 31.3% due to our efforts to decrease general and administrative costs in light of the COVID-19 pandemic; and

- a decrease of €1.4 million or 15.4% in payroll costs due to a decrease in SG&A staff. At December 31, 2020 we employed 24 SG&A staff as compared with 29 as of December 31, 2019.

Depreciation, amortization and provision expenses increased from €270 thousand in 2019 to €340 thousand in 2020, primarily due to the additional amortization of new facility leases in Paris (Oberkampf road and Faubourg Saint Antoine road).

1.4.1.4. Net income

1.4.1.4.1. Financial income and expenses

Net financial income changed by €2.7 million, from a €2.8 million income for the year ended December 31, 2020 to an income of €5.6 million for the year ended December 31, 2021. The increase was primarily attributable to the increase in foreign exchange gains on gross proceeds of our U.S. initial public offering held in a US dollar bank account.

Net financial income changed by €7.0 million, from a €4.1 million loss for the year ended December 31, 2019 to an income of €2.8 million for the year ended December 31, 2020. The increase was primarily attributable to the positive impact of a €4.8 million decrease in interest costs resulting from our updating of the EIB estimated loan royalties, for the year ended December 31, 2020 compared to a €4.4 million interest expense for the year ended December 31, 2019, partially offset by a €1.5 million increase in foreign exchange losses. The increase in foreign exchange losses was driven primarily by our retention of $113.3 million from the gross proceeds of our global offering, which included our U.S. initial public offering in a US dollar bank account. (€72.0 million as of December 31, 2020), and the impact associated with the closing of a bank account.

1.4.1.4.2. Income tax

Due to the losses incurred during the reporting period, the Company did not record any significant corporate tax expense. According to current legislation, the Company has tax deficits that can be carried forward in France for a total amount of €284 million. For financial years ending on or after December 31, 2013, carried forward losses are capped at €1 million, on top of which 50% of the profits above that amount can be included.

1.4.1.4.3. Net loss and net loss per share

The loss per share (average weighted number of shares during the year) amounted to €1.35 in 2021, €1.38 in 2020 and €2.35 in 2019.

1.4.2. Balance sheet analysis

1.4.2.1. Non-current assets

(€K)	As of December 31, 2021	As of December 31, 2020
Intangible assets	**4**	21
Property, plant and equipment	**8,186**	8,256
Financial assets	**519**	505
Total non-current assets	**8,709**	**8,782**

From 1 January 2019, the Company has adopted IFRS 16 – Leases, increasing its non-current, tangible assets. The rights of use related to these contracts relate primarily to the leases of the head office in Paris and the manufacturing site in Villejuif in France.

1.4.2.2. Current assets

(€K)	As of December 31, 2021	As of December 31, 2020
Research tax credit receivable	2,490	1,927
VAT receivable	1,058	971
Prepaid expenses	2,213	2,217
Other receivables	3,378	920
Other current assets	**9,139**	**6,035**

As of December 31, 2021, prepaid expenses mainly relate to research agreements related to MD Anderson agreement for €1.0 million, and insurance related to the Directors & Officers for €0.6 million.

As of December 31, 2020, prepaid expenses mainly relate to research agreements for €1.6 million, to the MD Anderson agreement, and to €185 thousand in insurance costs following its initial public offering on the Nasdaq.

Other receivables mainly comprised advances paid to suppliers in the amounts of €3,043 thousand as of December 31, 2021 as compared to €805 thousand as of December 31, 2020. This new advance is mainly related to the new ICON contract signed in conjunction with the launch of the 312 study.

(€K)	As of December 31, 2021	As of December 31, 2020
Cash and bank accounts	83,921	119,151
Net cash and cash equivalents	**83,921**	**119,151**

As of December 31, 2021, cash and bank accounts decreased by €35,230 thousand as compared with December 31, 2020 mainly due to the non-refundable upfront payment from LianBio, the payments made to PharmaEngine, the debt reimbursement related to the EIB loan and other cash flows used in operating activities.

(€K)	2021	2020
Cash flows used in operating activities	(29,872)	(27,538)
Cash flows used in investing activities	(242)	(112)
Cash flows from financing activities	(5,180)	111,769
Impact of exchange rates changes on cash	64	(63)
Net cash flow	**(35,230)**	**84,056**

(see note 1.4.4 Cash flow, capital financing)

1.4.2.3. Equity

The Company's equity on December 31, 2020 is €26,790 thousand compared to €70,468 thousand on December 31, 2020. The decrease is primarily due to the net losses in 2021 of €47,003 thousand.

1.4.2.4. Non-current liabilities

Non-current liabilities of €38,134 thousand at December 31, 2021 mostly include financial liabilities related to the loans and advances granted to the Company, including the fair value of the European Investment Bank loan for a nominal value of €30 million.

Details of the remaining amounts to be repaid as of December 31, 2021 can be found in Note 12 to the consolidated financial statements for the year ended December 31, 2021, prepared under IFRS, in Section 4.1. of the Universal Registration Document.

1.4.2.5. Current liabilities

(€K)	As of December 31, 2021	As of December 31, 2020
Current provisions	110	40
Current financial liabilities	8,204	4,872
Trade payables and other payables	6,482	7,106
Other current liabilities	5,531	7,022
Deferred revenues and contract liabilities	16,518	—
Total current liabilities	**36,845**	**19,041**

Under Sections L. 441-6-1 and D. 441-4 of the French Code of Commerce, the breakdown of the Company's supplier debts on the closing date of the last two financial years based on their respective maturity dates is presented below.

2021

Unpaid invoices received at the end of the financial year:

	1 to 30 days	31 to 60 days	61 to 90 days	91 days and more	Total (1 day and more)
(A) Late payment tranche					
Number of invoices					155
Total (incl. VAT)	€61k	€139k	€177k	€753k	€1,130k
Percentage of total purchases for the year (incl. VAT)	0.17 %	0.39 %	0.49 %	2.10 %	3.14 %
(B) Invoices excluded from (A) related to to disputed or unrecognized debts and receivables					
Number of invoices excluded	—	—	—	—	—
Total amount of invoices excluded (incl. VAT)	—	—	—	—	—
(C) Reference payment terms used (contractual or legal deadline - article L. 441-6 or article L. 443-1 of the French Commercial Code)					
Payment period used to calculate late payments	Contractual deadlines: deadlines for each invoice				

Unpaid invoices issued at the end of the financial year:

	1 to 30 days	31 to 60 days	61 to 90 days	91 days and more	Total (1 day and more)
(A) Late payment tranche					
Number of invoices					—
Total (incl. VAT)	—	—	—	—	—
Percentage of total purchases for the year (incl. VAT)					
Percentage of the financial year revenue (incl. VAT)	—	—	—	—	—
(B) Invoices excluded from (A) related to to disputed or unrecognized debts and receivables					
Number of invoices excluded	—	—	—	—	—
Total amount of invoices excluded (incl. VAT)	—	—	—	—	—
(C) Reference payment terms used (contractual or legal deadline - article L. 441-6 or article L. 443-1 of the French Commercial Code)					
Payment period used to calculate late payments	Contractual deadlines: deadlines on each invoice				

2020

Unpaid invoices received at the end of the financial year:

	1 to 30 days	31 to 60 days	61 to 90 days	91 days and more	Total (1 day and more)
(A) Late payment tranche					
Number of invoices					198
Total (incl. VAT)	€609k	€452k	€169k	€180k	€1,411k
Percentage of total purchases for the year (incl. VAT)	2,65%	1,97%	0,74%	0,78%	6,14%
(B) Invoices excluded from (A) related to to disputed or unrecognized debts and receivables					
Number of invoices excluded	—	—	—	—	—
Total amount of invoices excluded (incl. VAT)	—	—	—	—	—
(C) Reference payment terms used (contractual or legal deadline - article L. 441-6 or article L. 443-1 of the French Commercial Code)					
Payment period used to calculate late payments	Contractual deadlines: deadlines for each invoice				

Unpaid invoices issued at the end of the financial year:

	1 to 30 days	31 to 60 days	61 to 90 days	91 days and more	Total (1 day and more)
(A) Late payment tranche					
Number of invoices					5
Total (incl. VAT)	—	€14k	—	€47k	€62k
Percentage of total purchases for the year (incl. VAT)					
Percentage of the financial year revenue (incl. VAT)	—	24%	—	76%	100%
(B) Invoices excluded from (A) related to to disputed or unrecognized debts and receivables					
Number of invoices excluded	—	—	—	—	—
Total amount of invoices excluded (incl. VAT)	—	—	—	—	—
(C) Reference payment terms used (contractual or legal deadline - article L. 441-6 or article L. 443-1 of the French Commercial Code)					
Payment period used to calculate late payments	Contractual deadlines: deadlines on each invoice				

1.4.3. Outlook and subsequent events

1.4.3.1. Trends

To find out the main trends since December 31, 2021, see paragraph 1.1.3. of the Universal Registration Document.

1.4.3.2. Known trend, uncertainty, commitment request or reasonably sensitive event to affect the Company's outlook

For details about the impact of COVID-19 on the Group, see paragraph 1.1.3. of the Universal Registration Document.

1.4.3.3. Profit forecasts or estimates

The Company does not intend to forecast or estimate profits.

1.4.3.4. Significant change in financial or business situation

To the Company's knowledge, there has been no significant change in the Company's financial or commercial position since December 31, 2021.

However, given the great uncertainty regarding the evolution of COVID-19 pandemic, global confinement measures and a possible resulting economic downturn, the potential impact of the pandemic on the Group's activities and future results remains highly uncertain.

As of the date of the Universal Registration Document, the Company has adjusted its resourcing and operations to ensure flexibility to respond to the uncertainty caused by the pandemic. It will nevertheless continue to regularly assess the impact of COVID-19 on its business and will communicate any significant evolution on the subject to the market.

1.4.4. Cash flow, capital financing

Information about the Group's capital, liquidity and sources of financing.

As of December 31, 2021, the amount of cash and cash equivalents held by the Company was €83.9 million compared to €119.2 million as of December 31, 2020. Cash and cash equivalents include the Company's current availability and financial instruments (mainly composed of paid short-term bank deposits). These availability and investment securities are used to fund the Company's activities, including its research and development costs. As of the date of the Universal Registration Document, the Group has cash visibility up to the second quarter of 2023, allowing it to meet its off-balance sheet commitments and planned investments.

Capital financing

Refer to chapter 4 of the Universal Registration Document.

Financing through advances

See paragraph 1.4.2.4. of the Universal Registration Document.

Research Tax Credit financing

See Note 8.2 to the consolidated financial statements for the year ended December 31, 2021, prepared under IFRS, in Section 4.1. of the Universal Registration Document.

Off-balance sheet of commitment

See Note 22 to the consolidated financial statements for the year ended December 31, 2021, prepared under IFRS, in Section 4.1. of the Universal Registration Document.

Source and amount of cash flow

During the period presented, net cash flows are presented as shown in the table below.

(€K)	2021	2020
Cash flows used in operating activities	(29,872)	(27,538)
Cash flows used in investing activities	(242)	(112)
Cash flows from financing activities	(5,180)	111,769
Impact of exchange rates changes on cash	64	(63)
Net cash flow	**(35,230)**	**84,056**

Cash flows from operating activities

Net cash consumption at operating activities is primarily divided into cash flow over the period and changes in working capital requirements.

(€K)	2021	2020
Net loss for the period	**(47,003)**	**(33,590)**
Elimination of other non-cash, non-operating income and expenses		
Depreciation and amortization	1,560	1,754
Provisions	152	(48)
Expenses related to share-based payments	3,201	2,924
Cost of net debt	2,224	2,115
Loss on disposal	—	—
U.S. Initial public offering 2018 costs offset	—	—
Impact of deferred income related to financial liabilities discounting effect	(1,554)	(6,463)
Other charges with no impact on treasury	8	7
Cash flows used in operations, before tax and changes in working capital	**(41,412)**	**(33,300)**
Changes in operating working capital	**11,540**	**5,762**
Cash flows used in operating activities	**(29,872)**	**(27,538)**

Our net cash flows used in operating activities was €29.9 million and €27.5 million for the years ended December 31, 2021 and 2020, respectively. Net cash flows from operating activities for the year ended December 31, 2021 was primarily attributable to:

- €11.6 million in changes in working capital mainly composed of operating expenses reflecting the increase of the clinical development activities, especially driven by the launch of our global Phase III clinical trial for elderly head and neck cancer patients ineligible for platinum-based (cisplatin) chemotherapy (NANORAY-312).

These funds were partially offset by:

- €16.5 million relating to the LianBio upfront payment; and
- €4.9 million of impact of deferred income related to financial liabilities discounting effect.

Cash flow from investing activities

Cash consumption related to investment activities should be analysed by distinguishing flows directly related to the Company's operating activity and those related to its cash management policy.

(€K)	2021	2020
Acquisitions of intangible assets	(5)	(11)
Acquisitions of property, plant and equipment	(228)	(96)
Addition in non-current financial assets	(9)	(4)
Net cash flows from (used in) investing activities	**(242)**	**(112)**

Our net cash flows used in investing activities was €242 thousand for the year ended December 31, 2021 compared to €112 thousand for the year ended December 31, 2020. The increase of €130 thousand was primarily due to a €96 thousand increase in fixed asset acquisitions.

Cash flows from financing activities

Net flows from financing activities are mainly related to:

(€K)	2021	2020
Capital increases	—	113,650
Warrants subscription	43	5
Transaction costs	(349)	(10,359)
Increase in loans	—	10,350
Decrease in conditional advances	(2,833)	(250)
Repayment of lease liabilities [(2)]	(909)	(928)
Interest paid related to loans	(1,132)	(700)
Net cash flows from financing activities	**(5,180)**	**111,769**

Our net cash flows from financing activities were €(5.2) million and €111.8 million for the periods ended December 31, 2021 and 2020, respectively. The decrease of €116.9 million was primarily attributable to the €84.0 million of net proceeds, after deducting underwriting commissions and offering expenses, from our U.S. initial public offering in December 2020 and the €20.0 million of gross proceeds received in July 2020 as a result of a capital increase from a private placement of ordinary shares.

Information on repayable advance conditions and financing structure

The main terms of the repayable advances granted to the Company as of December 31, 2021 are described in paragraph 1.4.2. of the Universal Registration Document.

Restrictions to the use of Equity

(€K)	2021	2020
Treasury share - cash account	97	104
Deposits paid	421	401
TOTAL	**519**	**505**

Funding sources needed for the future

As outlined in paragraph 1.5.1.3. of the Universal Registration Document, the Company has sufficient net working capital to meet its obligations and operating cash requirements for the next twelve months following the date of the date of the Universal Registration Document.

1.4.5. Accounting and reporting on allocation of the profit

Important factors, including unusual or infrequent events or new developments, significantly affecting the issuer's operating income, indicating the measure in the world is affected.

In terms of the development stage of the Company's business, the main factors affecting the business and profit are:

- the scope of the R&D programs and compliance with their timetable; the existence of tax incentives for companies involved in technical and scientific research activities such as the research tax credit for which it benefits;
- entering into development agreements and/or licenses on part of its technology, or;
- obtaining grants and repayable advances.

In addition, the Company regularly grants financial instruments giving access to its capital to its employees, be they corporate officers or not, as well certain business partners. The Company's results are affected by the corresponding expense, recorded in the financial statements established according to the IFRS repository prepared under IFRS.

The Company did not find any unusual or infrequent events that could affect its operating income.

When financial statements show significant changes in net sales or net revenues, explain the reasons for these changes.

Not Applicable.

Mention any measures or factors of an administrative, economic, budgetary, monetary or political nature that have significantly or could have significant impact, directly or indirectly, on the issuer's operations.

Given the great uncertainty regarding the evolution of COVID-19 pandemic, global confinement measures and the resulting economic downturn, the potential impact of the pandemic on the Group's activities and future results remains highly uncertain. In addition, enrollment and retention of patients in clinical trials could be disrupted by geopolitical events, including civil or political unrest (such as the ongoing conflict between Ukraine and Russia), terrorism, insurrection or war, man-made or natural disasters, or public health pandemics or epidemics or other business interruptions, including, the current COVID-19 pandemic and future outbreaks of the disease.

1.4.6. Information on dividends

Dividends paid in the last three years

None.

Dividend distribution policy

There are no plans at this time to initiate a ~~short-term~~ dividend payment policy given the Company's stage of development.

1.4.7. Non-tax-deductible expenses

In accordance with the provisions of Article 223 quarter of the General Tax Code, the General Meeting of Shareholders approved, among other things, non- tax-deductible expenses and expenses covered by Section 39-4 of the same Code.

We indicate that the corporate accounts for the past year do not show any tax-deductible expenses or expenses as covered by section 4 of section 39 of the French General Tax Code.

1.4.8. Results for the last five years

INDICATORS (€K)	2017	2018	2019	2020	2021
I. Financial position at the end of the year					
a) Share Capital	589	589	672	1,033	1,045
b) Weighted average number of shares	19,633,373	19,633,373	21,631,514	24,385,827	34,733,418
c) Number of equity options that may be converted in shares	2,828,098	3,176,910	2,338,013	2,414,654	2,972,860
II. Overall results					
a) Turnover (excl VAT)	388,000	209,000	444,000	231,000	125,000
b) Loss before tax, depreciation and provisions	(23,343)	(30,751)	(44,772)	(36,734)	(46,788)
c) Research Tax credit	3,259	3,251	2,373	1,858	2,273
d) Profit/ (loss) after tax, amortization and depreciation	(20,560)	(28,117)	(43,574)	(35,720)	(45,146)
e) Dividends	—	—	—	—	—
III. Results assessed for one share					
a) Loss before tax, depreciation and provisions	(1.19)	(1.57)	(2.07)	(1.51)	(1.35)
b) Net loss	(1.05)	(1.43)	(2.01)	(1.46)	(1.30)
c) Dividend per share	—	—	—	—	—
IV. Employees					
a) Number of employees at the end of the year	75	89	85	71	75
b) Payroll cost	6,148	7,649	8,307	7,375	7,826
c) Social benefit expense during the year	2,448	3,044	3,439	3,551	4,091

1.5. RISK FACTORS

The Company operates in a changing environment involving risks, some of which are beyond its control.

The risks and uncertainties described below should be considered carefully, together with all of the other information in this chapter, before deciding whether to subscribe or purchase the Company's securities.

The Company has reviewed the risks that could materially and adversely affect the Group, its business, financial condition, operating results, prospects or ability to meet its objectives. As of the date of the Universal Registration Document, the Company is not aware of any significant risks other than those presented in this chapter.

The main risk factors relating to the Group and its business are grouped into four categories listed below, it being specified that, within each of these categories, the most important risk factor, based on the Company's assessment as of the date of the Universal Registration Document, is presented first.

The most important risk factors have been identified and assessed considering the likelihood of occurrence and the possible negative effect on the Company, in each case taking also into account corrective actions and risk management measures that have been put in place. The occurrence of new events, be they internal or external to the Company, is therefore likely to modify this ranking in the future.

	Risk	Likelihood	Impact
1.5.1	**Risks Related to the Group's Activity**		
1.5.1.1	The Group is heavily dependent on the successful development, pre-clinical or clinical, of NBTXR3	High	High
1.5.1.2	The commercial success and profitability of NBTXR3 and any other Group's products is not guaranteed	High	High
1.5.1.3	The Group's business is governed by a rigorous, complex and evolving regulatory framework	High	Medium
1.5.1.4	Due to its limited resources and access to capital, the Group's decisions to prioritize development of certain product candidates or certain indications may adversely affect its business prospects	High	Medium
1.5.1.5	The COVID-19 pandemic could have a significant impact on the Group's activities	High	Medium
1.5.1.6	Investments in the Company may be subject to prior governmental authorization under the French foreign investment control regime	N/A	N/A
1.5.2	**Risks Related to Organization and Operations**		
1.5.2.1	Claims related to product liability or other lawsuits could divert the Group's resources from other activities, expose it to significant liabilities and reduce the commercial potential of its product candidates	High	High
1.5.2.2	The Group relies on third parties who carry out its clinical trials and the collection and analysis of related data, with which it has entered or may enter into partnership in the future for the development and marketing of Hensify® and its other product candidates, and for the supply of various materials required for the production of all or part of its product candidates	Low	High
1.5.2.3	The Group may be held liable in connection with the use of hazardous chemical products in its business activities	Low	Medium

	Risk	Likelihood	Impact
1.5.2.4	The Group depends on key management personnel and its ability to attract and retain other qualified personnel	Medium	Medium
1.5.2.5	The Group's internal computer systems, or those of third-party subcontractors or consultants, may fail or suffer security breaches	Medium	Medium
1.5.2.6	Use of social media may materially and adversely impact the Group's reputation	Medium	Low
1.5.2.7	If current or future collaboration partners do not fulfill their obligations, this may cause delays in, or discontinuation of, partner-sponsored clinical trials, reduced revenue potential, and potentially litigation.	High	High
1.5.2.8	The Company may identify material weaknesses or otherwise fail to maintain an effective system of internal control over financial reporting, and as a result, investor confidence in the Company and the value of its shares could be materially and adversely affected.	Low	Medium
1.5.3	**Risks Related to Intellectual Property**		
1.5.3.1	A dispute concerning the infringement or misappropriation of intellectual property rights or the intellectual property rights of others could be time-consuming and costly, and an unfavorable outcome could harm the Group	Medium	High
1.5.3.2	The Group's ability to compete may decline if it does not adequately protect its intellectual property proprietary rights	Low	High
1.5.3.3	In the event the Group's trademarks and trade names are not adequately protected, the Group may not be able to build name recognition in its markets of interest	Low	High
1.5.4	**Financial and Market Risks**		
1.5.4.1	The Group will require additional funding, which may not be available on acceptable terms or at all. Failure to obtain this necessary capital in time may force the Group to delay, limit or terminate its product development efforts or other operations	High	High
1.5.4.2	The Group has incurred significant losses and anticipates that it will continue to incur significant losses for the foreseeable future	High	Medium
1.5.4.3	Shareholder participation could be diluted	High	High
1.5.4.4	Future use of tax loss carryforwards could be called into question	Low	Medium
1.5.4.5	The dual listing of the Company's shares requires the implementation of costly and complex compliance procedures	High	Low

1.5.1. Risks Related to the Group's Activity

1.5.1.1. The Group is heavily dependent on the successful development, pre-clinical or clinical, of NBTXR3.

The Group's business and future success depends heavily on its ability to develop and market its lead product candidate, NBTXR3, which is, at the date of the Universal Registration Document, being evaluated in several clinical trials worldwide. Through a partnership with the University of Texas MD Anderson Cancer Center, the Company's clinical program will include several clinical trials on several different types of cancer. The Group's success also depends on its ability to satisfy the necessary regulatory requirements for its marketing and sale. At the date of the Universal Registration Document, the NBTXR3 development programs for the treatment of different cancer indications are at varying

stages (from the pre-clinical stage in different oncological indications to the CE-marking in the STS indication).

In order to, as the case may be, obtain the requisite regulatory approvals or successfully complete the necessary conformity assessment procedures, the Group conducts clinical and preclinical programs for product candidates with the ultimate goal of marketing therapeutic solutions that aim to transform cancer treatments that rely on radiotherapy.

Preclinical testing and clinical trials are long, expensive and unpredictable processes that can encounter extensive delays. The Group cannot guarantee that clinical trials will be conducted as planned or completed on schedule, if at all.

In connection with clinical testing and trials, the Group faces a number of risks, including:

- A product candidate may be ineffective, inferior to existing approved treatments, unacceptably toxic, or have unacceptable side effects (both immediate or long-term);
- Patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;
- Extension studies on long-term tolerance may invalidate the use of the product;
- Results may not confirm the positive results of earlier testing or trials;
- The independent data monitoring committee assigned to review the Group's testing and trials may identify potential flaws in one or more of its trials or their design and recommend that they not be continued or adjusted;
- Results may not meet the level of statistical significance required by the ANSM, FDA or other regulatory agencies to establish the safety and efficacy of product candidates; and
- Because each of the trials the Group is undergoing or contemplating the NBTXR3 product, were one of these preclinical or clinical trials to reveal any issues regarding safety and/or therapeutic efficacy, the validity of the Group's nanotechnology platform itself could be questioned.

Human clinical trials are very expensive, time-consuming, and difficult to design, implement and complete. Commencement of clinical trials for product candidates may be delayed for a variety of reasons, including delays in:

- Demonstrating sufficient preclinical safety and efficacy to obtain regulatory approval to commence a clinical trial;
- Validating test methods to support quality testing of the product candidate;
- Manufacturing sufficient quantities of the product candidate necessary to conduct clinical trials;
- Obtaining institutional review board approval to conduct a clinical trial at a prospective clinical trial site;
- Determining dosing and clinical trial design; and
- Achieving patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant oncological indication and the eligibility criteria for the clinical trial.

Favorable results of preclinical studies do not necessarily predict clinical success, and larger and later-stage clinical trials may not produce the same results as earlier-stage clinical trials. To date, clinical trials of NBTXR3 in certain oncological indications have generated favorable security and efficacy data; however, the Group may adopt different enrollment criteria in its future clinical trials. Furthermore, the

data from certain clinical trials can only be considered as preliminary. Therefore, it is possible that the Group's results vary from previous clinical trials, or even from preliminary data. Obtaining favorable results in a clinical trial and/or market approval or marketing authorizations for a product in a specific indication (such as the CE-marking for NBTXR3 in the treatment of locally advanced STS) may not be sufficient. These results are not a gauge of effectiveness, job security, or the ability to obtain market approval or marketing authorizations for a product in another indication (such as a possible CE-marking for the treatment of head and neck cancers), regardless of rational scientific connection.

The completion of clinical trials for product candidates may also be delayed, suspended or terminated due to a number of factors, including:

- Adverse events, safety issues or side effects of the product candidates or their formulation;
- Unanticipated events during clinical trials requiring amendments to clinical trial designs or protocols;
- Inability to raise additional capital in sufficient amounts to continue funding clinical trials or development programs;
- Need to sequence clinical trials as opposed to conducting them concomitantly in order to save resources;
- Inability to enter into collaborations relating to the development and commercialization of product candidates;
- Failure to conduct clinical trials in accordance with regulatory requirements or clinical trial protocols;
- Inability to manufacture or obtain from third parties sufficient quantities of product candidates for use in preclinical studies and clinical trials or of raw materials necessary for their manufacture;
- Governmental or regulatory delays and changes in regulatory requirements, policy or guidance from regulatory authorities, including mandated changes in the scope or design of clinical trials or requests for supplemental information with respect to clinical trial results;
- Delays in patient enrollment, variability in the number and types of patients available for clinical trials, and lower-than-anticipated retention rates for patients in clinical trials;
- Difficulty in patient monitoring and data collection due to a loss of contact with the concerned patients following treatment;
- Varying interpretations of data collected during the Group’s clinical trials by the notified body, ANSM, EMA, FDA or any other regulatory agencies; and
- The need to identify alternative clinical trial sites to replace sites originally appointed for activation in Russia and Ukraine, which sites have been suspended in light of the Russian invasion of Ukraine that commenced in February 2022.

Many of these factors could potentially require additional time and investment in research and development to attempt to remedy the issues identified. It could also ultimately lead to the denial of marketing applications or the failure to complete applicable pre-marketing regulatory requirements (such as CE marking), or even call into question the marketing authorizations already granted for Hensify® or other product candidates, potentially impacting the development of each application of NBTXR3. In addition, due to the Group's limited financial resources, an unfavorable outcome in one or more trials may lead to a delay, reduction in scope, or elimination of one or more product development programs. Lastly, these types of situations could negatively impact the Group's image and, in certain cases, lead to amicable settlements or legal action.

Even though the Group has obtained the CE-marking for Hensify®, the name of NBTXR3 in the indication of locally advanced STS, it cannot be certain that NBTXR3 will receive regulatory approvals in other indications or in other territories or successfully complete the necessary conformity assessment procedures, as applicable, or be successfully commercialized, for any cancer indications, even if the Group successfully completes applicable pre-marketing regulatory requirements (such as a CE-marking). Please refer to sections 1.5.1.3. and 1.5.2.2. of the Universal Registration Document, for more information on these risks.

In February 2020, the Company received Fast Track designation from the FDA for NBTXR3 for the treatment of locally advanced head and neck cancers. Fast Track designation is a process designed to facilitate development and accelerate the review of treatments for serious conditions that have the potential to address unmet medical needs. However, such designation may not lead, in practice, to a faster development or regulatory review or approval process and does not increase the likelihood that NBTXR3 will receive regulatory approval.

1.5.1.2. The commercial success and profitability of NBTXR3 and any other Group's products is not guaranteed

The Group has a limited operating history that, to date, has been focused primarily on research and development and working towards the commercialization of a lead product candidate, NBTXR3. A key element of the Group's strategy is to use and expand its proprietary technology to continue to develop innovative product candidates designed to enhance the efficacy of radiotherapy and to progress these candidates through clinical development for the treatment of a wide variety of cancers. The nanotechnology underlying the Group's product candidates, specifically the use of nanosized radiation enhancers as a cancer treatment method, is a relatively new technology.

As of the date of the Universal Registration Document, the Group is not aware of any other products of the same type as NBTXR3 that have received a marketing authorization by a competent regulatory authority. As a result, the prospects for the development and profitability of NBTXR3 and its acceptance by patients, physicians and payors are uncertain. The Group has not generated any revenue from the sale of NBTXR3 yet and cannot guarantee the profitability of this product in the future.

In addition, given the Group's limited operating history, it does not currently have a sales or marketing infrastructure at the date of the Universal Registration Document and has limited experience in the sale, marketing or distribution of drug or medical device products. The Group may decide to directly market some of its products, by implementing its own sales and marketing organization while entering into arrangements with business partners for future marketing needs with respect to other products.

Factors that may inhibit the Group's efforts to market products on its own include:

- The inability to recruit, train, manage, motivate and retain adequate numbers of sales and marketing personnel. Recruiting and training a sales force is indeed expensive and time-consuming and could delay any product launch;
- Any delay or suspension of the commercial launch of a product candidate for which it has recruited a sales force and established marketing channels, which would lead to a premature or unnecessary investment.
- The inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to adopt any future products as part of a given treatment; and,
- Unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Indirect marketing, through partners, may also be limited by several factors (for more details on these risk factors, see section 1.5.2.2. of the Universal Registration Document.

Furthermore, candidates may not be commercialized for other reasons, including:

- Being subject to proprietary rights held by others (see section 1.5.3. of the Universal Registration Document);
- Being difficult or expensive to manufacture on a commercial scale;
- Failing to compete effectively with products or treatments commercialized by competitors, some of which, either alone or in collaboration with their business partners, may have significantly greater financial resources and expertise in research and development, preclinical testing, clinical trials, manufacturing, and marketing;
- Failing to show that the long-term benefits of Group products exceed their risks; or
- Shifting Group commercialization strategy based on its view that the market no longer supports commercialization of a particular product candidate.

Even if the Group successfully completes applicable pre-marketing regulatory requirements for the commercialization of a product candidate, the resulting approval or certification may carry conditions that limit the market for the product or put the product at a competitive disadvantage relative to alternative therapies. These restrictions could make it more difficult to market the product effectively.

Furthermore, the Group's ability to market any product candidates successfully will also depend in part on the extent to which coverage and adequate reimbursement for these products is available from governmental authorities and other third-party payors. Such entities determine which therapeutic treatments should be covered and establish reimbursement levels. Coverage and reimbursement may impact the demand for, or the price of, any Group product. If the Group is unable to have its products covered and reimbursed or if the level of reimbursement granted to such products is not sufficient or adequate for the medical community and patients' expectations, it may not successfully market NBTXR3 or any other product candidate for which it successfully completes the applicable pre-marketing regulatory requirements. In addition, due to the extensive number of third-party payors, the Group's products' coverage determination process may be costly and time and resource-consuming.

Notwithstanding the European marketing approval for NBTXR3 in the STS indication, the Group has not yet undertaken any commercialization activities. Following evaluation of the results from study 102 and NANORAY-312, the Group expects to undertake a strategic review and to determine where it believes it is best positioned to pursue commercialization, including its commercialization strategy with respect to Hensify® (the brand name of NBTXR3 in the STS indication).

1.5.1.3. The Group's business is governed by a rigorous, complex and evolving regulatory framework.

The development, screening, manufacturing and commercialization of therapeutic solutions for cancer treatment are governed by a rigorous, complex and evolving global regulatory environment (for more information on such environment, see Section 1.3.17. of the Universal Registration Document). Regulatory authorities, including the ANSM and the FDA, have imposed stringent requirements on the amount and types of data required to demonstrate the safety and efficacy of products prior to their marketing and sale. Moreover, following its initial approval or certification, any product approved for commercialization is reassessed on a regular basis in terms of its patient risk/benefit ratio. The potential discovery of new defects or side effects which were not detected during development and clinical trials can result in restrictions on sale, the suspension or withdrawal of the product from the market and an increased risk of litigation. Extensive restrictive global regulation has increased the cost of obtaining and maintaining the necessary marketing authorizations for therapeutic oncology solutions

and the costs related to the completion of the necessary conformity assessment procedures for these products. This increase in costs may limit the economic value of a new product and thus lessen the prospects for growth in this field, and consequently the prospects of the Group's product candidates.

In addition, clinical studies for Hensify® and the Group's other product candidates must be submitted to the relevant regulatory authorities of the countries in which the studies will be carried out. A negative opinion from such a regulatory authority with respect to any of the Group's clinical development programs could suspend or terminate such programs. Moreover, depending on the information provided to regulatory authorities during a clinical trial pursuant to the applicable regulation, particularly about the occurrence of undesirable side effects, the regulatory authorities could decide to suspend or terminate the clinical trial.

NBTXR3 has been classified as a ''Class III medical device'' in the European Union (EU) and as a ''drug'' in the United States. As a result, the Group must meet various specific requirements and deadlines, particularly in terms of CE-marking (or equivalents in all non EU jurisdictions where the Group intends to market its products) and in terms of marketing authorization for drugs in other countries around the globe (chiefly deadlines and conditions for registration, as, where no single authority exists, deadlines tend to be longer) and related transparency requirements. As soon as a product is classified as a drug candidate or medical device as appropriate, a competent authority or a notified body must approve or certify the conformity of said drug candidate or medical device before it can be commercialized, marketed, promoted or sold in those jurisdictions. The Group must provide these regulatory authorities with data from preclinical studies and clinical trials that demonstrate that its product candidates are safe and effective for a defined indication before they can be approved or certified for commercial distribution. It must provide data to ensure the strength, quality and purity of the product and its components. It must also assure the regulatory authorities that the characteristics and performance of the clinical batches will be replicated consistently in the commercial batches.

The regulatory framework may also change, particularly in key markets such as the EU, where rules on medical devices are set to be significantly tightened following the adoption of the MDR regulation (see Section 1.3.17.2. of the Universal Registration Document). Such changes in the regulatory environment could lead to the Group's products being limited to certain indications, being unauthorized for sale, or being ineligible for reimbursement by national authorities. The cost of ensuring compliance with existing regulations to maintain authorizations or certifications obtained previously is already significant and continues to increase. Even if the Group takes into account potential changes in regulations or standards in the countries where it intends to market its products, new regulatory requirements could prevent the Group from marketing its products in the event of marketing authorizations being suspended or withdrawn, or could make manufacturing them more costly and thereby slow down sales.

In light of the regulatory evolutions, the competent authorities of EU Member States could reconsider the classification of NBTXR3 as a medical device in the EU and decide to reclassify it as a drug (see Section 1.3.17.2. of the Universal Registration Document). If Hensify® or the other Group product candidates were to be classified as drugs in the EU, their clinical development would be subject to different regulatory framework. As a result, the development and commercialization process would be longer and more costly than expected. In an effort to minimize the impact of a potential reclassification of our product candidates, we are designing our clinical development programs so as to generate clinical evidence we believe will constitute a robust scientific basis, irrespective of classification.

The Group's current research and development and future commercialization operations expose it to broadly applicable federal and state healthcare laws in the EU, the U.S. and any other country the Group operates in (see Section 1.3.17. of the Universal Registration Document). These laws may impact, among other things, its research, proposed sales, marketing and education programs for product

candidates that successfully complete applicable pre-marketing regulatory requirements. Restrictions under applicable healthcare laws and regulations include:

- Laws and regulations with respect to anti-corruption, fraud and false statements in healthcare, which would apply to products of the Group that are covered by public agencies or third-party payors, including commercial insurers;
- Laws and regulations on marketing and/or transparency to which the Group is subject as manufacturer and producer of healthcare products;
- The laws and regulations relating to the protection of personal data, and in particular GDPR;
- Requirements for transparency on consideration granted to doctors and teaching hospitals and certain investments and interests held by doctors or members of their immediate family; or
- Law and regulations relating to anti-trust or competition.

Many of these laws differ from each other in significant ways and have different effects, thus complicating compliance efforts.

Furthermore, ensuring that the Group's activities and business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. In addition, it is possible that the competent governmental authorities will conclude that the Group's business practices do not comply with current or future healthcare laws, regulations or case law. In this event, the Group could be subject to severe civil, criminal or administrative sanctions, an obligation to pay punitive or contractual damages, or possible exclusion from healthcare programs financed by a country in which the Group markets its products. These actions could also damage the Group's reputation or result in lower profits and future earnings and a decrease in its business. Similarly, failure by a partner, supplier or any other co-contractor of the Group to comply with applicable laws and regulations could have negative consequences for the Group, its business or its reputation.

1.5.1.4. Due to its limited resources and access to capital, the Group's decisions to prioritize development of certain product candidates or certain indications may adversely affect its business prospects.

Because it has limited resources and access to capital to fund our operations, the Group must decide which product candidates to pursue and the amount of resources to allocate to each product. In addition, for product candidates under development, such as NBTXR3, it must decide which indications it intends to develop the product candidate for. As such, at the date of the Universal Registration Document, the Group primarily focused on the development of Hensify® and NBTXR3 in other indications, particularly for the treatment of patients with locally advanced head and neck cancers, while also evaluating other indications and building out a robust immuno-oncology program.

Decisions concerning the allocation of research, collaboration, management and financial resources to particular product candidates, oncological indications or therapeutic areas may not lead to the development of viable commercial products and may divert resources away from more promising opportunities. Similarly, potential decisions with respect to some product development programs may also prove not to be optimal and could cause the Group to miss valuable opportunities, delay or terminate partnerships, or require it to collaborate with third parties. If it does not accurately evaluate the commercial potential or target market for a particular product candidate, the Group may relinquish valuable rights to that product candidate through collaboration, licensing or other arrangements in cases in which it would have been more advantageous to retain sole development and commercialization rights. If the Group makes incorrect determinations regarding the market potential of its product candidates or misreads trends in the field of cancer treatment, its business prospects could be harmed.

1.5.1.5. The COVID-19 pandemic could have a significant impact on the Group's business.

The SARS-CoV-2 coronavirus pandemic, which spread over the world in the first half of 2020, has resulted in significant and evolving health threats in many countries, including countries in which the Group's clinical trials are planned or ongoing, such as France or the United States. As a result of the measures implemented by governmental authorities in their territories as well as on their border, which have in the past and, in certain countries, may still restrict the free movement of persons and goods, as well as of proactive measures taken by the Group, its suppliers and services providers to protect the health and safety of employees, the Group has experienced, and expects to continue to experience, disruptions and adverse impacts to its business, including delays in certain clinical trial activities, future projects and financial situation.

The degree to which the COVID-19 pandemic will ultimately impact the Group will depend on future developments, which are highly uncertain, in particular due to lock-down measures that have been and may be implemented in the future, and cannot be predicted. However at this stage, the Company believes that the main risk factors that the Group could face in this context are the following, it being specified this list is not exhaustive:

- disruptions or interruptions of the Group's clinical trial activities, whether conducted by the Group or in collaboration with its partners (such as MD Anderson), due in particular to delays or difficulties in recruiting patients, limitations or redirection of human or material resources normally allocated to these clinical trials, delays in receiving, or even lack of, the supplies and materials necessary for the performance of clinical trials, or travel restrictions imposed or recommended by local authorities (see Sections 1.5.1.1. and 1.5.2.2. of the Universal Registration Document);
- changes in local regulations due to the measures taken in response to the COVID-19 pandemic, which required the Company to modify the conditions of its clinical trials, resulting in unforeseen costs or even the interruption of these trials;
- delays in obtaining from regulatory authorities the approvals required to launch the clinical trials contemplated by the Company, as well as delays in the necessary interactions with local authorities or other important organizations and third-party partners (see Sections 1.3.17 and 1.5.1.3 of the Universal Registration Document);
- the refusal of regulatory authorities such as the FDA, the ANSM or the EMA to accept data from clinical trials conducted in these affected geographic areas (see Sections 1.3.17 and 1.5.1.3 of the Universal Registration Document);
- overall reduced operational productivity, including interruptions to our research and development activity, resulting from challenges associated with remote work arrangements and limited resources available to employees working remotely, as well as a potential decrease in Group employees' engagement following short-time working measures or long periods of remote work in particular during lockdown periods; or
- difficulties in accessing, in a timely manner or on acceptable terms, financing opportunities as a result of dislocations in the capital markets, liquidity constraints on potential commercial partners, and general disruptions to global and regional economies. (see Section 1.5.4.1. of the Universal Registration Document).

At the date of the Universal Registration Document, the Company remains in position to deliver data from its priority pathways in head and neck cancer and immuno-oncology on schedule. While recruitment and monitoring have slowed due to the crisis, delivery of data in these areas will proceed as planned based on patients already recruited.

1.5.1.6 Investments in the Company may be subject to prior governmental authorization under the French foreign investment control regime.

The Group is a clinical-stage biotechnology company focused on developing first-in-class product candidates that use its proprietary nanotechnology to transform cancer treatment by increasing the efficacy of radiotherapy.

Pursuant to the provisions of the French Monetary and Financial Code (code monétaire et financier), any investment:

i. by (a) any non-French citizen, (b) any French citizen not residing in France, (c) any non-French entity or (d) any French entity controlled by one of the aforementioned persons or entities;

ii. that will result in the relevant investor (a) acquiring control (within the meaning of article L. 233-3 of the French Commercial Code) of an entity registered in France, (b) acquiring all or part of a business line of an entity registered in France, or (c) for non-European Union or non-European Economic Area's investors crossing, directly or indirectly, alone or in concert, a 25% threshold of voting rights in an entity registered in France; and

iii. where this entity registered in France is developing activities in certain strategic industries related to (a) activity likely to prejudice national defense interests, participating in the exercise of official authority or are likely to prejudice public policy and public security (including weapons, double-use items, IT systems, cryptology, date capturing devices, gambling, toxic agents or storage of data), (b) activities relating to essential infrastructure, goods or services (including energy, water, transportation, space, telecom, public health, farm products or media), and (c) research and development activity related to critical technologies (including cybersecurity, artificial intelligence, robotics, additive manufacturing, semiconductors, quantum technologies, energy storage or biotechnology) or dual-use items,

is subject to the prior authorization of the French Ministry of Economy, which authorization may be conditioned on certain undertakings.

Additionally, in the context of the ongoing COVID-19 pandemic, the Decree (décret) n°2020 892 dated July 22, 2020, as amended by the Decree (décret) n°2020-1729 dated September 28, 2020 and by the Decree (décret) n°2021-1758 dated December 22, 2021, has created a new 10% threshold of the voting rights applicable until December 31, 2022 for the non-European investments in listed companies, in addition to the 25% above-mentioned threshold for certain activities.

A fast-track procedure shall apply for any non-European investor exceeding this 10% threshold who will have to notify the Minister of Economy who will then have 10 days to decide whether or not the transaction should be subject to further examination.

On November 5, 2020, the French Ministry of Economy informed the Company that its activities are subject to the foreign investment control regime described above. Therefore, investments in the Company meeting the above criteria are subject to prior authorization by the French Ministry of Economy.

Any investor willing to acquire of all or part of the Group's business or to cross the above-mentioned share capital thresholds may be subject to this prior governmental authorization. In such circumstances, the Company cannot guarantee that such investor will obtain the necessary authorization in due time. The authorization may also be granted subject to conditions that may deter a potential purchaser. The existence of such conditions to an investment in the Company could have a negative impact on the ability of the Company to raise the funds necessary to its development.

Similarly, certain existing investors could be subject to this control regime if regulatory thresholds are crossed due to the allocation of double voting rights in their favor.

In addition, failure to comply with such measures could result in significant consequences on the applicable investor (for a description of such consequences, see Section 1.3.17 of the Universal Registration Document). Such measures could also delay or discourage a takeover attempt, and we cannot predict whether these measures will result in a lower or more volatile market price of our ADSs or ordinary shares.

For more details on the French foreign investment control regime, see Section 1.3.17 of the Universal Registration Document.

1.5.2. Risks Related to the Group's Organization and Operations

1.5.2.1. Claims related to product liability or other lawsuits could divert the Group's resources from other activities, expose it to significant liabilities and reduce the commercial potential of its product candidates.

The risk of being sued on product liability claims is inherent to the development and commercialization of therapeutic products. Side effects, manufacturing defects, or improper physician administration of products that the Group develops could result in the deterioration of a patient's condition, injury or even death.

Although, as of the date of the Universal Registration Document, the Group has never been held liable for its products, in the event that one of these events were to occur, in the future, criminal or civil proceedings might be filed against the Group by patients, physicians, regulatory authorities, pharmaceutical companies or any other third party using or marketing its products. These actions could include claims resulting from acts by Group partners, potential licensees and subcontractors, over which the Group has little or no control. These lawsuits may divert management from pursuing business strategy and incur significant legal fees. In addition, if the Group is held liable in any of these lawsuits, it may incur substantial liabilities, deal with damage to its market reputation, and be forced to limit or forgo further commercialization of the affected products.

Although the Group believes it is sufficiently covered by the product insurance policies it has taken out for its clinical trials, this coverage may prove insufficient or ineffective to offset expenses or losses that the Group may incur (see Section 1.5.5. of the Universal Registration Document).

1.5.2.2. The Group relies on third parties who carry out its clinical trials and the collection and analysis of related data, with which it has entered or may enter into partnership in the future for the development and marketing of Hensify® and its other product candidates, and for the supply of various materials required for the production of all or part of its product candidates.

At the date of the Universal Registration Document, the Group relies, and expects to continue relying, on medical institutions, clinical research centers and research partners to carry out clinical trials and to perform data collection and analysis and, more generally, to develop certain of its product candidates. For example, LianBio, the Group's collaboration partner in the Asia-Region, has undertaken to contribute to enrollment in five global registrational studies for NBTXR3 (see Section 1.3.13. of the Universal Registration Document). The Group is also collaborating with MD Anderson on the development of NBTXR3 in various indications (e.g. head and neck, pancreatic, thoracic and lung cancers, etc.). Even if the Group managed to establish a relationship of trust with its existing associates and partners, it has limited control over them. In addition, since the Group faces competition in seeking

partnerships, it cannot guarantee that, when the time comes, it will be able to identify a suitable partner or enter into a partnership under the most favorable commercial conditions for the Group.

Development activity or clinical trials, as well as the marketing of products, conducted in collaboration with third parties may be delayed, suspended, or terminated if:

- Said third parties cannot devote or do not wish to devote a sufficient amount of time or effort to the proper performance of the Group's activities (due to internal constraints, such as budget limitations, lack of human resources or a change in strategic direction);
- Said third parties otherwise fail to meet regulatory obligations or expected deadlines or are unable to obtain, or believe they are unable to obtain, the required regulatory approvals or certifications;
- Said third parties delay the development or marketing of the Group's product candidates in favor of the development or marketing of another party's product candidates and, more generally, decide to develop a competing product outside of the collaboration agreement entered into with the Group;
- The quality or accuracy of the data obtained by third parties is compromised due to their failure to adhere to clinical protocols, regulatory requirements, or for other reasons;
- Said third parties challenge, including through legal channels, the performance of their obligations under the partnership, whether regarding development or marketing, the payment of expenses relating to the work carried out or the potential allocation of the revenue generated; or
- The Group changes one of its third-party partners.

The occurrence of one of these events may increase the Group's development costs, delay its ability to obtain regulatory approval or successfully complete pre-marketing certification procedures, and delay or prevent the commercialization of product candidates. The Group could also be held liable for the actions of its business partners, over which it has little or no control (see Section 1.5.2.2. of the Universal Registration Document).

While the Group believes that in many cases there are alternative service providers, it may not be able to enter into replacement arrangements without incurring delays or additional costs. The Group would in particular have to demonstrate that the change has no impact on the quality of its products. Furthermore, in the event of a default, bankruptcy or shutdown of, or a dispute with, a third party, the Group may be unable to enter into a new agreement with another third party on commercially acceptable terms.

The Group is also dependent on third parties for the supply of various materials that are necessary to manufacture Hensify® and its other product candidates for clinical trials. Although the Group has entered into agreements related to the supply of the raw materials used in the manufacture of nanoparticles, the supply could be reduced or interrupted at any time. In such case, the Group may not be able to find other suppliers of acceptable materials in appropriate quantities at a reasonable cost. Should it lose key suppliers or the supply of materials be diminished or discontinued, or in the event of a major or international crisis impacting mining or the extraction of minerals in certain regions, the Group may not be able to continue to develop, manufacture and market Hensify®, NBTXR3 or any other product candidate in a timely and competitive manner. In addition, these materials are subject to stringent manufacturing processes and rigorous testing. Delays in the completion and validation of facilities and manufacturing processes of these materials could adversely affect the Group's ability to complete trials and market its products in a cost-effective and timely manner. If it encounters difficulties in the supply of these materials, chemicals or other necessary products, or if it were unable to maintain its supply agreements or establish new supply agreements in the future, or incurred

increased production costs as a result of any of the above, product development and business prospects could be significantly compromised.

The production of NBTXR3 for use in clinical trials is contracted out to a number of manufacturers specialized in the manufacturing of high-precision products. In addition, the Group recently expanded its own manufacturing capabilities by opening an internal research and innovation center facility in Villejuif, just outside of Paris, France. The Group and its third-party manufacturers are subject to continuous and periodic regulatory inspections by the competent national authorities in EU Member States, the EMA, the FDA and other regulatory bodies to ensure compliance with the Current Good Manufacturing Practices (''**CGMP**'') and the guidelines of the International Organization for Standardizations (''**ISO**'').

Although the Group has trained its third-party manufacturers so as to ensure the proper implementation of its production methods and has taken the necessary steps to ensure adequate quality control through, in particular, the implementation of a monitoring system, it has limited control over the activities of these subcontractors. Any failure to follow and document adherence by the Group or its third-party manufacturers to CGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical trials. It may also result in a clinical trial being terminated or put on hold or may delay or prevent filing or approval of marketing applications or the completion of pre-marketing certification procedures, as applicable, for Group products.

Failure to comply with the applicable regulations could also result in the ANSM, EMA, FDA or other applicable regulatory authorities taking various actions, including:

- Levying fines and other civil penalties;
- Requiring the Group to suspend or put on hold one or more clinical trials;
- Suspending or withdrawing regulatory approvals or certifications;
- Delaying or refusing to approve pending applications or supplements to approved applications;
- Requiring the Group to suspend manufacturing activities or product sales, imports or exports;
- Requiring the Group to communicate with physicians, hospitals and other stakeholders about concerns related to actual or potential safety, efficacy, and other issues involving its products;
- Ordering or requiring product recalls or seizures;
- Imposing operating restrictions; and
- Seeking criminal prosecutions.

Finally, before any products could be approved for marketing in the United States, the EU or elsewhere, suppliers would have to pass an audit by the applicable regulatory agencies. The Group is dependent on its suppliers' cooperation and ability to pass such audits. Aside from the additional costs generated by these audits, the Group's subcontractors could find themselves unable to manufacture the Group's products in a timely manner and in the quantities required.

1.5.2.3. The Group may be held liable in connection with the use of hazardous chemical products in its business activities.

Research and development processes involve the controlled storage, handling, use and processing of hazardous materials, including toxins and chemical agents or radioactive substances. The risk of accidental contamination or discharge and any resultant injury from these materials cannot be eliminated. Furthermore, EU, U.S. or other local laws and regulations in countries in which the Group operates govern the use, manufacture, storage, handling and disposal of these hazardous materials and specific waste products, as well as the discharge of pollutants into the environment and issues relating to human health and safety. Compliance with environmental laws and regulations may be expensive could prove costly (in particular for the acquisition of appropriate control equipment), require operational changes, and hamper its research and development efforts.

Although, as of the date of the Universal Registration Document, the Group has never been held liable as a result of the use of hazardous chemicals in its business, the Group may be held liable for any injury or contamination resulting from use by the Group or third parties of these materials, and its liability may exceed any insurance coverage and commit all of its assets.

In addition, the Group cannot predict the impact on its business of any changes in applicable environmental legislation and regulations or in their interpretation and implementation.

1.5.2.4. The Group depends on key management personnel and its ability to attract and retain other qualified personnel.

The Group's success depends to a significant degree on the technical skills and continued service of certain members of its management team, particularly Laurent Levy, Ph.D., Chairman of the Executive Board. Although the Company has taken out key person insurance for Laurent Levy and the principal executives of the Group are subject to a non-competition and non-employment clause, the loss of the services of any member of the management team could have a material adverse effect on the Group.

The Group's success will also depend on its ability to attract and retain additional qualified management, research, medical, regulatory, technical, business development and sales and marketing executives and personnel. The failure to attract, integrate, motivate, and retain additional skilled and qualified personnel could have a material adverse effect on business. The Group competes for such personnel against numerous other companies, including larger, more established companies with significantly greater financial resources. In addition, were the Group to fail to successfully develop and market Hensify® or its other product candidates, it may make it more challenging to recruit and retain qualified personnel.

1.5.2.5. The Group's internal computer systems, or those of third-party subcontractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, internal computer systems, and those of third parties on which the Group relies, remain vulnerable to diverse threats, including computer viruses, malware, unauthorized accesses, natural disasters, acts of terrorism, acts of war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the internet.

Were such an event to occur, it could cause interruptions in Group systems and materially disrupt the Group’s operations. For instance, the loss of clinical trial data for product candidates could result in delays in regulatory approval, certification and commercialization processes. In addition, system redundancy may be ineffective or inadequate. The Group may be unable to retrieve lost data or may have to mobilize significant human and financial resources in order to recover said data. In addition, Group data or applications as well as data or applications relating to Group technology or product candidates may be damaged. Finally, confidential or proprietary information could be disclosed.

The Group could incur liabilities, damage to its reputation, and see delays in the further development of product candidates. In addition, it may not have adequate or effective insurance coverage to compensate for any losses associated with such events (see Section 1.5.2.1. of the Universal Registration Document).

1.5.2.6. Use of social media may materially and adversely impact the Group's reputation.

Rumour or inaccurate or negative information concerning or affecting the Group, including information regarding its products, product candidates or proprietary nanotechnology, may be posted on social media platforms and other similar tools at any time.

The Group may not be afforded an opportunity to redress or correct this rumour or information. Furthermore, such rumour or inaccurate information may require engaging in a defensive media campaign, which may divert the management team's attention or result in an increase in costs. In addition, the medical community and care prescribers could access the rumour or information and act accordingly without further research or verification and without concern for their accuracy. Such platforms also could be used for the dissemination of trade secret information or compromise other valuable company assets, any of which could harm the Group's business.

1.5.2.7. If current or future collaboration partners do not fulfill their obligations, this may cause delays in, or discontinuation of, partner-sponsored clinical trials, reduced revenue potential, and potentially litigation.

The Company's collaboration agreements, and those it may enter into in the future, generally require that its collaboration partners use commercially reasonable efforts to advance the development and/or potential commercialization of the Company's product candidates for certain indications and in specified geographies, typically in accordance with a jointly approved development plan. Such collaboration agreements generally include dispute resolution procedures, which permit both the Company and its collaboration partners to terminate the collaboration under certain circumstances, including upon any uncured material breach of the agreement. The failure of any collaboration partner to fulfill its obligations under a collaboration agreement may result in delays in clinical trial activities or the discontinuation of clinical trials sponsored and conducted by the Company's collaboration partner, which could limit the geographies in which the Company is able to effectively develop and commercialize its product candidates. Early termination of any collaboration agreement could result in additional costs and the loss of potential revenue opportunities. In addition, early termination of any collaboration agreement could result in disputes over intellectual property rights, responsibility for incurred costs or rights with respect to future revenue, which could lead to arbitration, litigation or other dispute resolution mechanisms. Disputes or litigation involving a collaboration partner may make it difficult for the Company to enter into a new agreement with another third party on commercially acceptable terms.

1.5.2.8. The Company may identify material weaknesses or otherwise fail to maintain an effective system of internal control over financial reporting, and as a result, investor confidence in the Company and the value of its shares could be materially and adversely affected.

As a public company in the United States, the Company is required to establish and maintain internal control over financial reporting. Pursuant to Section 404(a) of the United States Sarbanes- Oxley Act it is required to furnish a report by its management that assesses its internal control over financial reporting as of year-end in its Annual Reports on Form 20-F.

Prior to the issuance of the Company's interim financial statements as of and for the six months ended June 30, 2021, a deficiency, which constituted a material weakness[(1)] in its internal control over

financial reporting, was identified[1]. See Section 2.4.1.2.8 of the Universal Registration Document for more information.

Even though the identifies deficiency has since been remedied, the Company cannot guarantee that it will be able to maintain an effective system of internal control over financial reporting. In addition, the Company may discover other control deficiencies in the future, and it cannot be certain that it will not have a material weakness in future periods. Should the Company be unable to maintain such system or identify any new material weaknesses, the reliability of its financial reporting, investor confidence in the Company and the value of its shares could be materially and adversely affected.

(1) A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the Company's annual or interim financial statements will not be prevented or detected on a timely basis.

1.5.3. Risks Related to Intellectual Property

1.5.3.1. A dispute concerning the infringement or misappropriation of intellectual property rights or the intellectual property rights of others could be time-consuming and costly, and an unfavorable outcome could harm the Group.

There is significant litigation in the fields of pharmaceutical and medical device development regarding patent and other intellectual property rights. While the Group is not currently subject to any pending intellectual property litigation from any of its competitors, and is not aware of any such threatened litigation, it may be exposed to future litigation by third parties based on claims that its products, product candidates, processes, technologies or activities infringe on the intellectual property rights of others.

If the Group's development activities are found to infringe on any such patents, it may have to pay significant damages or seek licenses to such patents. A patentee could prevent the Group from using patented drugs, medical devices or compositions. The Group may need to resort to litigation to enforce a patent issued to it, to protect trade secrets, or to determine the scope and validity of third-party proprietary rights. From time to time, it may hire scientific personnel or consultants formerly employed by other companies involved in one or more areas similar to the activities conducted by the Group. The Group, including its personnel and its consultants, may be subject to allegations of trade secret misappropriation or other similar claims as a result of prior affiliations. Regardless of its outcome, a legal dispute could take up a large part of the Group's managerial and financial resources. It may not be able to afford the costs of such legal dispute. Any court ruling against the Group or its employees could require the Group to pay damages, limit its ability to develop or market products, or license all or parts of its products on unfavorable terms.

1.5.3.2. The Group's ability to compete may decline if it does not adequately protect its intellectual property proprietary rights.

The Group's commercial success depends in part on obtaining and retaining rights to its intellectual property and that of its partners granting it a license to such rights (the licensors), as well as on defending these rights against third parties. The Group will be able to protect its products, product candidates, processes and technologies from unauthorized use by third parties only if they are covered by valid and enforceable patents or effectively protected trade secrets. The Group's ability to obtain patent protection for its products, product candidates, processes and technologies is uncertain due to several factors, including:

- The Group or its licensors may not have been the first to invent the technology covered by its or their pending patent applications or issued patents;
- The Group cannot be certain that it or its licensors were the first to file patent applications covering products, product candidates, processes or technologies, as patent applications in the United States and most other countries are confidential for a period of time after filing;
- Third parties may independently develop identical, similar or alternative products, product candidates, processes and technologies;
- The disclosures in the Group's or its licensors' patent applications may not be sufficient to meet the statutory requirements for patentability;
- Any or all of the Group's or its licensors' pending patent applications may not result in issued patents;
- The Group or its licensors may not seek or obtain patent protection in countries or jurisdictions that may eventually provide a significant business opportunity;
- All patents issued to the Group or its licensors may not provide a basis for commercially viable products, product candidates, processes and technologies, may not provide any competitive advantages, or may be successfully challenged by third parties, which may result in the Group's or its licensors' patent claims being narrowed, invalidated or held unenforceable;
- The Group's or its licensors' products, product candidates, processes and technologies may not be patentable;
- Third parties may design around the Group's or its licensors' patent claims to produce competitive products, product candidates, processes and technologies that fall outside of the scope of the Group's or its licensors' patents;
- Third parties may identify prior art or other bases upon which to challenge and ultimately invalidate the Group's or its licensors' patents or in any case render them unenforceable.

As patent applications can take many years to issue, there may be currently pending applications unknown to the Group that may later result in issued patents that its products, product candidates, processes or technologies may infringe. These patent applications may have priority over patent applications filed by the Group or its licensors.

Group employees may claim intellectual property rights over, or demand compensation with respect to, inventions they helped to develop. The Group may not be able to negotiate intellectual property rights or compensation that is sufficient or under acceptable conditions for the inventions resulting from the use of the rights claimed by these employees. The terms of such agreements could also conflict with previous agreements.

The Group patent lives may not be sufficient to effectively protect Group products and business. Obtaining and maintaining a patent portfolio involves significant expenses and substantial resources. For this reason, the Group and its licensors could choose to waive the protection of specific inventions

or even deliberately or involuntarily terminate their patents or patent applications, resulting in a partial or complete loss of the patent rights in the relevant jurisdiction.

Even if the Group has or obtains patents covering its products, product candidates, processes and technologies, it may still be barred from making, using and selling products, product candidates, processes and technologies because of the patent rights of other market players, covering products, processes or technologies that are similar or identical to the Group's.

Similarly, patents held by the Group or its licensors could be subject to claims or other administrative proceedings. The Group's intellectual property could also be challenged due to potential changes or differences in interpretation with respect to patents in countries where the Group works to protect its intellectual property. Lastly, the Group's intellectual property could be called into question in the event of a dispute involving the Group (see Section 1.5.3.1. of the Universal Registration Document).

Such events associated with patents held by or applied for by the Group or its licensors could lead to the refusal or the reduction in scope of other patents held by or applied for by the Group or its licensors.

Furthermore, even if they are not challenged, the patents held by or applied for by the Group or its licensors may not adequately protect the Group's products, product candidates, processes or technologies, or may not prevent third parties from designing products or technologies that are similar or identical to those of the Group. Similarly, current or potential partners of the Group could be discouraged from working alongside the Group in the development or even the marketing of its products.

Any of these events could limit the Group's ability to capitalize on the full market potential of its inventions and could severely hinder its ability to develop and market its product candidates or sell its products, once approved.

In addition to patent protection, because the Group operates in the highly technical field of the development of therapies using nanotechnology, it relies in part on trade secret protections in order to protect its proprietary technology and processes. However, trade secrets are difficult to protect and require monitoring of unauthorized uses and disclosures. The Group enters into non-disclosure agreements with employees, consultants, external collaborators, sponsored researchers and other advisors. In addition to contractual measures, the Group tries to protect the confidential nature of its proprietary information using physical and technological security measures.

The Group cannot guarantee that the steps it has taken to protect its proprietary technologies and processes will be effective. The Group cannot guarantee that trade secrets and other proprietary and confidential information will not be disclosed, in particular to its competitors, or that the parties to its confidentiality agreements abide by their terms.

In the event its trade secrets are disclosed, the Group may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time consuming, and the outcome is unpredictable. Certain courts may be less willing to protect trade secrets. Furthermore, proprietary information may be independently developed by others in a manner that could prevent legal recourse by the Group.

If any of the Group's confidential or proprietary information, including trade secrets, were to be disclosed or misappropriated, or if any such information were to be independently developed by a competitor, its competitive position and activities could be harmed.

Some of the Group's patents may be eligible for a limited patent term extension under regulation in the EU, the United States or other countries. If the Group is unable to obtain patent term extension or the

term of any such extension is less than the Group requested, the period during which it can enforce its patent rights for that product will be shortened and its competitors may obtain approval to market competing products sooner.

1.5.3.3. In the event the Group's trademarks and trade names are not adequately protected, the Group may not be able to build name recognition in its markets of interest.

The Group's registered or unregistered trademarks or trade names may be challenged, infringed on, circumvented, declared generic or determined to be infringing on other marks. The Group may not be able to protect its rights to these trademarks and trade names, which it needs to build name recognition in its markets of interest, or may be forced, following possible lawsuits brought by partners or customers, to stop using said names and trademarks. If the Group is unable to establish name recognition based on trademarks and trade names, it may not be able to compete effectively, and business may be adversely affected.

1.5.4. Financial and Market Risks

The accounting data included in the paragraph comes from the Company's annual financial statements for the years ended December 31, 2020 and 2021.

1.5.4.1. The Group will require additional funding, which may not be available on acceptable terms or at all. Failure to obtain this necessary capital in time may force the Group to delay, limit or terminate its product development efforts or other operations.

The process of developing the Company's candidates is expensive, lengthy and risky. The Group expects its research and development expenses to increase substantially as it continues to develop NBTXR3 through its clinical development programs and identify new product candidates for development. Further, as a result of its increasing commercialization efforts with respect to NBTXR3 and the costs of operating as a publicly listed company, the Company expects its selling, general and administrative expenses to increase significantly in the next several years.

As of December 31, 2021, the Group had cash and cash equivalents of €83.9 million. The Company believes that its cash and cash equivalents will be sufficient to fund its operations until Q2 2023.

However, in order to continue its ongoing research and development efforts, pursue regulatory approval and certification, and advance its commercialization efforts, the Group will require substantial additional funding. Also, the Group's operating plan, which includes product candidate development plans, may change as a result of many currently unknown factors and it may need to seek additional funds sooner than planned, through public or private equity or debt financing, government or other third-party funding, marketing and distribution arrangements and other strategic alliances and licensing arrangements, or a combination of these approaches.

Furthermore, even if the Group believes it has sufficient funds for current or future operating plans, it may seek in the future additional capital if market conditions are favorable or in light of specific strategic considerations.

Any additional equity or debt financing could lead to several of the following repercussions:

- Shareholders' ownership interest may be diluted, or their rights modified, by the issuance of financial instruments granting specific rights to their holders,
- A portion of the Company's operating cash flow could be dedicated to the periodic payment of principal and interest on one or several loans taken out by the Group,

- The Group could enter into restrictive covenants that impose operating restrictions (debt, capital expenditures, distribution of dividends…),
- The Group may be required to relinquish some technologies, product candidates or revenue streams, license technologies or product candidates on unfavorable terms, or otherwise agree to less favorable or unfavorable terms,
- The Group's management's attention could be diverted from their day-to-day activities.

The Group entered into several loan agreements in particular with the European Investment Bank, Bpifrance Financement and HSBC France (for a description of these agreements, see Section 1.3.14 of the Universal Registration Document). A default in payment of all or part of these loans, in particular due to a request for early repayment by the European Investment Bank could result in other loans contracted by the Group becoming due and payable and have an adverse effect on the Group's reputation and financial position.

For more information on the Group's financial debt, see Note 12 to the consolidated financial statements for the year ended December 31, 2021, prepared under IFRS, in Section 4.1 of the Universal Registration Document.

In addition, the Group finances a part of its operations with the research tax credit (CIR). The Group cannot exclude the possibility that the tax authorities will call into question such credit (from previous or upcoming periods), due notably to changes in regulations or the authorities challenging the methods used to calculate the R&D expenses.

If the Group is unable to obtain funding on a timely basis, in sufficient amounts or under acceptable conditions, its growth prospects could be impaired, share price may decline, and the Group may be required to, among other things:

- Delay or reduce the number or extent of preclinical and clinical trials or eliminate them entirely;
- Grant licenses to Group technology to collaborative partners or third parties; or
- Enter into new collaboration agreements on less favorable conditions than those it would have been able to obtain under different circumstances.

1.5.4.2. The Group has incurred significant losses and anticipates that it will continue to incur significant losses for the foreseeable future.

The Group has not generated significant revenues and has incurred significant operating losses since its inception. To date, revenue and other income have been derived primarily from payments under exclusive license and collaboration agreements and research tax credits.

As of the date of the Universal Registration Document, the Group has not generated significant revenue to date from product sales or royalties, and it does not expect to generate significant revenue from product sales or royalties unless and until product candidates are successfully commercialized. The Group incurred net losses of €47 million for the year ended December 31, 2021.

To date, losses are primarily attributable to expenditures for nanotechnology development and the implementation of its clinical and preclinical programs. The Group expects to continue to incur significant expenses and losses for the foreseeable future. It anticipates that such expenses and capital requirements will increase substantially as the Group has set itself the following objectives:

- Continuing preclinical and clinical programs currently in progress;
- Expanding the scope of current clinical trials and launching new clinical trials to research new oncological applications for its nanotechnology;
- Expanding manufacturing capabilities for the production of product candidates and ensuring compliance with applicable manufacturing regulatory requirements;
- Seeking regulatory and marketing approvals, or implementing the necessary conformity assessment procedures, as applicable, for product candidates that successfully complete clinical trials;
- Establishing a market access, sales, marketing and distribution infrastructure to commercialize any products which may have successfully completed the applicable pre-marketing regulatory requirements;
- Advancing research and development efforts, which may include the acquisition of new technologies, products or licenses;
- Maintaining, protecting and expanding its intellectual property portfolio;
- Attracting new and retaining existing skilled personnel.

The amount of future net losses will also depend on Group's ability to raise equity through its marketing activities as well as the Group's ability to obtain funding through commercialization activities, through equity or debt financing or through research grants or collaborative partnerships.

The net losses incurred may fluctuate significantly from year-to-year or even from quarter-to-quarter, such that a period-to-period comparison of operating results may not be a good indication of future performance. In any particular period or periods, operating results could be below the expectations of securities analysts or investors, which could cause the price of shares to decline.

1.5.4.3. Shareholder participation could be diluted

Since its creation, the Company has issued or awarded stock options (OSA), warrants *(bons de souscription d'actions* or BSA), founders' warrants (*bons de souscription de parts de créateur d'entreprise* or BSPCE) and free shares (*actions attribuées gratuitement* or AGA).

As of the date of the Universal Registration Document, the full exercise of all instruments granted and outstanding giving access to the capital (assuming that all the conditions for the exercise or grant of such instruments are met) would lead to the subscription of 2,822,325 new shares representing a potential dilution of up to 8.01% on the basis of current capital (for a summary of the dilutive instruments issued by the Company and currently outstanding, see Section 5.1.4.5. of the Universal Registration Document).

In addition, the Company's shareholders could see their participation be diluted in the event that the Company raises additional capital through a capital increase or an issue of convertible financial instruments, in particular if such an increase is carried out without shareholders' preferential subscription rights.

In the future, as part of its incentive policy for managers and employees, and in order to attract new skill sets, the Company could issue or award new shares or financial instruments granting access to its

capital, which would lead to additional, potentially significant dilution for current and future shareholders.

1.5.4.4. Future use of tax loss carryforwards could be called into question

As of December 31, 2021, after taking into account the net loss for the period, the Company reported a tax loss carryforward of €284 million in France and $3.4 million in the United States, compared to €235 million in France and $4.4 million in the United States as of December 31, 2020.

Tax losses in France (i) can be carried forward for an unlimited period of time to be computed against any upcoming benefit-making result, being noted that (ii) such computation is capped annually at €1 million, plus 50% of the portion of profits in excess of that limit. The unused loss balance can be carried forward to upcoming periods under the same conditions.

As tax loss carryforwards, for the U.S. entity were generated before January 1, 2018, they will expire 20 years after they were generated. The tax loss carryforwards in the U.S. comply with the federal and each state's Net Operating Loss rules updated by the Tax Cuts and Jobs Act of 2017.

It is possible that, due to upcoming changes in corporate taxation in France, in the United States, or in any other relevant country, previous tax loss carryforwards to future revenues are called into question, in part or in whole, or, if it is not already the case, limited in time. In addition, tax losses would in principle be voided if ever the Company undertakes a "change of activity" under the meaning of French tax law, defined as any addition, cessation or transfer of an activity resulting in a variation of (i) the turnover or (ii) the average number of employees and the gross amount of the company's fixed assets, of more than 50% (in the fiscal year of its occurrence or in the following fiscal year, compared to the fiscal year preceding that of such addition, cessation or transfer).

1.5.4.5 The dual listing of the Company's shares requires the implementation of costly and complex compliance procedures.

Due to the listing of its shares, in the form of ADSs, in the United States on the NASDAQ Global Select Market, the Company is subject to a number of additional laws, rules and regulations, including the Securities Exchange Act and the reporting requirements thereunder, the Sarbanes-Oxley Act, the NASDAQ corporate governance requirements and other applicable securities laws, rules and regulations.

Compliance with these laws, rules and regulations requires the implementation of costly and complex compliance procedures that increases our legal and financial compliance costs, make some activities more difficult, time-consuming or costly, increase demand on our systems and resources and may divert the management's attention from the Group's other concerns.

In addition, the dual listing of the Company's shares on the regulated market of Euronext in Paris and on the NASDAQ Global Select Market in the United States requires compliance with both regulations and thus entails an increase in the legal requirements applicable to the Group, particularly in terms of disclosures of regulated information. The Company may not be able to ensure an equivalent level of disclosure in the information disclosed and published on the two stock exchanges. This may lead to uncertainty as to the determination of the applicable rules and regulations and increase costs related, in particular, to the implementation of good disclosure and corporate governance practices.

Legal actions may be initiated by competitors or third parties on the basis of the regulated information. In addition to the costs and consequences of the Group's potential loss of the legal actions, the legal proceedings themselves and the time and resources required to address them may force the Group to divert resources that would have been allocated to its business.

1.5.5. Insurance and risk coverage

The Group has implemented a policy of covering the main insurable risks with amounts of coverage that it considers compatible with its cash consumption requirements. Total premiums paid for all insurance policies for Nanobiotix S.A. and Nanobiotix Corp. amounted to 789,850 euros in 2020 and 2,241,860 euros in 2021.

The Company has taken out a number of policies, the main ones being as follows:

- A general civil liability policy which encompasses :
  - "product liability" coverage for damages caused to third parties, occurring in the context of professional activity with a total annual coverage limit of €10,000,000 and various sub-limits
  - “operations civil liability" coverage (Responsabilité Civile Exploitation) for damage, including bodily injury, caused to third parties and resulting from events occurring during the declared activities of the Company, whether inside or outside the Company, but not resulting from the performance of services, with a total annual coverage limit of €7,500,000 and various sub-limits;
- A “shipment, stock and transport of goods” policy, covering risks related to the worldwide shipment, stock and transport of the Group's products, with a total annual coverage limit of €1,400,000;
- A “staff business travel” policy, covering air and ground travel risks as well as certain damages that may occur during business travel by the Group’s staff, with a total annual coverage limit of €75,000,000, both ground and air travel risks included;
- A “Cyber Risk” policy, covering risk related to IT system.
- Two “Directors and officers liability” policies providing coverage for the civil liability for Directors of Nanobiotix and including an IPO coverage with a total annual limit of €20.000.000 and $1,000,000 for Nanobiotix Corp.;

In addition, the liability arising from the Group's clinical trials is covered by specific policies, the pricing and amounts of which depend on the local regulations applicable to the relevant clinical investigation center, the number of clinical trials, their location and the expected number of patients to be included in these clinical trials.

The Group cannot rule out the possibility that its liability may be sought beyond the coverage limits or for events that are not covered by the insurance policies it has taken out. The Group could thus be required to pay substantial compensation or incur expenses that would be partially reimbursed or not reimbursed at all by its insurers. The occurrence of one of these risks could have a significant impact on the Group's business, results, financial position and development.

The Group can not ensure that it will be able to maintain or underwrite equivalent guarantees at a reasonable price; meaning that the Group could be led to underwrite policies at higher prices and/or to bear higher risks as its activities will grow.

1.5.6. Legal and arbitration proceedings

To date, there are no governmental, legal or arbitration proceedings, including all proceedings of which the Company is aware and all pending or potential proceedings, that are likely to have or have had over the last 12 months any significant effect on the Group's financial position or profitability.

2. CORPORATE GOVERNANCE

2.1. ADMINISTRATIVE AND MANAGEMENT BODIES

2.1.1. Composition of the Company's Executive and Supervisory Boards

As of the date of the Universal Registration Document, the Executive Board and supervisory board of the company (the "**Supervisory Board**") consist of:

2.1.1.1. Executive Board composition

The composition of the Executive Board evolved in the course of 2021. On May 31, 2021, Philippe Mauberna resigned from his office of Executive Board member, effective immediately as well as from all other positions he holds within the Group. On the Same date, the Supervisory Board appointed Bart Van Rhijn to replace him as a member of the Executive Board.

As of the date of the Universal Registration Document, the Executive Board's composition is as follows:

Name	Corporate office	Main role in the Company	Main role outside the Company	Date of first appointment	End date of corporate office
Laurent LEVY	Chairman, Executive Board	Company Officer	None	05/27/04	Reappointed by the Supervisory Board on March 13, 2020, for a four-year term starting on April 28, 2020 and expiring at the end of the shareholders' meeting called to approve the financial statements for the financial year ending December 31, 2023.
Bart VAN RHIJN	Member of Executive Board	Administrative & Financial Officer	None	05/31/21	Appointed by the Supervisory Board on May 31, 2021, for the duration of the Executive Board's term of office, i.e. until the end of the shareholders' meeting called to approve the financial statements for the financial year ending December 31, 2023.
Anne-Juliette HERMANT	Member of Executive Board	Human Resources Officer	None	07/01/19	Reappointed by the Supervisory Board on March 13, 2020, for a four-year term starting on April 28, 2020 and expiring at the end of the shareholders' meeting called to approve the financial statements for the financial year ending December 31, 2023.

The professional address of Laurent Levy and Anne-Juliette Hermant is the registered office of the Company and Bart Van Rhijn's is the registered office of Nanobiotix Corp.

2.1.1.2. Supervisory Board composition

The composition of the Supervisory Board evolved in the course of 2021. On May 25, 2021, Laurent Condomine, member and chairman of the Supervisory Board, resigned with immediate effect. To fill this vacancy, on the same date, the Supervisory Board appointed Gary Phillips as a member of the Supervisory Board for the remainder of Laurent Condomine's term of office, subject to the ratification of the appointment by the next ordinary shareholders' meeting, and elected him as chairman of the Supervisory Board. Gary Phillips was also appointed on such date as a member of the Supervisory Board's audit committee and appointments and compensation committee. As of the date of the Universal Registration Document, the Supervisory Board comprises four members and one observer (*censeur*).

Name	Corporate office	Main role in the Company	Main role outside the Company	Date of first appointment	End date of corporate office
Gary PHILLIPS	Chairman (Independent Member*)	None	President and Chief Executive Officer at OrphoMed, Inc.	Nominated by the Supervisory Board held 05/25/2021, to be ratified by the next ordinary shareholders' meeting	At the end of the shareholders' meeting held to approve the financial statements of the financial year ended on December 31, 2022
Anne-Marie GRAFFIN	Vice-Chairwoman (Independent Member*)	None	Expert consultant for the pharmaceutical industry	Nominated by the Supervisory Board held 12/18/2013, ratified by the shareholders' meeting held 06/18/2014	At the end of the shareholders' meeting held to approve the financial statements of the financial year ended on December 31, 2023
Alain HERRERA	Independent Member	None	Managing Director of AOC	Nominated by the Supervisory Board held 12/18/2013, ratified by the shareholders' meeting held 06/23/2013	At the end of the shareholders' meeting held to approve the financial statements of the financial year ended on December 31, 2023
Enno SPILLNER	Independent Member*	None	Financial Officer at Evotec and member of the Management Board	06/18/2014	At the end of the shareholders' meeting held to approve the financial statements of the financial year ended on December 31, 2025
Christophe DOUAT	Observer	Observer	Chief Executive Office at Medincell	06/14/2017	At the end of the shareholders' meeting held to approve the financial statements of the financial year ended on December 31, 2022

** Within the meaning of the Code of corporate governance amended by MiddleNext in September 2021.*

The addresses of Supervisory Board members and of the observer are as follows:

- Gary PHILLIPS, OrphoMed Inc., 50 Francisco Street, Suite 245, San Francisco, CA 94133;
- Anne-Marie GRAFFIN: registered office of the Company;

- Alain HERRERA, Alain Oncology Consulting (AOC), 77 rue de Vaugirard 75006 Paris;
- Enno SPILLNER, EVOTEC, Manfred Eigen Campus, Essener Bogen 7, 22 419 Hamburg, Germany; and
- Christophe DOUAT, Medincell SA, 1 rue Charles Cros, 34830 Jacou.

The expertise and management experience of the members of the Executive and Supervisory Boards stems from the various salaried and management positions they previously held.

Observers to the Supervisory Board

The shareholders' meeting may appoint observers to the Supervisory Board. The Supervisory Board may also appoint observers directly, subject to the ratification of the appointment by the next shareholders' meeting.

Observers are appointed for a term of 6 years, ending at the end of the shareholders' meeting called to approve the financial statements for the past financial year and held in the year during which the appointment expires. Observers may be reelected.

The observers review any questions the Supervisory Board, its Chairman, or the Executive Board may submit to them. They attend the Supervisory Board meetings and take part in the deliberations in a strictly advisory capacity. Their absence does not impact the validity of the Supervisory Board's decisions.

The observers are convened to Supervisory Board meetings under the same conditions as the Supervisory Board members.

Censors are bound by the same duties and obligations as the members of the Supervisory Board, including a duty of loyalty.

The Supervisory Board may compensate the observers by deducting their compensation from the global amount of compensation allocated to the Supervisory Board members by the shareholders' meeting.

2.1.2. Other corporate offices

2.1.2.1. Other current corporate offices outside the Group

As of the date of the Universal Registration Document, the members of the Executive Board exercise the following corporate offices outside the Group:

	Other existing corporate offices	
	Nature of corporate office	**Company or Public Institution**
Laurent LEVY	Chairman of the Supervisory Board	VALBIOTIS*
Bart VAN RHIJN	Treasurer and Secretary	Slice of Media, Inc.
	Member of the Board of Directors	Biochealth Inc
	Venture Partner	1414 Ventures
Anne-Juliette HERMANT	Member of the Board of Directors	Mines-Telecom Institute
	Member of the Scientific Council	Ecole des Ponts Paris Tech
	Member of the Board of Directors	ISEP - Ecole d'ingénieurs du numérique

**Listed Company*

Members of the Supervisory Board

As of the date of the Universal Registration Document, the Supervisory Board members exercise the following corporate offices outside the Group:

	Other existing corporate offices	
	Nature of corporate office	**Company**
Gary PHILLIPS (Independent member)*	President, CEO & Member of the Board of Directors	OrphoMed, Inc.
	Member of the Board of Directors	Aldeyra Therapeutics
	Member of the Board of Directors	Rheon Medical SA
	Member of the Board of Directors	Zyla Life Sciences
Anne-Marie GRAFFIN (Independent Member)*	Member of the Supervisory Board	VALNEVA SE**
	Member of the Board of Directors	SARTORIUS STEDIM BIOTECH SA**
	Managing Director	SMAG CONSULTING
	Member of the Board of Directors	M2Care
Alain HERRERA (Independent Member)*	Member of the Board of Directors	IDDI (Belgium)
	Member of the Board of Directors	FONDATION ARCAD
	Member of the Board of Directors	ISOFOL**
	Member of the Board of Directors	PDC' LINE PHARMA
	Managing Director	AB BIO CONSULTING
	Chief Medical Officer & Member of the Board of Directors	ONWARD Therapeutics SA
	President	Onward Therapeutics France SAS
	Member of the Board of Directors	EMERCell
	Independent Member of the Board of Directors	ERVACCINE Technologies
	Managing Director	ALAIN ONCOLOGIE CONSULTING
	Member of the Board of Directors	Gustave Roussy Transfert
Enno SPILLNER (Independent Member)**	Financial Officer Member of the Management Board	EVOTEC**
	Member of the Supervisory Board	Leon Nanodrugs
Christophe DOUAT (Observer)	Chairman of the Executive Board	Medincell SA **
	Member of the Board of Directors	CM Biomaterials BV

**Within the meaning of the Code of corporate governance as amended by MiddleNext in September 2021 (see Section 2.1.6.1 of the Universal Registration Document).*
***Listed Company.*

2.1.2.2. Corporate offices exercised in the past five years, but which have ceased to date

Members of the Executive Board

Name	Nature of corporate office	Company
Laurent LEVY	None	
Bart VAN RHIJN	Member of Board of Directors	Stynt, Inc.
Anne-Juliette HERMANT	None	

Members of the Supervisory Board

Name	Nature of corporate office	Company
Gary PHILLIPS (Independent Member*)	Executive Vice President & Chief Strategy Officer Member of the Board of Directors Member of the Board of Directors	Mallinckrodt Pharmaceuticals Inotek Pharmaceuticals Envisia Therapeutics
Anne-Marie GRAFFIN (Independent Member*)	None	
Alain HERRERA (Independent Member*)	Managing Director	PharmaEngine Europe SARL (in liquidation proceedings)
Enno SPILLNER (Independent Member*)	None	
Christophe DOUAT (Observer)	None	

** Within the meaning of the Code of corporate governance as amended by MiddleNext in September 2017 (see section 2.1.6.1 of the Universal Registration Document)..*
***Listed Company.*

2.1.3. Biographies of members of the Company's corporate bodies

2.1.3.1. Biographies of Members of the Executive Board

The biographies of the members of the Executive Board can be found in Section 1.2.2. of the Universal Registration Document.

2.1.3.2. Biographies of Members of the Supervisory Board

The biographies of the members of the Supervisory Board are as follows:

GARY PHILLIPS – Chairman of the Supervisory Board (independent member)

Nationality: American

Age: 56

Corporate office appointment date: May 25, 2021

Corporate office term: At the end of the general meeting held to approve the financial statements for the financial year ended on December 31, 2022

Committee Member: Member of the audit committee and the appointments and compensation committee

BIOGRAPHY
Gary M. Phillips, M.D., has served as Chairman of the Supervisory Board since May 2021. With over two decades of experience in the pharmaceutical and healthcare industries, Dr. Phillips currently holds the position of President and CEO of OrphoMed. Prior, he was Executive Vice President and Chief Strategy Officer at Mallinckrodt Pharmaceuticals. Dr. Phillips has also served as Head of Global Health & Healthcare Industries at the World Economic Forum, President of Reckitt Benckiser Pharmaceuticals North America (now Indivior), and he held dual roles as President, U.S. Surgical and Pharmaceuticals and Global Head of Pharmaceuticals at Bausch & Lomb. Additionally, he has served in executive roles at Merck Serono, Novartis, and Wyeth. Dr. Phillips graduated Summa Cum Laude from the University of Pennsylvania, earning a B.A in biochemistry, holds an MBA from the Wharton School, and an M.D. with Alpha Omega Alpha distinction from the School of Medicine. He maintains an active medical license and practiced as a general medicine clinician/officer in the U.S. Navy, from which he was honorably discharged as a lieutenant commander.

ANNE-MARIE GRAFFIN – Vice President of the Supervisory Board (independent member)

Nationality: French

Age: 60

Corporate office renewal date: May 23, 2018

Corporate office term: At the end of the general meeting held to approve the financial statements for the financial year ended on December 31, 2023

Committee Member: Chairwoman of the appointments and compensation committee

BIOGRAPHY

Anne-Marie Graffin has served as a Supervisory Board member since 2013, as chairman of the appointments and compensation committee since 2017 and as vice chairwoman of the supervisory board since July 2017. She has over 20 years of experience in life sciences and pharmaceutical companies. She has served as a non-executive board member of Valneva SE (Nantes, FR – Vienna, AT) since 2013 and of Sartorius Stedim Biotech SA (Aubagne, FR – Goëttingen, Ger) since 2015. Anne-Marie Graffin has expertise in both developing market access strategies and driving biotechnology companies' growth. She has been a consultant to the pharmaceutical industry since 2011, developing many initiatives within the innovation and startups fields, connecting biotech and medtech startups with major EU venture capital firms and investors. Previously, she was a vice president at Sanofi Pasteur MSD, a European leader in the vaccine field, and acted as a member of the Executive Committee. Prior to working at Sanofi Pasteur MSD, she worked for five years at ROC as international brand manager. Anne-Marie Graffin graduated from ESSEC Business School Paris.

ALAIN HERRERA – Supervisory Board Member

Nationality: French

Age: 71

Corporate office renewal date: May 23, 2018

Corporate office term: At the end of the general meeting held to approve the financial statements for the financial year ended on December 31, 2023

Committee Member: Member of the appointments and compensation committee

BIOGRAPHY

Dr. Alain Herrera, MD, has served as a Supervisory Board member since 2013 and a member of the appointments and compensation committee since the same year. Dr. Herrera has more than 25 years of experience in the pharmaceutical industry with a strong focus in oncology drug development and marketing. Dr. Herrera currently works at Alain Oncologie Consulting, an oncology consultancy company he started. Previously, Dr. Herrera has served as Head of Corporate Development, Managing Director of PharmaEngine Europe Sarl, as well as the head of the Oncology business at Sanofi-Aventis for 10 years. He also served as Vice President for the Global Oncology Business Strategy and Development from 2007-2008 and Head of the Global Oncology Franchise from 1998-2007. While at Sanofi-Aventis, he contributed to the worldwide registration of Oxaliplatin (Eloxatin®) and Rasburicase (Fasturtec®/Elitek®), as well as the Gastric and Head & Neck indications for Docetaxel (Taxotere®). Prior to Sanofi-Aventis, he served as Chairman of Chiron Therapeutics Europe, Managing Director at Pierre Fabre Oncology Laboratories and Head of the Oncology Platform at Roger Bellon (Rhône Poulenc). Dr. Herrera has also served as a Hematologist Consultant at Antoine Beclere Hospital since 1991.

ENNO SPILLNER – Member of the Supervisory Board (independent member)

Nationality: German

Age: 52

Corporate office renewal date: April 28, 2020

Corporate office term: At the end of the general meeting held to approve the financial statements for the financial year ended on December 31, 2025

Committee Member: Chairman of the audit committee

BIOGRAPHY

Enno Spillner has served as a Supervisory Board member and chairman of the audit committee since 2014. He has 20 years of experience in the life science industry and currently serves as Chief Financial Officer and Member of the Management Board at German biotech company Evotec SE. From March 2013 until June 2016, he served as Chairman of the Management Board, Chief Executive Officer and Chief Financial Officer of 4SC AG. From September 2005 to March 2013 he acted as Chief Financial Officer of 4SC AG. Enno Spillner started his life science industry career as Head of Finance and Managing Partner of the Munich-based biotech venture fund, BioM AG. He was also Managing Director of two portfolio companies, ACTIPAC Biosystems GmbH and Munich innovative Biomaterials GmbH. Prior to moving into the life science field, he was engaged in the media and marketing industry. Enno Spillner earned his Dipl.-Kaufmann degree (Masters in Business) at the University of Bamberg, Germany.

CHRISTOPHE DOUAT - Observer

Nationality: French

Age: 57

Appointment Date: June 14, 2017

Corporate office term: At the end of the general meeting held to approve the financial statements for the financial year ended on December 31, 2022

Committee Member: Member of the audit committee (as an observer)

BIOGRAPHY

Christophe Douat serves as a Supervisory Board observer and is entitled, in this capacity, to attend all meetings of the Supervisory Board in a non-voting capacity. Christophe Douat previously served as member of the Supervisory Board from 2011 until 2017 and from 2006 to 2009 when he was the lead investor. He is currently CEO of Medincell (MEDCL, Euronext), a pharmaceutical company that specializes in drug delivery technologies. Christophe Douat worked at the venture capital company Matignon Investissement & Gestion from 2001 to 2009, where he invested in a broad range of companies, and cofounded Matignon Technologies II, one of Europe's largest funds specialized in medtech. Christophe Douat is also an alumnus of the Boston Consulting Group. He graduated from École des Mines de Paris, an engineering French "Grande Ecole" and holds a master's of science in engineering (U.S.A.) and an MBA (Canada).

2.1.4. Statements relating to members of the Executive Board and the Supervisory Board

There are no family connections between the persons listed above.

In the past five years, none of these persons:

- Have been convicted of fraud;
- Have been involved as an officer or director in any bankruptcy, sequestration or liquidation;
- Have been barred by a court from acting as a member of an administrative, management or supervisory body of an issuer or from participating in the management or conduct of the affairs of an issuer;
- Have been the subject of official public incrimination or sanctions by statutory or regulatory authorities (including designated professional bodies).

2.1.5. Operation of the Executive and the Supervisory Boards

Nanobiotix is a public limited Company (*société anonyme*) with an Executive Board and Supervisory Board whose memberships are listed in Section 2.1.1. above.

2.1.5.1. Company Management

During the financial year ended on December 31, 2021, the Executive Board met thirteen (13) times, it being specified that the Executive Board members meet informally on a weekly basis.

2.1.5.2. Supervisory Board

During the past financial year, the Supervisory Board of the Company met nine (9) times. The Chairman of the board presided over these meetings and each member participated in at least 100% of the board's meetings.

2.1.5.2.1. Tasks of the Supervisory Board

The Supervisory Board is subject to the provisions of the French Commercial Code, Articles 15 to 17 of the Bylaws of the Company and the internal rules that it has adopted. In particular, the Supervisory Board:

- continuously oversees the Executive Board's management of the Company;
- verifies and monitors the corporate and consolidated financial statements prepared by the Executive Board;
- appoints and dismisses members of the Executive Board, who are in charge of managing the Company and defining its strategy, and sets their compensation;
- authorizes the agreements and undertakings referred to in Articles L. 225-86 and L. 225-90-1 of the French Commercial Code;
- recommends the appointment of the statutory auditors to the shareholders' meeting;
- prepares the Corporate Governance Report referred to in Article L. 225-68 of the French Commercial Code; and
- prepares the draft resolutions referred to in Article L. 22-10-8 of the French Commercial Code, and the associated report.

It ensures the quality of information provided to the shareholders and the market.

In addition and based on recommendation n°14 of the MiddleNext code, starting after the shareholders' meeting held to approve the financial statements for the year ended December 31, 2021,

the Supervisory Board intends to conduct a yearly review of the voting results of each of the shareholders' meetings of the Company, especially as regards the negative votes on any decision submitted to its shareholders. The Board would in particular pay attention to how the majority of the Company's minority shareholders expressed themselves, and discuss whether any measures should be taken as a result.

2.1.5.2.2. Conditions for preparing and organizing the work of the Supervisory Board

The Executive Board regularly informs the Supervisory Board of the financial position, cash flow, financial commitments and significant events of the Company. Any new member of the Supervisory Board may ask for training on the specific characteristics of the Company and its Group, their business lines and sector activities. The Supervisory Board meets as often as required by Company interests and in any event at least once a quarter.

Every year, a provisional calendar of annual meetings is set. Members of the Supervisory Board are convened by letter, fax or email at least five (5) business days before each meeting. The board may also be convened by any other means, even verbally, if all the board members are present or represented at the meeting. All documents or draft documents are sent, submitted or made available to members of the Supervisory Board a reasonable amount of time before the meeting, so as to inform them of the agenda and of any matters that are submitted to the board for review. To participate effectively in the work and deliberations of the Supervisory Board, each member of the Supervisory Board is sent the documents that he or she considers to be useful. Requests to this end are made to the Executive Board or any other officer, as the case may be.

Furthermore, the Supervisory Board is informed during its meetings of the Company's financial position, cash flow situation and commitments. Each member of the Supervisory Board has the right to meet with the Company's main officers, provided that he/she notifies the Executive Board beforehand. Members of the Executive Board can attend these meetings, unless the relevant member of the Supervisory Board objects to their presence. Members of the Executive Board may be heard at any meeting of the Supervisory Board.

Members of the Supervisory Board may participate in the board meeting through videoconferencing or telecommunication technology. However, this method of participation is not valid when adopting decisions in relation with the verification and monitoring of the financial year's financial statements, including the consolidated accounts prepared in accordance with the IFRS norms, and the review of the management report and the Group's management report[(1)]. Moreover, the members of the Supervisory Board are allowed to take certain specific decisions by written consultation, such as convening a shareholders' meeting or making provisional appointments to the Supervisory Board in accordance with Article L. 225-78 of the French Commercial Code.

The technology used must allow for the identification of the participants and ensure their effective participation.

The minutes of the meeting must mention the participation of Supervisory Board members by means of videoconferencing or telecommunications technology, if any.

In accordance with the recommendations of the Code of corporate governance as amended in September 2021 by MiddleNext (the "**MiddleNext Code**"), the Supervisory Board shall conduct a yearly assessment of the operating methods of the board and committees, as well as on the preparation of its work. The assessment of the year 2021 was conducted and the Supervisory Board took note of it during its discussions on March 30, 2021.

[(1)]It being specified that such restriction has been temporally lifted in the context of the Covid-19 pandemic until July 31, 2022.

2.1.5.2.3. Balanced gender representation

The principle of balanced gender representation on the Supervisory Board (Law No. 2011–103 of January 27, 2011 – *loi du 27 janvier 2011 relative à la représentation équilibrée des femmes et des hommes au sein des conseils d'administration et de surveillance et à l'égalité professionnelle*) is also respected by the Company, as the Supervisory Board is composed of one woman and three men.

The Company continues to pursue a diversity and equity policy at all hierarchical levels. As of the date of the Universal Registration Document, women are represented at all levels of the Company. In particular, in addition to the Supervisory Board being composed of one woman and three men, the Executive Board is composed of two men and one woman. Overall, women represent 67% of the Company's employees.

2.1.5.3. Specialized Committees

At the date of the Universal Registration Document, the Company has two specialized committees set up by the Supervisory Board: an audit committee and an appointments and compensation committee.

2.1.5.3.1. Audit Committee

2.1.5.3.1.1. Composition

The Supervisory Board dated September 9, 2010 set up an audit committee, whose members adopted new internal rules of procedure, detailed below, on April 11, 2012, which were approved by the Supervisory Board on the same day. In the context of the Company's initial public offering on the Nasdaq Global Select Market, the Supervisory Board voted to amend the audit committee's internal rules of procedure (règlement intérieur) on November 20, 2020 in order to ensure compliance with all applicable requirements of the French Commercial Code, the United States Securities Exchange Act and the Nasdaq Global Market, as well as the rules and regulations of the United States Securities Exchange Commission.

The audit committee monitors the questions relating to the processing and control of accounting and financial information. To this end, it ensures the quality of the Company's internal controls and the reliability of information provided to shareholders and financial markets.

The duties specifically assigned to the audit committee by the Supervisory Board include, but are not limited to:

- monitoring the financial reporting process;
- monitoring the effectiveness of internal control and risk management systems;
- monitoring the legal audit of the annual and consolidated accounts of the statutory auditors;
- making recommendations regarding the selection of the Company's statutory auditors to be appointed by its shareholders, determining their compensation and ensuring their independence;
- making recommendations regarding the selection of any accounting firm, other than the Company's statutory auditors, to be appointed for non-audit services;
- examining the Company's procedures for the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters, as well as for the confidential, anonymous submissions by its employees of concerns regarding questionable accounting or auditing matters; and

- generally advising the Supervisory Board and making recommendations with respect to all of the areas above.

The audit committee may meet or consult with any member of the Executive Board and may conduct internal or external due diligence reviews with respect to any matter that may be relevant to the performance of its duties, so long as the Supervisory Board and the chairman of the Executive Board are informed in advance. In particular, the audit committee has the right to interview the persons involved in the preparation or control of the Company's financial statements, including the Chief Financial Officer and those persons responsible for significant areas within the Company's financial department.

The audit committee shall be comprised of at least two members from, and appointed by, the supervisory board, after consultation with the appointments and compensation committee. Members shall be independent in accordance with Nasdaq's listing rules and Rule 10A-3 of the United States Securities Exchange Act as well as the criteria established by the MiddleNext Code (see Section 2.1.6.1 of the Universal Registration Document). At least one member shall have specific financial and accounting skills. No member of the audit committee may be a person exercising any management function within the Company and its subsidiaries.

Currently, the audit committee is comprised of two members: Enno Spillner (chairman and independent member) and Mr. Gary Phillips (independent member), and one observer, Christophe Douat, who attends in a non-voting capacity. The Supervisory Board has determined that Enno Spillner is an "audit committee financial expert," as defined by SEC rules and regulations, and that each member qualifies as financially sophisticated under the Nasdaq listing rules.

The audit committee met five (5) times during the 2021 financial year.

2.1.5.3.2. Appointments and Compensation Committee

On February 28, 2019, to replace the former compensation committee, the Supervisory Board set up an appointments and compensation committee, whose members adopted internal rules of procedure, detailed below, on the same day, which were approved by the Supervisory Board. In the context of the Company's initial public offering on the Nasdaq Global Select Market, the Supervisory Board voted to amend the appointments and compensation committee's internal rules of procedure (règlement intérieur) on November 20, 2020 in order to ensure compliance with all applicable requirements of the French Commercial Code, the United States Securities Exchange Act and the Nasdaq Global Market, as well as the rules and regulations of the United States Securities Exchange Commission.

The appointments and compensation committee provides recommendations and proposals to the Executive and Supervisory Board members on the composition and compensation policies of the Executive and Supervisory Boards, and also prepares any related reports to be provided by the Company.

The principal duties and responsibilities of the appointments and compensation committee include, but are not limited to:

- making recommendations on the composition of the Executive and Supervisory Boards and the Supervisory Board's committees;
- annually evaluating independence and submitting to the Supervisory Board a list of its members who may qualify as independent members based on Nasdaq's listing rules and Rule 10A-3 of the United States Securities Exchange Act as well as the criteria set forth in the MiddleNext Code;

- establishing a succession plan for the Company's executive officers and assisting the Supervisory Board in the selection and evaluation of Executive and Supervisory Board members;
- reviewing the main objectives recommended by management regarding the compensation granted to the non-executive officers of the Company, including under free share and stock option plans;
- reviewing equity incentive plans, including free share plans and stock options or stock purchase options, pension and contingency schemes and benefits in kind for non-executive officers;
- making recommendations to the Supervisory Board regarding:
    - the compensation, pension and contingency schemes, benefits in kind and other various pecuniary rights, including termination, of the members of the Executive Board. The committee makes recommendations on the amount and structure of Executive Board member compensation, taking into account strategy, objectives, outcomes, and general market practice, and
    - the free share and stock option plans, as well as any similar equity incentive instrument and in particular, the allocation to members of the Executive Board,
- making recommendations to the Supervisory Board regarding compensation, including equity-based compensation and expense reimbursement, for the members of the Supervisory Board, taking into account corporate goals and objectives and performance of Supervisory Board members in light of such goals and objectives;
- preparing and presenting the reports provided for in the Supervisory Board internal rules of procedure (règlement intérieur);
- making any other recommendation that might be requested by the Supervisory Board regarding compensation; and
- generally advising the Supervisory Board and making recommendations with respect to all of the areas above.

The appointments and compensation committee shall be comprised of at least two members from and appointed by the Supervisory Board. No member of the appointments and compensation committee may be a person exercising any management function within the Company and its subsidiaries. Currently, the appointments and compensation committee is comprised of three members: Anne-Marie Graffin (chairman and independent member), Dr. Alain Herrera and Gary Phillips (independent members).

This committee was, from 2010 to 2019, solely a compensation committee whose principal duties and responsibilities concerned solely compensation matters.

The compensation and appointments committee met four (4) times during the 2021 financial year.

2.1.6. Conflict of interests

2.1.6.1. Review of the members' independence and potential conflicts of interest

The MiddleNext Code sets out the following five criteria to be used to evaluate the independence of supervisory board members, which are characterized by the absence of any significant financial, contractual or family relationship likely to affect a member's independence of judgment. Each supervisory board member:

- must not be a salaried employee or corporate officer of us or any of our affiliates and must not have held such a position within the last five years;
- must not be in a significant business relationship with us or any of our affiliates (e.g., client, supplier, competitor, provider, creditor, banker, etc.) and must not have been in such a relationship within the last two years;
- must not be a reference shareholder or hold a significant number of voting rights;
- must not have close relationships or family ties with any of our corporate officers or reference shareholders; and
- must not have been our auditor within the last six years.

The Supervisory Board is tasked with examining the situation of its members on a case by case basis in light of these criteria. Subject to the justification of its position, the Supervisory Board may consider one of its members to be independent when he or she does not meet all of these criteria; conversely, the Board may also consider one of its members not to be independent when he or she does meet all of these criteria.

The Supervisory Board believes that all of its current members are independent with regard to the MiddleNext Code.

In addition, under U.S. listing requirement and the rules of Nasdaq, the Company is not required to have independent members on the Supervisory Board, except with respect to the audit committee. The Supervisory Board has undertaken a review of the independence of its members and determined that all of its members qualify as "independent directors" as defined under applicable rules of Nasdaq and the independence requirements contemplated by Rule 10A-3 under the United States Securities Exchange Act.

2.1.6.2. Conflicts of interest of the Executive Board and Supervisory Board

Members of the Executive Board who make up the executive team as well as some Supervisory Board members are shareholders of the Company and/or hold securities giving them access to the Company's capital. See Section 2.2.8 of the Universal Registration Document for more information.

2.1.6.3. Information on service agreements binding members of the Executive Board and Supervisory Board with the Group

There is no service agreements between members of the Executive Board and any of the Group Companies or between members of the Supervisory Board and any of the Group Companies. As far as the Company is aware, there is no contract, arrangement or agreement whatsoever with the shareholders, customers, suppliers or others according to which a member of the Executive Board or the Supervisory Board has been appointed.

2.1.7. Agreements referred to in article L.225-37-4 of the French Commercial Code

In order to fulfill the new legal requirements regarding current agreements, the Executive Board shall inform the Supervisory Board on an annual basis on current agreements entered into during the past financial year. It shall review the purpose and financial conditions of these agreements and confirm or deny their classification as current agreements. In the 2021 financial year, no current agreements were entered into.

2.2. COMPENSATION AND BENEFITS FOR MEMBERS OF THE EXECUTIVE BOARD AND THE SUPERVISORY BOARD

The information is based on the MiddleNext Code. The tables in Appendix 2 of AMF position and recommendation no. 2021-02 are presented below.

The composition of both the Supervisory Board and the Executive Board evolved in the course of 2021. On May 25, 2021, Laurent Condomine, member and chairman of the Supervisory Board, resigned with effect immediately. To fill this vacancy, on the same date, the Supervisory Board appointed Gary Phillips as a member of the Supervisory Board for the remainder of Laurent Condomine's term of office, subject to the ratification of the appointment by the next ordinary shareholders' meeting, and elected him as chairman of the Supervisory Board. On May 31, 2021, Philippe Mauberna, member of the Executive Board, resigned from his office effective immediately. On the same date, the Supervisory Board appointed Bart Van Rhijn to replace him as a member of the Executive Board with effective date of June 1, 2021.

The reader may refer to the details, if any, provided in the tables below.

2.2.1. Compensation and benefits paid to the Executive Board members

Table No. 1: Summary of compensation and dilutive instruments allotted to each executive board member

Summary table of compensation and stock-options and free shares granted to each corporate officer		
Corporate officer	**2021 Financial Year**	**2020 Financial Year**
Laurent LEVY - Chairman of the Executive Board		
Compensation due for the financial year [1]	€553,065	€513,025
Value of the free shares granted during the financial year [2]	€2,417,400	—
Value of the stock options granted during the financial year [2]	€763,920	€304,800
TOTAL	**€3,734,385**	**€817,825**
Bart VAN RHIJN[3] – Chief Financial Officer		
Compensation due for the financial year [1]	€268,885	—
Value of the free shares granted during the financial year [2]	—	—
Value of the stock options granted during the financial year [2]	€458,400	—
TOTAL	**€727,285**	**—**
Anne-Juliette HERMANT – Chief People Officer		
Compensation due for the financial year [1]	€287,543	€300,000
Value of the free shares granted during the financial year [2]	€1,208,700	€287,000
Value of the stock options granted during the financial year [2]	€254,640	€152,400
TOTAL	**€1,750,883**	**€739,400**
Philippe MAUBERNA[4] – Chief Financial Officer		
Compensation due for the financial year [1]	€381,615	€350,000
Value of the free shares granted during the financial year [2]	—	—
Value of the stock options granted during the financial year [2]	—	€152,400
TOTAL	**€381,615**	**€502,400**
Edwina BASKIN-BEY[5] – Chief Medical Officer		
Compensation due for the financial year [1]	—	—
TOTAL	**—**	**—**
TOTAL	**€6,594,168**	**€2,059,625**

(1) See Table no. 2 " Summary of the compensation of each corporate officer" below

(2) The valuation of the stock option and/or free shares according to the method used for the consolidated financial statements.

(3) Bart Van Rhijn entered into an employment agreement with Nanobiotix Corp. on May 11, 2021, effective on June 1st, 2021, and was appointed as a member of the Executive Board, effective June 1st, 2021, by the Supervisory Board held on May 31, 2021. The above figures reflect the compensation he received under his employment agreement during his term as a member of the Executive Board, i.e. 7 months.

(4) Philippe Mauberna resigned from his corporate office as Executive Board member, effective on May 31, 2021, it being specified that Philippe Mauberna continued to receive compensation under his employment agreement until his departure from the Company, i.e. until June 30, 2021. The above amounts reflect his compensation for the entire 2020 financial year and the first six months of the 2021 financial year.

(5) Edwina Baskin-Bey was appointed as a member of the Executive Board, effective July 1st, 2019, by the Supervisory Board held on June 20, 2019. Her corporate office as a member of the Executive Board was terminated with immediate effect by the Supervisory Board on April 6, 2020.

(6) The euro to dollar exchange rate used to convert the compensation of Bart Van Rhijn is equal to 1€ = $1.1326.

No multi-year variable compensation was granted to Executive Board members during the 2020 and 2021 fiscal years.

2.2.2. Compensation and benefits paid to the Executive and Supervisory Board members

Table No. 2: Summary of compensation for each corporate executive officer

Summary table of compensation for each corporate officer				
Corporate officer	**2021 Financial Year**		**2020 Financial Year**	
	Amounts due [1]	**Amounts paid [2]**	**Amounts due [1]**	**Amounts paid [2]**
Laurent LEVY - Chairman of the Executive Board				
Annual fixed compensation [3]	€380,000	€380,000	€330,000	€330,000
Annual variable compensation [4]	€155,040	€165,000	€165,000	€132,000
Exceptional compensation [5]	—	—	—	—
In kind benefits (corporate officer private unemployment insurance or "*Garantie Sociale du Chef d'entreprise*")	€18,025	€18,025	€18,025	€18,025
TOTAL	**€553,065**	**€563,025**	**€513,025**	**€480,025**
Bart VAN RHIJN – Chief Financial Officer[8,9]				
Annual fixed compensation [6,7,8]	€195,715	€195,715	—	—
Annual variable compensation [4]	€73,170	—	—	—
Exceptional compensation	—	—	—	—
In kind benefits	—	—	—	—
TOTAL	**€268,885**	**€195,715**	**—**	**—**
Anne-Juliette HERMANT – Chief People Officer				
Annual fixed compensation [6,7]	€210,000	€210,000	€200,000	€200,000
Annual variable compensation [4]	€77,543	€100,000	€100,000	€54,000
Exceptional compensation	—	—	—	—
In kind benefits	—	—	—	—
TOTAL	**€287,543**	**€310,000**	**€300,000**	**€254,000**
Philippe MAUBERNA – Chief Financial Officer [10]				
Annual fixed compensation [6,7]	€100,741	€100,741	€242,000	€242,597
Annual variable compensation [4]	€25,874	€108,900	€108,000	€96,800
Exceptional compensation [10]	€255,000	€255,000	—	—
In kind benefits	—	—	—	—
TOTAL	**€381,615**	**€464,641**	**€350,000**	**€339,397**
Edwina BASKIN-BEY – Chief Medical Officer [11]				
Annual fixed compensation [7]	—	—	—	—
Annual variable compensation [4]	—	—	—	—
Exceptional compensation	—	—	—	—
In kind benefits	—	—	—	—
TOTAL	**—**	**—**	**—**	**—**
TOTAL EXECUTIVES BOARD MEMBERS	**€1,491,108**	**€1,533,381**	**€1,163,025**	**€1,073,422**

(1) For the financial year, the amount of which is unlikely to change regardless of the payment date, on a gross basis before tax.

(2) During the financial year, on a gross basis before tax.

(3) Laurent Levy is compensated solely for his corporate office as Chairman of the Executive Board. His fixed compensation is set annually by the Supervisory Board.

(4) Variable compensation corresponds to an annual bonus equal to 60% for Laurent Levy and 50% for the other executive board members of the annual fixed compensation paid on the basis of performance criteria linked to the achievement of the Company's objectives (for 80%) and on the individual leadership qualities of each member of the Executive Board (for 20%). The Company's objectives are set by the Executive

Board, reviewed by the appointment and remuneration committee and approved by the Supervisory Board; achievement of said objectives is assessed by the same committees according to the same procedure.

(5) The exceptional compensation, if applicable, will relate to newly filed patented inventions.

(6) Compensation granted under an employment agreement.

(7) The variations between the amounts due and amounts paid are due to the treatment of paid leave.

(8) Bart Van Rhijn entered into an employment agreement with the Company on May 11, 2021, effective on June 1, 2021, and was appointed as a member of the Executive Board by the Supervisory Board on May 31, 2021, effective June 1st, 2021. His fixed yearly salary amounts to $380,000, to which is added variable compensation of up to 50% of his fixed compensation, i.e., up to $190,000. His fixed salary in 2021 amounted (on a prorate basis) to $221,666, to which was added variable compensation of up to 50% of his fixed salary, i.e., up to $110, 833, i.e. a total of €268,885.

(9) The euro to dollar exchange rate used to convert the compensation of Bart Van Rhijn is equal to 1€ = $1.1326

(10) Philippe Mauberna entered into an employment agreement with the Company on April 1, 2019 and was appointed as a member of the Executive Board by the Supervisory Board on June 20, 2019, effective July 1st, 2019. He resigned from his corporate office as Executive Board member, effective on May 31, 2021. The Company and Philippe Mauberna, mutually agreed to terminate his employment agreement, effective June 30, 2021 and, in this context, entered into a termination agreement on May 19, 2021, the terms of which were approved by the Supervisory Board on April 6, 2021. Pursuant to this agreement, Philippe Mauberna is in particular entitled to an exceptional indemnity of €255,000. He shall also keep the benefit of his 2021 variable compensation (on a prorata basis), subject however to the achievement of the performance objectives set by the Executive Board.

(11) Edwina Baskin-Bey entered into an employment agreement with the Company on April 1, 2019 and was appointed as a member of the Executive Board by the Supervisory Board on June 20, 2019, effective July 1st, 2019. Her corporate office as a member of the Executive Board was terminated with immediate effect by the Supervisory Board on April 6, 2020. She received no compensation during 2020 financial year. She did not receive any variable compensation or compensation in respect of her duties as a member of the Executive Board

The Company and Philippe Mauberna, member of the Executive Board and Chief Financial Officer of the Group, mutually agreed to terminate his employment agreement, effective June 30, 2021 and, in this context, entered into a termination agreement on May 19, 2021, the terms of which were approved by the Supervisory Board on April 6, 2021. Pursuant to this agreement, Philippe Mauberna is in particular entitled to an exceptional indemnity of €255,000. He shall also keep the benefit of his 2021 variable compensation (on a prorata basis), subject however to the achievement of the performance objectives set by the Executive Board. In addition, the Executive Board decided to lift, as from June 30, 2021, the continued service condition to which the exercise or definitive acquisition of all incentive instruments held by Philippe Mauberna are subject, notwithstanding the termination of his positions within the Group, and to accelerate the vesting of the OSA 2020 he holds, enabling Philippe Mauberna to exercise all of them. In order to avoid a negative impact on the Company's share price, Philippe Mauberna agreed that the sale of his shares would be restricted. Finally, as from June 30, 2021, Philippe Mauberna was released from his non-compete undertaking.

Furthermore, on May 31, 2021, Philippe Mauberna resigned from his office of Executive Board member, effective immediately as well as from all other positions he holds within the Group. For more information on the compensation policy applicable to Philippe Mauberna for the 2021 financial year, see Section 2.2.9 of the Company’s 2020 universal registration document filed with the AMF on April 7, 2021, under number D.21 0272.

Table No. 3: Compensation (e.g. attendance fees) and other compensation received by non-Executive Board members

This table is included in Section 2.2.3. of this Universal Registration Document.

Table No. 4: Stock options (*Options de Souscription d'Actions, OSA*) awarded during the financial year to each corporate officer by the Company and any company of Group

Stock-options granted during the financial year to each Executive Board member by the Company and any Group company						
Name of the Executive Board member	**Plan name and date**	**Nature of the stock options (purchase or subscription)**	**Value of the options [1]**	**Number of options awarded during the financial year**	**Exercise price**	**Exercise period**
Laurent LEVY	Name: OSA 2021-04-Performance Date: April 20, 2021	subscription	[1]	180,000	€13.74	10 years[2]
Bart VAN RHIJN	Name: OSA 2021-06-Performance Date : June 21, 2021	subscription	[1]	60,000	€12.99	10 years[3]
	Name: OSA 2021-06-Ordinary Date : June 21, 2021	subscription	[1]	60,000	€12.99	10 years[4]
Anne-Juliette HERMANT	Name: OSA 2021-04-Performance Date: April 20, 2021	subscription	[1]	60,000	€13.74	10 years[2]
TOTAL				**360,000**	—	-

(1) Valuation of the options according to the method used for consolidated financial statements
(2) The OSA 2021-04 Performance may be exercised under the following conditions:

- *10% of the OSA 2021-04 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €24;*
- *an additional 10% of the OSA 2021-04 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €30;*
- *an additional 40% of the OSA 2021-04 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €40;*
- *an additional 40% of the OSA 2021-04 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €60;*

it being specified that (i) among such OSA 2021-04 Performance that may be exercised, and subject to, for each increment, a continued service condition, their holders may only exercise (x) up to 10% of such OSA 2021-04 Performance as from April 20, 2022, (y) an additional 30% of such OSA 2021-04 Performance as from April 20, 2023, and (z) the balance, i.e., 60% of such OSA 2021-04 Performance as from April 20, 2024 and (ii) such additional vesting condition shall be automatically waived in the event of a change of control. In addition, the exercise of the OSA 2021-04 Performance granted to members of the Executive Board is subject to the determination of the recommended dose for two of the three patient cohorts enrolled in the NBTXR3-1100 clinical study, in order to be able to define the next stage of the development plan in immuno-oncology before April 20, 2022. The satisfaction of this performance condition shall be acknowledged by the Executive Board with the approval of the Supervisory Board.

(3) The OSA 2021-06 Performance may be exercised under the following conditions:

- *10% of the OSA 2021-06 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €24;*
- *an additional 10% of the OSA 2021-06 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €30;*
- *an additional 40% of the OSA 2021-06 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €40; and*
- *an additional 40% of the OSA 2021-06 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €60,*

it being specified that (i) among such OSA 2021-06 Performance that may be exercised, and subject to, for each increment, a continued service condition, their holders may only exercise (x) up to 10% of such OSA 2021-06 Performance as from June 21, 2022, (y) an additional 30% of such OSA 2021-06 Performance as from June 21, 2023 and (z) the balance, i.e., 60% of such OSA 2021-06 Performance as from June 21, 2024 and (ii) such additional vesting condition shall be automatically waived in the event of a change of control. The exercise of the OSA 2021-06 Performance is also subject to the determination of the recommended dose for two of the three patient cohorts enrolled in the NBTXR3-1100 clinical study, in order to be able to define the next stage of the development plan in immuno-oncology before June 21, 2022. The satisfaction of this performance condition shall be acknowledged by the Executive Board with the approval of the Supervisory Board.

(4) The OSA 2021-06 Ordinary may be exercised as follows:

- *up to one-third of the OSA 2021-06 Ordinary as from June 21, 2022;*
- *an additional one-third of the OSA 2021-06 Ordinary as from June 21, 2023; and*
- *the balance, i.e., one-third of the OSA 2021-06 Ordinary as from June 21, 2024,*

subject to, for each increment, a continued service condition. The exercise of the OSA 2021-06 Ordinary is also subject to the determination of the recommended dose for two of the three patient cohorts enrolled in the NBTXR3-1100 clinical study, in order to be able to define the next stage of the development plan in immuno-oncology before June 21, 2022.

Table No. 5: Stock options exercised during the financial year by each corporate officer

None

Table No. 6: Free shares awarded by the Company to Executive Board members

Free shares awarded by the Company to each Executive Board member during the financial year						
	Plan name and date	**Number of shares awarded during the financial year**	**Valuation of the shares [1]**	**Acquisition date**	**Availability date**	**Performance conditions**
Laurent LEVY	Name: AGA 2021 Date: April 20, 2021	180,000	€2,417,400	20/04/2023	20/04/2024	(2)(3)
Anne-Juliette HERMANT	Name: AGA 2021 Date: April 20, 2021	90,000	€1,208,700	20/04/2023	20/04/2024	(2)(3)
Total		**270,000**	**€3,626,100**	-	-	-

(1) Valuation of the shares according to the method used for consolidated financial statements.
(2) The exercise of the AGA 2021 granted to members of the Executive Board are conditioned upon the determination of the recommended dose for two out of the three patient cohorts enrolled in the NBTXR-1100 clinical study in order to define the next steps of the immuno-oncology development plan before April 20, 2022. The satisfaction of this condition must be acknowledged by the Executive Board, with the prior approval of the Supervisory Board, before April 20, 2023. Furthermore, the AGA 2021 will be subject to a one-year holding period starting at the end of the two-year acquisition period, i.e. starting April 20, 2023.

(3) See also "Continued Service Condition" and "Change of Control" in Section 5.1.4.4. of the Universal Registration Document.

It is also specified that the Executive Board dated April 20, 2021 granted Philippe Mauberna one free share that lapsed upon his departure from the Company.

Between December 31, 2021 and the date of the Universal Registration Document, the Company has not granted free shares to members of the Executive Board.

Table No. 7: Free shares that became available for each member of the Executive Board

Free shares that became available for each member of the Executive Board member during the financial year			
Free shares that became available for each member of the Executive Board	**Plan name and date**	**Number of shares that became available and that were exercised during the financial year**	**Acquisition condition**
Anne- Juliette HERMANT	Name : AGA 2020 Date: Date: March 11, 2022	50,000	(1)
TOTAL		**50,000**	-

(1) The definitive acquisition of the AGA 2020 granted to Anne-Juliette HERMANT as member of the Executive Board was subject to the achievement of clinical and strategic objectives in the head and neck indication, the completion of which was acknowledged by the Executive Board, under the approval of the Supervisory Board, on March 17, 2020. The AGA 2020 are nevertheless subject to a one-year conservation period from their acquisition date, i.e. until March 11, 2023.

Table No. 8: History of allotments of securities giving access to capital

The history of allotments of securities giving access to capital can be found in Section 5.1.4. of this Universal Registration Document.

Table No. 9: Securities giving access to capital granted to the top ten employees who are not corporate officers and options exercised by them

This table can be found in paragraph 5.7.1.2. of this Universal Registration Document.

Table No. 10: Free share grants

The history of free shares grants can be found in Section 5.1.4.4. of this Universal Registration Document.

Table No. 11: Terms of compensation and other benefits granted solely to corporate officers

	Employment Agreement		**Additional pension plan**		**Indemnity or benefits due or likely to be due in the event of termination or change in position**		**Indemnity due to a non-compete clause**	
Executive Board members	**YES**	**NO**	**YES**	**NO**	**YES**	**NO**	**YES**	**NO**
Laurent LEVY								
Chairman of the Executive Board		**X**		**X**	**X** (1)			**X**
Corporate office Start Date	May 27, 2004							
Term of corporate office	At the shareholders' meeting held to approve the financial statements for the financial year ended December 31, 2023							
Philippe MAUBERNA								
Executive Board member	**X** (2)			**X**		**X**	**X** (3)	
Corporate office Start Date	August 28, 2013							
Term of corporate office	May 31, 2021							
Anne-Juliette HERMANT								
Executive Board member	**X** (4)			**X**		**X**	**X** (5)	
Corporate office Start Date	July 1st, 2019							
Term of corporate office	At the shareholders' meeting called to decide on the financial statements for the financial year ended December 31, 2023							
Bart VAN RHIJN								
Executive Board member	**X** (6)			**X**		**X**	**X** (7)	
Corporate office Start Date	June, 1st, 2021							
Term of corporate office	At the shareholders' meeting held to approve the financial statements for the financial year ended December 31, 2023							
Edwina BASKIN-BEY								
Executive Board member	**X** (8)			**X**		**X**	**X** (9)	
Corporate office Start Date	July, 1st, 2019							
Term of corporate office	April 6, 2020							

(1) On July 2, 2013, the Supervisory Board re-specified the terms of a previous decision from May 27, 2004, under the terms of which Laurent Levy would be entitled to a severance payment in case of a forced departure from the Company (see Section 5.6.2. of the Universal Registration Document).

(2) On May 23, 2013, Philippe Mauberna entered into an employment agreement with the Company. Following his appointment as a member of the Executive Board of the Company, the Supervisory Board held on August 28, 2013 authorized the combination of Mauberna's employment agreement with his corporate office.

(3) Philippe Mauberna was bound by a non-competition clause for a period of 12 months from the termination of his employment agreement. During this period, he was entitled to a special fixed monthly indemnity equal to two thirds of his annual base salary for his last month of service with the Company. However, the Supervisory Board waived this non-competition clause on April 6, 2021.

(4) On April 1, 2019, Anne-Juliette Hermant entered into an employment agreement with the Company. Following her appointment as a member of the Executive Board of the Company, the Supervisory Board held on June 20, 2019 authorized the combination of Anne-Juliette Hermant's employment agreement with her corporate office.

(5) Anne-Juliette Hermant is bound by a non-competition clause for a period of 12 months from the termination of her employment agreement. During this non-compete period, Anne-Juliette Hermant is entitled to a monthly compensation amounting to 66% of her annual base salary.

(6) On May 11, 2021 Mr. Bart Van Rhijn entered into an employment agreement with Nanobiotix Corp, effective on June 1, 2021.

(7) Bart Van Rhijn is bound by a non-competition clause for a period of 12 months from the termination of his employment agreement. During this non-compete period, Bart Van Rhijn is entitled to a monthly compensation amounting to 80% of his annual base salary abd his variable compensation.

(8) On April 1, 2019, Edwina Baskin-Bey entered into an employment agreement with the Company. Following her appointment as a member of the Executive Board of the Company, the Supervisory Board held on June 20, 2019 authorized the combination of Edwina Baskin-Bey's employment agreement with her corporate office. While her corporate office as a member of the Executive Board was terminated with immediate effect by the Supervisory Board on April 6, 2020, her employment agreement with the Company was terminated on October 10, 2019.

(9) Edwina Baskin-Bey was bound by a non-competition clause for a period of 12 months from the termination of her employment agreement, i.e. until October 10, 2020. During this non-compete period, Edwina Baskin-Bey was entitled to a monthly compensation amounting to two thirds of her gross monthly compensation for her last month of service with the Company.

2.2.3. Compensation and benefits allocated to Supervisory Board members

Table No. 3: Compensation (e.g. Director fees) and other compensation received by Supervisory Board members

Non-executive corporate officers	2021 Financial year		2020 Financial year	
	Amounts due	Amount paid	Amounts due	Amount paid
Laurent CONDOMINE[1]				
Compensation	€26,250	€49,000	€49,000	€21,429
Value of the BSA awarded during the financial year[2, 4]	€0	€0	€0	€0
Other compensation	—		—	
Gary PHILLIPS[3]				
Compensation	€36,750	€0	€0	€0
Value of the BSA awarded during the financial year[2, 4]	€0	€0	€0	€0
Other compensation	—		—	
Alain HERRERA				
Compensation	€35,000	€30,000	€30,000	€10,714
Value of the BSA awarded during the financial year[2, 4]	€0	€0	€0	€0
Other compensation	—		—	
Anne-Marie GRAFFIN				
Compensation	€42,000	€36,000	€36,000	€12,857
Value of the BSA awarded during the financial year[2, 4]	€0	€0	€0	€0
Other compensation	—		—	
Enno SPILLNER				
Compensation	€50,000	€40,000	€40,000	€14,286
Value of the BSA awarded during the financial year[2, 4]	€0	€0	€0	€0
Other compensation	—		—	
Christophe DOUAT[5] (Observer)				
Compensation	€35,000	€30,000	€30,000	€10,714
Value of the BSA awarded during the financial year[2, 4]	€0	€0	€0	€0
Other compensation	—		—	

(1) On May 25, 2021, Laurent Condomine, member and president of the Supervisory Board, resigned with immediate effect.

(2) The members of the Supervisory Board members and the observer were granted warrants (BSA) during the 2020 and 2021 financial years, the subscription price of which reflects the market value of those warrants at their grant date, according to the Black-Scholes model. Once subscribed, and if the exercise conditions are met, these BSA allow their holder to subscribe to the underlying shares at a price defined at the grant date (see Section 5.1.4.2 of the Universal Registration Document for more details on these BSA).

(3) On May 25, 2021, the Supervisory Board named Dr. Gary Phillips as a member of the Supervisory Board to replace Laurent Condomine for the remainder of Laurent Condomine's term of office, subject to the ratification of the appointment by the next ordinary shareholders' meeting, and elected him as chairman of the Supervisory Board.

(4) All the Supervisory Board members and the observer subscribed the BSA they were granted in 2020 and 2021, at an issue price of €0.29 per BSA granted in 2020 and €2.95 per BSA granted in 2021. In the 2020 and 2021 financial years, the Supervisory Board members and the observer thus paid the Company an amount of €1,153.04 € and €42,571.45 respectively for Laurent Condomine, €1,114.47 and €25,075 for Anne-Marie Graffin, €926.55 and 27,219.65 for Alain Herrera, €1,110.41 and €24,190 for Enno Spillner, and €915.53 and €22,847.75 for Christophe Douat.

(5) As part of his role as observer, Christophe Douat is granted compensation for his contribution to the Supervisory Board. Such compensation is calculated on the same basis as the compensation granted to the Supervisory Board members.

2.2.4. Directors' and employees' compensation ratios

In accordance with articles L. 22-10-9 6° and L. 22-10-78 of the French Commercial Code, the below ratios are calculated based on the fixed and variable compensation due for each executive officers (as detailed in Sections 2.2.2 and 2.2.3 of the Universal Registration Document, annualized for those who left during the year), divided by the average or median compensation of all of the Company's employees, excluding corporate officers. The valuation of dilutive instruments such as free shares and stock options has not been taken into account as per the uncertainty on the valuation of such long term incentives for the whole Company. The average compensation of employees is calculated on a full-time basis, excluding the compensation of the Executive Board members.

Comparisons between the level of compensation of executive officers and that of Group employees

Laurent LEVY - Chairman of the Executive Board	**2021**	**2020**	**2019**	**2018**	**2017**
Ratio[3] vs. average employee compensation	4.87	4.87	5.72	5.46	4.48
Ratio[3] vs. median employee compensation	7.76	7.53	7.45	7.59	7.22

Philippe MAUBERNA - Chief Financial Officer[1]	**2021**	**2020**	**2019**	**2018**	**2017**
Ratio[3] vs. average employee compensation	2.96	3.44	4.20	4.01	3.19
Ratio[3] vs. median employee compensation	4.72	5.32	5.47	5.58	5.14

Anne-Juliette HERMANT - Chief People Officer	**2021**	**2020**	**2019**	**2018**	**2017**
Ratio[3] vs. average employee compensation	2.57	2.95	2.16	-	-
Ratio[3] vs. median employee compensation	4.09	4.56	2.81	-	-

Bart Van RHIJN - Chief Financial Officer[2]	**2021**	**2020**	**2019**	**2018**	**2017**
Ratio[3] vs. average employee compensation	4.11	-	-	-	-
Ratio[3] vs. median employee compensation	6.54	-	-	-	-

(1) Philippe Mauberna resigned from his corporate office as Executive Board member, effective on May 31, 2021.

(2) Bart Van RHIJN was appointed as a member of the Executive Board, effective June 1st, 2021, by the Supervisory Board held on May, 31, 2021.

(3) Calculations are based on theoretical level of compensation of executive officers as if each were paid fully during the fiscal year for those having started or finished employment during the fiscal year.

Gary PHILLIPS – Chairman of the Supervisory Board	**2021**	**2020[1]**	**2019[1]**	**2018[1]**	**2017[1]**
Ratio vs. average employee compensation	-	0.21	0.26	0.26	0.25
Ratio vs. median employee compensation	-	0.33	0.33	0.36	0.41

[1] Laurent CONDOMINE as chairman prior Gary Phillips nomination

Annual changes in the compensation of Executive Board members and Company employees in light of Company performance over the last five years

As a key performance indicator for a biotechnology company, the Company monitors rigorously the resources allocated to research and development (R&D) compared to the total operating expenses incurred.

	2021 vs. 2020	2020 vs. 2019	2019 vs. 2018	2018 vs. 2017	2017 vs. 2016
Laurent LEVY					
Compensation	€553,065	€513,025	€479,757	€464,530	€384,545
Evolution (in absolute numbers)	€40,040	€33,268	€15,227	€79,985	€46,883
Evolution (in %)	7.80%	6.96%	3.28%	20.80%	13.88%
Bart VAN RHIJN(1)					
Compensation	€268,885	-	-	-	-
Evolution (in absolute numbers)	-	-	-	-	-
Evolution (in %)	-	-	-	-	-
Anne-Juliette HERMANT					
Compensation	€287,543	€300,000	€144,000	-	-
Evolution (in absolute numbers)	€(12,457)	€156,000	-	-	-
Evolution (in %)	(4.15)%	108.33%	-	-	-
Philippe MAUBERNA(2)					
Compensation	€382,515	€350,000	€338,800	€328,405	€261,360
Evolution (in absolute numbers)	€32,515	€11,200	€10,395	€67,045	€15,664
Evolution (in %)	9.29%	3.31%	3.17%	25.65%	6.38%
Average employee compensation(4)					
Compensation	107,053	€101,695	€93,761	€93,283	€85,729
Evolution (in absolute numbers)	5,358	€7,934	€478	€7,554	€12,662
Evolution (in %)	5.27%	8.46%	0.51%	8.81%	17.33%
Proportion of resources allocated to R&D compared to the total operating expenses incurred (4)					
Proportion	73%	73%	74%	77%	76%
Evolution (in %)	12%	-19%	33%	22%	30%

(1) Bart Van RHIJN was appointed as a member of the Executive Board, effective June 1st, 2021, by the Supervisory Board held on May 31,2021.

(2) Philippe Mauberna resigned from his corporate office as Executive Board member, effective on May 31, 2021.

(3) Average gross salary, including variable pay, on a full-time basis.

2.2.5. Restriction on the sale by members of the Executive Board and the Supervisory Board of their stake in the company

There is no such restriction, other than (i) the one applicable to free shares during their holding period and (ii) pursuant to article L. 225-197-1, whereby members of the Executive Board are required to keep at least 10% of the free shares they were granted until the termination of their duties within the Company.

2.2.6. Summary of the operations of the managers and of the persons mentioned in article L.621-18-2 of the Monetary and Financial Code (*"Code Monétaire et Financier"*) on the Company's securities carried out during the financial year ended December 31, 2021

None.

2.2.7. Amounts provisioned by the Company for the payment of pensions, retirement and other benefits for the members of the Executive Board and the Supervisory Board

The Company has not provisioned any amounts for the payment of pensions, retirements and other benefits for members of the Executive Board and Supervisory Board, except for the sums allotted for corporate officer private unemployment insurance (*"Garantie Sociale du Chef d'entreprise"*), taken out at the benefit of Levy for the 2020 and 2021 financial years, with a premium amounting to €18,025 and €18,025, respectively, and the statutory retirement benefits of Mauberna and Hermant.

The Company has not granted any new hiring or severance bonuses or other severance or benefits to these persons, with the exception of the departure indemnity Levy is entitled to (see Section 5.6.2. of the Universal Registration Document).

2.2.8. Warrants (BSA) and/or founders' warrants (BSPCE) allocated and free shares allocated to members of the Executive Board and the Supervisory Board

As of the date of the Universal Registration Document, the direct and indirect shareholdings of the members of the Executive Board and the Supervisory Board, as well as the number of financial securities giving access to the Company's share capital that they hold, are as follows:

Executive Board

Name	Shares		Securities granting access to capital
	Number	% of capital	
Laurent LEVY Chairman of the Executive Board	959,060	2.75%	A total of 1,130,400 potential shares derived from the exercise of: * 21,000 BSPCE 09-2014 founders' warrants granting the right to subscribe to 21,000 shares at a price per share of €18.68 * 24,000 BSPCE 2015-1 granting the right to subscribe to 24,000 shares at a price per share of €18.57 *23,500 BSPCE 2016 Ordinary granting the right to subscribe to 23,500 shares at a price per share of €14.46 *23,500 BSPCE 2016 Performance granting the right to subscribe to 23,500 shares at a price per share of €14.46 *26,400 BSPCE 2017 Ordinary granting the right to subscribe to 26,400 shares at a price per share of €15.93 *32,000 BSPCE 2017 granting the right to subscribe to 32,000 shares at a price per share of €15.93 *500,000 OSA LLY 2019 (stock options) granting the right to subscribe to 500,000 shares at a price per share of €6.41 *120,000 OSA 2020 granting the right to subscribe to 120,000 shares at a price per share of €6.25 *180,000 AGA 2021 (free shares) 180,000 OSA 2021-04 Performance granting the right to subscribe to 180,000 shares at a price per share of €13.74

Name	Shares		Securities granting access to capital
	Number	% of capital	
Bart VAN RHIJN Member of the Executive Board	0	0.00%	A total of 120,000 potential shares derived from the exercise of: * 60,000 OSA Ordinary 2021-06 granting the right to subscribe to 60,000 shares at a price per share of €12.99 * 60,000 OSA Performance 2021-06 granting the right to subscribe to 60,000 shares at a price per share of €12.99
Anne-Juliette HERMANT Member of the Executive Board	50,000	0.00%	A total of 210,000 potential shares derived from the exercise of: *60,000 OSA 2020 granting the right to subscribe to 60,000 shares at a price per share of €6.25 *90,000 AGA 2021 (free shares) *60,000 OSA 2021-04 Performance granting the right to subscribe to 60,000 shares at a price per share of €13.74

Supervisory Board

Name	Shares		Securities granting access to capital
	Number	% of capital	
Gary PHILLIPS Chairman of the Supervisory Board	0	0.00%	None.
Anne-Marie GRAFFIN Vice-Chairman of Supervisory Board	0	0.00%	A total of 23,143 potential shares derived from the exercise of: * 5,000 BSA 2015-1 granting the right to subscribe to 5,000 shares at a price of €17.67 per share *2,900 BSA 2018 granting the right to subscribe to 2,900 shares at a price of €13.55 per share *2,900 BSA 2019-1 granting the right to subscribe to 2,900 shares at a price of €11.66 per share *3,843 BSA 2020 granting the right to subscribe to 3,843 shares at a price of €6.59 per share

Name	Shares		Securities granting access to capital
	Number	% of capital	
Alain HERRERA Member of the Supervisory Board	0	0.00%	A total of 27,222 potential shares derived from the exercise of: * 4,000 BSA 2014 granting the right to subscribe to 4,000 shares at a price of €17.67 per share * 5,000 BSA 2015-1 granting the right to subscribe to 5,000 shares at a price of €17.67 per share *2,900 BSA 2018 granting the right to subscribe to 2,900 shares at a price of €13.55 per share *2,900 BSA 2019-1 granting the right to subscribe to 2,900 shares at a price of €11.66 per share *3,195 BSA 2020 granting the right to subscribe to 3,195 shares at a price of €6.59 per share
Enno SPILLNER Member of the Supervisory Board	0	0.00%	A total of 20,029 potential shares derived from the exercise of: *4,000 BSA 2018 granting the right to subscribe to 4,000 shares at a price of €13.55 per share *4,000 BSA 2019-1 granting the right to subscribe to 2,900 shares at a price of €11.66 per share *3,829 BSA 2020 granting the right to subscribe to 3,829 shares at a price of €6.59 per share
Christophe DOUAT Observer	0	0.00%	A total of 16,702 potential shares derived from the exercise of: *2,900 BSA 2018 granting the right to subscribe to 2,900 shares at a price of €13.55 per share *2,900 BSA 2019-1 granting the right to subscribe to 2,900 shares at a price of €11.66 per share *3,157 BSA 2020 granting the right to subscribe to 3,157 shares at a price of €6.59 per share

For more information on the securities held by the Executive and Supervisory Board members, including their exercise conditions, see Section 5.1.4 of the Universal Registration Document.

2.2.9. Compensation policy applicable to corporate officers for the 2022 financial year

Pursuant to Article L. 22-10-26 of the French commercial code, the Supervisory Board submits for approval to the shareholders' meeting convened to approve the financial statements of the year ended December 31, 2021 to approve compensation policy for corporate officers for the 2022 financial year, which must be consistent with the Company's corporate interest and contribute to its long-term viability and be in line with its strategy. This policy describes all the components of the fixed and variable compensation payable to members of the Executive Board and the Supervisory Board for the performance of their duties for the 2022 financial year. It also explains the decision-making process followed for its determination, review and implementation.

The principles and criteria of this compensation policy, determined by the Supervisory Board upon the recommendation of the appointments and compensation committee, are presented below.

2.2.9.1. Executive Board

2.2.9.1.1. Laurent Levy, Chairman of the Executive Board

Compensation elements	Principles	Determining criteria
Fixed compensation	The chairman receives fixed compensation	The gross annual amount of this fixed compensation has been set at 380,000 Euros for the 2022 financial year.
Variable compensation	The Chairman may receive variable compensation up to 60% of his fixed compensation.	The final amount of the variable compensation due to the chairman will be determined by the supervisory board in accordance with the principles described in section 2.2.9.1.4 below.
Exceptional compensation	The Chairman may be awarded exceptional compensation.	This exceptional compensation would be intended to compensate specific performance on one or more projects that have a major impact on the Company's development, such as acquisitions, mergers or change of control.
Benefits in kind	The Chairman benefits from a GSC Insurance (Corporate officer unemployment insurance)	-
Supplementary retirement plan	The Chairman does not benefit from any supplementary retirement plan.	-

In addition, Laurent Levy will be entitled to a termination indemnity in the event of forced departure from the Company.

The Chairman of the Executive Board may be granted stock options and/or free shares subject to continued service and performance conditions.

Finally, it is specified that Laurent Levy does not receive any compensation of any kind whatsoever in respect of his duties within the Company's subsidiaries, and does not benefit from a long-term multi-annual compensation mechanism, other than, on a case-by-case basis, the granting of stock options and/or free shares subject to continued service and/or performance conditions.

Pursuant to Article L. 22-10-34 of the French Commercial code, the amounts resulting from implementation of the aforementioned compensation policy will be submitted for shareholder approval during the shareholders' meeting called to approve the Company's financial statements for the 2022 financial year, with payment of variable and exceptional compensation remaining subject to the shareholders' approval during the next annual shareholders' meeting.

2.2.9.1.2. Bart Van Rhijn, member of the Executive Board

It should be noted that all compensation received by Bart Van Rhijn is in respect of his salaried duties. For more information on Bart Van Rhijn's employment agreement, including its term and termination conditions, see Section 5.6.2. of the Universal Registration Document:

Compensation elements	Principle	Determining criteria
Fixed compensation	Bart Van Rhijn receives a fixed compensation granted as part of an employment agreement.	The gross annual amount of this fixed compensation has been set at €350,000 (USD 390,667) for the 2022 financial year.(*)
Variable compensation	Bart Van Rhijn may receive variable compensation up to 50% of his fixed compensation.	The final amount of the variable compensation due to Bart Van Rhijn, if any, will be determined by the supervisory board in accordance with the principles described in section 2.2.9.1.4 below.
Non-competition clause	Bart Van Rhijn is bound by a non-competition clause for a period of 12 months from termination of his employment agreement.	Payment of compensation during the non-compete period at a rate equal to 80% of his annual base salary and variable compensation.
Exceptional compensation	Bart Van Rhijn may be awarded exceptional compensation.	Such exceptional compensation may be used to provide compensation for exceptional performance on one or more projects that have had a major impact on the Company's development.
Benefits in kind	N/A	N/A
Supplementary retirement plan	Bart Van Rhijn does not benefit from any supplementary retirement plan.	-

(*) applicable amount according to the employment agreement is in USD. The euro to dollar exchange rate used is $ 1.12, (I.e. the average exchange rate for the February-March 2022 period).

Additionally, Bart Van Rhijn may be granted stock options and/or free shares subject to continued service and performance conditions.

Finally, it is specified that Bart Van Rhijn does not receive any compensation of any kind whatsoever in respect of his duties within the Company's subsidiaries other than Nanobiotix Corp., and does not benefit from a long-term multi-annual compensation mechanism, other than, on a case-by-case basis, the granting of stock options and/or free shares subject to continued service and/or performance conditions.

Pursuant to Article L. 22-10-34 of the French Commercial code, the amounts resulting from implementation of the aforementioned compensation policy will be submitted for shareholder approval during the shareholders' meeting called to approve the Company's financial statements for the 2022 financial year, with payment of variable and exceptional compensation remaining subject to the shareholders' approval during the next annual shareholders' meeting.

2.2.9.1.3. Anne-Juliette Hermant, member of the Executive Board

It should be noted that all compensation received by Anne-Juliette Hermant is in respect of her salaried duties. For more information on Anne-Juliette Hermant's employment agreement, including its term and termination conditions, see Section 5.6.2. of the Universal Registration Document.

Compensation elements	Principle	Determining criteria
Fixed compensation	Anne-Juliette Hermant receives a fixed compensation granted as part of an employment agreement.	The gross annual amount of this fixed compensation has been set at €210,000 for the 2022 financial year.
Variable compensation	Anne-Juliette Hermant may receive variable compensation up to 50% of her fixed compensation.	The final amount of the variable compensation due to Anne-Juliette Hermant, if any, will be determined by the supervisory board in accordance with the principles described in section 2.2.9.1.4 below.
Non-competition clause	Anne-Juliette Hermant is bound by a non-competition and loyalty clause for a period of 12 months from termination of her employment agreement.	Payment of a special fixed monthly indemnity equal to 2/3 of her gross monthly compensation for her last month of service with the Company.
Exceptional compensation	Anne-Juliette Hermant may be awarded exceptional compensation.	Such exceptional compensation may be used to provide compensation for exceptional performance on one or more projects that have had a major impact on the Company's development.
Benefits in kind	N/A	N/A
Supplementary retirement plan	Anne-Juliette Hermant does not benefit from any supplementary retirement plan.	-

Additionally, Anne-Juliette Hermant may be granted stock options and/or free shares subject to continued service and performance conditions.

Finally, it is specified that Anne-Juliette Hermant does not benefit from a long-term multi-annual compensation mechanism, other than, on a case-by-case basis, the granting of stock options and/or free shares subject to continued service and/or performance conditions.

Pursuant to Article L. 22-10-34 of the French Commercial code, the amounts resulting from implementation of the aforementioned compensation policy will be submitted for shareholder approval during the shareholders' meeting called to approve the Company's financial statements for the 2022 financial year, with payment of variable and exceptional compensation remaining subject to the shareholders' approval during the next annual shareholders' meeting.

2.2.9.1.4. Executive Board's members variable compensation calculation principles

The final amount of the variable compensation due to each member of the Executive Board for the 2022 financial year shall be determined by the Supervisory Board in accordance with the following principles:

- The individual performance percentage will be based on a matrix combining:
    - the 'What': the achievement of specific operational individual criteria determined by the Supervisory Board based on recommendation of the appointments and compensation committee, it being specified that these criteria are not made public for confidentiality reasons,

  and
    - the 'How': the individual ability to role-model Nanobiotix leadership values.

  Those two dimensions will be each assessed through a 5-level scale (significantly under expectations, under expectations, meets expectations, below expectations, significantly below expectations)

multiplied by

- The Company performance factor; this Company performance factor shall be established based on the achievement of the Company-wide yearly performance criteria. They are fully derived from the Company's strategic plan (defined as the 'critical path') and are organized around four pillars that are expected to sustain the Company's development:

Pillars	KPIs	Weight
Head and neck registration path	Achievement of the targets as per the critical path for NBTXR3	25%
Immuno-oncology registration path	Achievement of the targets as per the critical path for NBTXR3	25%
Prepare NBTXR3 to market	Achievement of a target figures specified in the critical path	25%
Ensure organizational scalability	Achievement of target figures specified in the critical path	25%

The achievement of the Company performance criteria as well as the individual performance of each member of the Executive Board will be assessed by the Supervisory Board based on the recommendations of the appointments and compensation committee, it being specified that the appointments and compensation committee may be assisted by the chairman of the Executive Board in its assessment of the other members of the Executive Board's ability to role-model Nanobiotix leadership values.

The main changes in this compensation policy for the Executive Board for the 2022 financial year in comparison with the 2021 financial year are the following:

- based on executive compensation experts' recommendations as well as on an international benchmark, the calculation rules for the Executive Board members' variable compensation for the 2022 financial year have been fully aligned with the rules for calculating the variable compensation of Group employees;
- a multiplier between the Company's yearly performance and each Executive Board member's individual performance has been implemented;
- such multiplier aligns the risk-sharing between Executive Board members and shareholders in the light of the Company development by ensuring a strong correlation between each Executive Board member's compensation and the achievement of the Company-wide yearly performance criteria;
- therefore, the event of an underachievement (i.e. the achievement of the Company-wide yearly performance criteria below what was expected), if and when assessed as such by the

Supervisory Board, will proportionally decrease the variable compensation of each Executive Board member, even if he/she has fully achieved his/her personal performance criteria. In contrast, the event of an overachievement (i.e. the achievement of the Company-wide yearly performance criteria exceeds expectations), if and when assessed as such by the Supervisory Board, will proportionally increase each Executive Board member's variable compensation, even if he/she has not fully achieved his/her personal performance criteria. This new multiplication mechanism nullifies the previous capping of any bonus earned for the achievement of Company-wide yearly performance criteria at 100% of each Executive Board member's variable compensation.

2.2.9.2. Members of the Supervisory Board

The members and observers, if any, of the Supervisory Board are entitled to compensation within the limits of the global annual amount set by the shareholders' meeting (compensation for serving on the Supervisory Board and each of the committees set up by the Supervisory Board – formerly known as attendance fees). The shareholders' general meeting dated April 28, 2021 set such compensation to an annual aggregate amount of up to €260,000 for the 2021 financial year and for each subsequent financial year, until a decision to the contrary is made by the shareholders of the Company at an ordinary shareholders' meeting.

The Supervisory Board determines (within the range of limits voted on by the shareholders' meeting) the amount awarded to each member and observer, if any, based on the principles described below:

(i) an amount not exceeding €63,000 may be granted to the Chairman of the Supervisory Board;
(ii) an amount not exceeding €35,000 may be granted to each member of the Supervisory Board (excluding the Chairman but including the observer(s), if any);
(iii) an additional amount not exceeding €7,000 may be granted to the chairperson of the appointments and compensation committee; and
(iv) an additional amount not exceeding €15,000 may be granted to the chairperson of the audit committee.

Each of the members and observers, if any, of the Supervisory Board must attend 80% of all meetings of the Supervisory Board and committees of the Supervisory Board, as applicable, in order to receive this compensation.

In addition, members and observers, if any, of the Supervisory Board may receive a compensation for special assignments that may be delegated to them by the Supervisory Board and that would be the subject of regulated agreements put to the vote at the shareholders' meeting. The amount of such compensation will be set by the Supervisory Board based on the nature of the specific assignment entrusted to the concerned member or observer, as applicable.

Furthermore, travel expenses are reimbursed for each physical attendance upon presentation of an expense report.

Lastly, the members of the supervisory board may be offered the option of subscribing, under market conditions, for warrants, the issue price of which will be determined on the day of issuance of the warrants on the basis of their characteristics, if necessary with the assistance of an independent expert.

2.2.9.3. Compensation paid or due by a company within the consolidation scope in line with article L. 233-16 of the Code of Commerce

No compensation of this kind is provided for in the compensation policy.

2.2.9.4. Explanation of how total compensation complies with the adopted compensation policy, including the way it contributes to the Company's long-term performance and how performance criteria have been applied

The compensation of the Executive Board members is determined by the Supervisory Board, based on proposals from its appointments and compensation committee.

Each member of the Executive Board receives a fixed compensation, the chairman in respect of his duties and the other members of the Executive Board in respect of an employment contract. In addition, in accordance with the compensation policy approved by the shareholders' meeting of April 28, 2021, the Supervisory Board may grant variable annual compensation to the chairman of the Executive Board up to 60% of the fixed annual compensation and any other member up to 50% of the fixed annual compensation of the concerned member. This variable compensation is determined on the basis of the achievement of performance criteria related to the Company's objectives (for 50% of the bonus), the achievement of individual objectives set by the Supervisory Board upon the appointments and compensation committee's proposal (for 30% of the bonus), and the individual leadership qualities of the member concerned (for the remaining 20%). The Company's objectives are set by the Executive Board, reviewed by the appointments and compensation committee and approved by the Supervisory Board. The achievement of these objectives is assessed according to the same procedure. With regard to the 2021 financial year, the Supervisory Board decided on March 30, 2022, based on its review and evaluation of the achievement of the Company's objectives for the 2021 financial year, including its assessment of the quality of the leadership of each member of the Executive Board, to set the annual variable compensation for each member of the Executive Board accordingly and as further detailed in section 2.2.2. of the Universal Registration Document.

The same principles apply to the other Nanobiotix employees, each of whom is eligible for variable compensation linked, in part, to the objectives of his or her department and, in part, to personal objectives. Performance criteria are applied on the basis of the achievement of departmental objectives assessed by the executive board, on the one hand, and on the basis of the achievement of personal objectives assessed by the managers concerned and reported to each member of their team during annual interviews, on the other.

Each year, the Company asks its shareholders to grant it the necessary authorizations and delegations of authority to proceed, where appropriate, with the granting of instruments giving access to the Company's capital (stock options and/or free shares) to all Group employees. The Executive Board, after authorization by the Supervisory Board, on the advice of the appointments and compensation committee, shall decide on the granting of such instruments when these bodies deem it appropriate, in particular with regard to market conditions.

For the 2022 financial year, the shareholders' meeting called to approve the financial statements for the year ended December 31, 2021 will be asked to vote to modify the principles used for the calculation of the Executive Board members' variable compensation. See Section 2.2.9.1.4 of the Universal Registration Document for more information.

2.2.9.5. Way in which the last shareholders' ordinary meeting vote, as provided for in section II of article L. 225-100 of the French commercial code has been taken into account

The compensation policy for the members of the Executive Board and the Supervisory Board complies with the votes cast at the last shareholders' meeting, and the amounts paid have been or will be paid in accordance with the compensation policy approved by the shareholders' meeting.

2.2.9.6. Deviation from the procedure for implementing the compensation policy and any waiver applied in accordance with the second paragraph of III of Article L. 225-37-2, including an explanation of the nature of the exceptional circumstances and an indication of the specific elements from which a waiver is made

No deviation was identified during the reference period.

2.3. GOVERNANCE

For the sake of transparency and public information and in order to comply with the requirements of Article L. 22-10-10 (former L. 225-37-4) of the Code of Commerce, the Supervisory Board, during its meeting held on April 11, 2012, decided to refer to the MiddleNext Code, which is available on the MiddleNext website (www.middlenext.com), as a corporate governance reference code.

Implementation of the "comply or explain" rule
The Company's objective is to comply with all of the recommendations of the MiddleNext Code.

As such, the Company regularly reviews its governance in relation to the recommendations of this Code. The table below showcases the Company's position on all of the recommendations issued by the MiddleNext Code as of the date of this Universal Registration Document:

Middlenext Code Recommendations	Adopted	Will be adopted	Under consideration
Supervisory power			
R1: Code of conduct for board members	X		
R2: Conflicts of interest	X		
R3: Composition of the board - Attendance by independent members	X		
R4: Information of the board members	X		
R5: Training of the board members			X(1)
R6: Organization of board and committee meetings	X		
R7: Setting up of committees	X		
R8: Implementation of a specialized Corporate Social and environmental Responsibility (CSR) committee			X(2)
R9: Setting up internal board regulations[3]	X		
R10: Selection of each board member	X		
R11: Length of board members' terms of office	X		
R12: Compensation for board members	X		
R13: Establishing an assessment of the board's work	X		
R14: Shareholders relations		X(3)	
Executive power			
R15: Company diversity and equity policy	X(4)		
R16: Definition and transparency of executive directors' compensation	X		
R17: Preparation for the succession of directors		X(5)	
R18: Combination of employment agreements and corporate offices	X		
R19: Severance packages	X(6)		
R20: Supplementary retirement plans	X		
R21: Stock options and free shares	X(7)		
R22: Review of points to be watched	X		

(1) *The Company intends to reflect on the implementation of a three-year training plan for its Supervisory Board and will set up an annual follow-up of this process.*

(2) *The Company intends to reflect on the implementation of a specialized Corporate Social and environmental Responsibility (CSR) committee of the Supervisory Board and will set up an annual follow-up of this process.*

(3) *Starting after the shareholders' meeting held to approve the financial statements for the year ended December 31, 2021, the Supervisory Board intends to conduct a yearly review of the voting results of each of the shareholders' meetings of the Company, especially as regards the negative votes on any decision submitted to its shareholders. The Board would in particular pay attention on how the majority of the Company's minority shareholders expressed themselves, and discuss whether any measures should be taken as a result.*

(4) *The Company continues to pursue a diversity and equity policy at all hierarchical levels. As of the date of the Universal Registration Document, women are represented at all levels of the Company. In particular, the Executive Board is composed of two men and one woman, and the Supervisory Board is composed of three men and one woman (see Section 2.1.5.2.3 for more information on the balanced gender representation on the Supervisory Board). Overall, women represent 67% of the Company's employees.*

(5) *The Company intends to continue its reflection on the succession of its executives in 2022 and has set up an annual follow-up of this process.*

(6) *The Company has granted Laurent Levy a severance indemnity in the event of forced departure from the Company, it being specified that such severance payments, as well as any non-competition payments that Laurent Levy may be entitled to receive, cannot exceed twice the amount of his total compensation during the year in which his duties were terminated. See Section 5.6.2 of the Universal Registration Document for more information.*

(7) *The exercise of a portion of the BSPCEs that have been granted in the past by the Company to some members of the Executive Board is not subject to performance conditions. However, the Company has since made the exercise and/or acquisition of dilutive instruments granted to its corporate officers subject to performance conditions. See Section 5.1.4 for more information on the dilutive instruments granted to corporate officers of the Company.*

2.4. INTERNAL CONTROL AND RISK MANAGEMENT PROCEDURES IMPLEMENTED BY THE COMPANY

2.4.1. General principles of internal control

2.4.1.1. Definition

The Company has adopted the definition for an internal audit proposed by the French Financial Markets Authority (AMF)[(1)], which states that an internal audit is a mechanism implemented by a Company to ensure:

- Compliance with laws and regulations;
- Implementation of the instructions and guidelines laid down by the governing board;
- Proper operation of the Company's internal procedures;
- The reliability of financial information;

and, generally contributes to control over its activities, the effectiveness of its operations and the efficient use of its resources. During the financial year, the Company has continued to implement an internal audit process designed to "guarantee the relevance and reliability of the information used and disseminated in-house relating to the Company's activities". However, internal auditing cannot provide absolute guarantee that the Company's objectives will be achieved, nor that risks of error or fraud are fully controlled or eliminated.

(1) Guide to implementation of internal audit frameworks suitable for small caps and midcaps, updated on July 22, 2010.

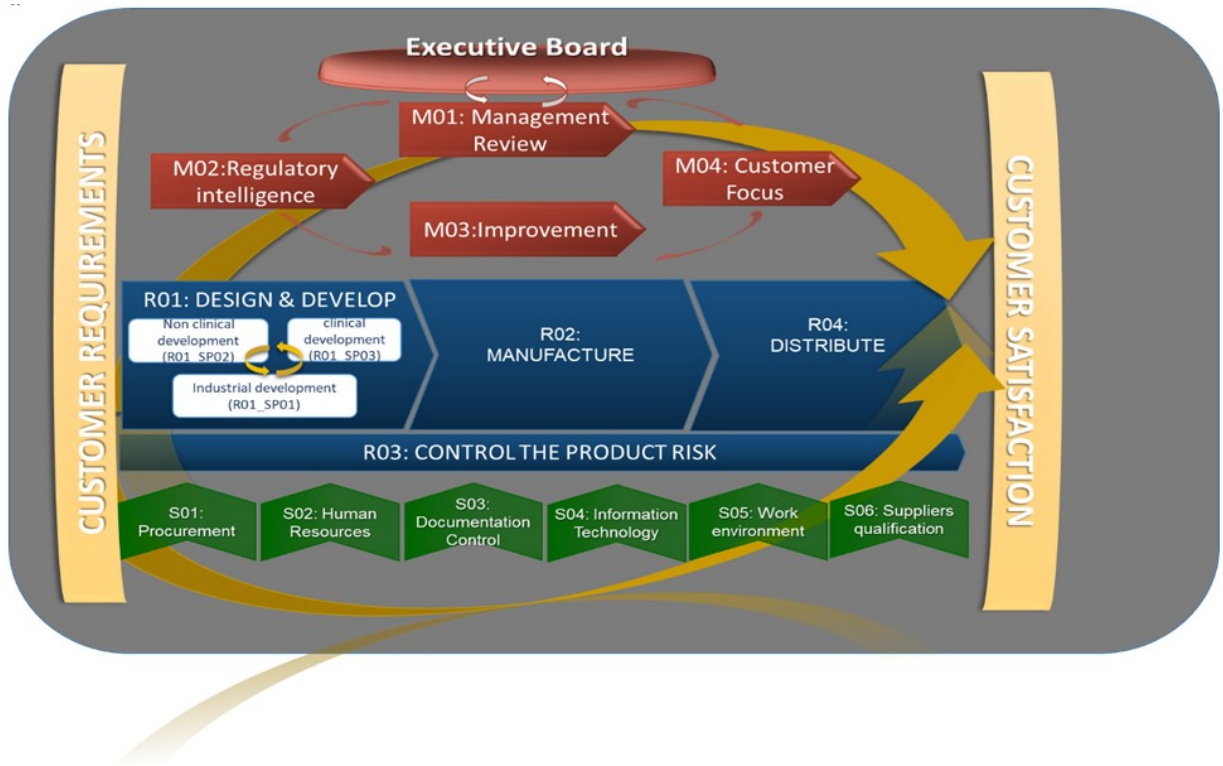
2.4.1.2. Components of internal audits

2.4.1.2.1. General organization

The organization of the internal audit and risk management procedures within the Company is based on the following principles and tools:

- Organizational charts and job descriptions, regularly updated under the supervision of each business manager, are maintained centrally by the human resources department. Job descriptions contain an in-depth description of each employee's expected duties, responsibilities, and skill sets. These cover all staff members, and for key roles, they are reviewed under the direct supervision of the Executive Board Members;
- The rules for assuming and delegating authority that apply to the different managers, specified in the job descriptions themselves;
- The Quality Assurance manual defines a detailed mapping of all key business processes, that interact with the aim of achieving the expected performance and responding to diverse compliance issues. The mapping is consequently established based on the following process typology:
  - "Management" processes,
  - "Performance" processes, and
  - "Support" processes.

The system is thus based on an agile approach to the processes providing robustness and flexibility as the Company evolves.



- **Formalized tracking of access rights to the information system** and main documents. Access rights are split up by business area and read and write permissions are determined for each group of team members. In addition, whenever a new employee is hired, the department managers determine the new employee's access rights for their collaborative workspace for each sub-group falling within their area of responsibility.
- **Skills management**, directly linked to the strategic plan, the definition of responsibilities, the training plan and the regulatory and standards reference documents applicable to the tasks defined in the job descriptions.

During the annual individual performance review, detailed objectives are set out and a corresponding personal action plan is defined in a document validated by the employee, his/her immediate supervisor and a member of the Executive Board. The annual review is formalized in an "annual review assessment sheet" that includes a detailed performance evaluation based on the Company's defined general objectives and each team member's individual objectives. Staff recruitment and dismissals are initiated and approved by the Executive Board.

Annual follow-up is formalized in an HR information system that allows for regular monitoring of achievement of set individual objectives and for ongoing assessment of available resources and means made available throughout the year.

The Company's internal audit mechanism is also based on the dissemination and analysis of information necessary for managing the business:

2.4.1.2.2. Project management interaction

- **Meetings chaired by the Executive Board**: organized at least two times per year, or more regularly if the Company's current situation requires it. They allow formal communication on the progress of key activities, strategic decisions and progress toward achieving corporate objectives; they allow formal communication on the progress of key activities and strategic decisions;
- **Leadership reviews:** prepared and led by the Quality Assurance Director, under the supervision of the Executive Board. The calendar is established on a yearly basis with a schedule of four meetings per year. These leadership reviews make it possible to gain a global vision of the company's performance using strategic axes broken up into annual objectives for all processes, functions and employees. Leadership reviews are an opportunity to review the sustainability and suitability of the current organizational structure, to establish and make decisions about opportunities for improvement and change, and to evaluate the company's policies and objectives on a quarterly basis at a minimum. Dashboards bringing together key indicators are used to determine corrective and preventive actions to be developed across different functions.
- **Project reviews:** with the aim of maintaining the effectiveness of resources deployed and their suitability for the objectives defined, a project management-based approach has been implemented in order to support the business's strategic plan.

Project management makes it possible to establish a structural view that ensures the availability of a multi-functional team dedicated to the project's success. Each project identifies a Project Manager who oversees the proper allocation of resources and deliverables within the allotted time. Each project is monitored at a strategic level during meetings with the Executive Board, every six weeks or according to critical project milestones. Each project is matched up with a defined set of monitoring and performance indicators making it possible to gain a holistic vision through the use of dashboards.

2.4.1.2.3. Tracking processes and tools

Tracking processes and tools assessing interdependence across the Company's different strategic and operational axes have been put in place. These processes and tools make it possible to anticipate potential drift and to optimize implementation of corrective actions used to mitigate impact in terms of timelines and human and financial resources.

Consequently, in order to support the vision set by the Executive Board, measurements and tracking indicators are identified within each department, down to an individual level. Accordingly, each department has a responsibility to monitor the performance of these action plans and has the ability to rapidly inform the Executive Board of any potential discrepancies that are noted or anticipated in order to make corrections to the initial plan.

2.4.1.2.4. Risk management process

Risk management is an essential component of decision-making mechanisms within the Company, not only for patient safety, but also for the adequacy and prioritization of activities to address strategic issues.

Consequently, the risk management process is expressed at the organizational level through each of the Company's key processes (see process mapping in Section 2.4.1.2.1. Overall Organization) and at the product level throughout their whole life cycle, beginning with design of the initial prototypes up until verification and validation, followed by production/post production, use and disposal.

These approaches are underpinned by active application of international standards developed for medical device manufacturers, ISO 13485: 2016 and ISO 14971, whose concepts are widely adopted across the healthcare industry through the use of various tools such as FMEA. These are also applied to the Company's risk management activities.

The holistic, document-based methodology sets up a multidisciplinary forum that is shaped and facilitated by the quality assurance department on a regular basis and tailored to the issues at hand.

Each stakeholder contributes their vision, and the combined vision of the various participants makes it possible to identify and quantify risk scenarios, in order to prioritize them according to severity, occurrence and the means of detectability available.

The remediation plan established subsequently ensures that these risk situations are controlled, not only for the product, patients, users, third parties and the environment, but also to guarantee the company's good reputation.

This plan, like all scenarios, is regularly reviewed to take into account technical developments and the associated current state of the art, as well as external and internal developments within the company.
All the documentation complies with the procedures of the Company's Quality system and provides proof that the risks inherent in the Company's activities are effectively controlled. The overall acceptability of residual risk is approved by the Executive Board primarily during management reviews.

2.4.1.2.5. Auditing activities

2.4.1.2.5.1. Auditing activities linked to regulatory compliance

Due to the nature of its activities, the Company is subject to local French, European and international regulations. To this end, it has implemented a regulatory monitoring process in its management processes to analyze and implement any changes in these regulations and to ensure the compliance of the Company's activities at all levels.

The Company must comply, among other things, with European Regulation 2017/745 ("MDR") establishing the implementation of requirements applicable to medical devices, which will require that the Company's European activities, looking ahead of commercialization, be brought into compliance starting as of the date on which it comes into force, i.e., from May 26, 2021. While the quality system of the Company is complying with prior European Directive 93/42/EEC relating to medical devices and has submitted its NANORAY 312 trial referencing compliance to some MDR sections, a process to finalize the full compliance is currently ongoing.

Also, with a view to complying with regulations, the Company has established a program to implement the requirements of the General Data Protection Regulation (GDPR) 2016/679, the provisions of which have been in force since May 25, 2018. This compliance takes place throughout the Company and its communication and data storage channels, and more specifically in the HR and clinical research processes. The Company has appointed a data protection officer who is responsible for the implementation of the global data protection policy for internal activities and those outsourced to third parties.

The quality management system and its policy provide the necessary framework for defining the operations involved in the application of regulations, to ensure the compliance of operations through the application of approved procedures and operating methods. The control of the application of all these procedures is carried out primarily through improvement processes that include internal and subcontractor audits and the presentation of performance indicators and monitoring of key processes to the Executive Board, mainly at management reviews.

Additionally, as the Company has been involved in a voluntary corporate certification process through ISO 13485 since 2015, it has been hosting auditors from the French notified body annually to assess the compliance of its quality management system with respect to regulatory requirements, required standards and legal provisions. Since the start of the process, the company has been keen to extend the scope of these audits on a regular basis without receiving any unfavorable opinions from the various third parties involved.

2.4.1.2.5.2. Auditing activities linked to outsourced processes

In order to optimize resources and skills, the company has delegated all or part of its activities to subcontractors competent in its various fields of activity.

The choice and deployment of third party operations is underpinned by a robust selection and qualification process. This process therefore makes it possible to establish an ongoing relationship between the Company and its subcontractors based on trust, by ensuring that technical and regulatory requirements are met within a clear and formalized legal framework.

The following activities have therefore been totally or partially outsourced:

- Manufacturing of products and their associated analytical quality control;
- Non-clinical product validation studies;
- Monitoring activities for clinical research sites, and electronic data management using suitable and validated software;
- Electronic management and storage of patient safety events;
- Intellectual property management;
- Production of financial statements;
- Fiscal and payroll management.

The Company sets up documented procedures to ensure the compliance of activities and implements the necessary audits to ensure that subcontractors satisfies the requirements needed to achieve predetermined objectives.

Among these auditing activities, the Company conducts audits of all of its partners. These audits are carried out by the Quality Department, regardless of the activities that are audited. Each audit is planned during the management review based on internal procedures and a formalized risk assessment. Ongoing audits of activities by the Company's departments and the audit results are analyzed during these reviews and enable active monitoring of the quality of provided services and continual reassessment of the initial qualification of contractors.

All subcontracting agreements include a right to audit which is regularly exercised depending on the criticality of the delegated activities.

The production of financial statements is outsourced to an accounting firm. In addition to its mission of presenting the financial statements, the selected firm provides a monthly review of the operations recorded in the accounts.

Taking in account the Company's size, reliance on subcontracted or co-contracted solutions allows for broad technical and strategic objectives to be established and for the procurement of data whose accuracy and traceability has been inspected by the subcontractor and by the Company's business managers.

2.4.1.2.6. Audits related to data protection and physical security

The protection of data protection and know-how are subject to rigorous procedures and inspections. In particular, the Company has set up redundant servers and backup procedures meeting current security standards. In order to protect itself as effectively as possible against attempted intrusions, internet access servers and data servers are kept completely separate.

The Company's premises include a secure room equipped with several strong, fireproof cabinets containing all research work and contracts.

With regard to the requirements of the French Labor Code, the Company has developed a Unique Risk Assessment Document (DUERP (Document Unique d'Evaluation des Risques - Unique Risk Assessment Document) to assess the potential risks to which employees are exposed and to describe the prevention measures and methods used to ensure the safety and to protect the health of its employees.

This document is regularly updated to accurately reflect the company's general health and safety environment as well as the annual program of risk prevention actions to reduce risks. These safety measures are systematically referred to when welcoming a newcomer by presenting them with orientation handbooks and routinely for all employees by providing ongoing training within the Company.

2.4.1.2.7. Monitoring of internal audit system

Due to its size, the Company does not require a permanent internal audit function.

There are several internal auditing structures within the Company for ensuring compliance with the provisions established by the organization or its regulatory and economic environment.

Each person is *de facto* responsible for the quality and compliance of the operations under their supervision, through the application of approved procedures and the traceability of the results generated during the performance of their activities. Auditing operations make it possible to confirm the level of quality and compliance achieved based on a representative sample or on the Company's entire production (data or physical products).

An independent internal audit is also carried out by the quality assurance department, which reports the results of these audits directly to the Executive Board, primarily during management reviews. Scheduling for these audits is determined using a risk management approach and guarantees maximum independence among auditors and the entities being audited so that reliable improvement plans can be established.

2.4.1.2.8. Internal audit procedures relating to the preparation and processing of accounting and financial information

Since the business's accounting activities have been internalized, the use of an external accounting firm is now limited to the review of accounts and the preparation of the consolidated financial statements. Similarly, management of fiscal obligations (taxation related to the Company's earnings, local taxation, etc.) is also handled by this firm. The firm also performs an administrative review in connection with payroll through the use of payroll audits, auditing of monthly and quarterly social security contributions, end-of-contract documents, etc.

Finally, the Company continues to improve its procedures, as well as its tools for cost analysis and control.

As a public company in the United States, the Company is required to establish and maintain internal control over financial reporting. Pursuant to Section 404(a) of the United States Sarbanes- Oxley Act it is required to furnish a report by its management that assesses its internal control over financial reporting as of year-end in its Annual Reports on Form 20-F.

Prior to the issuance of the Company's interim financial statements as of and for the six months ended June 30, 2021, a deficiency, which constituted a material weakness in its internal control over financial reporting, was identified. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the Company's annual or interim financial statements will not be prevented or detected on a timely basis. A material adjustment was made to the Company's interim financial statements as of and for the six months ended June 30, 2021 prior to their issuance which resulted from a deficiency in the controls over the evaluation of certain contracts and the related accounting. The identified deficiency related to the timing of the recognition of expenses associated with new contracts signed with certain contract research organizations for one of the Company's clinical trials. Specifically, the Company made advance payments that were recorded as expenses of the period instead of prepaid expenses (which in turn inappropriately increased the R&D expenses). Consequently, a material weakness was disclosed in connection with the reporting of the Company's interim financial statements.

During the remainder of the 2021 financial year, the Company remediated the identified deficiencies in internal control over financial reporting. Based on the results of its evaluation, the Company concluded that as of December 31, 2021, it had maintained effective internal control over financial reporting.

2.5. ITEMS LIKELY TO HAVE AN IMPACT IN THE EVENT OF A PUBLIC OFFER

2.5.1. Capital structure of the Company

See Section 5.1. of the Universal Registration Document.

2.5.2. Statutory restrictions on the exercise of voting rights and transfers of shares or clauses of agreements brought to the Company's attention in application of article L. 233-11 of the French Commercial Code

None.

2.5.3. Direct or indirect shareholdings in the Company's capital of which it is aware pursuant to Articles L. 233-7 and L. 233-12 of the French Commercial Code

See Section 5.2. of the Universal Registration Document.

2.5.4. List and description of holders of any securities with special control rights

The Company is not aware of the existence of any special control rights.

2.5.5. Control mechanisms provided for in any employee shareholding system, when the control rights are not exercised by the employee

The Company has not set up an employee shareholding system that may contain control mechanisms when control rights are not exercised by employees.

2.5.6. Shareholder agreements of which the Company is aware and which may result in restrictions on the transfer of shares and the exercise of voting rights

The Company is not aware of any such agreement.

2.5.7. Rules governing the appointment and replacement of members of the Supervisory Board or Executive Board and amendments to the Company's bylaws

Members of the Executive Board are appointed in accordance with French law by the Supervisory Board.

Members of the Supervisory Board are appointed in accordance with French law by the shareholders of the Company at shareholders' meetings. By exception, if a member of the Supervisory Board dies or resigns between annual meetings, the Supervisory Board may appoint a temporary member to fill the vacancy, subject to ratification at the next ordinary general meeting. If such vacancy results in a number of Supervisory Board members below three, the Executive Board must call an ordinary shareholders' meeting in order to fill the vacancy.

The bylaws are amended by shareholders during shareholder's meetings.

2.5.8. Powers of the Executive board, in particular regarding the issuance or repurchase of shares

See Sections 5.1.3.1. and 5.1.5 of the Universal Registration Document.

2.5.9. Agreements entered into by the Company that are amended or terminated in the event of a change of control of the Company

The Group has entered into several agreements to finance its operations, some of which provide for the possibility of early repayment in the event of a change of control.

In addition, the rights to exercise certain dilutive instruments issued by the Company are accelerated in the event of a change of control of the Company (see Section 5.1.4. of the Universal Registration Document).

2.5.10. Agreements providing for compensation for members of the Executive Board or employees if they resign or are dismissed without real and serious cause or if their employment is terminated due to a public offer

Laurent Levy may be entitled to severance payment in the event of forced departure from the Company and Anne-Juliette Hermant and Bart Van Rhijn may be entitled to indemnities in the context of termination of their employment agreement (see Section 5.6.2. of the Universal Registration Document).

3. NANOBIOTIX AND CORPORATE SOCIAL RESPONSIBILITY

3.1. Nanobiotix and corporate social responsibility

Incorporated in 2003, Nanobiotix is a leading, clinical-stage nanomedicine company pioneering new approaches to significantly change patient outcomes by bringing nanophysics to the heart of the cell.

The Nanobiotix philosophy is rooted in designing pioneering, physical-based approaches to bring highly effective and generalized solutions to address unmet medical needs and challenges. Nanobiotix's first-in-class, proprietary lead technology, NBTXR3, aims to expand radiotherapy benefits for millions of cancer patients, while its Immuno-Oncology program has the potential to bring a new dimension to cancer immunotherapies.

This chapter describes the activities led by the Company in terms of employment and well-being of its people, the environment and the Company in a wider sense. This chapter is for the period from January 1st, 2021 to December 31st, 2021 and relates to the activities of the parent company as well as its subsidiaries, Nanobiotix Corp, created in September 2014, Nanobiotix GmbH, created in October 2017, Nanobiotix S.L.U., created in December 2017 and Curadigm SAS, created in July 2019.

The Company is keen to include and consider the main stakes of Corporate Social Responsibility (CSR) in order to contribute to the sustainable development and to ensure an overall, consistent, performance of its activities. Research and development being its main value-added activities, one of the Company's objective is to register patents for its inventions, being the source of intellectual property. In this regard, the Company's employees are therefore deemed its main resource. The work environment that exists within the Company allows, amongst other things, to attract, motivate, train and retain talent, this being a crucial component for the development of the Company.

Although the Company's environmental impact is negligible, the Company ensures that it follows a responsible management of its resources and waste.

Finally, in terms of social responsibility, the Company participates and is an active player in the development of nanomedicine-related knowledge and the treatment of cancer and therefore increases its involvement with various stakeholders.

3.2. Our Vision

At Nanobiotix, we believe that the purpose behind what we do is just as important as the products we develop. For us, that purpose is something we call "Expanding Life". To Expand Life is to go beyond what you know to create a new possibility. We never set out to treat any specific disease, but instead we asked ourselves the question, "What if we could impact the physical properties of a cell without touching it?" This led us to discover that we could develop innovative treatment solutions for patients by bringing nanophysics to the heart of the cell, which in turn led to NBTXR3 for the treatment of cancer among other first-in-class nanotechnology applications.

Moving forward, we will continue to ask bold questions and take actions based on our expertise that are meant to improve the lives of millions around the world.

3.2.1. Description of the main activities, markets, customers and stakeholders in our activities

Since its creation, most of the Company's resources have been devoted to the development of "NBTXR3" and other formulations including related intellectual property rights, enabling Nanobiotix to offer an unprecedented approach to cancer treatment.

By relying on our nanotechnology products, we aim to improve patient outcomes and respond to important medical benefit that remain unmet nowadays. We have strong assets to carry out our mission and position ourselves as a leading figure in the development of nanomedicine, through:

- An advanced pipeline and promising clinical data, in various oncology indications.
- A considerable market opportunity in solid tumors: At some point, nearly 60% of cancer patients receive radiation therapy in their care journey. As a result, we are convinced that the mode of action of NBTXR3 is likely to benefit all populations of oncology patient candidates for radiation therapy. In addition, we believe NBTXR3 is a real vector of hope for patients with cancers ineligible for radiation therapy because of the sensitivity of the tissues surrounding the tumor.
- An improved benefit/risk ratio through an injection directly into the heart of the tumor.
- A product-candidate that is highly compatible and complementary to current standards of care.
- Actively protected intellectual property and preserved know-how.
- A recently established production site with a high capacity.

NBTXR3 is currently being evaluated in several clinical trials worldwide.

In August 2012, we entered into an exclusive license and collaboration agreement with PharmaEngine for the development and commercialization of NBTXR3 in the Asia-Pacific region which was terminated in March 2021.

In January 2019, we entered a large-scale comprehensive clinical collaboration with The University of Texas MD Anderson Cancer Center to cover 9 additional clinical trials in different indications.

In May 2021, we entered into an exclusive license and collaboration agreement with LianBio for the development and commercialization of NBTXR3 in the Asia-Pacific region.

Overall, NBTXR3 will be evaluated in several clinical trials worldwide, in different cancer patient populations.

The Company currently conducts several nanomedicine researches programs whose concepts differ from NBTXR3. In May 2019, we announced the launch of Curadigm, a new nanotechnology platform for healthcare that is dedicated to redefining the therapeutic balance between bioavailability, toxicity, and efficacy across the pharmaceutical industry. Curadigm's concepts is based in particular on the development of new objects from nanotechnology to answer the question "Is it possible to increase the useful dose or to reduce the unnecessary dose of a therapeutic agent administered in a patient to optimize its bioavailability and/or reduce its toxicity?" To answer this question, the Curadigm team has created different types of nanoparticles with specific physical-chemical properties (called nanoprimers) allowing them to accumulate in the liver in order to temporarily occupy the main liver elimination pathways of targeted therapeutic agents and thus increase their useful dose and/or decrease their potential toxicity. The different nanoprimers created aim to adapt to the different families of therapeutic agents affected by a strong liver elimination, mainly nanomedicines. Nanoprimers therefore open new possibilities in their development and could improve the effectiveness of different therapeutic agents.

3.2.2. Our resources

Nanobiotix counts 100 employees at the end of 2021, supervised by complementary and highly experienced management as well as a Supervisory Board consisting of experts in their respective fields. Such teams include discovery and non-clinical teams, the medical and regulatory affairs departments as well as the development and quality assurance departments. In addition to these operational departments, additional departments work across all functions to support them.

As at December 2021, 73 employees were dedicated to research and development, while 27 were working in supporting departments.

The workforce at as December 31 was as follows:

	2021	**2020**	**2019**	**2018**	**2017**
Cadres	**90**	**77**	**99**	93	77
non cadre	**10**	**11**	**11**	9	8
Total headcount	**100**	**88**	**110**	102	85
Split men/ women	**38/62**	**32/68**	**30/70**	34/66	33/67
Number of men	**38**	**28**	**33**	35	28
Number of women	**62**	**60**	**77**	67	57
Split R&D/ SG&A	**73/27**	**66/24**	**81/29**	79/23	65/20
Number of R&D staff	**73**	**66**	**81**	79	65
Number of SG&A staff	**27**	**24**	**29**	23	20

Women consistently represent a large majority of the workforce, representing 62% of the total headcount as at December 31, 2021. Nanobiotix's workforce is highly qualified and includes 90 cadres as at December 31, 2021, representing 90% of the workforce. In addition, 36 employees held a PhD, MD or PharmD.

Nanobiotix also has a relatively young workforce, with an average age of 41 years old.

The workforce's age was as follows:

	Number	**Percentage**
Less than 25 years old	3	3%
From 26 to 35 years old	34	34%
From 36 to 45 years old	27	27%
More than 46 years old	36	36%

3.2.3. Description of the economic model

Commercialization

Subject to successfully completing applicable pre-marketing regulatory requirements, we expect to commence commercialization activities and establish a global commercial infrastructure by building commercial capabilities and evaluating partnering opportunities. Through our global medical science liaison team, we have established important strategic relationships and enhanced awareness of NBTXR3 with a number of key opinion leaders, hospitals, clinics and cancer treatment centers in the United States and in key European markets. As part of our clinical trial efforts, we have involved more than 400 physicians. We believe that our planned commercial organization will be able to target the community of physicians who are the key specialists in treating the patient populations for which NBTXR3 is being developed. We may enter into additional development and commercialization agreements with third parties in selected geographic territories for any of our product candidates that successfully completed applicable pre-marketing regulatory requirements. In May 2021, we entered into an exclusive license and collaboration agreement with LianBio for the development and commercialization of NBTXR3 in the Asia-Pacific region.

We also plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with leaders in relevant fields of medicine.

Coverage and Reimbursement

A pharmaceutical manufacturer's ability to commercialize any approved drug product successfully depends in part on the extent to which coverage and adequate reimbursement for such drug product and related treatments will be available from third-party payors, including government health administration authorities, private health insurers, health maintenance organizations and other organizations.

Therefore, coverage and adequate reimbursement is critical to new drug product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

(Refer to chapter 1 of the Universal Registration Document for further details)

3.2.4. Outlook and strategy

Our goal is to become a leader in the biotechnology industry, with a fully integrated chain of operations, based on the systematic combination of NBTXR3 and radiotherapy either alone or in combination with immuno-therapies or chemotherapies in the treatment of solid tumors. The key elements of our strategy to achieve this goal include the following:

- **Complete the development of, and satisfy applicable EU and U.S. regulatory requirements for, NBTXR3 for the treatment of locally advanced head and neck cancers.** Based on encouraging results from Study 102 Escalation, Nanobiotix is conducting Study 102 Expansion to collect additional preliminary efficacy data. We presented updated clinical results from Study 102 Expansion at ASTRO's Annual Meeting in October 2021 showing a mOS of 18.1 months and a mPFS of 10.6 months in the evaluable population (n=41). As of September 3, 2021 cut-off, there were 41 evaluable patients in the Study 102 Expansion. Investigator-assessed rates remained consistent with previously reported results from the dose escalation and dose expansion study, showing a best observed target (injected) lesion ORR of 85.4%, and a best observed target lesion CRR of 63.4% at a median follow up of 9.5 months. The best observed target lesion response rates include one patient recorded by the principal investigator of the study as an unconfirmed complete response. NBTXR3 administration remained feasible and well-tolerated. A total of eight Grade 3-4 NBTXR3-related AEs were observed in eight patients, representing 1.3% of all AEs. Of these AEs related to NBTXR3, five SAEs were observed including dysphagia, sepsis, soft tissue necrosis, stomatitis and tumor hemorrhage. Of the SAEs, one death from sepsis occurred, which the investigator assessed as possibly related to NBTXR3, radiotherapy, and cancer. See "1.3.6.2. of the Universal Registration Document." A review of data as of the February 22, 2022 cut off date from Expansion Study 102 shows median overall survival (mOS) of 23 months in evaluable patients (n=44) demonstrating continued improvement relative to the analysis presented at ASTRO 21 and consistent with data reported from the dose escalation phase of Study 102. We commenced NANORAY-312, a global Phase III clinical trial for elderly patients with locally advanced head and neck squamous cell carcinoma who are ineligible for platinum-based chemotherapy, randomizing the first patient having been in January 2022. In the United States, where NBTXR3 is classified as a drug, we were granted Fast Track designation from the FDA in February 2020 for NBTXR3 for the treatment of locally advanced head and neck cancers, which we believe could allow for expedited clinical development. We expect approximately 500 patients to be treated in this global Phase III trial, including 100 patients to be enrolled by LianBio. The initial readout will be based on event-driven progression-free survival ("PFS"), and the final readout will be based on overall survival ("OS"). A futility analysis is expected approximately 18 months after the first patient is randomized, and the interim analysis for PFS superiority is expected approximately 30 months after first patient randomization. The final analysis will report on PFS and OS. .

- **Establish NBTXR3 as a complementary product to immune checkpoint inhibitors.** Nanobiotix is conducting, and continue to further develop, a global I-O development program to explore the use of NBTXR3 as a complement to immune checkpoint inhibitors across several solid tumor indications. In preclinical studies, NBTXR3 activated by radiation therapy in combination with immune checkpoint inhibitors demonstrated potential to convert checkpoint inhibitor non-responders into responders, provide better local and systemic control and increase survival. We are conducting Study 1100, a Phase I basket trial of NBTXR3 in combination with anti-PD-1 checkpoint inhibitors in patients with LRR or R/M HNSCC or with lung or liver metastases from any primary cancer eligible for anti-PD-1 therapy. We presented updated clinical results from ongoing Study 1100 at ASTRO's Annual Meeting in October 2021. We believe that these updated results suggest that NBTXR3 could benefit this patient population with the potential to increase the proportion of patients that respond to immune checkpoint inhibitors, and we have initiated discussions with regulatory authorities regarding the potential registration pathway for

this immunotherapy combination. See "1.3.6.4. of the Universal Registration Document" for additional detail. In addition, pursuant to our collaboration with MD Anderson, we are planning to evaluate NBTXR3 in combination with various checkpoint inhibitors (anti-PD-1, anti-PD-L1, and anti-CTLA-4) across several cancer indications.

- **Expand the opportunity for NBTXR3 as a treatment for solid tumor indications.** We believe that NBTXR3's physical mode of action could make it broadly applicable across a multitude of solid tumor indications. In addition to head and neck cancers and STS, we intend to continue to develop and pursue NBTXR3 for other indications, and we have already gathered data from clinical trials in liver cancers in the EU, prostate cancer in the United States, and rectal cancer in Taiwan. In December 2018, we entered into a collaboration with MD Anderson as part of which we intend to conduct multiple clinical trials in the United States to evaluate NBTXR3 plus radiotherapy, either alone or in further combination with immuno-therapies or chemotherapies, across several cancer types. If we are able to demonstrate the applicability of NBTXR3 to solid tumor cancers in our current and planned clinical trials, Nanobiotix believes it would would be able to increase the addressable patient population of NBTXR3 to encompass a significant portion of the patients who receive radiotherapy as part of their solid tumor cancer treatment.

- **Complete post-approval trials for NBTXR3 for the treatment of locally advanced STS in the EU.** Following positive results from our Phase II/III clinical trial in April 2019, NBTXR3 became the first ever radioenhancer to have a CE mark, allowing it to be commercialized for the treatment of locally advanced STS under the brand name Hensify. We are currently preparing Study 401 (MS01 01) to continue evaluating safety and efficacy while providing patients in the EU with access to Hensify.

- **Build an effective clinical development program and establish a global commercial infrastructure for NBTXR3.** Nanobiotix has conducted clinical trials involving multiple therapeutic areas throughout the United States and the EU, in which more than 400 physicians have been involved. In addition, Nanobiotix's global medical science liaison team has consulted closely with a number of physicians, hospitals, clinics, and cancer treatment centers in the United States and key European markets to better understand their needs as clinicians and institutions and to tailor NBTXR3 accordingly. Nanobiotix plans to focus our commercialization and marketing efforts for NBTXR3 in Europe and the United States, subject to the grant of any marketing authorization by, among others, health regulatory agencies. Nanobiotix has entered into an agreement with LianBio for the development and potential commercialization of NBTXR3 in key countries in Asia. Nanobiotix retains development and commercialization rights to NBTXR3 in all other geographies, and may develop and commercialize NBTXR3 in other specific regions, independently or through collaboration agreements.

3.3. Our main CSR risks and opportunities

In 2019, Nanobiotix carried out a mapping of its main CSR risks and opportunities in order to identify the major and relevant subjects related to its business model.

First, a CSR risks and opportunities universe was established based on sectoral risks, the challenges introduced by article 225 of the Grenelle II law and the risks previously identified by the quality department. The identified elements cover the entire value chain and stakeholders of Nanobiotix and are distributed on 3 main themes:

- Social,
- Societal and
- Environmental.

In order to embrace a broad vision of the Company's challenges, the assessment and prioritization of these CSR stakes involved several key departments of the Company (quality, finance, human resources, development, manufacturing and innovations).

During process/departments dedicated workshops, the question "What might go wrong?" was used to identify the risks during execution of a task/activities (processes) and accordingly identifying possible negative consequences (harm) for the organization. Risks are identified together with master process pilot (PP), experts or persons involved in the process, Global head of department (GHF) and Quality Assurance.

A risk register allows compilation of the risk control measure and where Nanobiotix needs to implement improvement or additional action to demonstrate that risks are under control. Implementation is followed through risk review.

The risk review is a continual and iterative process in which risk control measures are periodically reviewed to ascertain whether the implemented management activities remains effective and relevant, taking into account emerging knowledge and experience. This review is scheduled on annual basis with people involved in the activities, the risk review and risk process as well, are documented by issuing risk matrices and its updates associated with risk register. Unscheduled review may arise in case of evolution of higher risk priority level, if regulation or organization changes including modification on suppliers, or if new risk occurs. This could be linked to Corrective Action and change control process.

If implemented actions are not being carried out effectively or if risk impact is increasing and cannot be resolved, it should be escalated to the upper management to implement appropriate measures.

Full risk matrices and related update are reviewed and approved by the Executive Board.

At the end of the prioritization process, the following 7 CSR risks were identified as relevant regarding the activities of Nanobiotix:

Risk number	Risk description	Definition
Our employees		
Risk 1	Employees' health and safety	Health and Safety conditions (both at work as well as during commuting) have a direct impact on salary costs through decreased productivity. Controlling the well-being and safety risks of the employees is necessary for the Group's good economic and financial performance as well as for the preservation of its reputational image, attractiveness and employee commitment.
Risk 2	Working conditions	Poor working conditions can be due to inadequate management approaches. This can lead to an increase in psychosocial risks and a decrease in productivity within the Company. Ensuring good working conditions for all employees is critical for the proper performance of the Company's operations.

Our environment		
Risk 3	Waste management	Being a biotechnology company, Nanobiotix spends a considerable amount of efforts in research and development for a class III medical device in Europe. The Company therefore considers that the impact it has on the environment is low, given that most of the research activities are performed in labs while development activities are largely subcontracted.

Risk number	Risk description	Definition
Our patients		
Risk 4	Patients' safety during clinical trials	All Clinical Trials Sponsored by Nanobiotix or Business partners are executed with respect to the highest standards in the industry according to the national and international Regulations, Directives, Guidance and Recommendations. The main guidelines supporting clinical trials compliance are developed within the guidance for good clinical practice ICH E6(R2) (which discusses approaches to clinical trial design, conduct, oversight, recording, and reporting as well as updated standards regarding electronic records and essential documents), "good clinical Practice" (GCP) being an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.
Risk 5	Safety and quality of the products	The development, screening, manufacturing and commercialization of therapeutic solutions for cancer treatment are governed by a rigorous, complex and evolving global regulatory environment. Regulatory authorities, including the ANSM and the FDA, have imposed stringent requirements on the amount and types of data required to demonstrate the safety and efficacy of products prior to their marketing and sale. Moreover, following its initial approval or certification, any product approved for commercialization is reassessed on a regular basis in terms of its patient risk/benefit ratio. The potential discovery of new defects or side effects which were not detected during development and clinical trials can result in restrictions on sale, the suspension or withdrawal of the product from the market and an increased risk of litigation.
Risk 6	Protection of personal data	Despite the implementation of security measures, internal computer systems, and those of third parties on which the Group relies, remain vulnerable to diverse threats, including computer viruses, malware, unauthorized accesses, natural disasters, acts of terrorism, acts of war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the internet.

Our suppliers		
Risk 7	Responsible partnering	Since the opening of the manufacturing site in the BioPark, the Company has been performing manufacturing tests for its patented product candidate, NBTXR3. The model chosen by the Company relies on the systematic use of partners for the manufacturing of NBTXR3. Given the criticality of regulatory and product quality compliance in this industry, it has been decided to include CSR-related criteria in the decision-making process to identify subcontractors the Company works with. These criteria come in addition to those already existing, being ISO 9001, GCP and GMP.

3.4. Our employees

3.4.1. Risk 1: Employees' health and safety

Health and Safety conditions (both at work as well as during commuting) have a direct impact on salary costs through decreased productivity and cost resulting from employee turnover. Controlling the well-being and safety risks of the employees is necessary for the Group's good economic and financial performance as well as for the preservation of its reputational image, attractiveness and employee commitment.

Our key objectives

- Inform the employees, including new starters about health and safety risks,
- Maintain our health and safety training efforts at work, and
- Reduce the number of accidents at work or during employees' commute as recognised by health authorities.

Governance

In terms of governance, the HR department collaborates tightly with the Assurance Quality department, which they meet on a bi-yearly basis during the management review to discuss the KPIs, and the employees' representative body, the *Comité Social et Economique(CSE)*, which meets once every two months. KPIs are reviewed with the CSE every six months.

Policies and action plans

Risks and key attention points related to health and safety for each type of position are defined in the *Document Unique (DUERP)*, available as soon as a new starter joins the Company and all along their employment agreement.

In 2021, the Company noted:

(i) In terms of training:
  - 1,5 days dedicated to Health & Security at work.

(ii) In terms of accidents on the premises or during employees' commute:
  - No accident at the workplace as recognised by health authorities
  - No accident during commuting as recognised by health authorities
  - No leave due to work-related sickness;
  - No collective agreement was signed in 2020 regarding health and safety at work.

Findings

Indicator	2021	2020	2019	2018	2017
Health and safety-related trainings (days)	1,5	—	3.3	2	4
Number of accidents	—	—	6	—	2

3.4.2. Risk 2: Working conditions

Poor working conditions can be due to inadequate management approaches or inadequate facilities and workspace arrangements. This can lead to an increase in psychosocial risks and a decrease in productivity within the Company. Ensuring good working conditions for all employees is critical for the proper performance of the Company's operations.

Our key objective

Ensure optimum working conditions for all employees while respecting work-life balance.

Governance

In terms of governance, the HR department performs a regular review of indicators, always in collaboration with the employees' representative body, the *Comité Social et Economique (CSE)* and the work inspection authorities (*inspection du travail*).

Policies and action plans

From a practical point of view, the Company invested in the fit out and organisation of the newly rented space (749 m^2) at the head office in Paris, including:

- Functional and agreeable workspaces
- An additional equipped kitchen
- Large and friendly break areas
- Additional meeting rooms, fully equipped to foster effective communication within the room as well as from another location (large screens, visio, etc.)

The Company also pursued the development of the working from home policy for every employee, which started in 2018 via two schemes. Due to the COVID situation and in order to ensure our employees' safety in line with the national recommendations, the working from home policy has been extended to all eligible employees. The Company has developed support to all employees in these particular circumstances, such as virtual company calls every two weeks, dedicated support to managers for distant management and an open line with independent coaches for mental health support.

In addition, the Company also developed some support to managers to assist them with the individual performance appraisal process, through meetings and written documentation to further improve the quality of half yearly appraisal meetings with their teams. Team members also received support to better prepare for their appraisal meetings.

Finally, ad-hoc coaching has been made available for managers as and when required to allow them to be fully equipped to perform their role.

Findings

Indicator	2021	2020	2019	2018	2017
Number of employees having signed an amendment to their employment agreement allowing them to work from home	All	All due to the COVID situation	36	25	—
Turnover rate	24,8%	27.3%	21.8%	23.5%	12%
Absenteeism rate	1.65%	1.72%	3.4%	2.2%	2.9%

Comments on the evolution of indicators

As in 2021, the Company continued to evolve its structure to adapt to its growth.

3.5. Our environment

3.5.1. Risk 3: Waste management

Being a biotechnology company, Nanobiotix spends a considerable amount of efforts in research and development for a class III medical device in Europe. The Company therefore considers that the impact it has on the environment is low, given that most of the research activities are performed in labs while development activities are largely subcontracted.

It should be noted that for its research activities, the Company follows a strict regulatory framework and has obtained all the required agreements.

Our key objective

Ensure that waste coming out of Nanobiotix's labs is managed in accordance with and complies with the regulatory framework currently in place so that the Company's activities have the least impact on the environment.

Governance

The lab managers are responsible for waste management. They are responsible for the compliance with procedures in place, their updates and the monitoring of related costs. Every new joiner is given a welcome booklet which includes a section on "working in the lab", which includes instructions in terms of safety and environment.

Standard Operating Procedures are reviewed on a regular basis and were updated in 2019. An internal training session was organised across all functions working in the lab in order to maximise their understanding of the various safety aspects and the risks related to this activity.

Policies and action plans

Nanobiotix signed a contract with the company subcontracted for waste management in order to improve further the process.

The Company has implemented a number of procedures for chemical and biological lab waste, which detail the process for chemical products and waste management. The Company also separates the recycling and collection separately for potentially infectious clinical waste (DASRI), performed by its subcontractor. The aim of this collection and recycling is to eliminate this waste while complying with applicable laws.

Findings

Indicator	2021	2020	2019	2018	2017
Wattignies - Potentially infectious clinical waste (kg)	1,384	754	1,164	1,272	664
Wattignies - Chemical waste (kg)	449	240	618	656	452
BioPark - Chemical waste (T)	7.3	2.3	1.5	4.8	—

Comments on the evolution of indicators

The amount of waste generated by Wattignies in relatively stable year on year. However, the mount of chemical waste generated by the manufacturing (BioPark) site has increased in 2021 due to an increase of the production to meet the clinical needs (as 2020 was impacted by the COVID situation, the production has considerably decreased in 2020)

3.6. Our patients

3.6.1. Risk 4: Patients safety during clinical trials

All Clinical Trials Sponsored by Nanobiotix or Business partners are executed with respect to the highest standards in the industry according to the national and international Regulations, Directives, Guidance and Recommendations. The main guidelines supporting clinical trials compliance are developed within the guidance for good clinical practice ICH E6(R2) (which discusses approaches to clinical trial design, conduct, oversight, recording, and reporting as well as updated standards regarding electronic records and essential documents), "Good Clinical Practice" (GCP) being an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.

Compliance with this standard provides Nanobiotix assurance that the rights, safety, and well-being of patients enrolled in the clinical trials are protected, consistent with the principles coming from the Declaration of Helsinki, and that the clinical trial data are credible, meaning that quality and integrity of the data gathering during the trials can be demonstrated during and after the trial termination.

In addition, clinical trials and then protection of patients during the activities is framed by additional guidance established in the same concept and outlines within ICH E2A regarding "clinical safety data management" and ICH E8 "general consideration for clinical trials", which sets out the general scientific principles for the conduct, performance and control of clinical trials. The Guideline addresses a wide range of subjects in the design and execution of clinical trials.

As the goal of the Clinical Trial Regulation framework is to create an environment that is favorable to conducting clinical trials, with the highest standards of safety for participants and increased transparency of trial information Nanobiotix has identified several processes with objectives driving continuous compliance towards those regulation.

Our key objective

Ensuring safe participation of all patients treated with NBTXR3 in the context of any clinical trial, regardless the region or country where the trial is conducted.

Governance

The Executive Board is directly involved in the execution of the global clinical development plan. They make strategic decisions and provide appropriate resources to achieve clinical trial objectives and the supervision of safety for patients enrolled in the clinical trials.

While Clinical research associates (CRA's) work closely with the hospitals, ensuring sites' compliance and meeting ICH-GCP guidelines, the Safety Vigilance department is specifically dedicated to the collection, review and evaluation of all Adverse Events/Effects. All these events are duly reported to the appropriate national competent authorities, ethic committees and all parties involved in the clinical trials. The Safety Vigilance department is responsible for evaluation the potential patients-related risks in relation to the use of the product and establishing risk-minimization measures.

Policies and action plans

Oversight of clinical trials compliance and execution are defined through numerous procedures within the organization which are currently evaluated for Clinical Risk Management (CRM). Starting from the definition of regulatory and statutory requirements, Nanobiotix has defined a policy regarding regulatory intelligence to keep abreast of new or modified regulations and standard and to contribute in the company regulatory compliance.

The applicable regulatory and statutory requirements are outlines in Nanobiotix's procedures in the framework of the quality management system to ensure that operations are executed accordingly, particularly to ensure clinical project management and to control the execution of protocols as well as *Good Clinical Practice* compliance through monitoring.

Findings

Based on the CRM discussed above and feedback from trial quality controls and audits, a full review of the organization and the related procedures was set up, within a plan for critical clinical processes supporting patients' safety and rights as a paramount and data reliability.

An annual audit program established on a risk-based approach also supports GCP compliance during the trials, including audits of the CROs involved in Nanobiotix's projects, investigational sites, the Principal Investigators' responsibilities for the site as well as internal audits.

So far, Nanobiotix has provided a set of key performance indicators demonstrating the high level of control executed by the clinical trial teams including data integrity and reliability to demonstrating a good safety profile of the product and respect for Human Safety protection.

Although Nanobiotix tracks SAEs (clinical trial-related injury and serious adverse events), this KPI in itself isn't deemed to be as relevant as the actions taken in order to address these SAEs, which are used to establish the safety profile of the product before the product is available on the market and more importantly, whether these SAEs have been communicated to the appropriate regulation authorities, depending on the country the events arise in, in compliance with the country's deadlines for reporting (the NCA, National Competent Authorities), the Independent Ethics Committees (IECs) and the Company's Safety Management Plan, established at the beginning of each trial.

The deadlines differ, depending on the country and whether the product is a drug or a medical device amongst the factors. Typically, depending on the severity of the event and the factors mentioned above, the deadline for submission could be 24 hours, 2 calendar days, 7 calendar days or longer.

Indicator	2021	2020	2019	2018	2017
% of SAEs (clinical trial-related injury and serious adverse events) reported on time	96%	100%	99%	100%	99%

Comments on the evolution of indicators

Nanobiotix consistently meets the regulatory compliance requirements in terms of patients' safety.

3.7. Risk 5: Safety and quality of the products

The development, screening, manufacturing and commercialization of therapeutic solutions for cancer treatment are governed by a rigorous, complex and evolving global regulatory environment. Regulatory authorities, including the ANSM and the FDA), have imposed strict requirements on the amounts and types of data required to demonstrate the safety and efficacy of products prior to their marketing and sale. Moreover, following its initial approval or certification, any product approved for commercialization is reassessed on a regular basis in terms of its patients' risk/benefit ratio. The potential discovery of new defects or side effects which were not detected during the development of the product and clinical trials can result in restrictions on sale, the suspension or withdrawal of the product from the market and an increased risk of litigation.

Our key objectives

- Ensure that our product complies with the appropriate and expected specifications regarding safety, efficacy and quality, and
- Ensure that any modification during product development life cycle continue to promote a high level of quality for patient safety and treatment efficacy.

Governance

Nanobiotix has developed its product in line with ICHQ8 "Quality by Design", ICH Q9 "Risk management" and ICHQ10 "Pharmaceutical Quality system" to ensure the manufacturing of a safe product from the earliest times of the development activities.

A Quality Board is in place, which is accountable for the decision making regarding all product quality-related topics developed or commercialized by Nanobiotix, specifically on the following matters:

- Manufacturing and post-manufacturing activities related to the product,
- Regulatory application status and follow up,
- Changes that could have an impact on the quality of the product or its application,
- Status of critical suppliers involved in the production and post-production activities,
- Major deviations that could affect the quality of the product,
- Outcomes of audits performed internally and on our suppliers.

The Quality board includes as a minimum the Chief Operating Officer (COO), the Qualified Person, the head of manufacturing, the head of regulatory affairs, and the head of quality assurance.

The application of decisions and action plans to be executed are monitored through the quality management system and escalated to the Executive Board through KPIs at least on a quarterly basis.

Policies and action plans

From the design Phase of its products, Nanobiotix implements a risk-based approach process to determine the best solution to achieve their safety, efficacy and quality in line with ICH Q8, Q9 and Q10 (Quality by Design, Risk management and Pharmaceutical Quality system).

Based on the knowledge of the product and process development, Nanobiotix has established a Continuous Verification Process (CVP) approach to demonstrate the robustness of the manufacturing process, producing the expected quality.

The manufacturing process has been carried out based on and is monitored through a science-based and a risk-based approach based on the FMEA (Failure Mode and Effects Analysis) model. Regulatory requirements in relation to the medical devices and sterile medicinal products have been implemented in the quality system in order to support the science-based process and controls with a "built-in a quality" approach, ensuring compliance and quality for NBTXR3.

In addition, Nanobiotix has selected the EN ISO 14971 standard as recognized guidelines to conduct the product risk management process to achieve the compliance with the normative and regulatory requirements all along the product's life cycle, from design to production and post-production phase:

- Possible hazards have been identified and managed based on the FMEA model. If any risk has been deemed unacceptable, it has been reduced to acceptable levels by appropriate measures to control the risk.
- In 2022, the Quality Board's functional teams, being the manufacturing, quality and regulatory have focused their effort on the manufacturing site (BioPark).

In addition, the monitoring of routine production allowing the release of the product for clinical and non-clinical development have continuously been performed over the year.

Manufacturing high quality products for cancer patients

Definition of the risks

Manufacturing a high quality products requires multiple inputs such as suppliers of raw materials, external quality laboratories, contract development and manufacturing organizations (CDMO) and employees. All contributors introduce risks in the manufacturing process. The Nanobiotix Quality Management System has controls in place to ensure we produce a high-quality product for cancer patients.

Nanobiotix quality system is designed towards zero risk in the case of safety and quality and to comply with applicable reference standards such as GxP and ISO. All Nanobiotix processes are documented in a formal Quality Management System (QMS) to ensure full traceability of every batch of product manufactured. Nanobiotix' QMS:

i. Identify the processes needed and their application throughout the organization
ii. Determine the sequence and execution of these processes
iii. Evaluate the execution of these processes within Nanobiotix and all of its subcontractors during management reviews and internal QMS audits as required by the regulatory bodies
iv. Implement actions necessary to achieve results and improve effectiveness of these processes
v. Evaluate reporting requirements for changes and related communication to Regulatory Bodies
vi. Ensure that any changes to applicable regulations, standards and directives are assessed and implemented if applicable to our processes
vii. Before product release, perform an in-depth review of all manufactured product.

Processes that are outsourced are being monitored and controlled to ensure all applicable regulation, standards and directives are followed. These controls include written quality agreements.

The Nanobiotix' QMS ensures that all of our processes are reproducible and allow teams to demonstrate this through internal and external audit. Nanobiotix is certified to develop, manufacture, distribute and sell nanomaterials used as medical devices in oncology fields and complies with the requirements of the international standards ISO 13485:2016 – NF EN ISO 13485:2016

Nanobiotix reviews a number of KPIs on a regular basis in order to ensure consistency and quality of the processes and the results of manufacturing activities, one of which being the percentage of campaigns

that are deemed to be, following a thorough and lengthy process, compliant with Nanobiotix's and the industry's standards. In 2021, all finished product batches were released to conduct Nanobiotix development plan including non-clinical and clinical research activities without any relevant or significant issue from a quality point of view.

Indicator	2021	2020	2019	2018
% of campaigns that have successfully gone through the quality control process	100%	100%	On-going controls	On-going controls

Over the last few years, all of the activities and data published on the manufacturing side were performed externally on a small scale manufacturing process. In 2021 we made substantial progress to scale up our manufacturing process to fulfill the future clinical development and potential commercialization needs across multiple indications. During 2021, we achieved the pre-validation steps of that process, we received positive feedback from the FDA on the equivalence of our product from the up-scaled manufacturing process with the previous small scale manufacturing process. We also received positive feedback from the FDA on our CMC plan to support our New Drug Application (NDA) filling planned with the results of the NANORAY-312 trials in Head and Neck cancer.

The new manufacturing process strictly differentiates the Drug substance from the Drug Product stage.

The drug substance is manufactured in our new manufacturing site in Villejuif, France. In 2021, following a site inspection of our Drug Product manufacturing site by the ANSM, we received our cGMP certificate. The first drug substance batch was released in 2021.

The drug Product manufacturing process is done by our partner, Fareva at their Valdepharm GMP facilities in Val-de-Reuil. The release by Fareva of the first drug product batch took place on February 11th 2022.

3.8. Risk 6: Protection of personal data

Despite the implementation of security measures, internal computer systems, and those of third parties on which the Group relies, remain vulnerable to diverse threats, including computer viruses, malware, unauthorized accesses, natural disasters, acts of terrorism, acts of war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the internet.

2018 was the year GDPR (General Data Protection Data Regulation) became effective. The GDPR aims to reinforce and unify the protection of data for all individuals within the European Union. Nanobiotix is dedicated to guarantee the confidentiality and the safety of data that is collected and ensures that these data never be used for fraudulent purposes or in ways that would be against current regulations, in particular, act number 78-17, dated January 6, 1978, "Data Protection Act", ordinance number 2018-1125 dated June 28, 2018 and the EU regulation 2016/679 of the European parliament and of the counsel dated April 27, 2016 ("GDPR").

Our key objectives

Ensure that Nanobiotix complies with the laws and regulations in place, for its employees as well as all patients taking place in its clinical trials and any third party that may be impacted and that no breaches are reported.

If breaches are reported that appropriate measures are taken to ensure quick remediation and processes are implemented to avoid reoccurrence.

Governance

The Company has been working with specialists in order to identify actions to implement in order to ensure compliance, inform employees about the new requirements as introduced by the GDPR and nominated a Data Protection Officer (DPO) to the CNIL (*Commission Nationale de l'Informatique et des Libertés*).

Policies and action plans

IT and security measures

Data and know-how protection are subject to rigorous processes and controls. In 2018, the Company has set up back up servers and back up procedures in line with the current safety standards. In order to best protect the Company from hacking attempts, servers dedicated to internet and servers hosting data only have been set up so that they are entirely independent from one another. The Company's premises have a dedicated, secured room, where research and development documents and contracts are safely stored.

In 2019, an incidents and breaches log was implemented. The current data breach procedure is tracked through the Quality Management System's corrective and preventive actions process.

In early 2020, several measures were taken:

- Reinforcement of the password security policy
- Regular IT and cybersecurity awareness communication to employees
- Review and update of the IT Charter to place further restrictions against the dissemination of personal and confidential information of the Company
- Reinforcement of security through web filters against phishing and restrictions of access to certain websites with a monitoring of internet activity

In 2021, we have strengthened our IT security through a series of IT actions:

- Conducted an IT security audit and addressed the critical recommendations.
- Conducted an IT pentest (according to 3 scenarios: 1 external and 2 internal) which did not reveal any major flaws.
- Conducted a phishing awareness campaign with an assessment/training questionnaire.
- Implemented an automatic patching system for Windows laptops.

- Started to outsource the Nanobiotix IT in a Datacenter with a new business continuity solution (in progress)
- Started to deploy our Mobile security policy (in progress)
- Started to replace our encryption solution for a more automatic and efficient solution for Windows laptops (in progress)

Other activities

Actions to be carried out in the GDPR compliance program are either general (i.e. at the Company level) or defined for each identified data processing activities. In addition, these actions can be either organizational (e.g. updating the Data Protection Policy or establish privacy notices for particular situations), operational (e.g. minimizing data collection by all departments or check the compliance of sub-contractors) or technical (e.g. 'cookies in use' button for the website).

The company is focusing on the core principles of GDPR to address all identified gaps within the organization:

Consent: Patients' data used in clinical trials being particularly sensitive, the Company has continued to focus its efforts to provide additional information to healthcare professionals collecting patient's data and to ensure data protection for personal data collected from both investigators and patients. Data subject consent can be traced, so that it is continuously governed and administered across the business' systems and processes in accordance with the permissions granted.

Process: Every department is responsible for documenting a detailed and comprehensive view of what personal data they have, where it is and how it is being used, secured, stored and eventually deleted. This is captured in the records of data processing activities, which must be regularly updated.

Data governance: The Company is contemplating the set-up of a governance team composed of staff with the right skills and business unit perspectives, including IT, that would report to the Data Protection Officer.

Transparency: Transparency obligations under GDPR begin at the data collection stage and apply throughout the life cycle of data processing. The Company is working on informing data subjects by all means, free of charge, using a vocabulary that is easily understandable by all.

Accountability: The Company documents its data protection strategy as well as all data protection related actions, to provide evidence of compliance to applicable legislations and demonstrate that the requirements are consistently met.

Results

Key Performance Indicators will be set in 2020 and monitored going forward, on a regular basis, with the support of the governance team.

3.9. Our suppliers

3.9.1. Risk 7: Responsible partnering

The Company relies on the systematic use of partners for the manufacturing of NBTXR3. Given the criticality of regulatory and product quality compliance in this industry, it has been decided to include CSR-related criteria in the decision-making process to identify subcontractors the Company works with.

These criteria come in addition to those already existing, being ISO 9001 (Quality Management System), GCP (Good Clinical Practice, where guidelines are dictated by the International Conference on Harmonization (ICH)) and GMP (Good Manufacturing Practice).

Although this approach is true for the manufacturing of NBTXR3, it is also adopted for all significant subcontractors the Company works with, so as to ensure the highest standards and quality are ultimately, directly or indirectly, provided to patients who take part in NBTXR3 clinical trials.

Our key objective

Ensure that suppliers provide a high quality of service or product in line with Nanobiotix's and the industry's standards through the elaboration of strategic partnerships.

Governance

A dedicated function was created in 2019 within the Company in order to foster an effective partnerships' mindset and collaborations with the Company's strategic suppliers. The team's aim is to coordinate and improve interactions the Company has with potential partners as well as those already in place.

A cross functional team is set up for each new project where a partnership is required, including the heads of each departments as required. These teams define the technical, quality and regulatory requirements as a minimum, in terms of regulators' expectations from a GxP point of view, regulatory strategy and the financial aspects of the project.

Strategic partnership decisions are identified by the functional team and approved by the Executive board.

Policies and action plans

Strategic subcontractors/partners with whom the Company works follow the existing regulation currently in place at all times. The Company performs pre-qualifying visits and regular audits of the key sub-contractors in order to ensure a regular and rigorous monitoring of the manufacturing of products.

At the early stages of the product development and to support the Company's activities, Nanobiotix has identified the most appropriate source of material and services, respectively provided by suppliers or sub-contractors. The selection and qualification of suppliers are defined within an internal document, explaining the process that contributes to the selection of the suppliers/ subcontractors which can answer to the Company's technical, quality and financial requirements. Technicality and quality are the foundation of this process as suppliers must provide assurance that products or services to be provided are in line with Nanobiotix's expectations and executed within the appropriate quality framework, including typical ISO certification and GxP compliance, especially GCP and GMP.

A continuous follow up of the quality provided by suppliers and subcontractor is performed through the quality management system and through the consolidation of a number of elements, an evaluation is performed at least annually. The consolidated elements include risk-based approach audit programs, continuous evaluation of purchases, process monitoring of activities delegated, quality control before use, formalized agreements. For all critical suppliers who have an impact on the quality of the product, Nanobiotix classifies them as "class I" (critical supplier) and ensures that agreements are in place which specify the roles and responsibility of each party within the regulatory framework.

Results

In 2020, Nanobiotix has initiated two major partnerships: one with a CRO supporting the Company's activities for some of its clinical trials, and another one in manufacturing. Audit programs have contributed to ensure the initial or confirmation of the qualification of these suppliers, as well as the existing ones.

No critical findings were identified as a result of the Company's suppliers' audits, although suggestions for improvement were made. Audit programs have contributed to ensure the initial or confirmation of the qualification of these suppliers, as well as the existing ones.

No critical findings were identified as a result of the Company's suppliers' audits, although suggestions for improvement were made.

4. 2021 ANNUAL FINANCIAL STATEMENTS

4.1. CONSOLIDATED FINANCIAL STATEMENTS FOR THE FISCAL YEAR ENDED DECEMBER 31, 2021

4.1.1. Consolidated statement of financial position

Amounts in thousands of euros

	Notes	2021	2020
Non-current assets			
Intangible assets	**5**	4	21
Property, plant and equipment	**6**	8,186	8,256
Non-current financial assets	**7**	**519**	**505**
Total non-current assets		**8,709**	**8,782**
Current assets			
Trade receivables	**8.1**	—	62
Other current assets	**8.2**	9,139	6,035
Cash and cash equivalents	**9**	83,921	119,151
Total current assets		**93,060**	**125,248**
TOTAL ASSETS		**101,769**	**134,030**
Shareholders' equity			
Share capital	**10.1**	1,045	1,033
Premiums related to share capital	**10.1**	255,767	255,735
Accumulated other comprehensive income		643	555
Treasury shares		(202)	(196)
Reserve		(183,459)	(153,069)
Net loss for the period		(47,003)	(33,590)
Total shareholders' equity		**26,790**	**70,468**
Non-current liabilities			
Non-current provisions	**11.2**	318	414
Non-current financial liabilities	**12**	37,816	44,107
Total non-current liabilities		**38,134**	**44,522**
Current liabilities			
Current provisions	**11.1**	110	40
Current financial liabilities	**12**	8,204	4,872
Trade payables and other payables	**13.1**	6,482	7,106
Other current liabilities	**13.2**	5,531	7,022
Deferred revenues and contract liabilities	**13.3**	16,518	—
Total current liabilities		**36,845**	**19,041**
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY		**101,769**	**134,030**

4.1.2. Consolidated income statement

Amounts in thousands of euros (except per share numbers)

	Notes	For the year ended December 31, 2021	2020
Revenues and other income			
Revenues	**15**	10	50
Other income	**15**	2,637	2,462
Total revenues and other income		**2,647**	**2,512**
Research and development expenses	**16.1**	(30,378)	(24,330)
Selling, general and administrative expenses	**16.2**	(19,434)	(14,611)
Other operating income and expenses	**16.5**	(5,414)	—
Total operating expenses		**(55,226)**	**(38,941)**
Operating income (loss)		**(52,579)**	**(36,428)**
Financial income	**18**	6,360	201
Financial expenses	**18**	(780)	2,646
Financial income (loss)		**5,580**	**2,847**
Income tax	**19**	(5)	(9)
Net loss for the period		**(47,003)**	**(33,590)**
Basic loss per share (euros/share)	**21**	(1.35)	(1.38)
Diluted loss per share (euros/share)	**21**	(1.35)	(1.38)

4.1.3. Consolidated statement of comprehensive loss

Amounts in thousands of euros

	Notes	For the year ended December 31, 2021	2020
Net loss for the period		**(47,003)**	**(33,590)**
Actuarial gains and losses on retirement benefit obligations (IAS 19)	**11.1**	182	(4)
Tax impact		—	—
Other comprehensive loss that will not be reclassified subsequently to income or loss		**182**	**(4)**
Currency translation adjustment		**(94)**	**125**
Tax impact		—	—
Other comprehensive income that may be reclassified subsequently to income or loss		**(94)**	**125**
Total comprehensive loss		**(46,915)**	**(33,469)**

4.1.4. Statements of consolidated changes in shareholders' equity

Amounts in thousands of euros (except number of shares)

	Notes	Share capital Ordinary shares		Premiums related to share capital	Accumulated other comprehensive income (loss)	Treasury shares	Reserve	Net loss for the period	Total shareholders' equity
		Number of shares	Amount						
As of December 31, 2019		**22,415,039**	**672**	**153,139**	**433**	**(169)**	**(105,070)**	**(50,915)**	**(1,908)**
Net loss for the period		—	—	—	—	—	—	(33,590)	(33,590)
Currency translation adjustments		—	—	—	125	—	—	—	125
Actuarial gains and losses (IAS 19)	**11.2**	—	—	—	(4)	—	—	—	(4)
Total comprehensive loss		**—**	**—**	**—**	**121**	**—**	**—**	**(33,590)**	**(33,469)**
Allocation of prior period loss		—	—	—	—	—	(50,915)	50,915	—
Capital increase		12,017,083	361	102,591	—	—	(10)	—	102,942
Subscription of warrants	**10.3**	—	—	5	—	—	—	—	5
Share based payment	**17**	—	—	—	—	—	2,924	—	2,924
Treasury shares		—	—	—	—	(27)	—	—	(27)
As of December 31, 2020		**34,432,122**	**1,033**	**255,735**	**555**	**(196)**	**(153,070)**	**(33,590)**	**70,468**
Net loss for the period		—	—			—	—	(47,003)	(47,003)
Currency translation adjustments		—	—	—	(94)	—	—	—	(94)
Actuarial gains and losses (IAS 19)	**11.2**	—	—	—	182	—	—	—	182
Total comprehensive loss		**—**	**—**	**—**	**88**	**—**	**—**	**(47,003)**	**(46,915)**
Allocation of prior period loss		—	—	—	—	—	(33,590)	33,590	—
Capital increase		393,750	12	—	—	—	(12)	—	—
Subscription of warrants	**10.3**	—		32	—	—	11	—	43
Share based payment	**17**	—	—	—	—	—	3,201	—	3,201
Treasury shares		—	—	—	—	(6)	—	—	(6)
As of December 31, 2021		**34,825,872**	**1,045**	**255,767**	**643**	**(202)**	**(183,460)**	**(47,003)**	**26,790**

4.1.5. Statements of consolidated cash flows

Amounts in thousands of euros

	Notes	For the year ended December 31, 2021	2020
Cash flows used in operating activities			
Net loss for the period		(47,003)	(33,590)
Elimination of other non-cash, non-operating income and expenses			
Depreciation and amortization	**16.4**	1,560	1,754
Provisions		152	(48)
Expenses related to share-based payments	**17**	3,201	2,924
Cost of net debt		2,224	2,115
Impact of deferred income related to financial liabilities discounting effect		(1,554)	(6,463)
Other charges with no impact on treasury		8	7
Cash flows used in operations, before tax and changes in working capital		**(41,412)**	**(33,300)**
(Increase) / Decrease in trade receivables	**8.1**	62	(51)
(Increase) / Decrease in Research tax credit receivable	**8.2**	1,927	5,688
Increase in other receivables	**8.2**	(5,034)	(721)
Increase in trade and other payables	**13.1**	(281)	(995)
Increase / (Decrease) in other current liabilities	**13.2**	(1,652)	1,840
Increase in deferred income and contract liabilities	**13.3**	16,518	—
Changes in operating working capital		**11,540**	**5,762**
Net cash flows used in operating activities		**(29,872)**	**(27,538)**
Cash flows from (used in) investing activities			
Acquisitions of intangible assets	**5**	(5)	(11)
Acquisitions of property, plant and equipment	**6**	(228)	(96)
Addition in non-current financial assets	**7**	(9)	(4)
Net cash flows from (used in) investing activities		**(242)**	**(112)**
Cash flows from financing activities			
Capital increases	**10.1**	—	113,650
Warrants subscription	**10.1**	43	5
Transaction costs	**10.1**	(349)	(10,359)
Increase in loans and conditional advances	**12**	—	10,350
Loans repayments	**12**	(2,833)	(250)
Payment of lease liabilities	**12**	(909)	(928)
Interest paid	**12**	(1,132)	(700)
Charges of lease debt interest		—	—
Net cash flows from financing activities		**(5,180)**	**111,769**
Effect of exchange rates changes on cash		64	(63)
Net increase (decrease) in cash and cash equivalents		**(35,230)**	**84,056**
Net cash and cash equivalents at beginning of period		**119,151**	**35,094**
Net cash and cash equivalents at end of period	**9**	**83,921**	**119,151**

4.1.6. Notes to the consolidated financial statements for the year ended December 31, 2021

4.1.6.1. Information related to the Company

4.1.6.1.1. Presentation of the Company

Nanobiotix S.A. was incorporated in 2003 as a spin-off from the State University of New York (SUNY) in Buffalo. Nanobiotix S.A. (together with its subsidiaries, the "Company"), is headquartered in Paris, France.

The Company is a clinical-stage biotechnology company focused on developing first-in-class product candidates that use proprietary nanotechnology to transform cancer treatment, as well as the utility and efficacy of radiotherapy. Its lead product candidate, NBTXR3, is an aqueous suspension of functionalized crystalline metallic nanoparticles approximately 50 nanometers (50 billionths of a meter) in diameter, designed for injection directly into a malignant tumor. When exposed to ionizing radiation, NBTXR3 amplifies the localized, intratumor killing effect of that radiation. NBTXR3 is designed to enhance the overall efficacy of radiotherapy without resulting in additional side effects on the surrounding healthy tissues.

Alongside the Company's core NBTXR3 development program, the Company is also pursuing a development program to explore the use of radiotherapy-activated NBTXR3 in combination with immune checkpoint inhibitors across several solid tumor indications.

The Company is listed on the Euronext regulated market in Paris (under the ticker symbol "NANO"; Code ISIN: FR0011341205, Bloomberg code: NANO:FP) and on the Nasdaq Global Select Market (under the ticker symbol "NBTX").

4.1.6.1.2. Key events of the fiscal year ended December 31, 2021

Significant events of the period

Nanobiotix and PharmaEngine mutually agree to terminate their collaboration

In March 2021, in light of disagreements over a number of issues with respect to the development of NBTXR3 in the Asia-Pacific region, Nanobiotix and PharmaEngine mutually agreed to terminate the licensing and collaboration agreement entered into in August 2012. Accordingly, on March 4, 2021, Nanobiotix and PharmaEngine entered into a termination and release agreement (the "Termination Agreement"). Under the Termination Agreement, Nanobiotix retained all rights to the development and commercialization of NBTXR3 in the Asia-Pacific region. Nanobiotix agreed to make total termination payments to PharmaEngine of up to $12.5 million in the aggregate as described below.

PharmaEngine was eligible for and received a $2.5 million payment following the announcement of Nanobiotix's collaboration with LianBio for the Asia-Pacific region. During the six months ended June 30, 2021, PharmaEngine also received $4.0 million in conjunction with the completion of various administrative steps in connection with the winding-up of the collaboration.

PharmaEngine will be eligible to receive an additional $1.0 million in administrative fees and a final payment of an additional $5.0 million upon a second regulatory approval of an NBTXR3-containing product in any jurisdiction of the world for any indication. PharmaEngine is entitled to receive a low-single digit tiered royalty based on net sales of NBTXR3 in the Asia-Pacific region for a 10-year period commencing on the corresponding first date of sales in the region. As of December 31, 2021, these future payments were not accrued because the triggering events have not occurred.

As part of the Termination Agreement, PharmaEngine re-assigned to Nanobiotix rights for the development, manufacture, commercialization and exploitation of NBTXR3 in the Asia-Pacific region, as well as all development data, regulatory materials, and all regulatory approvals that are in the name of PharmaEngine or its affiliates. Consequently, NBTXR3 clinical trials conducted by PharmaEngine in Asia are in the process of being concluded or terminated.

Nanobiotix and PharmaEngine also agreed to a mutual release of all claims against the other party and its respective affiliates.

Nanobiotix partners with LianBio for the development and commercialization of NBTXR3 in several oncology indications and in combination with several anti-cancer therapies, in China and other Asian markets

In May 2021, Nanobiotix entered into a partnership with LianBio, a biotechnology company dedicated to bringing paradigm-shifting medicines to patients in China and major Asian markets, to develop and commercialize Nanobiotix's lead product candidate, NBTXR3 into Greater China (mainland China, Hong Kong, Taiwan, and Macau), South Korea, Singapore and Thailand.

LianBio will collaborate in the development of NBTXR3 in Asia Pacific, and contribute to patient enrollment in five future global registrational studies across several tumor types and therapeutic combinations including immunotherapy. LianBio will also support the expansion of global phase III registrational study in head and neck cancer into Greater China with longer term strategic alignment across multiple tumor indications and therapeutic combinations.

Under the terms of the agreement, the Company received a $20 million upfront payment and is entitled to receive up to an aggregate of $220 million in potential contingent, development and commercialization milestone payments. The Company will also be eligible to receive tiered, low double-digit royalties based on net sales of NBTXR3 in the licensed territories. LianBio will fund all development and commercialization expenses in the collaboration territory, and the Company will continue to fund all development and commercialization expenses in all other geographies.

Nanobiotix announces the appointment of Dr. Gary Phillips as Chairman of the Supervisory Board

In May 2021, Dr. Gary Phillips was appointed Chairman of the Company's supervisory board of the Company ("the "Supervisory Board"). Dr Phillips succeeded Laurent Condomine, who retired from the Supervisory Board after 11 years of leadership.

Nanobiotix announces the appointment of Bart Van Rhijn as Chief Financial Officer and member of the executive board of the Company to support its international expansion

On June 1, 2021, the Company announced the appointment of Bart Van Rhijn, MBA, as Chief Financial Officer and member of the executive board of the Company (the "Executive Board"). Bart Van Rhijn brings proven capabilities in global financial management, business development and pharmaceutical commercialization as the Company prepares for the planned launch of its second clinical registration study for NBTXR3 in head and neck cancer (NANORAY-312), continued development in immunotherapy, and planned expansion across solid tumor types and therapeutic combinations. He succeeded Philippe Mauberna, who stepped down from his roles as Chief Financial Officer and Executive Board member after 8 years of service to the Company.

4.1.6.2. General Information, Statement of Compliance and Basis of Presentation

4.1.6.2.1. General principles

The statement of consolidated financial position as of December 31, 2021 and 2020 and the statements of consolidated operations, the statements of consolidated comprehensive loss, the consolidated changes in shareholders' equity and statements of consolidated cash flows for the years ended December 31, 2021 and 2020 were prepared under management's supervision and were approved by the Executive Board of the Company (the "Executive Board") and reviewed by the Supervisory Board of the Company (the "Supervisory Board") on March 30, 2022.

All amounts presented in the consolidated financial statements are presented in thousands of euros, unless stated otherwise. Some figures have been rounded. Accordingly, the totals in some tables may not be the exact sums of component items.

The preparation of the consolidated financial statements in accordance with International Financial Reporting Standards (''IFRS'') requires the use of estimates and assumptions that affect the amounts and information disclosed in the financial statements (see Note 3.2 for additional information).

The consolidated financial statements have been prepared using the historical cost measurement basis, with the exception of financial assets and liabilities, which are measured at fair value.

The consolidated financial statements were prepared on a going concern basis. The Executive Board determined it is appropriate to apply a going concern assumption because the Company's historical losses are due to the innovative nature of the products it is developing, which necessitates a research and development phase spanning several years. With cash and cash equivalents of €83,921 thousand as of December 31, 2021, as compared to €119,151 thousand as of December 31, 2020, the Company believes it has sufficient resources to continue operating for at least twelve months following the consolidated financial statements' publication.

4.1.6.2.2. Statement of Compliance and Basis of Presentation

The consolidated financial statements have been prepared in accordance with IFRS, International Accounting Standards ("IAS") as issued by the International Accounting Standards Board ("IASB") as well as interpretations issued by the IFRS Interpretations Committee ("IFRS-IC") and the Standard Interpretations Committee (the "SIC"), which application is mandatory as of December 31, 2021. The consolidated financial statements are also compliant with IFRS as adopted by the European Union.

Those are available on the European Commission website:
https://ec.europa.eu/info/law/international-accounting-standards-regulation-ec-no-1606-2002

The accounting principles used to prepare the consolidated financial statements for the fiscal year ended December 31, 2021 are identical to those used for the previous year except for the standards listed below that required adoption in 2021.

Application of New or Amended Standards and Interpretations

The Company adopted the following standards, amendments and interpretations, whose application was mandatory for periods beginning on or after January 1, 2021:

- Amendments to IAS 39, IFRS 9, IFRS 7 and IFRS 16 related to the interest rate benchmark reform - Phase 2; and
- Amendments to IFRS 16 - Covid-19 related rent concession.

The application of these standards had no impact on the consolidated financial statements of the Company.

Application of New or Amended Standards and Interpretations early adopted by the Company

The Company elected to early adopt no new standards, amendments and interpretations which application was not yet mandatory for the year ended December 31, 2021.

Application of New or Amended Standards and Interpretations not yet applied by the Company

The application of the following new standards, amendments and interpretations was not yet mandatory for the year ended December 31, 2021:

- IFRS 17 - *Insurance contracts* and related amendments. No significant impact expected on the financial statements.

- Amendment to IAS 1 - *Classification of Liabilities as Current or Non-Current, Disclosure of significant accounting policies, and Update of Practice Statement 2 "Making materiality"*. No significant impact expected on the financial statements.

- Amendment to IAS 37 - *Onerous Contracts - Cost of Fulfilling a Contract*. No significant impact expected on the financial statements.

- Amendment to IFRS 3 - *Conceptual framework*. No significant impact expected on the financial statements.

- Amendment to IAS 8 - *Definition of an accounting estimate*. No significant impact expected on the financial statements.

- Amendments to IAS 16 - *Property, Plant and Equipment: Proceeds before Intended Use*. No significant impact expected on the financial statements.

4.1.6.3. Consolidation principles and methods

4.1.6.3.1. Basis of consolidation

Accounting policy

In accordance with IFRS 10 – Consolidated Financial Statements, an entity is consolidated when it is controlled by the Company. The Company has decision-making authority over the financial and operating policies of all its subsidiaries and holds greater than 50% of the voting rights of each subsidiary. Accordingly, each of the Company's subsidiaries has been fully consolidated from the date on which the Company obtained control over it. A subsidiary would be deconsolidated as of the date on which the Company no longer exercises control.

All intra-Company balances, transactions, unrealized gains and losses resulting from intra-Company transactions and all intra-Company dividends are eliminated in full.

The accounting methods of the Company's subsidiaries are aligned with those of the Company.

The consolidated financial statements are presented in euros, which is the reporting currency and the functional currency of the parent company, Nanobiotix S.A. The financial statements of consolidated foreign subsidiaries whose functional currency is not the euro are translated into euros for statement of financial position items at the closing exchange rate at the date of the statement of financial position and for the statement of operations, statement of comprehensive loss and statement of cash flow items at the average rate for the period presented, except where this method cannot be applied due to significant exchange rate fluctuations during the applicable period. The dollar to euro exchange rate used in the consolidated financial statements to convert the financial statements of the U.S. subsidiary were $1.1326 as of December 31, 2021 and an average of $1.1835 for the year ended December 31, 2021 (source: Banque de France) compared with $1.2271 and $1.1413, for 2020, respectively. The resulting currency translation adjustments are recorded in other comprehensive income (loss) as a cumulative currency translation adjustment.

Consolidated entities

As of December 31, 2021, the Company involves one parent entity, "Nanobiotix S.A.," and five wholly owned subsidiaries:

- Nanobiotix Corp., incorporated in the State of Delaware in the United States in September 2014;
- Nanobiotix Germany GmbH, incorporated in Germany in October 2017;
- Nanobiotix Spain S.L.U., incorporated in Spain in December 2017;
- Curadigm S.A.S., incorporated on July 3, 2019 and located in France; and
- Curadigm Corp., a wholly-owned subsidiary of Curadigm S.A.S., incorporated in the State of Delaware on January 7, 2020 and headquartered in Boston, Massachusetts.

The consolidated financial statements as of and for the year ended December 31, 2021 include the operations of each of these subsidiaries from the date of their incorporation.

Accordingly, the consolidated financial statements as of and for the year ended December 31, 2020 include the operations of each of these subsidiaries from the date of their incorporation.

4.1.6.3.2. Use of judgement, estimates and assumptions

The preparation of consolidated financial statements in accordance with IFRS requires the use of estimates and assumptions that affect the amounts and information disclosed in the financial statements. The estimates and judgments used by management are based on historical information and on other factors, including expectations about future events considered to be reasonable given the circumstances. These estimates may be revised where the circumstances on which they are based change. Consequently, actual results may vary significantly from these estimates under different assumptions or conditions. The main items affected by the use of estimates are share-based payments, deferred tax assets, clinical trials accruals, revenue recognition and the fair value of financial instruments.

Measurement of share-based payments

The Company measures the fair value of stock options (OSA), founders' warrants (BSPCE), warrants (BSA) and free shares (AGA) granted to employees, members of the Supervisory Board and consultants based on actuarial models. These actuarial models require that the Company use certain calculation assumptions with respect to characteristics of the grants (e.g., vesting terms) and market data (e.g., expected share volatility) (see Note 17).

Deferred tax assets

Deferred taxes are recognized for temporary differences arising from the difference between the tax basis and the accounting basis of the Company's assets and liabilities that appear in its financial statements. The primary temporary differences are related to the tax losses that can be carried forward or backward, depending on the jurisdiction. Enacted tax rates are used to measure deferred taxes (see Note 19).

The deferred tax assets are recorded in the accounts only to the extent that it is probable that the future profits will be sufficient to absorb the losses that can be carried forward or backward. Considering its stage of development, which does not allow income projections judged to be sufficiently reliable to be made, the Company has not recognized deferred tax assets in relation to tax losses carryforwards in the Statements of Consolidated Financial Position.

Clinical trial accruals

Clinical trial expenses, although not yet billed in full, are estimated for each study and a provision accrual is recognized accordingly. See Note 13.1 for information regarding the clinical trial accruals as of December 31, 2021 and 2020.

Revenue recognition

In order to determine the amount and timing of revenue under the contract with LianBio, the Company is required to use significant judgments, mainly with respect to identifying performance obligations of the Company and determining the timing of satisfaction of support services provided to LianBio.

See Note 15 for additional detail regarding the Company's accounting policies for its additional sources of revenue.

Fair value of financial assets and liabilities

The fair value measurement of the loan granted by European Investment Bank ("EIB") requires the Company to assess the amount of additional interest ("royalties", as defined by the royalty agreement with EIB) that will be due according to the loan agreement during a royalty calculation period commencing on January 1, 2021. The royalties due during this period will be determined and calculated based on the number of tranches that have been withdrawn and will be indexed to the Company's annual sales turnover. For the purpose of measuring the fair value of the EIB loan, the Company forecasts the sales that it expects to generate during the royalty period, taking into consideration the operational assumptions such as market release dates of the products, growth and penetration rate in each market. (see notes 4.2 and 12 for details about this loan and the accounting treatment applied).

4.1.6.4. Significant transactions

4.1.6.4.1. LianBio

In May 2021, Nanobiotix announced a partnership with LianBio a biotechnology company dedicated to bringing paradigm-shifting medicines to patients in China and major Asian markets, to develop and commercialize NBTXR3 into Greater China (mainland China, Hong Kong, Taiwan, and Macau), South Korea, Singapore and Thailand.

LianBio will collaborate in the development of NBTXR3 in Asia Pacific, and contribute to patient enrollment in five future global registrational studies across several tumor types and therapeutic combinations. LianBio will also support the expansion of the global phase III registrational study in head and neck cancer into Greater China, while supporting longer term strategic alignment across multiple tumor indications and therapeutic combinations.

As of December 31, 2021, a non-refundable upfront payment of $20 million has been collected by the Company at the signature of the LianBio Agreement. The Company is entitled to receive up to an aggregate of $220 million in potential contingent, development and commercialization milestone payments. Nanobiotix will also be eligible to receive tiered, low double-digit royalties based on net sales of NBTXR3 in the licensed territories.

See Note 15 Revenues and other income for further details on this new partnership.

4.1.6.4.2. PharmaEngine

In August 2012, the Company entered into an Exclusive License and Collaboration Agreement (as amended in 2014, the ‘‘License and Collaboration Agreement’’) with PharmaEngine, a biopharmaceutical company specializing in the development of new drugs for the treatment of cancer in Asia. Under the terms of the License and Collaboration Agreement, PharmaEngine will receive the exclusive right to further develop NBTXR3 to obtain regulatory approval, leverage the data generated by the Company’s development activities and commercialize NBTXR3 in multiple countries throughout the Asia-Pacific region. Under the same Agreement, PharmaEngine is responsible for developing (non-clinical and clinical research) and commercializing NBTXR3 throughout the contractual territory and making certain development and minimum commercial milestone payments to the Company. Key provisions of the License and Collaboration Agreement include:

- An exclusive perpetual license granted to PharmaEngine, with the right to sublicense the Company’s technology in order to exploit or have NBTXR3 exploited and use the Company’s trademark in connection with the exploitation of NBTXR3 in the contractual territory (with exploitation including among others developing, obtaining and maintaining regulatory approval, commercializing, distributing, promoting and marketing);

- The Company’s commitment to furnish PharmaEngine with know-how necessary and useful to develop and commercialize NBTXR3 in the contractual territory, know-how meaning any results of experimentation and pre-clinical, clinical and non-clinical trial data by providing PharmaEngine with access to an electronic data platform; and

- The Company’s commitment to supplying or having supplied PharmaEngine with all quantities of NBTXR3 required and used by PharmaEngine for clinical testing and subsequent commercialization if and when regulatory approvals are obtained.

In return, PharmaEngine commits to use commercially reasonable efforts to develop NBTXR3 in the contractual territory at PharmaEngine’s cost.

Under the License and Collaboration Agreement, the Company has received and/or is entitled to receive:

- A $1.0 million up-front payment on signature of the contract, fully received in 2012;
- Payments upon the achievement of development milestones, including key stages of product development, first filing for regulatory approval, and first regulatory approval in the contractual territory;
- Payments upon the achievement of commercial milestones based on specified sales thresholds;
- Up to double-digit royalties based on net product sales in the Asia-Pacific region; and
- Payments for the supply of NBTXR3.

Potential development and commercial milestone payments, including those paid to date, amount to an aggregate of up to $56 million.

The Company and PharmaEngine amended the agreement in October 2014, as part of which PharmaEngine agreed:

- To join the global pivotal clinical trial of NBTXR3 for the treatment of Soft Tissue Sarcoma sarcoma initiated by the Company in the Asia-Pacific area, with each party committing itself to share clinical trial results in order to increase the tested population and to accelerate growth and value creation;
- To pay the first development milestone ($1 million, received by the Company in 2014) and share external clinical research organization costs charged to the Company in proportion to its contribution in recruiting the patient population included in the clinical trial; and
- To pay the development milestone ($1 million, received by the Company in 2016) related to the launch of the first Phase II of the pivotal study.

As of December 31, 2020, $3.0 million has been received since the signature of the License and Collaboration Agreement. The next potential milestone payment under the agreement will become payable only if PharmaEngine files a commercialization authorization of NBTXR3 in their region.

In November 2020, Nanobiotix notified PharmaEngine of a material breach of the terms of the License and Collaboration agreement. While both Nanobiotix and PharmaEngine believe in the potential of NBTXR3 to improve treatment outcomes for patients with cancer, the parties have had disagreements regarding the optimal strategy for development in the Asia-Pacific region. As such, after discussion between the two parties, Nanobiotix and PharmaEngine have mutually agreed to discontinue the collaboration. This agreement to terminate the License and Collaboration agreement represents a full resolution of outstanding disagreements over a number of issues with respect to the development of NBTXR3 in the Asia-Pacific region. See Note 24 – Subsequent events for additional detail regarding the collaboration of the termination and see Note 15 for additional detail regarding the accounting policy applied to the License and Collaboration Agreement.

In March 2021, the Company and PharmaEngine mutually agreed to terminate the License and Collaboration agreement.

As of December 31, 2021, the Company paid a cumulative amount of $6.5 million to PharmaEngine in accordance with the termination agreement signed between the parties. PharmaEngine will receive additional payments of $1 million upon receipt by the Company of certain clinical study reports and of

$5 million upon the second regulatory approval of NBTXR3 in any jurisdiction of the world for any indication. The Company has also agreed to pay royalties to PharmaEngine at low single-digit royalty rates with respect to sales of NBTXR3 in the Asia-Pacific region for a 10-year period beginning at the date of the first sales in the region. These future payments were not accrued because the triggering events have not occurred.

4.1.6.4.3. Financing agreement with the European Investment Bank ("EIB")

In July 2018, the Company signed a non-dilutive financing agreement with the EIB to borrow up to €40 million in order to fund its research, development and innovation activities related to NBTXR3 in various therapeutic indications, subject to achieving a set of agreed-upon performance criteria. This financing is divided in three tranches:

- a first tranche of €16 million, received in October 2018, subject to a 6% fixed rate and that will be fully repaid in 2023 at the latest;

- a second tranche of €14 million, received in March 2019, subject to a 5% fixed rate, that with repayments beginning in 2021 and continuing into 2024; and,

- a last tranche of €10 million, subject to a 4% fixed interest rate, that will be fully repaid after a period of five years, which begins within one year of obtaining it. The deadline for requesting this third tranche, initially scheduled as of July 26, 2020, was delayed by 12 months to July 31, 2021. As the conditions have not been met by July 31, 2021, the Company will not request the final tranche of the EIB loan.

In connection with this financing agreement, the Company also entered into a royalty agreement with EIB pursuant to which the Company is required, during a six-year royalty calculation period commencing on January 1, 2021, to pay (on each June 30 with respect to the preceding year within the calculation period) royalties to EIB. The amount of royalties payable is calculable based on low single-digit royalty rates, which vary according to the number of tranches that have been drawn, and indexed on the Company's annual sales turnover.

The €14 million second tranche, which was received in March 2019, was disbursed on the basis of achieving the following criteria:

- Determination of the recommended dose at 22% of the tumor volume for head and neck cancers treatment following the end of the Phase I clinical trial with NBTXR3; and

- Positive evaluation of the clinical benefit/risk ratio of NBTXR3 in the Phase II/III clinical trial in soft tissue sarcomas by the clinical expert mandated by the French notified body covering medical devices, GMED.

See Note 22 for discussion of royalties that may be due in the case of early repayment or change of control after repayment of the loan.

4.1.6.4.4. Collaboration Agreement with the University of Texas MD Anderson Cancer Center

In January 2019, the Company and the University of Texas MD Anderson Cancer Center, world prominent center of research, education, prevention and care for cancer patients announced a large-scale research collaboration.

The collaboration will support multiple new Phase I/II clinical trials involving around 340 patients with Nanobiotix's first-in-class agent NBTXR3 for use in treating several cancer types –, including head and neck, pancreatic, thoracic, lung, gastrointestinal and genitourinary cancers.

As part of the funding for this collaboration, Nanobiotix is committed to pay approximately $11 million for those clinical trials during the collaboration, and made an initial $1.0 million payment at the commencement of the collaboration and a second $1.0 million payment on February 3, 2020. Additional payments will be made in the six months following patients enrollment, with the balance payable upon enrollment of the final patient for all studies.

Nanobiotix may also be required to pay an additional one-time milestone payment upon (i) grant of the first regulatory approval by the Food and Drug Administration in the United States and (ii) the date on which a specified number of patients have been enrolled in the clinical trials. The milestone payment increases on an annual basis ranging from $2.2 million to $16.4 million.

As of December 31, 2021 and 2020, the Company recognized prepaid expenses for €1.0 million and €1.6 million respectively. Expenses will be recorded during the course of the collaboration in the statement of consolidated operations based on the patients enrolled during the relevant period. See Note 8.2 for further details on other current assets.

4.1.6.5. Intangible assets

Accounting policies

In accordance with IAS 38 – *Intangible Assets*, intangible assets are carried at their acquisition cost.

Research and Development costs

Research costs are recorded in expenses in the period during which they are incurred. Under IAS 38 – *Intangible Assets*, development costs may only be capitalized as intangible assets if the following criteria are met:

- it is technically feasible to complete the development of the intangible asset so that it will be available for use or sale;
- the Company intends to complete the development of the intangible asset and use or sell it;
- the Company has the ability to use or sell the intangible asset;
- it is probable that the intangible asset will generate future economic benefits;
- adequate technical, financial and other resources are available to complete the development of the intangible asset; and
- the Company is able to reliably measure the expenditures attributable to the development of the intangible asset.

The Company believes that because of the risks and uncertainties related to the grant of regulatory approval for the commercialization of its product candidates, the technical feasibility of completing its development projects will only be demonstrated when requisite approvals are obtained for the commercialization of products. Accordingly, pursuant to IAS 38, the Company has recognized all of its research and development costs incurred as an expense in 2021 and prior periods.

Patents

Costs incurred by the Company in connection with the filing of patent applications are recognized as an expense until such time as the relevant patents are obtained, in line with the treatment of research and development costs. Once the patents are obtained from relevant authorities, their related patent costs are amortized on a straight-line basis over the patent protection period. The useful life of the patents is reassessed each year, according to IAS 36.

Software

The costs of acquiring software licenses are recognized as assets on the basis of the costs incurred to acquire and implement the software to which the license relates. These costs are amortized on a straight-line basis over the life of the license.

Recoverable amount of intangible assets

Intangible assets with a definite useful life are tested for impairment when there are events or changes in circumstances that indicate that the asset might be impaired. Impairment tests involve comparing the carrying amount of an intangible asset with its recoverable amount. The recoverable amount of an asset is the higher of (i) its fair value less costs to sell and (ii) its value in use. If the recoverable amount

of any asset is below its carrying amount, an impairment loss is recognized to reduce the carrying amount to the recoverable amount.

Detail of intangible assets

The change in intangible assets breaks down as follows:

(€k)	As of January 1st, 2021	Increases	Decreases	Transfer	Currency translation	As of December 31, 2021
Patents	65	—	—	—	—	65
Software	651	5	—	—	—	657
Intangible assets in progress	—	—	—	—	—	—
Gross book value of intangible assets	**717**	**5**	**—**	**—**	**—**	**722**
Patents	(65)	—	—	—	—	(65)
Software	(630)	(22)	—	—	—	(652)
Accumulated depreciation of intangible assets [(1)]	**(695)**	**(22)**	**—**	**—**	**—**	**(717)**
Net book value of intangible assets	**21**	**(17)**	**—**	**—**	**—**	**4**

(1) *Expenses for the period are detailed in Note 16.4 Depreciation, amortization and provisions expenses*

(€k)	As of January 1st, 2020	Increases	Decreases	Transfer	Currency translation	As of December 31, 2020
Patents	65	—	—	—	—	65
Software	584	11	(5)	61	—	651
Intangible assets in progress	61	—	—	(61)	—	—
Gross book value of intangible assets	**710**	**11**	**(5)**	**—**	**—**	**717**
Patents	(65)	—	—	—	—	(65)
Software	(483)	(152)	5	—	—	(630)
Accumulated depreciation of intangible assets [(1)]	**(548)**	**(152)**	**5**	**—**	**—**	**(695)**
Net book value of intangible assets	**163**	**(141)**	**—**	**—**	**—**	**21**

(1) *Expenses for the period are detailed in Note 16.4 Depreciation, amortization and provisions expenses*

4.1.6.6. Property, plant and equipment

Accounting policies

Property, plant and equipment are recorded at their acquisition cost. Major renovations and improvements necessary to bring an asset to the working condition for its use as intended by the Company's management are capitalized. The cost of repairs, maintenance and other renovation work is expensed as incurred.

Property, plant and equipment are depreciated on a straight-line basis according to the estimated useful life of the relevant assets.

The depreciation periods used are as follows:

- General fixtures and fittings, building work: 5 to 10 years;
- Technical installations, equipment and industrial tooling: 3 to 10 years; and
- Office and IT equipment and furniture: 1 to 10 years.

Recoverable amount of property, plant and equipment

Property, plant and equipment with a definite useful life are tested for impairment when there are events or changes in circumstances that indicate that the asset might be impaired. An impairment loss is recognized for the excess of the carrying amount of the asset over its recoverable amount. The recoverable amount of an asset is equal to the higher of (i) its fair value less costs to sell and (ii) its value in use.

Detail of property, plant and equipment

The change in property, plant and equipment is as follows:

(in thousands of euros)	**As of January 1st, 2021**	**Increases**	**Decreases**	**Transfer**	**Currency translation**	**As of December 31, 2021**
Fixtures, fittings and installations	3,313	5	—	—	—	3,318
Right of use – Buildings	7,171	1,362	(139)	—	—	8,393
Technical equipment	2,061	73	—	1	—	2,135
Office and IT equipment	988	53	(35)	—	4	1,010
Transport equipment	31	—	—	—	3	33
Right of use – Transport equipment	65	—	(38)	—	1	28
Tangible assets in progress	1	97	—	(0)	—	98
Prepayments on tangible assets	—	—	—	(0)	—	—
Gross book value of tangible assets	**13,630**	**1,590**	**(212)**	**—**	**8**	**15,017**
Fixtures, fittings and installations	(1,320)	(320)	—	—	—	(1,641)
Right of use – Buildings	(1,739)	(901)	30	—	—	(2,610)
Technical equipment	(1,466)	(178)	—	—	—	(1,644)
Office and IT equipment	(783)	(124)	34	—	(3)	(875)
Transport equipment	(31)	—	—	—	(3)	(33)
Right of use – Transport equipment	(36)	(12)	20	—	(1)	(28)
Accumulated depreciation of tangible assets[(1)]	**(5,374)**	**(1,534)**	**84**	**—**	**(6)**	**(6,831)**
Net book value of tangible assets	**8,256**	**56**	**(129)**	**—**	**3**	**8,186**

[(1)] *Expenses for the period are detailed in Note 16.4 Depreciation, amortization and provisions expenses*

The €1,362 thousand increase in Right of use – Buildings mainly relates to to the extension of Villejuif leases for 4 years following changes in the ownership for €1,390 thousand reduced by the €25 thousand related to the rent indexation impact.

The €139 thousand decrease in Right of use – Buildings mainly relates to the termination of a lease contract in Faubourg Saint-Antoine in Paris, France.

(in thousands of euros)	**As of January 1st, 2020**	**Increases**	**Decreases**	**Transfer**	**Currency translation**	**As of December 31, 2020**
Fixtures, fittings and installations	3,297	16	—	—	—	3,313
Right of use – Buildings	6,766	418	(14)	—	—	7,171
Technical equipment	2,019	42	—	—	—	2,061
Office and IT equipment	957	37	(1)	—	(4)	988
Transport equipment	34	—	—	—	(3)	31
Right of use – Transport equipment	115	—	(41)	(5)	(4)	65
Tangible assets in progress	11	1	—	(11)	—	1
Prepayments on tangible assets	—	—	—	—	—	—
Gross book value of tangible assets	**13,197**	**515**	**(57)**	**(15)**	**(11)**	**13,630**
Fixtures, fittings and installations	(1,001)	(320)	—	—	—	(1,320)
Right of use – Buildings	(829)	(911)	—	2	—	(1,739)
Technical equipment	(1,272)	(194)	—	—	—	(1,466)
Office and IT equipment	(629)	(157)	1	—	2	(783)
Transport equipment	(34)	—	—	1	3	(31)
Right of use – Transport equipment	(45)	(35)	42	—	1	(36)
Accumulated depreciation of tangible assets[(1)]	**(3,811)**	**(1,616)**	**43**	**4**	**6**	**(5,374)**
Net book value of tangible assets	**9,386**	**(1,101)**	**(14)**	**(12)**	**(4)**	**8,256**

[(1)] *Expenses for the period are detailed in Note 16.4 Depreciation, amortization and provisions expenses*

In 2020, the €418 thousand increase in Right of use – Buildings mainly relates to:

- two new lease contracts: one in Oberkampf Street in Paris, France for €155 thousand, the other in Faubourg Saint-Antoine in Paris, France for €140 thousand,
- the termination of a lease contract by Curadigm SAS for €43 thousand;
- The addition of a parking under the leases for the Villejuif facility for €30 thousand, and
- the impact of an annual rent adjustment for the Wattignies and Villejuif leases based on the INSEE (National Institute of Statistics and Economic Studies) index for €35 and €15 thousand, respectively.

4.1.6.7. Non-current financial assets

Accounting policies

Non-current financial assets are recognized and measured in accordance with IFRS 9 – Financial Instruments.

Pursuant to IFRS 9 – Financial Instruments, financial assets are classified in two categories according to their nature and the intention of management:

- Financial assets at fair value through profit and loss;
- Financial assets at fair value through other comprehensive income; and
- Financial assets at amortized cost.

All regular way purchases and sales of financial assets are recognized at the settlement date.

Financial assets at fair value through profit or loss

This category includes marketable securities, cash and cash equivalents. They represent financial assets held for trading purposes, i.e., assets acquired by the Group to be sold in the short-term. They are measured at fair value and changes in fair value are recognized in the consolidated statements of operations as financial income or expense, as applicable.

Financial assets at amortized cost

This category includes other financial assets (non-current), trade receivables (current) and other receivables and related accounts (current). Other financial assets (non-current) include advances and security deposits and guarantees granted to third parties as well as term deposits and restricted cash, which are not considered as cash equivalents.

They are non-derivative financial assets with fixed or determinable payments that are not listed on an active market. They are initially recognized at fair value plus transaction costs that are directly attributable to the acquisition or issue of the financial asset, except trade receivables that are initially recognized at the transaction price as defined in IFRS 15.

After initial recognition, these financial assets are measured at amortized cost using the effective interest rate method when both of the following conditions are met:

- The financial asset is held within a business model whose objective is to hold financial assets in order to collect contractual cash flows; and
- The contractual terms of the financial asset give rise on specified dates to cash flows that are solely payments of principal and interest on the principal amount outstanding.

Gains and losses are recorded in the consolidated statements of operations when they are derecognized, subject to modification of contractual cash flows and/or impaired.

IFRS 9 – *Financial Instruments* requires an entity to recognize a loss allowance for expected credit losses on a financial asset at amortized cost at each Statement of Financial Position date. The amount of the loss allowance for expected credit losses equals: (i) the 12 - month expected credit losses or (ii) the full lifetime expected credit losses. The latter applies if credit risk has increased significantly since initial recognition of the financial instrument. An impairment is recognized, where applicable, on a case–by–

case basis to take into account collection difficulties which are likely to occur based on information available at the time of preparation of the financial statements.

Disputed receivables are written-off when certain and precise evidence shows that recovery is impossible, and existing credit loss allowance are released.

Financial assets and liabilities are monitored for any indication of impairment. Under IFRS 9, the impairment model is based on the accounting on expected credit losses during the life of the financial assets. A financial asset is impaired if its credit risk, determined with both historic and prospective data, increased significantly since its initial booking. The loss will impact the net income (loss) recorded to the statement of operations.

Detail of non-current financial assets

The change in non-current financial assets breaks down as follows:

(€k)	**Liquidity contract - Cash account[(1)]**	**Other long-term investments pledged as collateral**	**Security deposits paid**	**Total**
Net book value as of December 31, 2019	**131**	**—**	**399**	**529**
Additions	—	—	9	9
Decreases	(27)	—	(5)	(31)
Currency translation adjustments	—	—	(2)	(2)
Net book value as of December 31, 2020	**105**	**—**	**401**	**505**
Additions	—	—	9	9
Decreases	(6)	—	—	(6)
Reclassification	—	—	8	8
Currency translation adjustments	—	—	3	3
Net book value as of December 31, 2021	**98**	**—**	**421**	**519**

(1) *See note 10.2 Treasury shares*

In 2021, non-current financial assets increased by €14 thousand compared to 2020. In 2020, non-current financial assets decreased by €24 thousand compared to 2019. In 2021, the Security deposits paid increased by €20 thousand, mainly due to the new €9 thousand deposit paid in connection with the Nanobiotix Corp headquarters' lease contract in Cambridge, Massachusetts, United States.

The decrease of the liquidity contract – cash account corresponds to treasury shares transactions whose counterpart is recorded as capital on the "treasury shares" line in the statement of change in shareholders' equity.

4.1.6.8. Trade receivables and other current assets

4.1.6.8.1. Trade receivable

In 2020, trade receivables related mainly to invoices issued to PharmaEngine, in connection with the charging-back of shared external clinical research organization costs under the License and Collaboration Agreement as amended (see Note 4 for more detail on the License and Collaboration Agreement). This agreement terminated in March 31, 2021, and thus the related receivables have been settled.

(€k)	As of December 31, 2021	As of December 31, 2020
Trade receivables	—	62
Trade receivables	**—**	**62**

Trade receivables break down as follows:

(€k)	As of December 31, 2021	As of December 31, 2020
Due in 3 months or less	—	62
Due between 3 and 6 months	—	—
Due between 6 and 12 months	—	—
Due after more than 12 months	—	—
Trade receivables	**—**	**62**

4.1.6.8.2. Other current assets

Other current assets break down as follows:

(€k)	As of December 31, 2021	As of December 31, 2020
Research tax credit receivable	2,490	1,927
VAT receivable	1,058	971
Prepaid expenses	2,213	2,217
Other receivables	3,378	920
Other current assets	**9,139**	**6,035**

As of December 31, 2021, prepaid expenses mainly relate to:

- research agreements related to MD Anderson agreement (see Note 4.4 – Collaboration Agreement with the University of Texas MD Anderson Cancer Center) for €1.0 million, and
- insurance related to the Directors & Officers for €0.6 million.

As of December 31, 2020, prepaid expenses mainly relate to research agreements related to MD Anderson agreement (see Note 4.4 – Collaboration Agreement with the University of Texas MD Anderson Cancer Center) for €1.6 million.

Other receivables mainly comprised advances paid to suppliers in the amounts of €3,043 thousand as of December 31, 2021 as compared to €805 thousand as of December 31, 2020. This advance payment is mainly related to the new ICON contract signed in 2021 in conjunction with the launch of the 312 study.

4.1.6.8.3. Research tax credit

The Company receives a research tax credit (*Crédit d'Impôt Recherche*, or ''CIR'') from the French tax authorities. See Note 15 for additional details on the CIR research tax credit.

The research tax credit for 2021 was €2.5 million (€2.3 million for Nanobiotix S.A. and €218 thousand for Curadigm SAS), while the amount for 2020 was €1.9 million (€1.9 million for Nanobiotix S.A. and €69 thousand for Curadigm SAS).

The 2020 research tax credit was collected by the Company in November 2021, while the 2019 research tax credit was collected in July 2020.

The change in CIR receivables breaks down as follows:

(€k)

Receivable as of December 31, 2019	**5,688**
Refund of 2018 research tax credit – Nanobiotix SA	(3,251)
Refund of 2019 research tax credit – Nanobiotix SA	(2,374)
Refund of 2019 research tax credit – Curadigm SAS	(64)
2020 research tax credit – Nanobiotix SA	1,858
2020 research tax credit – Curadigm SAS	69
Receivable as of December 31, 2020	**1,927**
Refund of 2020 research tax credit – Nanobiotix SA	(1,858)
Refund of 2020 research tax credit – Curadigm SAS	(69)
2021 research tax credit – Nanobiotix SA	2,272
2021 research tax credit – Curadigm SAS	218
Receivable as of December 31, 2021	**2,490**

4.1.6.9. Cash and cash equivalents

Accounting policies

Cash equivalents are held for the purpose of meeting short-term cash commitments rather than for investment or other reasons. They are easily converted into known amounts of cash and are subject to an insignificant risk of changes in value. Cash and cash equivalents consist of liquid assets that are available immediately and term deposits.

Cash equivalents are measured at amortized cost.

Detail of cash and cash equivalents

(€k)	As of December 31, 2021	As of December 31, 2020
Cash and bank accounts	83,921	119,151
Net cash and cash equivalents	**83,921**	**119,151**

As of December 31, 2021, Cash and bank accounts decreased by €35,230 thousand as compared with December 31, 2020 mainly due to:

- the non-refundable upfront payment from LianBio in June 2021 for €16.5 million ($20.0 million);
- the payments made to PharmaEngine for a total of €5.4 million in 2021 pursuant to the PharmaEngine Termination Agreement;
- the debt reimbursement related to the EIB loan for €3.0 million and to the Bpifrance loan for €0.5million; and
- other cash flows used in operating activities.

4.1.6.10. Share Capital

4.1.6.10.1. Capital issued

Accounting policies

Ordinary shares are classified in shareholders' equity. The cost of equity transactions that are directly attributable to the issue of new shares or options is recognized in shareholders' equity as a deduction from the proceeds of the issue.

Detail of share capital transactions

(in thousands, except number of shares)	Nature of transaction	Share Capital	Premiums related to share capital	Number of shares
December 31, 2019		**672**	**153,139**	**22,415,039**
March 6, 2020	Capital increase	9	—	316,083
June 24, 2020	Subscription of 2020 warrants	—	1	—
June 26, 2020	Subscription of 2020 warrants	—	1	—
June 29, 2020	Subscription of 2020 warrants	—	2	—
June 30, 2020	Subscription of 2020 warrants	—	1	—
July 27, 2020	Capital increase	—	—	6,000
July 28, 2020	Dawn IV Capital increase	99	20,030	3,300,000
July 28, 2020	Dawn IV Capital increase transaction costs	—	(1,387)	—
December 16, 2020	U.S. Initial public offering initial deal € - Nasdaq (€11.14)	56	20,609	1,855,000
December 16, 2020	U.S. Initial public offering initial deal $ - Nasdaq ($13.50)	163	60,494	5,445,000
December 18, 2020	U.S. Initial public offering green shoe $ - Nasdaq ($13.50)	33	12,165	1,095,000
December 18, 2020	U.S. Initial public offering costs	—	(9,322)	—
December 31, 2020		**1,033**	**255,735**	**34,432,122**
March 31, 2021	Capital increase AGA 2018-1	1	—	24,500
March 31, 2021	Capital increase AGA 2019-1	11	—	369,250
April 20, 2021	Warrants attribution	—	(11)	—
May 31, 2021	Warrants subscription (BSA 2021)	—	43	—
December 31, 2021		**1,045**	**255,767**	**34,825,872**

As of December 31, 2021, the share capital was €1,044,776.16 divided into 34,825,872 fully paid in ordinary shares each with a par value of €0.03, as compared with the 2020 share capital of €1,032,963.66 divided into 34,432,122 fully paid in ordinary shares, each with a par value of €0.03 and the 2019 share capital of €672,451.17 divided into 22,415,039 fully paid in ordinary shares each with a par value of €0.03.

In 2021, the increase in share capital is inherent to the conversion of fully vested warrants related to the AGA 2018-1 and AGA 2019-1 plans.

In 2020, the increase in share capital is mainly related to the U.S. initial public offering, which closed in December 2020. In the global offering, a total of 8,395,000 ordinary shares was issued, as follows:

- 5,445,000 ordinary shares in the form of ADSs were issued in the United States at $13.50 per ADS;
- 1,855,000 ordinary shares were issued through a concurrent offering in certain jurisdictions outside of the United States to certain investors at €11.14 per ordinary share; and,
- the underwriters for the global offering exercised in full their option to purchase 1,095,000 additional ADSs at the same public offering price of $13.50 per ADS.

As of December 31, 2020, €10.7 million of transaction costs had been recorded, €9.3 million of which were related to the initial public offering in the United States, and are recognized as a reduction to premiums related to share capital. Those transaction costs were almost paid in full as of December 31, 2020. The remaining €349 thousand were paid in 2021.

4.1.6.10.2. Treasury shares

On December 31, 2021, the Company held 15,456 treasury shares under a liquidity contract compared to 12,970 treasury shares as of December 31, 2020. This liquidity contract complies with the general regulations of, and market practices accepted by, the French Financial Markets Authority ("AMF"), entered into following the Company's French initial public offering in 2012. These shares were deducted from IFRS equity in the amount of €202 thousand and €196 thousand as of December 31, 2021 and 2020, respectively.

4.1.6.10.3. Founders' warrants (BSPCE), warrants (BSA), stocks options (OSA) and allocation of free shares (AGA)

Accounting policies

Accounting policies for share-based payments are described in Note 17.

Detail of change in founders' warrants, warrants and stock options and free shares

As of December 31, 2021, and 2020, the Company had the following type of equity plans in place: founders' warrant (BSPCE) plans, warrant (BSA) plans, stock option (OSA) plans and free shares (AGA) plans.

The following tables summarize activity in these plans during the years ended December 31, 2020 and 2021.

Founders' warrants (BSPCE)

Type	Grant date	Exercise price (in euros)	Outstanding at January 1, 2021	Issued	Exercised	Forfeited	Outstanding at December 31, 2021	Number of shares issuable
BSPCE 2012-2	12/18/2012	6.63	100,000	—	—	—	100,000	100,000
BSPCE 08-2013	08/28/2013	5.92	50,000	—	—	—	50,000	50,000
BSPCE 09-2014	09/16/2014	18.68	86,150	—	—	—	86,150	86,150
BSPCE 2015-1	02/10/2015	18.57	68,450	—	—	—	68,450	68,450
BSPCE 2015-3	06/10/2015	20.28	30,700	—	—	(350)	30,350	30,350
BSPCE 2016	02/02/2016	14.46	202,617	—	—	(1,776)	200,841	200,841
BSPCE 2017	01/07/2017	15.93	180,850	—	—	(1,350)	179,500	179,500
Total			**718,767**	**—**	**—**	**(3,476)**	**715,291**	**715,291**

Type	Grant date	Exercise price (in euros)	Outstanding at January 1, 2020	Issued	Exercised	Forfeited	Outstanding at December 31, 2020	Number of shares issuable
BSPCE 2012-2	12/18/2012	6.63	100,000	—	—	—	100,000	100,000
BSPCE 08-2013	08/28/2013	5.92	50,000	—	—	—	50,000	50,000
BSPCE 09-2014	09/16/2014	18.68	92,100	—	—	(5,950)	86,150	86,150
BSPCE 2015-1	02/10/2015	18.57	70,950	—	—	(2,500)	68,450	68,450
BSPCE 2015-3	06/10/2015	20.28	38,400	—	—	(7,700)	30,700	30,700
BSPCE 2016	02/02/2016	14.46	212,969	—	—	(10,352)	202,617	202,617
BSPCE 2017	01/07/2017	15.93	187,166	—	—	(6,316)	180,850	180,850
Total			**751,585**	**—**	**—**	**(32,818)**	**718,767**	**718,767**

By way of exception, the Executive Board decided to lift, for three former employees and for two former members of the Executive Board, the continued service condition, and, where applicable for a former Executive Board member, the performance conditions to which the exercise of certain BSPCEs was subject, notwithstanding the termination of their employment agreement and/or corporate offices.

The impact of share-based payments on income is detailed in Note 17.

The probability of meeting the performance conditions for the 2016 BSPCE, BSA and OSA performance plans was reassessed as of December 31, 2021. As a consequence, no new instrument became issuable.

Warrants (BSA)

Type	Grant date	Exercise price (in euros)	Outstanding at January 1, 2021	Issued	Exercised	Forfeited	Outstanding at December 31, 2021	Number of shares issuable
BSA 04-12	05/04/2012	6.00	30,000	—	—	—	30,000	30,000
BSA 2013	04/10/2013	6.37	6,000	—	—	—	6,000	6,000
BSA 2014	09/16/2014	17.67	10,000	—	—	—	10,000	10,000
BSA 2015-1	02/10/2015	17.67	21,000	—	—	—	21,000	21,000
BSA 2015-2(a)	06/25/2015	19.54	64,000	—	—	—	64,000	64,000
BSA 2015-2(b)	06/25/2015	19.54	—	—	—	—	—	—
BSA 2016	02/02/2016	13.74	36,208	—	—	(36,208)	—	—
BSA 2016-2	11/03/2016	15.01	8,000	—	—	(8,000)	—	—
BSA 2017	01/07/2017	15.76	18,000	—	—	—	18,000	18,000
BSA 2018-1	03/06/2018	13.55	28,000	—	—	—	28,000	28,000
BSA 2018-2	07/27/2018	16.10	5,820	—	—	—	5,820	5,820
BSA 2019-1	03/29/2019	11.66	18,000	—	—	—	18,000	18,000
BSA 2020	03/17/2020	6.59	18,000	—	—	—	18,000	18,000
BSA 2021 (a)	04/21/2021	13.47	—	48,103	—	(33,672)	14,431	14,431
BSA 2021 (b)	04/21/2021	13.64	—	30,000	—	—	30,000	30,000
Total			**263,028**	**78,103**	**—**	**(77,880)**	**263,251**	**263,251**

Type	Grant date	Exercise price (in euros)	Outstanding at January 1, 2020	Issued	Exercised	Forfeited	Outstanding at December 31, 2020	Number of shares issuable
BSA 04-12	05/04/2012	6.00	30,000	—	—	—	30,000	30,000
BSA 2013	04/10/2013	6.37	6,000	—	—	—	6,000	6,000
BSA 2014	09/16/2014	17.67	10,000	—	—	—	10,000	10,000
BSA 2015-1	02/10/2015	17.67	21,000	—	—	—	21,000	21,000
BSA 2015-2(a)	06/25/2015	19.54	64,000	—	—	—	64,000	64,000
BSA 2015-2(b)	06/25/2015	19.54	6,000	—	—	(6,000)	—	—
BSA 2016	02/02/2016	13.74	36,208	—	—	—	36,208	36,208
BSA 2016-2	11/03/2016	15.01	8,000	—	—	—	8,000	8,000
BSA 2017	01/07/2017	15.76	18,000	—	—	—	18,000	18,000
BSA 2018-1	03/06/2018	13.55	28,000	—	—	—	28,000	28,000
BSA 2018-2	07/27/2018	16.10	5,820	—	—	—	5,820	5,820
BSA 2019-1	03/29/2019	11.66	18,000	—	—	—	18,000	18,000
BSA 2020	03/17/2020	6.59	—	18,000	—	—	18,000	18,000
Total			**251,028**	**18,000**	**—**	**(6,000)**	**263,028**	**263,028**

At a meeting on April 20, 2021, the Executive Board, acting pursuant to the delegation granted by the Company's shareholders' meeting held on November 30, 2020 granted 48,103 warrants to members and observers of the Supervisory Board, each entitling its holder to subscribe one ordinary share, each with a par value of €0.03 and at a price of €13.47 (share premium included). The designated warrants included 18,103 warrants that were issued in replacement of certain 2016 ordinary warrants that became null on February 2, 2021. The subscription period is open from the date of the meeting of the Executive Board until September 30, 2021, inclusive. As of December 31, 2021, 14,431 warrants have been subscribed by their beneficiaries.

The warrants can be exercised at any time during a 10-year period, subject to the satisfaction of the following conditions:

- the subscription by the relevant beneficiary of his/her warrant;
- the relevant holder has attended at least 75% of the Supervisory Board meetings held during the twelve months preceding the exercise of the warrants or, as the case may be, the date the holder ceases to be part of the Group; and
- the recommended dose for two out of the three patient cohorts enrolled in the study 1100 has been determined in order to define the next steps of the immuno-oncology development plan.

It is being specified that (i) the Executive Board, with the prior approval of the Supervisory Board, shall acknowledge the satisfaction of such condition and (ii) such condition shall automatically be waived in the event of a change of control.

At the same meeting, the Executive Board, acting pursuant to the above mentioned delegation, also granted 30,000 warrants to a consultant of the Company, each warrant giving its holder the right to subscribe one ordinary share, each with a par value of €0.03 and at a price of €13.64 (share premium included) at any time during a ten-year period subject to (i) the subscription by such consultant of the warrants and (ii) the drafting by such consultant of a Chemistry, Manufacturing, Control (CMC) risk assessment report. The corresponding subscription period has been fixed from the date of the meeting of the Executive Board until July 20, 2021 inclusive. As of December 31, 2021, no warrants have been subscribed by the beneficiary. In addition, as of December 31, 2021 the report is not prepared yet. Therefore, the warrants are not vested yet.

At a meeting on March 17, 2020, the Executive Board, acting pursuant to the delegation granted by the thirty-fourth resolution of the annual shareholders' meeting dated April 11, 2019 and following the approval granted by the Supervisory Board on March 13, 2020, granted 18,000 warrants to members of the Supervisory Board, each entitling the holder to subscribe to a defined number of ordinary shares with a par value of €0.03, at a price of €6.59. The holders subscribed to the warrants prior to the end of the subscription period on September 30, 2020.

Stock options (OSA)

Type	Grant date	Exercise price (in euros)	Outstanding at January 1, 2021	Issued	Exercised	Forfeited	Outstanding at December 31, 2021	Number of shares issuable
OSA 2016-1	02/02/2016	13.05	400	—	—	—	400	400
OSA 2016-2	11/03/2016	14.26	4,000	—	—	—	4,000	4,000
OSA 2017	01/07/2017	14.97	500	—	—	—	500	500
OSA 2018	03/06/2018	12.87	52,000	—	—	—	52,000	52,000
OSA 2019-1	03/29/2019	11.08	28,750	—	—	(500)	28,250	28,250
OSA LLY 2019	10/24/2019	6.41	500,000	—	—	—	500,000	500,000
OSA 2020	03/11/2020	6.25	400,709	—	—	(13,253)	387,456	387,456
OSA 2021-04	04/20/2021	13.74	—	571,200	—	(80,000)	491,200	491,200
OSA 2021-06	06/21/2021	12.99	—	120,000	—	—	120,000	120,000
Total			**986,359**	**691,200**	**—**	**(93,753)**	**1,583,806**	**1,583,806**

Type	Grant date	Exercise price (in euros)	Outstanding at January 1, 2020	Issued	Exercised	Forfeited	Outstanding at December 31, 2020	Number of shares issuable
OSA 2016-1	02/02/2016	13.05	400	—	—	—	400	400
OSA 2016-2	11/03/2016	14.26	4,000	—	—	—	4,000	4,000
OSA 2017	01/07/2017	14.97	500	—	—	—	500	500
OSA 2018	03/06/2018	12.87	54,000	—	—	(2,000)	52,000	52,000
OSA 2019-1	03/29/2019	11.08	30,250	—	—	(1,500)	28,750	28,750
OSA LLY 2019	10/24/2019	6.41	500,000	—	—	—	500,000	500,000
OSA 2020	03/11/2020	6.25	—	407,972	—	(7,263)	400,709	400,709
Total			**589,150**	**407,972**	**—**	**(10,763)**	**986,359**	**986,359**

At a meeting on April 20, 2021, the Executive Board, acting pursuant to delegations granted by the Company's shareholders' meeting held on November 30, 2020, granted to certain employees of the Group and members of the Executive Board 571,200 stock options (including 143,200 stock options and 428,000 performance stock options), each giving its holder the right to subscribe one ordinary share, each with a par value of €0.03 and at a price of €13.74 (share premium included). Such stock options are governed by the 2020 stock option plan adopted by the Executive Board on February 9, 2021 and approved by the Company's annual shareholders' meeting held on April 28, 2021 (the "2020 Stock Option Plan").

The ordinary stock options are exercisable as follows:

- up to one-third of the ordinary stock options as from April 20, 2022;
- an additional one-third of the ordinary stock options as from April 20, 2023,
- the balance, i.e., one-third of the ordinary stock options as from April 20, 2024, subject to, for each increment, a continued service condition, and in any case,
- no later than 10 years after the date of grant, it being specified that stock options which have not been exercised by the end of this ten-year period will be forfeited by law.

The performance stock options may be exercised under the following conditions:

- 10% of the stock options may be exercised when the market price of the Company's shares on the regulated market of Euronext in Paris reaches €24.00,
- an additional 10% of the stock options may be exercised when the market price of the Company's shares on the regulated market of Euronext in Paris reaches €30.00,
- an additional 40% of the stock options may be exercised when the market price of the Company's shares on the regulated market of Euronext in Paris reaches €40.00,
- an additional 40% of the stock options may be exercised when the market price of the Company's shares on the regulated market of Euronext in Paris reaches €60.00, and
- at the latest within 10 years of the date of grant, it being specified that stock options which have not been exercised by the end of this 10-year period will be forfeited by law.

It being specified that (i) among such performance stock options that may be exercised, and subject to, for each increment, a continued service condition, their holders may only exercise (x) up to 10% of such performance stock options as from April 20, 2022, (y) an additional 30% of such performance stock options as from April 20, 2023, and (z) the balance, i.e., 60% of such performance stock options as from April 20, 2024, and (ii) such additional vesting condition shall be automatically waived in the event of a change of control.

The number of ordinary and performance stock options that may be exercised under the above exercise schedules would always be rounded down to the nearest whole number.

At a meeting on June 21, 2021, the Executive Board, acting pursuant to the delegation granted by the shareholders' meeting held on November 30, 2020 granted 60,000 ordinary stock options to Bart Van Rhijn following his entry into the Company and his appointment as a Member of the Executive Board. Such stock options are governed by the 2020 Stock Option Plan. Acting pursuant to a delegation granted by the Company's annual shareholders' meeting held on April 28, 2021, it also decided to adopt the 2021 stock option plan and to grant to Bart Van Rhijn 60,000 performance stock options governed by such plan. Each of such 120,000 stock options (whether ordinary and performance) gives it holders the right to subscribe one ordinary share, each with a par value of €0.03 and at a price of €12.99 (share premium included).

The exercise conditions of the 143,200 ordinary stock options and 428,000 performance stock options granted on April 20, 2021 described above shall apply mutatis mutandis to these 60,000 ordinary stock options and 60,000 performance stock options respectively, save for the anniversary date which shall be June 30 rather than April 20. In addition, in accordance with French regulation, the exercise of the above stock options (whether ordinary and performance) are subject to an additional performance condition as soon as they are granted to a member of the Executive Board: determination of the recommended dose for two of the three patient cohorts enrolled in the NBTXR3-1100 clinical study, in order to be able to define the next stage of the development plan in immuno-oncology.

At a meeting on March 11, 2020, the Executive Board adopted the 2019 Stock Option Plan and, acting pursuant to the authorization granted by the thirty-second resolution of the annual shareholders' meeting dated April 11, 2019, granted 407,972 stock options (the "OSA 2020"), 300,000 of which to members of the Executive Board and Alain Dostie and the remaining 107,972 to employees of the Company, under such 2019 Stock Option Plan. Each OSA 2020 entitles its holder to subscribe one ordinary share of the Company with a par value of €0.03, at an exercise price of €6.25 (issue premium included).

The OSA 2020 may be exercised as follows:

- up to one-third of the OSA 2020 as from March 11, 2021;
- an additional one-third of the OSA 2020 as from March 11, 2022; and
- the balance, i.e., one-third of the OSA 2020 as from March 11, 2023, subject to, for each increment, a continued service condition.

In addition, the Executive Board decided that the exercise of the OSA 2020 granted to members of the Executive Board and Alain Dostie would also be subject to the achievement of positive results in the 1100 study in 2020. The satisfaction of this performance condition was acknowledged by the Executive Board, with the approval of the supervisory board, on March 17, 2021.

Free shares (AGA)

Type	Grant date	Exercise price (in euros)	Outstanding at January 1, 2021	Issued	Exercised	Forfeited	Outstanding at December 31, 2021	Number of shares exercisable
AGA 2018-1	03/06/2018	n.a.	24,500	—	(24,500)	—	—	—
AGA 2018-2	07/27/2018	n.a.	—	—	—	—	—	—
AGA 2019-1	03/29/2019	n.a.	372,000	—	(369,250)	(2,750)	—	—
AGA 2020	03/11/2020	n.a.	50,000	—	—	—	50,000	50,000
AGA 2021	04/20/2021	n.a.	—	362,515	—	(2,003)	360,512	360,512
Total			**446,500**	**362,515**	**(393,750)**	**(4,753)**	**410,512**	**410,512**

Type	Grant date	Exercise price (in euros)	Outstanding at January 1, 2020	Issued	Exercised	Forfeited	Outstanding at December 31, 2020	Number of shares exercisable
AGA 2018-1	03/06/2018	n.a.	355,250	—	(316,083)	(14,667)	24,500	24,500
AGA 2018-2	07/27/2018	n.a.	6,000	—	(6,000)	—	—	—
AGA 2019-1	03/29/2019	n.a.	385,000	—	—	(13,000)	372,000	372,000
AGA 2020	03/11/2020	n.a.	—	50,000	—	—	50,000	50,000
Total			**746,250**	**50,000**	**(322,083)**	**(27,667)**	**446,500**	**446,500**

At a meeting on April 20, 2021, the Executive Board, acting pursuant to the authorization granted by Company's shareholders' meeting on November 30, 2020, granted 362,515 free shares, each with a par value of €0.03 to certain employees of the Group and members of the Executive Board. Such free shares will be subject to a one-year holding period starting at the end of the two-year acquisition period, i.e. starting on April 20, 2023. Such free shares are governed by the 2020 free share plan adopted by the Executive Board on February 9, 2021.

Furthermore, the final vesting of the free shares granted to members of the Executive Board is conditioned upon the determination of the recommended dose for two out of the three patient cohorts enrolled in the NBTXR3-1100 clinical study in order to define the next steps of the development plan in immuno-oncology.

At a meeting on March 11, 2020, the Executive Board, acting pursuant to the authorization granted by the thirty-third resolution of the annual shareholders' meeting dated April 11, 2019, granted 50,000 free shares (the "AGA 2020") with a par value of €0.03 to Anne-Juliette Hermant, a member of the Executive Board.

In addition to the acquisition and holding conditions detailed below, the acquisition of the AGA 2020 granted to Hermant is conditioned upon the achievement of positive results in Study 1100 in 2020. The

satisfaction of this performance condition was acknowledged by the Executive Board, with the approval of the Supervisory Board, on March 17, 2021.

Free share vesting conditions

The AGA 2020 and AGA 2021 are subject to, for French tax residents, a two-year acquisition period and a one-year holding period, and, for foreign tax residents, a three-year acquisition period. The free shares granted by the Company are definitively acquired at the end of the acquisition period as set by the Executive Board. At the end of such period, the beneficiary is the owner of the shares. However, during the holding period (as set by the Executive Board), if any, the shares may not be sold, transferred or pledged.

Unless otherwise decided by the supervisory and executive boards of the Company, the AGA 2020 and the AGA 2021 are subject to continued service during the acquisition period (i.e., for the AGA 2020, until March 11, 2022 and for AGE 2021, until April 20, 2023), it being specified that, failing such continued service, the beneficiary definitively and irrevocably loses his or her right to acquire the relevant AGA 2020 or AGA 2021.

Unless otherwise decided by the supervisory and executive boards of the Company, in the event of disability or death of a beneficiary before the end of the acquisition period, the relevant free shares shall be definitely acquired at, respectively, the date of disability or the date of the request of allocation made by his or her beneficiary in the framework of the inheritance, provided that such request is made within six months from the date of death.

At a meeting on September 22, 2020, the Executive Board acknowledged the definitive acquisition of 6,000 free shares granted on July 27, 2018 following a two-year acquisition period, thus acknowledging the related share capital increase of €180.

In accordance with the terms of the free shares, the Executive Board decided to lift, for seven Company's employees and a former Executive Board member, the continued service condition to which the definitive acquisition of their free shares is subject, notwithstanding the termination of their employment agreement or corporate office. The impact of share-based payments on income is discussed in Note 17. As of December 31, 2021, the assumptions related to the estimated vesting of the founders' warrants, the warrants and performance stock-options have been updated (see Note 17).

4.1.6.11. Provisions

Accounting policies

Provisions for contingencies and charges

Provisions for contingencies and charges reflect obligations resulting from various disputes and risks which due dates and amounts are uncertain, that the Company may face as part of its normal business activities.

A provision is recognized when the Company has a present obligation (legal or constructive) as a result of a past event, where it is probable that an outflow of resources embodying economic benefits will be required to settle the obligation and a reliable estimate can be made of the amount of the obligation.

The amount recorded in provisions is a best estimate of the outflow of resources that will be required to settle the obligation, discounted, if required, at year-end.

Provisions for retirement obligations

Company employees receive the retirement benefits provided for by law in France:

- Lump-sum retirement benefit paid by the Company to employees upon retirement (defined benefit plan); and

- Pension benefits paid by social security agencies, which are financed through employer and employee contributions (State defined contribution plan).

The cost of retirement benefits payable under defined benefit plans is estimated using the projected credit unit cost method.

Based on this method, the cost of retirement is recorded in income such that the amount is distributed uniformly over the term of the employee’s career. Past service cost related to non-vested benefits is recognized as an expense (increase in the benefits granted) or as income (reduction in the benefits granted) when the plan amendment or curtailment occurs. Actuarial gains and losses are recognized directly and in full in other comprehensive income (loss) under equity.

Retirement benefit obligations are measured at the present value of future estimated payments by reference to market yields on high quality corporate bonds with a maturity equivalent to that estimated for the plan. The Company uses experts to carry out an annual valuation of the plans. The Company's payments to defined contribution plans are recognized as expenses in each period to which they relate.

As of December 31, 2021, and 2020, the Company updated the parameters for calculating the lump-sum retirement benefit plan to take recent changes into account. The salary increase rate, staff turnover and discount rate were all updated (see Note 11.2 for further details on assumptions used).

Detail of provisions

(in €K)	As of January 1st, 2021	Increases	Decreases	As of December 31, 2021
Lump-sum retirement benefits	414	—	(97)	318
Non-current provisions	**414**	**—**	**(97)**	**318**
Provisions for disputes	40	54	—	94
Provision for charges	—	16	—	16
Current provisions	**40**	**70**	**—**	**110**
Total provisions	**454**	**70**	**(97)**	**428**

(in €K)	As of January 1st, 2020	Increases	Decreases[(1)]	As of December 31, 2020
Lump-sum retirement benefits	331	83	—	414
Non-current provisions	**331**	**83**	**—**	**414**
Provisions for disputes	—	40	—	40
Provision for charges	164	—	(164)	—
Current provisions	**164**	**40**	**(164)**	**40**
Total provisions	**495**	**123**	**(164)**	**454**

(1) *See Statement of consolidated cash flows and Note 16.4 for the nature of these decreases*

4.1.6.11.1. Current Provisions

Provisions for disputes comprise employee disputes in progress. The increase during 2021 and 2020 of €54 thousand and €40 thousand, respectively, were due to a new employee dispute that occurred during the respective years.

In 2020, the reversal of provisions for charges of €164 thousand were related to termination costs accounted for in 2019 following an employee departure.

4.1.6.11.2. Non-current Provisions

Commitments for retirement benefits

(€K)	As of December 31, 2021	As of December 31, 2020
Provision as of beginning of period	**414**	**331**
Cost of services	84	76
Interests / discounting costs	1	3
Expense for the period	**85**	**79**
Gains or losses related to experience	(133)	(61)
Gains or losses related to change in demographic assumptions	(5)	3
Gains or losses related to change in financial assumptions	(43)	62
Actuarial gains or losses recognized in other comprehensive income	**(182)**	**4**
Provision as of end of period	**318**	**414**

The assumptions used to measure lump-sum retirement benefits are as follows:

Measurement date	**December 31, 2021**	**December 31, 2020**
Retirement assumptions	*Management: Age 66* *Non-management: Age 64*	*Management: Age 66* *Non-management: Age 64*
Social security contribution rate	42.01 %	44 %
Discount rate	0.98 %	0.33 %
Mortality tables	Regulatory table INSEE 2015 -2017	Regulatory table INSEE 2014 -2016
Salary increase rate (including inflation)	Executive: 3% Non-Executive: 2.5%	Executive: 3% Non-Executive: 2.5%
Staff turnover	Constant average rate of 5.86%	Constant average rate of 5.86%
Duration	20 years	17 years

The rights granted to Company employees are defined in the Collective Agreement for the Pharmaceutical industry (manufacturing and sales of pharmaceutical products).

The staff turnover rate was determined using a historical average over the 2015-2019 period.

The sensitivity to the discount rate and to the salary growth is as follows:

Discount rate	**0.73%**	**0.98%**	**1.23%**
Defined Benefit Obligation as of December 31, 2021 (in thousands of euros)	333	318	303

The company does not expect to pay a material amount of benefits for the five next years.

4.1.6.12. Financial liabilities

Accounting policies

The Company receives assistance in the form of grants, conditional advances and interest-free loans.

Under IFRS, a repayable advance that does not require the payment of annual interest is considered to be an interest-free loan. The difference between the amount of the advance at historical cost and the advance discounted at the Company's average borrowing rate is considered to be a government grant. These grants are deferred over the estimated duration of the projects they finance.

The long-term (more than one year) portion of conditional advances is recognized in non-current financial liabilities and the short-term portion in current financial liabilities.

Non-repayable conditional loans are treated as government grants when there is reasonable assurance that the Company will comply with the conditions for non-repayment. Otherwise, they are classified in liabilities.

Government grants made available to offset expenses or losses already incurred, or as immediate financial assistance to the Company with no future related costs, are recognized in income in the period in which the grant is allocated.

Financial liabilities are recognized and measured in accordance with IFRS 9 – *Financial Instruments*. Financial liabilities, including trade and other payables are valued at amortized cost.

Financial liabilities at amortized cost

Loans and other financial liabilities are recognized and measured in accordance with IFRS 9 – *Financial Instruments*.

They are recognized at amortized cost, which is defined under IFRS 9 as the initial value of a financial asset or liability, after deduction of reimbursement of principal, increased or decreased by the accumulated amortization, calculated using the effective interest rate method.

Transaction costs directly attributable to the acquisition or issuance of financial liabilities are deducted from the financial liabilities. The costs are then amortized on an actuarial basis over the life of the liability using the effective interest rate, namely the rate that exactly discounts estimated future cash flows to the net carrying amount of the financial liability in order to determine its amortized cost.

Details of financial liabilities

(in thousands of euros)	As of December 31, 2021	As of December 31, 2020
Lease liabilities – Short term	1,126	1,197
Repayable BPI loan advances - Short term	800	500
PGE*	1,086	141
EIB Loan – Short term	5,192	3,033
Total current financial liabilities	**8,204**	**4,872**
Lease liabilities – Long term	5,393	4,991
Repayable BPI loan advances – Long term	2,259	2,975
PGE*	8,982	9,922
EIB loan – Long term	21,182	26,218
Total non-current financial liabilities	**37,816**	**44,107**
Total financial liabilities	**46,020**	**48,979**

(*)"PGE"or in French "Prêts garantis par l'Etat" are state-guaranteed loans

Bpifrance and OSEO conditional advances

The Company receives repayable advances from Banque Publique d'Investissement (formerly known as OSEO Innovation). Some of these advances are interest-free and are fully repayable in the event of technical and/or commercial success. In 2018, the Company was informed that the initial date of reimbursement of the Bpifrance repayable advance was deferred for 18 months.

The other advances are bearing 1.56% interest. The amount to be reimbursed corresponds to the amount received to date, €2.1 million, increased by the interest amount (see Note 12.1).

In June 2020, Curadigm SAS obtained a €500 thousand conditional advance from Bpifrance, €350 thousand of which was received at the signature date while the remaining amount had been scheduled to be received by Curadigm at the end of the work, expected as of March 1, 2022 at the latest, but Curadigm SAS requested an extension of the work period to Bpifrance as a result of COVID-19 which - in case of Bpifrance's approval - could result in collectibility of the remaining €150 thousand. As of December 31, 2021, the work had not been completed and the balance, therefore, has not been paid.

EIB loan

In July 2018, the Company obtained a fixed rate loan from the EIB. The loan could reach a maximum amount of €40 million, divided in three tranches. The first tranche, with a nominal value of €16 million, was received in October 2018 and will be repaid in full in 2023. The accumulated fixed-rate interest related to this tranche will be paid at the same time. The second tranche, with a nominal value of €14 million, was received in March 2019 and will be repaid between 2021 and 2024. The accumulated fixed-rate interest related to this second tranche will be paid twice a year together with the principal due.

The third tranche, which abides by specific conditions (NBTXR3 should obtain the European Commission trademark and reach the main performance criteria for the Phase III pivot, for head and neck cancer treatment), has not been requested by the Company. The deadline for requesting this third tranche, initially scheduled as of July 26, 2020, had been delayed by 12 months to July 31, 2021. As the conditions were not met by July 31, 2021, the Company will not be able to request the final tranche of the EIB loan.

Pursuant to the terms of the loan, the Company is also required, during a six-year royalty calculation period commencing on January 1, 2021, to pay (on each June 30 with respect to the preceding year within the calculation period) additional interest in the form of royalties, calculated according to the number of tranches that have been withdrawn and indexed on the annual sales turnover (see Note 4.2). Initially, the Company calculated estimated future royalties based on its forecast of future annual sales turnover, and this estimated amount was included in the amortized cost of the loan. When the Company revises its forecasts of estimated royalties, the carrying value of the liability is subsequently adjusted based on the revised estimate of future royalties, which is discounted at the original effective interest rate. The related impact on the carrying value of the liability is recorded as financial income or expense, as applicable. Due to the delay caused by COVID-19 in clinical trials and the revision of the related sales development plan, the sales forecasts were updated resulting in a change in estimate of the accrued royalties (see Note 12 of our consolidated financial statements for details about the impact of this sales forecast update). A 10% increase of the estimated future net sales would result in an immaterial change of the EIB loan valuation recorded as of December 31, 2021.

PGE loan

The Company announced in June 2020 that it has received approval for financing from both HSBC and Bpifrance for €5 million each in the form of state-guaranteed loans (“Prêts Garantis par l’Etat”, or “PGE” in France); the €5 million from HSBC (the ‘‘HSBC PGE Loan’’) was received in June 2020. This loan is booked at amortized cost for a minimum of 12 months and allows the Company to delay the reimbursement of this 12 months loan by 1 to 5 years. The Company uses this option and the reimbursement date was delayed by 1 year and will start in September 2022. The effective interest rate amounts to 0.31%.

On July 10, 2020, the Company entered into the second €5 million PGE loan with Bpifrance (the ‘‘Bpifrance PGE Loan’’). The Bpifrance PGE loan has a six-year term and is 90% guaranteed by the French State. The Bpifrance PGE loan did not bear any interest for the first 12-month period but, following such 12-month period and for the subsequent 5 years, bears an interest rate of 2.25% per annum, inclusive of an annual State guarantee fee of 1.61% per annum. The principal and interest of the Bpifrance PGE loan will be reimbursed in 20 quarterly installments as from October 31, 2021 until July 26, 2026.

4.1.6.12.1. Conditional advances, bank loan and loans from government and public authorities

The tables below show the detail of liabilities recognized on the statements of financial position by type of conditional advances, bank loan and loans from government and public authorities.

Conditional advances and loans from government and public authorities

(€K)	Bpifrance advance	Interest-free Bpifrance loan	EIB Loan	Curadigm Bpifrance advance	Total
As of January 1, 2020	**2,165**	**1,210**	**34,746**	**—**	**38,121**
Principal received	—	—	—	350	350
Impact of discounting and accretion	19	14	(1,736)	(65)	(1,769)
Accumulated fixed interest expense accrual	32	—	1,731	—	1,763
Accumulated variable interest expense accrual	—	—	(4,789)	—	(4,789)
Repayment	—	(250)	(700)	—	(950)
As of December 31, 2020	**2,216**	**974**	**29,251**	**285**	**32,727**
Principal received	—	—	—	—	—
Impact of discounting and accretion	17	19	(5,817)	16	(5,765)
Accumulated fixed interest expense accrual	32	—	1,758	—	1,790
Accumulated variable interest expense accrual	—	—	4,214	—	4,214
Repayment	—	(500)	(3,033)	—	(3,533)
As of December 31, 2021	**2,266**	**493**	**26,374**	**300**	**29,433**

The impact of discounting and accretion of €5.8 million, in 2021 relates to impact from the “catch-up method” related to the variable compensation further to the royalty component in the EIB loan that is linked to future revenue expectations. When the Company revises its forecasts of estimated royalties, the carrying value of the liability is subsequently adjusted based on the revised estimate of future royalties, which is discounted at the original effective interest rate. The related impact on the carrying value of the liability is recorded as financial income or expense, as applicable. The rest of the catch up impact is presented on the line variable interest future payments.

The expected royalty payments to be made in the future, initially estimated as €17.2 million as of December 31, 2020 have been updated to €3.4 million as of December 31, 2021.

Bank loan

(€K)	HSBC "PGE" [1]	Bpifrance "PGE" [1]	Total
As of January 1, 2020	**—**	**—**	**—**
Principal received	5,000	5,000	10,000
Impact of discounting and accretion	14	34	47
Accumulated fixed interest expense accrual [2]	7	10	17
As of December 31, 2020	**5,020**	**5,044**	**10,064**
Principal received	17	(14)	3
Impact of discounting and accretion	26	120	146
Accumulated fixed interest expense accrual [3]	(33)	(112)	(145)
As of December 31, 2021	**5,030**	**5,038**	**10,068**

[1]"PGE"or in French "Prêts garantis par l'Etat" are state-guaranteed loans

[2] In 2020 the fixed interest accrual refers to guarantee fee of 0.25% of the principal of the HSBC PGE loan and to a guarantee fee of 0.25% added to a fixed interest rate of 1.36% for the Bpifrance PGE loan, respectively.

[3] In 2021 the fixed interest accrual refers to guarantee fee of 0.25% of the principal of the HSBC PGE loan and to a guarantee fee of 0.25% added to a fixed interest rate of 1.36% for the Bpifrance PGE loan, respectively.

4.1.6.12.2. Lease Liabilities

The table below shows the detail of changes in lease liabilities recognized on the statements of financial position:

(€K)	Lease liabilities
As of January 1, 2020	**6,405**
New lease contracts	**521**
Impact of discounting of the new lease contracts	**(94)**
Fixed interest expense	**333**
Repayment of lease	**(928)**
Early termination of lease contracts	(49)
As of December 31, 2020	**6,188**
Engagement	1,476
Impact of discounting and accretion	(110)
Accumulated fixed interest expense accrual	288
Repayment of lease	(1,195)
Early termination of lease contracts	(128)
As of December 31, 2021	**6,519**

4.1.6.12.2. Due dates of the financial liabilities

The due dates for repayment of the advances, loans at their nominal value and including fixed-rate interest accrued as well as due dates for repayment of lease liabilities are as follows:

	As of December 31, 2021			
(€K)	**Less than 1 year**	**Between 1 and 3 years**	**Between 3 and 5 years**	**More than 5 years**
Bpifrance	300	1,300	808	—
Interest-free Bpifrance loan	500	—	—	—
Curadigm interest-free Bpifrance advance	—	200	150	—
HSBC "PGE" [(1)]	661	2,572	1,904	—
Bpifrance "PGE" [(1)]	425	2,662	2,237	—
EIB fixed rate loan	5,192	28,762	—	—
Lease liabilities	1,126	2,252	2,247	1,714
Total	**8,204**	**37,747**	**7,346**	**1,714**

[(1)]"The Company will reimburse the two "PGE"or ("Prêts garantis par l'Etat" or state-guaranteed loans) over 5 years with a deferral of 1 year (last reimbursement being in 2026), for the reasons mentioned in the paragraph below.

The long-term debt obligations relate to the fixed rate interest and principal payable on repayable advances, the interest-free Bpifrance loan, EIB loan, PGE loans and the lease liabilities. These amounts do not include the discounting impact, but only reflect the committed amounts under those contracts as of December 31, 2021.

The outstanding balance of the EIB loan included in the table above was €33.9 million as of December 31, 2021, including €7.0 million of total fixed rate interest to be paid over the term of the loan, out of which €1.8 million was accrued as of December 31, 2021. The balance in the table above does not include €3.4 million of estimated variable rate interest, based on the consolidated forecasted sales expected to be generated by the Company during the six-year period beginning January 1, 2021 (see Notes 3.2, 4.3 and 12.1).

On April 07, 2021, the Company received the approval of HSBC on its debt rescheduling request. The HSBC PGE loan will be reimbursed at the same pace as the Bpifrance loan, starting on September 2022.

4.1.6.13. Trade payables and other current liabilities

4.1.6.13.1. Trade and other payables

Accounting policies

Accounting policies for Trade and other payables are described in Note 12, "Financial liabilities".

Accrued expenses

Taking into account the time lag between the time at which treatment costs are incurred in studies or clinical trials and the time at which such costs are invoiced, the Company estimates an amount of accrued expenses to record in the financial statements at each reporting date.

The treatment costs for patients were estimated for each study based on contracts signed with clinical research centers conducting the trials, taking into account the length of the treatment and the date of injection of each patient. The total amount estimated for each study has been reduced by the amount included in invoices received at the closing date.

Details of trade and other payables

	For the year ended December 31,	
(€K)	**2021**	**2020**
Accrued expenses - clinical trials	1,486	1,532
Other trade payables	4,996	5,574
Total trade and other payables	**6,482**	**7,106**

Trade payables are not discounted, as none of the amounts were due in more than one year.

Other trade payables include €447 thousand of costs relating to the ICON contract not yet paid, as of December 31, 2021.

4.1.6.13.2. Other current liabilities

	For the year ended December 31,	
(€K)	**2021**	**2020**
Tax liabilities	258	283
Payroll tax and other payroll liabilities	4,820	6,248
Other payables	453	491
Other current liabilities	**5,531**	**7,022**

Payroll tax and other payroll liabilities consist primarily of payroll taxes, namely the employer costs to be paid on free shares, accrued bonuses, vacation days and related social charges.

Payroll tax and other payroll liabilities decreased by €1.4 million from €6.2 million as of December 31, 2020 to €4.8 million as of December 31, 2021 as a result of the decrease in social charges accrual related to free shares and to bonuses.

4.1.6.13.3. Deferred revenues and contract liabilities

	For the year ended December 31,	
(€K)	**2021**	**2020**
Deferred revenues and contract liabilities	16,518	—
Deferred revenues and contract liabilities	**16,518**	—

Change in deferred revenues and contract liabilities as of December 31, 2021 consists of contract liabilities relating to the LianBio contract in the amount of €16.5 million, accounted for in accordance with IFRS 15. See Note 15 Revenues and other income for more details.

4.1.6.14. Financial instruments on the balance sheet and effect on income

Accounting policies

Accounting policies for financial instruments included in the statements of financial position and impact on income are described in Note 7, "Non-current financial assets", Note 8, "Trade receivables and other current assets", Note 9, "Cash and cash equivalents" and Note 12, "Financial liabilities".

Detail of financial instruments included in the statements of financial position and impact on income

	As of December 31, 2021			
(€K)	**Book value on the statement of financial position**	**Financial assets carried at fair value through profit or loss**	**Assets and liabilities carried at amortized cost**	**Fair value[(1)]**
Non-current financial assets				
Non-current financial assets	519	97	421	519
Trade receivables	—	—	—	—
Cash and cash equivalents	83,921	—	83,921	83,921
Total assets	**84,440**	**97**	**84,343**	**84,440**
Financial liabilities				
Non-current financial liabilities	38,733	—	38,733	38,733
Current financial liabilities	7,288	—	7,288	7,288
Trade payables and other payables	**6,482**	**—**	**6,482**	**6,482**
Total liabilities	**52,503**	**—**	**52,503**	**52,503**

[(1)]The fair value of current and non-current liabilities include loans, repayable advances from Bpifrance and the EIB loan, recorded at amortized cost was assessed using unobservable "level 3" inputs, in the IFRS 13 classification for fair value.

	As of December 31, 2020			
(in €K)	**Book value on the statement of financial position**	**Financial assets carried at fair value through profit or loss**	**Assets and liabilities carried at amortized cost**	**Fair value[(1)]**
Non-current financial assets				
Non-current financial assets	505	104	401	505
Trade receivables	62	—	62	62
Cash and cash equivalents	119,151	—	119,151	119,151
Total assets	**119,717**	**104**	**119,613**	**119,717**
Financial liabilities				
Non-current financial liabilities	44,107	—	44,107	44,107
Current financial liabilities	4,872	—	4,872	4,872
Trade payables and other payables	**7,106**	**—**	7,106	7,106
Total liabilities	**56,085**	**—**	**56,085**	**56,085**

[(1)]The fair value of current and non-current liabilities include loans, repayable advances from Bpifrance, the EIB loan and the HSBC and Bpifrance state-guaranteed loans, recorded at amortized cost was assessed using unobservable "level 3" inputs, in the IFRS 13 classification for fair value.

Management of financial risks

The principal financial instruments held by the Company are instruments classified as cash and cash equivalents. These instruments are managed with the objective of enabling the Company to finance its business activities. The Company's policy is to not use financial instruments for speculative purposes. It does not use derivative financial instruments.

The principal risks faced by the Company are liquidity, foreign currency exchange, interest rate and credit risks.

Liquidity risk

Given the amount of cash and cash equivalents held by the Company as of December 31, 2021 (see Note 9), the Company does not believe that it is exposed to short-term liquidity risk.

Foreign Currency Exchange Risk

The functional currency of Nanobiotix S.A. is the euro. Exposure to foreign currency exchange risk is derived almost entirely from intragroup transactions between Nanobiotix S.A. and its U.S. subsidiary, for which the functional currency is the U.S. dollar, as well as trade relations with customers and suppliers outside the euro zone.

At this stage of its development, the Company does not use hedging to protect its business against exchange rate fluctuations. However, a significant increase in its business activity could lead to a greater exposure to foreign currency exchange risk. If this occurs, the Company may implement a suitable hedging policy for these risks.

The following table shows the impact of a 10% increase or decrease in the exchange rate between the euro and the U.S. dollar, calculated on the amounts of capital contributions and loans to the Company's U.S. subsidiary as of December 31, 2021 and December 31, 2020.

For the year ended December 31, 2021

Impact	**Net income**		**Equity**	
(€K)	**Increase**	**Decrease**	**Increase**	**Decrease**
USD / Euro exchange rate	45	(45)	87	(87)
Total	**45**	**(45)**	**87**	**(87)**

For the year ended December 31, 2020

Impact	**Net income**		**Equity**	
(€K)	**Increase**	**Decrease**	**Increase**	**Decrease**
USD / Euro exchange rate	5	(5)	124	(124)
Total	**5**	**(5)**	**124**	**(124)**

Credit risk

Credit risk arises from cash and cash equivalents, derivative instruments and deposits with banks and other financial institutions as well as from exposure to customer credit, in particular unpaid receivables and transaction commitments.

The credit risk related to cash and cash equivalents and to current financial instruments is not material given the quality of the relevant financial institutions.
Customer credit risk is limited, due in part to low trade receivables as of December 31, 2021 and in part to the public authority's high credit rating for other receivables.

Interest rate risk

The Company's exposure to interest rate risk is primarily related to cash equivalents and investment securities, which consist of money market mutual funds (SICAVs). Changes in interest rates have a direct impact on the interest earned from these investments and the cash flows generated.

Fair value

The fair value of financial instruments traded on an active market is based on the market price on the reporting date. The market prices used for the financial assets held by the Company are the bid prices in the market on the measurement date.

The carrying value of receivables and current liabilities is assumed to approximate their fair value.

4.1.6.15. Revenues and other income

Accounting policies

Revenue

Under IFRS 15, revenue is recognized when the Company satisfies a performance obligation by transferring a distinct good or service (or a distinct bundle of goods and/or services) to a customer, i.e. when the customer obtains control of these goods or services. An asset is transferred when the customer obtains control of the asset (or service).

Given the wide spectrum of therapeutic research and development opportunities, aside from the fields that the Company intends to research and develop with its own scientific and financial resources, the Company has entered and expects to enter into license and collaboration agreements with third parties in certain specific fields that have generated or will generate revenue.

Therefore, each agreement has been and will be analyzed, on a case-by-case basis to determine whether the arrangement contains performance obligations to the other party and, if so, to identify the nature of these performance obligations in order to determine the appropriate accounting under IFRS 15 principles of the amounts that the Company has received or is entitled to receive from the other party e.g.:

- Development services performed by the Company to create or enhance an intellectual property controlled by the client, for which revenue is recognized over time, when services are rendered;
- A transfer of control of an existing intellectual property of the Company for which revenue is recognized at the time such control is transferred;
- A license:
    - If the license is assessed to be a right to access the Company's intellectual property as it exists throughout the license period, revenue is recognized over the license period; or
    - If the license is a right to use the Company's intellectual property as it exists (in term of forms and functionality), revenue is recognized when the other party is able to use and benefit from the license; or
- Product supply for which the revenue is recognized once the control over the delivered products is transferred.

Contingent revenue arising from successful milestones or sales-based royalties are not recognized before the related milestone has been reached or sale has occurred.

Application to the license and collaboration agreement with PharmaEngine

Under the License and Collaboration Agreement, the Company's and PharmaEngine's rights are clearly identified and, financial terms are defined in the contract. The contract has commercial substance (the Company's cash flows have been affected by the terms of the contract) and the Company has collected and is entitled to collect in the future consideration in exchange for the goods and services transferred to PharmaEngine.

The Company identified three performance obligations in the License and Collaboration Agreement described under Note 4 above:

- the license of the right to use the Company's patent and know-how;
- the support provided by the Company to PharmaEngine until the first regulatory approval is granted in PharmaEngine's territory that the Company views as a series of distinct periods of access to information and experience that is satisfied over time; and
- the supply of NBTXR3 to PharmaEngine.

An upfront payment of $1.0 million was fully recognized as revenue when the license was transferred to PharmaEngine in 2012.

Development milestones constitute variable payments that are recognized over-time. As milestone payment timing was defined to reflect the efforts of both parties over time and were amended to reflect all changes in the contractual development plan, the Company concluded that the terms of variable payments reflect its efforts to satisfy the performance obligation related to each development phase and that no portion if any of such consideration that would relate to the license would impact the timing of recognition because of the highly probable collectability requirement. On this basis, the first milestone payment of $1 million (upon signature of the first amendment that allowed PharmaEngine to benefit from the results of the Company's clinical studies for soft-tissue sarcoma indication) and the second milestone payment of $1 million (first patient's injection with NBTXR3 in soft tissue sarcoma study in Asia) were received and recognized in 2014 and 2016, respectively. The next milestone will be received following the first filing for regulatory approval for marketing NBTXR3 in PharmaEngine 's territory, which had not occurred as of December 31, 2021.

Royalties are considered at market conditions and will be fully recognized once the subsequent sales occur.

In March 2021, the Company and PharmaEngine mutually agreed to terminate the license and collaboration agreement. See note 4 Significant Transactions.

Application of IFRS 15 to the license and collaboration agreement with LianBio

Under the clause 8.5 of the license and collaboration agreement between the Company and LianBio, LianBio has the final decision on development and marketing activities in its territory. Consequently, the agreement does not qualify as a partnership under IFRS 11, which requires joint control and unanimous approval of strategic decisions by both parties. The agreement falls within the scope of IFRS 15 as the license, development services and product revenues are revenues of the Company.

We identified the separate performance obligations of the contract under IFRS 15. The partnership includes the following obligations to LianBio:

- an exclusive license, under the Company's intellectual property, to develop and market the licensed products;
- the right to actively participate in global Phase III registration trials to obtain marketing approval in China;
- if a pivotal trial is initiated by the Company in another country, the right to obtain a license and the right to reference efficacy data from the study and regulatory filings and approvals;
- if a Phase I and Phase II trial is initiated by the Company, the right to obtain access to and a license to all clinical data and regulatory filings relating to such clinical trial; and
- the requirement to purchase products under license to the Company.

The Company's know-how as disclosed and made available to LianBio could not technically be used by LianBio, or by a third party, to manufacture the licensed products. The provision of additional know-how data and information by the Company is necessary to enable a third party to manufacture the licensed products. This information will only be provided if the Company, at any time following a change of control of the Company, fails to provide at least 80% of LianBio's forecasted need for licensed products in a given calendar year. The license cannot be separated because LianBio cannot benefit from the license alone (i.e. without the ongoing manufacturing service provided by the Company). On this basis, we concluded that the license and the manufacturing service are not distinct.

As the license is not separate, any services performed in connection with the clinical trials cannot be analyzed as a separate service provided by the Company to LianBio, because LianBio cannot benefit from the clinical trials alone.

LianBio has the exclusive right to purchase and sell the licensed products in its territory but has no enforceable obligation to make the purchases.

Accordingly, the agreement contains only one performance obligation: the manufacturing and the supply by Nanobiotix to LianBio of the licensed products.

In consideration for this exclusive right to purchase and sell the licensed products granted to LianBio, the Company received on June 15, 2021, a non-refundable upfront payment of $20 million and may receive up to $220 million in potential additional payments upon the achievement of certain development and commercialization milestones. The development milestones events refer to the effort provided by LianBio to register the licensed product as a drug and to enroll patients in the global phase III registrational study in head and neck within 18 months and the receipt of marketing authorization for the Licensed Product in the territory for any indication in the field. The Company is entitled to receive sales milestones payments, once the aggregate net sales of the Licensed product in the territory achieve graduated amounts.

No revenue is to be recognized when such a right is granted. The upfront payment and milestone payment are considered as advance payments for future deliverables. Therefore, no revenue will be recognized until the first sales of the licensed products occur. In accordance with paragraph 106 of IFRS 15, upon receipt of an upfront payment from LianBio, the Company shall recognize a contractual liability to the extent of the upfront payment. The Company shall derecognize this contractual liability (and recognize revenue) when it transfers the licensed products.

The upfront payment and milestone payments must be allocated to the sales of licensed products. Significant judgment will be required to determine how to allocate the upfront payments to the sales of licensed products.

Nanobiotix will also be eligible to receive tiered, low double-digit royalties based on net sales of NBTXR3 in the licensed territories. The method of recognizing these revenues is also yet to be determined.

Grants

Due to its innovative approach to nanomedicine, the Company has received various grants and other assistance from the government of France and French public authorities since its creation. The funds are intended to finance its operations or specific recruitments. Grants are recognized in income as the corresponding expenses are incurred and independently of cash flows received.

Research tax credit

The French tax authorities grant a research tax credit (Crédit d'Impôt Recherche, or "CIR"), to companies in order to encourage them to conduct technical and scientific research. Companies demonstrating that they have incurred research expenditures that meet the required criteria (research expenses in France or, since January 1, 2005, other countries in the European Community or the European Economic Area that have signed a tax treaty with France containing an administrative assistance clause) receive a tax credit that can theoretically be compensated with the income tax due on the profits of the financial year during which the expenses have been incurred and the following three years. Any unused portion of the credit is then refunded by the French Treasury. If the Company can be qualified as small and medium-sized enterprises, in France the "PME", it can request immediate refund of the remaining tax credit, without application of the three-year period).

The Company has received research tax credits since its creation. These amounts are recognized as "Other income" in the fiscal year in which the corresponding charges or expenses were incurred. The portion related to capitalized expenses is deducted from the amount of capitalized expenses on the statements of financial position and from the amortization charges for these expenses on the statements of operations.

Detail of revenues and other income

The following table summarizes the Company's revenues and other income for the years ended December 31, 2021 and December 31, 2020.

	For the year ended December 31,	
(€K)	**2021**	**2020**
Services	5	50
Other sales	5	—
Total revenues	**10**	**50**
Research tax credit	2,490	1,927
Subsidies	126	526
Other	21	10
Total other income	**2,637**	**2,462**
Total revenues and other income	**2,647**	**2,512**

The Company's revenue of €10 thousand in 2021 and €50 thousand in 2020 were derived mainly from the charging-back of shared external clinical research organization costs in connection with the

development support provided by the Company to PharmaEngine as part of the 2014 amendment to the Company's License and Collaboration Agreement.

100% of the revenues recognized in 2021 and in 2020 were derived from the arrangement with PharmaEngine (see Note 4.1).

In 2020, the Company's other income, other than the research tax credit, mainly derives from French State subsidies of €312 thousand provided as part of the ''partial unemployment measure,'' a National plan allowing companies facing economic challenges during the COVID-19 crisis to receive from the French State approximately 84% of specific employees' net salary, as well as the €350 thousand received by Curadigm in connection with the Bpifrance Deep Tech Funding, €187 thousand of which was recognized as revenue for the years ended December 31, 2020.

4.1.6.16. Operating expenses

Accounting policies

Leases included in the practical expedients under the IFRS 16 standard and used by the Company (low value asset and short-term leases) are recognized in operating expenses. Payments made for these leases are expensed, net of any incentives, on a straight-line basis over the contract term (see note 22. Commitments for further details).

Accounting policies for research and development expenses are described in Note 5.

4.1.6.16.1. Research and development (R&D) expenses

	For the year ended December 31,	
(€K)	**2021**	**2020**
Purchases, sub-contracting and other expenses	(19,562)	(12,734)
Payroll costs (including share-based payments)	(9,605)	(10,306)
Depreciation, amortization and provision expenses[(1)]	(1,211)	(1,290)
Total research and development expenses	**(30,378)**	**(24,330)**

[(1)] *see note 16.4 Depreciation, amortization and provision expenses*

Purchases, sub-contracting and other expenses increased by €6.9 million, or 54% for the year ended December 31, 2021 as compared with the same period in 2020. This reflects the increase of the clinical development activities, especially driven by the launch of our global Phase III clinical trial for elderly head and neck cancer patients ineligible for platinum-based (cisplatin) chemotherapy (NANORAY-312).

Payroll costs decreased by €774 thousand, or 8% for the year ended December 31, 2021 as compared with the same period in 2020. This variation is mainly due to a change in the mix and in the location of our research and development staff.

As of December 31, 2021, the Company's workforce amounted to 75 research and development staff, including 9 additional positions created during the year ended December 31, 2021.

As of December 31, 2020, the Company's workforce amounted to 66 research and development staff, including a decrease of fifteen positions created during the year ended December 31, 2020.

The impact of share-based payments (excluding employer's contribution) on research and development expenses amounted to €677 thousand in 2021 as compared with €629 thousand in 2020.

4.1.6.16.2. Selling, General and Administrative (SG&A) expenses

	For the year ended December 31,	
(€K)	**2021**	**2020**
Rent, fees and other expenses	(9,638)	(6,482)
Payroll costs (including share-based payments)	(9,379)	(7,789)
Depreciation, amortization and provision expenses [(1)]	(417)	(340)
Total SG&A expenses	**(19,434)**	**(14,611)**

[(1)] *see note 16.4 Depreciation, amortization and provision expenses*

In 2021, purchases, fees and other expenses increased by €3,156 thousand, or 49% for the year ended December 31, 2021 as compared with the same period in 2020. This variation reflects two main impacts, first the legal expenses relating to partnership agreements as well as consulting fees, legal and compliance expenses as a result of being a U.S. public company. The second main impact relates to recruitment expenses.

In 2020, wages, salaries and payroll costs, together, amounted to €15.1 million as compared with €16.8 million in 2019. This is mainly due to a decrease in staff over the period because of the COVID 19 pandemic and to the reversal of a provision related to employer's contribution following the exercise by beneficiaries of their right to free shares.

Payroll costs increased by €1.6 million or 21% in 2021, mainly due to a change in the mix and location changes of our staff in SG&A functions (more US based employees) and a one-time severance payment related to the departure of Philippe Mauberna, the prior CFO.

As of December 31, 2021, the Company's workforce amounted to 25 staff in SG&A functions in comparison with a Company's workforce of 24 staff in SG&A functions during the year ended December 31, 2020.

The impact of share-based payments (excluding employer's contribution) on SG&A expenses amounted to €2.5 million, as compared in 2021 with €2.3 million in 2020.

4.1.6.16.3. Payroll costs

	For the year ended December 31,	
(€K)	**2021**	**2020**
Wages and salaries	(11,391)	(11,141)
Payroll taxes	(4,308)	(3,953)
Share-based payments	(3,201)	(2,924)
Retirement benefit obligations	(84)	(76)
Total payroll costs	**(18,984)**	**(18,094)**
Average headcount	96	97
End-of-period headcount	100	90

As of December 31, 2021, the Company's workforce totaled 100 employees, compared with 90 December 31, 2020.

In 2021, wages, salaries and payroll costs, together, amounted to €15.7 million as compared with €15.1 million in 2020. This is mainly due to the 10 additional positions created during the year ended December 31, 2021.

In 2020, wages, salaries and payroll costs, together, amounted to €15.1 million as compared with €16.8 million in 2019. This is mainly due to a decrease in staff over the period because of the COVID 19 pandemic and to the reversal of a provision related to employer's contribution following the exercise by beneficiaries of their right to free shares.

In accordance with IFRS 2 – Share-based Payment, the share-based payment amount recognized in the statements of operations reflects the expense associated with rights vesting during the fiscal year under the Company's share-based compensation plans. The share-based payment expenses amounted to €3.2 million for the year ended December 31, 2021, as compared with €2.9 million as of December 31, 2020 (see Note 17).

4.1.6.16.4. Depreciation, amortization and provision expenses

Depreciation, amortization and provision expenses by function are detailed as follows:

	2021		
(€k)	**R&D**	**SG&A**	**Total**
Amortization expense of intangible assets	(34)	(10)	(45)
Amortization expense of tangible assets	(1,109)	(406)	(1,515)
Provision for charges	(68)	—	(68)
Total depreciation, amortization and provision expenses	**(1,211)**	**(416)**	**(1,628)**

	2020		
(€k)	**R&D**	**SG&A**	**Total**
Amortization expense of intangible assets	(152)	(23)	(176)
Amortization expense of tangible assets	(1,250)	(329)	(1,579)
Utilization of provision for disputes	145	—	145
Provision for charges	—	(40)	(40)
Reversal of provision for disputes	—	19	19
Total depreciation, amortization and provision expenses	**(1,257)**	**(373)**	**(1,630)**

4.1.6.16.5. Other operating income and expenses

	For the year ended December 31,	
(€K)	**2021**	**2020**
Contract termination indemnity (PharmaEngine)	(5,414)	—
Total Other operating income and expenses	**(5,414)**	**—**

The Company has made payments for a cumulative amount of $6.5 million (€5.4 million converted at the exchange rate on the payment date) to PharmaEngine in accordance with the termination and release agreement signed between the parties. See Note 4.2 PharmaEngine.

4.1.6.17. Share-based payments

Accounting policies

The Company has adopted a number of compensation plans since its inception. As of December 31, 2021, the Company had nine (9) outstanding founders' warrant plans, twelve (12) outstanding warrant plans, nine (9) stock option plans and two (2) outstanding free shares plans.

These share-based compensation plans are settled in equity instruments.

The Company has applied IFRS 2 – *Share-based Payment* to all equity instruments granted to employees since 2006.

As required by IFRS 2 – *Share-based Payment*, the cost of compensation paid in the form of equity instruments is recognized as an expense, with a corresponding increase in shareholders' equity for the vesting period during which the rights with respect to the equity instruments are earned.

The fair value of the equity instruments granted to employees is measured using the Black-Scholes or Monte Carlo model, as described below.

Detail of share-based payments

The Company has granted stock options (option sur actions, ''OSA''), warrants (bons de souscription d'actions, ''BSA''), founders' warrants (bons de souscription de parts de créateur d'entreprise, ''BSPCE'') and free shares (attributions gratuites d'actions, ''AGA'') to corporate officers, employees and members of the Supervisory Board and consultants. In certain cases, exercise of the options and warrants is subject to performance conditions. The Company has no legal or contractual obligation to pay the options in cash.

The number of options and warrants outstanding on December 31, 2021 and their main characteristics, are detailed below.

Founders' warrants

	Pre-2021 founders' warrant plans				
	BSPCE 2012-2	**BSPCE 08-2013**	**BSPCE 09-2014**	**BSPCE 2015-1**	**BSPCE 2015-03**
Number of founder's warrants granted	100,000	50,000	97,200	71,650	53,050
Date of shareholders' resolution approving the plan	04/05/2012	28/06/2013	18/06/2014	18/06/2014	18/06/2014
Grant date	18/12/2012	28/08/2013	16/09/2014	10/02/2015	10/06/2015
Contractual expiration date	18/12/2022	28/08/2023	16/09/2024	10/02/2025	10/06/2025
Grant price	—	—	—	—	—
Exercise price	€6.63	€5.92	€18.68	€18.57	€20.28
Number of founders' warrants as of December 31, 2021	**100,000**	**50,000**	**86,150**	**68,450**	**30,350**
Number of founders' warrants exercised	—	—	—	—	—
Of which founders' warrants exercised during the period	—	—	—	—	—
Number of founders' warrants lapsed or canceled	—	—	11,050	3,200	22,700
Of which founders' warrants lapsed or canceled during the period	—	—	—	—	*350*

	Pre-2021 founders' warrant plans			
	BSPCE 2016 Ordinary	**BSPCE 2016 Performance**	**BSPCE 2017 Ordinary**	**BSPCE 2017**
Number of founder's warrants granted	126,400	129,250	117,650	80,000
Date of shareholders' resolution approving the plan	25/06/2015	25/06/2015	23/06/2016	23/06/2016
Grant date	02/02/2016	02/02/2016	07/01/2017	07/01/2017
Contractual expiration date	02/02/2026	02/02/2026	08/01/2027	07/01/2027
Grant price	—	—	—	—
Exercise price	€14.46	€14.46	€15.93	€15.93
Number of founders' warrants as of December 31, 2021	**100,567**	**100,274**	**99,500**	**80,000**
Number of founders' warrants exercised	333	—	—	—
Of which founders' warrants exercised during the period	—	—	—	—
Number of founders' warrants lapsed or canceled	25,500	28,976	18,150	—
Of which founders' warrants lapsed or canceled during the period	*350*	*1,426*	*1,350*	—

Warrants:

	Pre-2021 BSA plans and outstanding						
	BSA 04-2012	**BSA 2013**	**BSA 2014**	**BSA 2015-1**	**BSA 2015-2 (a)**	**BSA 2015-2 (b)**	**BSA 2016 Ordinary**
Number of warrants granted	52,500	10,000	14,000	26,000	64,000	6,000	18,103
Date of shareholders' resolution approving the plan	04/05/2012	04/05/2012	18/06/2014	18/06/2014	18/06/2014	25/06/2015	25/06/2015
Grant date	04/05/2012	10/04/2013	16/09/2014	10/02/2015	25/06/2015	25/06/2015	02/02/2016
Contractual expiration date	04/05/2022	10/04/2023	16/09/2024	10/02/2025	25/06/2025	25/06/2020	02/02/2021
Grant price	€0.60	€2.50	€4.87	€4.87	€5.00	€2.80	€1.67
Exercise price	€6.00	€6.37	€17.67	€17.67	€19.54	€19.54	€13.74
Number of warrants as of December 31, 2021	**30,000**	**6,000**	**10,000**	**21,000**	**64,000**	**—**	**—**
Number of founders' warrants exercised	22,500	—	—	—	—	—	—
Of which warrants exercised during the period	—	—	—	—	—	—	—
Number of founders' warrants lapsed or canceled	—	4,000	4,000	5,000	—	6,000	18,103
Of which warrants lapsed or canceled during the period	—	—	—	—	—	—	*18,103*

	Pre-2021 BSA plans and outstanding						
	BSA 2016 performance	**BSA 2016-2**	**BSA 2017**	**BSA 2018-1**	**BSA 2018-2**	**BSA 2019-1**	**BSA 2020**
Type of warrants	18,105	8,000	18,000	28,000	5,820	18,000	18,000
Number of warrants granted	25/06/2015	23/06/2016	23/06/2016	14/06/2017	23/05/2018	23/05/2018	11/04/2019
Contractual expiration date	02/02/2016	03/11/2016	07/01/2017	06/03/2018	27/07/2018	29/03/2019	17/03/2020
Grant date	02/02/2021	03/11/2021	07/01/2022	06/03/2023	27/07/2028	29/03/2029	17/03/2030
Grant price	€1.67	€2.03	€2.26	€1.62	€2.36	€1.15	€0.29
Exercise price	€13.74	€15.01	€15.76	€13.55	€16.10	€11.66	€6.59
Number of warrants as of December 31, 2021	**—**	**—**	**18,000**	**28,000**	**5,820**	**18,000**	**18,000**
Number of warrants exercised	—	—	—	—	—	—	—
Of which number of warrants exercised during the period	—	—	—	—	—	—	—
Number of warrants lapsed or canceled	18,105	8,000	—	—	—	—	—
Of which number of warrants lapsed or canceled during the period	*18,105*	*8,000*	—	—	—	—	—

	2021 warrants	
	BSA 2021 (a)	**BSA 2021 (b)**
Type of warrants	48,103	30,000
Number of warrants granted	30/11/2020	30/11/2020
Contractual expiration date	20/04/2021	20/04/2021
Grant date	20/04/2031	20/04/2031
Grant price	€2.95	€0.68
Exercise price	€13.47	€13.64
Number of warrants as of December 31, 2021	**14,431**	**30,000**
Number of warrants exercised	—	—
Of which number of warrants exercised during the period	—	—
Number of warrants lapsed or canceled	33,672	—
Of which number of warrants lapsed or canceled during the period	*33,672*	—

Stock options:

	Pre-2021 OSA plans and outstanding						
	OSA 2016-1 Performance	**OSA 2016-2**	**OSA 2017 Ordinary**	**OSA 2018**	**OSA 2019-1**	**OSA LLY 2019**	**OSA 2020**
Number of options granted	6,400	4,000	3,500	62,000	37,500	500,000	407,972
Date of shareholders' resolution approving the plan	06/25/2015	06/23/2016	06/23/2016	06/14/2017	05/23/2018	04/11/2019	04/11/2019
Grant date	02/02/2016	11/03/2016	01/07/2017	03/06/2018	03/29/2019	10/24/2019	03/11/2020
Contractual expiration date	02/02/2026	11/03/2026	01/07/2027	03/06/2028	03/29/2029	10/24/2029	03/11/2030
Grant price	—	—	—	—	—	—	—
Exercise price	€13.05	€14.26	€14.97	€12.87	€11.08	€6.41	€6.25
Number of options as of December 31, 2021	**400**	**4,000**	**500**	**52,000**	**28,250**	**500,000**	**387,456**
Number of options exercised	—	—	—	—	—	—	—
Of which options exercised during the period	—	—	—	—	—	—	—
Number of options lapsed or canceled	6,000	—	3,000	10,000	9,250	—	13,253
Of which options lapsed or canceled during the period	—	—	—	—	*500*	—	*13,253*

	2021 stock options plans	
	OSA 2021-04	**OSA 2021-06**
Number of options granted	571,200	120,000
Date of shareholders' resolution approving the plan	11/30/2020	04/28/2021
Grant date	04/20/2021	06/21/2021
Contractual expiration date	04/20/2031	06/21/2031
Grant price	—	—
Exercise price	€13.74	€12.99
Number of options as of December 31, 2021	**491,200**	**120,000**
Number of options exercised	—	—
Of which options exercised during the period	—	—
Number of options lapsed or canceled	80,000	—
Of which options lapsed or canceled during the period	*80,000*	—

Free shares:

	Pre-2021 free share plan not yet vested				2021 free shares plan
	AGA 2018-1	**AGA 2018-2**	**AGA 2019-1**	**AGA 2020**	**AGA 2021**
Number of free shares granted	396,250	6,000	438,250	50,000	362,515
Date of shareholders' resolution approving the plan	06/14/2017	05/23/2018	05/23/2018	04/11/2019	11/30/2020
Grant date	03/06/2018	07/27/2018	03/29/2019	03/11/2020	04/20/2021
Grant price	—	—	—	—	—
Exercise price	—	—	—	—	—
Number of free shares as of December 31, 2021	**—**	**—**	**—**	**50,000**	**360,512**
Number of free shares exercised	340,583	6,000	369,250	—	—
Including free shares exercised during the period	*24,500*	—	*369,250*	—	—
Number of free shares lapsed or canceled	55,667	—	69,000	—	2,003
Including free shares lapsed or canceled during the period	—	—	*2,750*	—	*2,003*

	BSPCE	BSA	OSA	AGA	Total
Total number of shares underlying grants outstanding as of December 31, 2021	715,291	263,251	1,583,806	410,512	**2,972,860**

	BSPCE	BSA	OSA	AGA	Total
Total number of shares underlying grants outstanding as of December 31, 2020	718,767	263,028	986,359	446,500	**2,414,654**

The measurement methods used to estimate the fair value of stock options, warrants and free shares are described below:

- The share price on the grant date is equal to the exercise price, except for the BSA 2014 which exercise price was set at €40, taking into account both the average share price on the 20 days preceding the grant date and the expected development perspectives of the Company;
- The risk-free rate was determined based on the average life of the instruments; and
- Volatility was determined based on a sample of listed companies in the biotechnology sector on the grant date and for a period equal to the life of the warrant or option.

The performance conditions for all of the plans were assessed as follows:

- Performance conditions unrelated to the market were analyzed to determine the likely exercise date of the warrants and options and expense was recorded accordingly based on the probability these conditions would be met; and
- Market-related performance conditions were directly included in the calculation of the fair value of the instruments.

Except for the 2012-1 founders' warrants, the fair value of the warrants and options was measured using the Black-Scholes model.

The fair value of 2012-1 founders' warrants was determined using the Monte Carlo valuation model to take into account the exercise conditions, which depend on the realized gain compared to the expected stock market listing price.

The probability of meeting the performance conditions for the 2016 BSPCE, BSA and OSA performance plans was reassessed as of December 31, 2021. As a consequence, no new instrument became issuable.

Expenses of BSPCE outstanding plans as of December 31, 2021:

Plan	Share price *(in euros)*	Exercise price *(in euros)*	Volatility	Maturity *(in years)*	Risk-free rate	Yield	Value of initial plan *(in thousands of euros)*	Expense 2021 *(in thousands of euros)*	Expense 2020 *(in thousands of euros)*
BSPCE 2012-1	5.26	5.26	41%	3.49	0.20%	0.00%	307	—	—
BSPCE 2012-2	6.65	6.63	44,3% - 47,6%	5 - 7.30	0.84% - 1.22%	0.00%	288	—	—
BSPCE 04-2013	6.30	6.30	56%	5	0.90%	0.00%	167	—	—
BSPCE 08-2013	6.30	5.92	256%	7	0.90%	0.00%	152	—	—
BSPCE 09-2014	18.68	18.68	58%	5.5/6/6.5	0.64%	0.00%	932	—	—
BSPCE 2015-1	18.57	18.57	58% - 62% - 61%	5.5/6/6.5	0.39%	0.00%	50	—	—
BSPCE 2015-2	18.57	18.57	58% - 62% - 61%	5.5/6/6.5	0.39%	0.00%	650	—	—
BSPCE 2015-3	20.28	20.28	61% - 62% - 61%	5.5/6/6.5	0.56%	0.00%	483	—	—
BSPCE 2016 Ordinary	14.46	14.46	59% - 62% - 60%	5.5/6/6.5	0.32%	0.00%	1,080	—	—
BSPCE 2016 Performance	14.46	14.46	59%	5	0.19%	0.00%	1,212	32	99
BSPCE 2017 Ordinary	15.93	15.93	58% - 61% - 59%	5.5/6/6.5	0.23%	0.00%	1,000	—	8
BSPCE 2017 Performance	15.93	15.93	59%	5	0.11%	0.00%	622	—	—
BSPCE 2017	15.93	15.93	59%	5	0.11%	0.00%	627	—	—
BSPCE 2017 Project	15.93	15.93	59%	5	0.11%	0.00%	94	—	—
Total BSPCE	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**32**	**107**

Expenses of BSA outstanding plans as of December 31, 2021:

Plan	Share price *(in euros)*	Exercise price *(in euros)*	Volatility	Maturity *(in years)*	Risk-free rate	Yield	Value of initial plan *(in thousands of euros)*	Expense 2021 *(in thousands of euros)*	Expense 2020 *(in thousands of euros)*
BSA 2012	6.00	6.00	49%	10	0.96%	0.00%	183	—	—
BSA 2013	6.30	6.37	156%	6	0.90%	0.00%	1	—	—
BSA 2014	18.68	17.67	57%	5	0.41%	0.00%	—	—	—
BSA 2015-1	17.67	17.67	58%	5	0.26% - 0.27%	0.00%	63	—	—
BSA 2015-2	17.67	19.54	58%-58%-57%-58%	5/5.1/5.3/5.4	0.39%	0.00%	16	—	—
BSA 2015-3	19.54	19.54	58% - 60%	4.6 – 9.6	0.25% - 0.91%	0.00%	284	—	—
BSA 2016o-1	13.74	13.74	57%	2.4	—%	0.00%	37	—	—
BSA 2016p-1	13.74	13.74	57%	2.4	—%	0.00%	143	—	—
BSA 2016-2	15.01	15.01	57%	2.4	—%	0.00%	—	—	—
BSA 2017o-1	15.76	15.76	33%	2.4	0.00%	0.00%	—	—	—
BSA 2018-1	13.55	13.55	38%	4.8	0.7% - 0.10%	0.00%	2	—	—
BSA 2018-2	16.10	16.10	38%	4.8	0.7% - 0.10%	0.00%	1	—	—
BSA 2019-1	11.66	11.66	37%	9.8/9.9	0.16% - 0.50%	0.00%	24	—	—
BSA 2020	—	6.59	38%	10	-0.13%/-0.07%	0.00%	19	—	19
BSA 2021 (a)	13.47	13.47	39.1%	10	0.27%	—	44	44	—
BSA 2021 (b)	n.a.	13.64	n.a.	10	0.27%	0.00%	—	—	—
Total BSA	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**44**	**19**

Expenses of OSA outstanding plans as of December 31, 2021:

Plan	Share price *(in euros)*	Exercise price *(in euros)*	Volatility	Maturity *(in years)*	Risk-free rate	Yield	Value of initial plan *(in thousands of euros)*	Expense 2021 *(in thousands of euros)*	Expense 2020 *(in thousands of euros)*
OSA 2016 Ordinary	13.05	13.05	59% - 62% - 60%	5.5 / 6 /6.5	0.32%	0.00%	117	—	—
OSA 2016 Performance	13.05	13.05	59%	5	0.19%	0.00%	69	—	—
OSA 2016-2	14.26	14.26	58% - 62% - 59%	5.5 / 6 /6.5	0.04%	0.00%	27	—	—
OSA 2017 Ordinary	15.93	14.97	58% - 61% - 59%	5.5 / 6 /6.5	0.23%	0.00%	31	—	—
OSA 2017 Performance	15.93	14.97	59%	5	0.11%	0.00%	35	—	—
OSA 2018	12.87	12.87	35%	5.5 / 6 /6.5	—%	0.00%	252	—	7
OSA 2019-1	11.08	11.08	38.10% / 37.40%	6 /6.5	0.103% / 0.149%	0.00%	140	17	49
OSA 2019-2	6.41	6.41	37%	10	0.40%	0.00%	252	—	—
OSA 2020	6.25	6.25	38%	10	0.31%	0.00%	939	329	453
OSA 2021-04 O	13.60	13.74	38.9% - 37.8% - 38.3 %	5.5 / 6 /6.5	0.38%/0.33%/0.28%	0.00%	684	188	—
OSA 2021-04 P	13.60	13.74	39%	10	0.03%	0.00%	1,816	131	—
OSA 2021-06 O	12.20	12.99	39.2% - 37.9% - 38.1 %	5.5 / 6 /6.5	0.35 % / 0.3 % / 0.26 %	0.00%	246	79	—
OSA 2021-06 P	12.20	12.99	39%	10	0.13%	0.00%	212	16	—
Total OSA	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**760**	**509**

Expenses of AGA outstanding plans as of December 31, 2021:

Plan	Share price *(in euros)*	Exercise price *(in euros)*	Volatility	Maturity *(in years)*	Risk-free rate	Yield	Value of initial plan *(in thousands of euros)*	Expense 2021 *(in thousands of euros)*	Expense 2020 *(in thousands of euros)*
AGA 2018-1	12.87	—	n.a.	n.a.	—%	0%	4,951	16	268
AGA 2018-2	12.87	—	n.a.	n.a.	—%	0%	75	—	21
AGA 2019-1	10.90	—	n.a.	n.a.	0.19% / 0.141%	0%	4,776	422	1,884
AGA 2020	5.90	—	n.a.	n.a.	-0.74%/ -0.69%	0%	287	144	116
AGA 2021	13.60	—	n.a.	n.a.	0.63% / 0.59%	0%	4,869	1,784	—
Total AGA	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**2,366**	**2,289**

(€K)	BSPCE	BSA	OSA	AGA	Total
Expense for the year ended December 31, 2021	32	44	760	2,366	**3,202**

(€K)	BSPCE	BSA	OSA	AGA	Total
Expense for the year ended December 31, 2020	107	19	509	2,289	**2,924**

4.1.6.18. Net financial income (Loss)

(€K)	2021	2020
Income from cash and cash equivalents	—	—
Foreign exchange gains	6,347	104
Other financial income	13	97
Total financial income	**6,360**	**201**
Interest cost [(1)]	(383)	4,676
IFRS 16 related interests	(288)	(333)
Foreign exchange losses	(109)	(1,697)
Total financial expenses	**(780)**	**2,646**
Net financial income (loss)	**5,580**	**2,847**

For the year ended December 31, 2021, the interest cost was a negative net amount of €383 thousands, mainly due to the EIB loan interest and discounting impact (see Note 12.1 Conditional advance, bank loan and loans from government and public authorities) which was a net income of €4.2 million in 2021 as a result of the EIB royalties sales reforecast catch up effect and the accretion of the debt cost, offset by €1.8 million impact of EIB fixed interest cost.

For the year ended December 31, 2020, the interest cost was a positive net amount of €4.7 million, substantially due to the EIB loan interests and discounting impact (see Note 12.1 Conditional advance, bank loan and loans from government and public authorities) which was a net income of €4.8 million in 2020 as a result of the EIB royalties sales reforecast catch up effect and the accretion of the debt cost, offset by €1.7 million impact of EIB fixed interest cost.

In 2021, the Company had foreign exchange gains for the total amount of €6.3 million. This impact was primarily arising from the foreign exchange gains realized by the Company related to the HSBC bank account denominated in U.S. dollars.

In 2020, the Company had foreign exchange losses for the total amount of €1.7 million. This impact was first arising from retaining $113.3 million from the gross proceeds of the global offering in a US dollar bank account.

4.1.6.19. Income Tax

Accounting policies

The Company and its subsidiaries are subject to income tax in their respective jurisdictions.

Deferred taxes are recognized on a full provision basis using the liability method for all temporary differences between the tax basis and accounting basis of assets and liabilities in the financial statements.

The main temporary differences relate to tax loss carryforwards. The prevailing income tax rates on the reporting date are used to determine deferred taxes. Deferred tax assets, which mainly arise as a result of tax loss carryforwards, are only recognized to the extent that it is probable that sufficient taxable income will be available in the future against which to offset the tax loss carryforwards or the temporary differences. Management uses its best judgment to determine such probability. Given the Company's current stage of development and its short-term earnings outlook, the Company is unable to make sufficiently reliable forecasts of future earnings and accordingly, deferred tax assets have not been recognized and offset only to the extent of deferred tax liabilities in the same taxable entities.

Income tax

As of December 31, 2021, in accordance with the applicable legislation, the Company has €284 million of evergreen tax losses in France, in comparison with €235 million and €184.3 million of evergreen tax losses in France as of December 31, 2020 and 2019, respectively. For fiscal years ended on or after December 31, 2018, the use of tax loss carryforwards in France is capped at €1.0 million, plus 50% of the portion of profits in excess of that limit.

The cumulative tax loss carryforwards for the U.S. entities of the Company totaled $3.4 million as of December 31, 2021, $4.4 million as of December 31, 2020 and $4.8 million in the United States as of December 31, 2019. The tax loss carryforwards that were generated before January 1, 2018 will expire 20 years after they were generated; those generated after that date have an indefinite carryforward. The tax loss carryforwards in the U.S. comply with the federal and each state's Net Operating Loss ("NOL") rules updated by the Tax Cuts and Jobs Act ("TCJA") of 2017.

The following table reconciles the Company's theoretical tax expense to its effective tax expense:

(€K)	**2021**	**2020**
Net loss	(47,003)	(33,590)
Effective tax expense	5	9
Recurring loss before tax	**(47,058)**	**(33,581)**
Theoretical tax rate (statutory rate in France)	26.50 %	28.00 %
Theoretical tax (benefit) expense	**(12,470)**	**(9,403)**
Share-based payment	848	819
Other temporary differences	117	(6)
Other non-taxable items	(644)	(540)
Unrecognized tax losses	12,154	9,138
Effective tax expense	**5**	**9**
Effective tax rate	**—**	**—%**

The cumulative net unrecognized deferred tax assets amounted to €75.4 million in 2021, including €14.0 million of 2021 net operating loss carryforwards in comparison with €60.2 million in 2020, including €59.6 million of 2020 net operating loss carryforwards and €51.0 million in 2019, including €49.6 million of 2019 net operating loss carryforwards.

The deferred tax rate of the Company is 25.8% in 2021, 26.5% in 2020, and 25.49% in 2019, based on enacted tax rate reductions in future years.

4.1.6.20. Segment reporting

In accordance with IFRS 8 – *Operating Segments*, reporting by operating segment is derived from the internal organization of the Company's activities; it reflects management's viewpoint and is established based on internal reporting used by the chief operating decision maker (the Company's Chief Executive Officer and Chairmen of the Executive Board and of the Supervisory Board) to allocate resources and to assess performance.

The Company operates in a single operating segment: research and development in product candidates that harness principles of physics to transform cancer treatment.

The assets, liabilities and operating loss realized are primarily located in France.

Revenue in 2021 and 2020 was derived mainly from the charging-back of shared external clinical research organization costs, in connection with the development support provided by the Company to PharmaEngine as part of the Company's License and Collaboration Agreement in Asia by Nanobiotix S.A. (see Note 15).

For territorial analysis purposes, management allocates revenue based on the place of delivery of licenses or on the place in which services are provided.

4.1.6.21. Loss per share

Accounting policies

Loss per share is calculated by dividing the net loss due to shareholders of the Company by the weighted average number of ordinary shares outstanding during the period.

The diluted loss per share is calculated by dividing the results by the weighted average number of common shares in circulation, increased by all dilutive potential common shares. The dilutive potential common shares include, in particular, the share subscription warrants, stock options and founder subscription warrants as detailed in Note 17.

Dilution is defined as a reduction of earnings per share or an increase of loss per share. When the exercise of outstanding share options and warrants decreases loss per share, they are considered to be anti-dilutive and excluded from the calculation of loss per share.

Detail of loss per share

	2021	2020
Net loss for the period (in thousands of euros)	(47,063)	(33,590)
Weighted average number of shares	34,733,418	24,385,827
Basic loss per share (in euros)	**(1.35)**	**(1.38)**
Diluted loss per share (in euros)	**(1.35)**	**(1.38)**

Instruments providing deferred access to the capital are considered to be anti-dilutive because they result in a decrease in the loss per share. Therefore, diluted loss per share is identical to basic loss per share as all equity instruments issued but not granted, representing as of December 31, 2021, 3,006,532 potential additional ordinary shares, have been considered antidilutive.

4.1.6.22. Commitments

4.1.6.22.1 Obligations under the loan agreement with the EIB

In the event the EIB loan is repaid early, or in the event of a change of control after repayment of the loan, the amount of royalties due will be equal to the net present value of the royalties as determined by an independent expert, such amount not to be less than €35.0 million.

The EIB finance contract contains covenants that impose restrictions on the operation of the Company's business but no financial covenants that the Company is required to comply with.

In certain circumstances, including any material adverse change, a change of control of the Company or if Dr. Laurent Levy, Chairman of the Executive Board, ceases to hold office, the Company may be required to pay a cancellation fee. If Dr. Laurent Levy ceases to hold a certain number of shares or ceases to be an officer, the EIB may require early repayment of the loan.

4.1.6.22.2 Obligations under the terms of the rental agreements part of the IFRS 16 exemptions

The obligations of the Company related to the leases falling under the practical expedients (leases related to low value assets and short-term leases) are as follow:

- One short term lease for an office by Nanobiotix Corp., of which the annual rent is €140 thousand; and
- Leases related to low-value assets for Nanobiotix S.A.'s printers, of which the annual rent is around €10 thousand.

4.1.6.22.3 Obligations related to the MD Anderson agreement

In January 2019, the Company and MD Anderson announced a large-scale research collaboration.

The collaboration will support multiple phase I/II clinical trials involving around 340 patients with NBTXR3 for use in treating several cancer types – including head and neck, pancreatic, thoracic, lung, gastrointestinal and genitourinary cancers.

As part of the funding for this collaboration, Nanobiotix is committed to pay approximately $11 million for the clinical trials contemplated by the agreement during the course of the collaboration on the basis of patients enrolled during the relevant period. As of June 30, 2021, $2 million have already been invoiced and paid since the beginning of the collaboration. An additional payment will also occur in the event of a successful first registration of NBTXR3 with the FDA. The amount will be determined based on the number of patients enrolled in these clinical trials as of the date of FDA registration. This number increases every year and varies between $2.2 million (if it had been payable in 2020) and $16.4 million (if payable in 2030).

As of December 31, 2021, €1.8 million have already been invoiced since the beginning of the collaboration and €1.0 million remain in prepaid expenses. An additional payment will also occur in the event of a successful first registration of NBTXR3 with the FDA.

4.1.6.22.4 Obligations related to the termination of the PharmaEngine agreement

In March 2021, the Company and PharmaEngine mutually agreed to terminate the license and collaboration agreement entered into in August 2012.

During the year ended December 31, 2021, the Company paid $6.5 million to PharmaEngine (€5.4 million converted at the exchange rate on the payment date) in accordance with the termination agreement signed between the parties. PharmaEngine is eligible to receive additional payments of $1 million upon receipt by the Company of clinical study reports and of $5 million upon the second regulatory approval of NBTXR3 in any jurisdiction in the world and for any indication. The Company has also agreed to pay royalties to PharmaEngine at low single-digit royalty rates with respect to sales of NBTXR3 in the Asia-Pacific region for a 10-year period beginning at the date of the first sales in the region.

4.1.6.23. Related parties

Key management personnel compensation

The compensation presented below, granted to the members of the Executive Board and Supervisory Board was recognized in expenses over the period shown:

(€K)	2021	2020
Salaries, wages and benefits	1,245	1,073
Share-based payments	2,018	1,723
Supervisory Board's fees	375	70
Total compensation to related parties	**3,638**	**2,866**

The methods used to measure share-based payments are presented in Note 17.

4.1.6.24. Auditors' fees

The fees of the Independent Auditors for the audit and certification of the 2021 financial statements amounted to €762 thousand and breaks down as follow:

2021 Auditors' fees			Total
(€K)	**Grant Thornton**	**Ernst & Young**	
Statutory audit	115	647	**762**
Services other than the certification of accounts	40	108	**148**

4.1.6.25. Subsequent events

Accounting policies

The statement of consolidated financial position and the statement of consolidated operations are adjusted to reflect subsequent events that alter amounts related to situations that exist as of the reporting date. Non-adjusting subsequent events are disclosed. The adjustments and disclosures are made until the date the consolidated financial statements are approved and authorized for issuance by the Supervisory Board.

Detail of Subsequent Events

Considerations arising from the Russia-Ukraine war

Russia launched in February 2022 the invasion of Ukraine, which, in addition to creating humanitarian concerns, may also impact the health care ecosystem in the form of delayed clinical trials. Clinical trial sites originally appointed in Russia and Ukraine for the clinical trial NANORAY-312 were not actively opened at the time of such conflict and, consequently, did not recruit patients. While backup options are being identified and the replacement of such sites by sites located in other countries is actively conducted by the Company, however it is currently impossible to excluded any delay in this clinical trial activity, even if no significant delay has been identified as of the date of issuance of this report.

Share capital increase

On March 11, 2022, the share capital of the Company was increased by a nominal amount of €1,500, through the issuance of 50,000 new ordinary shares with a nominal value of €0.03 each, increasing the Company's share capital from €1,044,776.16 to €1,046,276.16, as a result of the definitive acquisition of 50,000 AGA 2020. Such acquisition was acknowledged by the Executive Board on March 11, 2022.

4.2. STATUTORY AUDITOR'S REPORT ON THE 2021 CONSOLIDATED FINANCIAL STATEMENTS

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ERNST & YOUNG et Autres

This is a translation into English of the statutory auditors' report on the consolidated financial statements of the Company issued in French and it is provided solely for the convenience of English-speaking users. This statutory auditors' report includes information required by European regulations and French law, such as information about the appointment of the statutory auditors or verification of the information concerning the Group presented in the management report and other documents provided to shareholders. This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.

Nanobiotix
Year ended December 31, 2021

Statutory auditors' report on the consolidated financial statements

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Commissaire aux Comptes
Membre de la compagnie
régionale de Versailles et du Centre

Nanobiotix
Year ended December 31, 2021

Statutory auditors' report on the consolidated financial statements

To the Annual General Meeting of Nanobiotix,

Opinion

In compliance with the engagement entrusted to us by your Annual General Meeting we have audited the accompanying consolidated financial statements of Nanobiotix for the year ended December 31, 2021.

In our opinion, the consolidated financial statements give a true and fair view of the assets and liabilities and of the financial position of the Group as at December 31, 2021 and of the results of its operations for the year then ended in accordance with International Financial Reporting Standards as adopted by the European Union.

The audit opinion expressed above is consistent with our report to the Audit Committee.

Basis for Opinion

- **Audit Framework**

We conducted our audit in accordance with professional standards applicable in France. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Our responsibilities under those standards are further described in the *Statutory Auditors' Responsibilities for the Audit of the Consolidated Financial Statements* section of our report.

- **Independence**

We conducted our audit engagement in compliance with the independence requirements of the French Commercial Code *(Code de commerce)* and the French Code of Ethics for Statutory Auditors *(Code de déontologie de la profession de commissaire aux comptes)* for the period from January 1, 2021 to the date of our report and specifically we did not provide any prohibited non-audit services referred to in Article 5(1) of Regulation (EU) No. 537/2014.

Justification of Assessments - Key Audit Matters

Due to the global crisis related to the COVID-19 pandemic, the financial statements for this period have been prepared and audited under special circumstances. Indeed, this crisis and the exceptional measures taken in the context of the health emergency have had numerous consequences for companies, particularly on their operations and their financing, and have led to greater uncertainties regarding their future prospects. Some of these measures, such as travel restrictions and remote working, have also had an impact on companies' internal organization and on the performance of audits.

It is in this complex, evolving context that, in accordance with the requirements of Articles L. 823-9 and R. 823-7 of the French Commercial Code *(Code de commerce)* relating to the justification of our assessments, we inform you of the key audit matters relating to risks of material misstatement that, in our professional judgment, were of most significance in our audit of the consolidated financial statements of the current period, as well as how we addressed those risks.

These matters were addressed in the context of our audit of the consolidated financial statements as a whole and in forming our opinion thereon, and we do not provide a separate opinion on specific items of the consolidated financial statements.

- **Recognition of revenue from the licensing, development and marketing agreement signed with the company LianBio Oncology Limited in 2021**

Risk identified	Our response
Note 15 “Revenues and other income” to the consolidated financial statements, sets out that your Company signed in 2021 a license, development, and commercialization agreement with LianBio, that consist of: the licensing of rights to technology, research and development programs, participation in the funding of the clinical trials and the exclusive right to buy and sell the licensed products in its territory. Your Company evaluated this agreement to determine the single performance obligation, including performance obligation to which non-refundable upfront payment relates, the transaction price, the allocation of the transaction price to the performance obligation, and the timing of the satisfaction of the performance obligation. Under this license, development and commercialization agreement, the Company received a $20.0 million non-refundable upfront payment. Based on its analysis, your Company determined that this non-refundable upfront payment related to the single performance obligation that had not been satisfied yet and consequently differed the revenue until the occurrence of the first sales of the licensed product. Given the complexity of determining if the license, development and collaboration agreement contains only one performance obligation and this performance obligation is fulfilled, requiring Management’s judgement, we consider the estimation of the revenue recognition as a key audit matter.	In this context, we have: • analyzed the license, development and collaboration agreement signed in 2021 with LianBio; • familiarizing ourselves with internal control procedures implemented to analyze the license, development, and commercialization agreement and determine the satisfaction of the related performance obligations; • analyzed the accounting note prepared by Management and its counsels documenting identification and the satisfaction of the performance obligation related to this agreement in accordance with IFRS 15.

- **Estimation of invoices not received relating to expenses incurred for the realization of clinical trials**

Risk identified	Our response
In the context of the development of its products, your Company carries out clinical trials in collaboration with contract research organizations. Note 13.1 "Trade and other payables" to the consolidated financial statements sets out the method applied to determine an estimation of the costs incurred in that respect according to the progress of the clinical studies. At year-end, Management estimates the costs not yet invoiced, for each study, taking into account the duration of the treatment as well as each patient's injection date, and records such estimate as accrued expenses for the financial year. The identification of all the clinical trials on-going at year-end, the actual costs incurred and the correct estimate of the accruals at year end constitute a risk. A misstatement would lead to an improper estimate of the amount presented in "Research and development expenses" in the consolidated income statement. Given the complexity of determining the key assumptions used to determine the research and development expenses, and their estimation method at year end requiring Management judgement, we consider the estimation of the clinical trial accrued expenses incurred as a key audit matter.	Our audit procedures mainly consisted in assessing the valuation and the factors underlying the assumptions used by Management to determine the amount of accrued expenses. In this context, we have: • performed procedures to evaluate internal control procedures implemented to identify and estimate the costs to be recognized as accruals at year end; • tested key controls set up regarding the number of patients injected over the period, the update of the average cost per patient based on contracts entered into with clinical trial centers, and the clearance of the provision; • analyzed the information drawn up by Management documenting the cost per patient of the trials performed; • read the significant contracts entered into with clinical trial centers; • tested the invoices billed by the contract research organizations during the subsequent period to assess the consistency of the management's estimate; • reconciled the number of patients recruited and the treatment start dates declared by the clinical trial centers with the number of patients and the treatment dates taken into account to calculate the accrual.

- **Estimation of the financial debt relating to the loan granted by the EIB**

Risk identified	Our response
Note 4.3 “Financing agreement with the European Investment Bank (“EIB”)” to the consolidated financial statements sets out that your Company received the first tranche of €16 million in October 2018 and the second tranche of €14 million in March 2019, of a loan from the European Investment Bank (“EIB”) of a maximum of € 40 million over a period of five years, subject to achieving a set of agreed-upon performance criteria. The first tranche and the related accumulated fixed-rate interest shall be reimbursed in 2023 and the second tranche and the related accumulated fixed-rate interest is being reimbursed from 2021 to 2024. Your Company also committed to pay additional interests as royalties on net sales that occur for six years starting from January 1, 2021. Note 12 “Financial liabilities” to the consolidated financial statements presents the valuation method of financial liabilities measured at amortized cost, calculated using the effective interest rate method. Management estimated the amounts to be paid overtime including royalties in order to estimate the effective interest rate considering the market release date of the product, growth and penetration rate. The estimate of the sales forecast to which the royalty rate would be applied represents a risk. A misstatement would lead to an improper estimate of the “Financial liabilities” in the consolidated financial position and the “Financial expenses” in the statements of consolidated operations. Given the complexity in determining the future sales forecast to calculate the royalties and the underlying assumptions made by management such as product launch dates, growth and penetration rates in each market, we consider the valuation of the financial liabilities related to the EIB loan as a key audit matter.	Our audit procedures mainly consisted in familiarizing ourselves with the method used to calculate the valuation at amortized cost and factors justifying the key assumptions made by Management to determine the amount of royalties to be paid in the future. In this context, we have: • analyzed the Loan Agreement and the Royalties Agreement entered into between the Company and the EIB; • analyzed the future sales forecast drawn up by Management as of the closing date, approved by the Executive and Supervisory Boards, used to estimate the amount of royalties; • assessed the reasonableness of management's assumptions to determine expected product first commercialization dates given the progress of clinical trials; • assessed the growth and penetration rate assumptions on each market established by management with regard to specialized scientific publications; • reconciled the assumptions of sales used in the calculation of the fair value of the financial debt at year end with the elements approved by the Supervisory Board and communicated to the EIB.

Specific verifications

We have also performed, in accordance with professional standards applicable in France, the specific verifications required by laws and regulations of the information relating to the Group given in the Executive board's Management Report of Directors.

We have no matters to report as to its fair presentation and its consistency with the consolidated financial statements.

Report on Other Legal and Regulatory Requirements

- **Format of preparation of the consolidated financial statements intended to be included in the annual financial report**

We have also verified, in accordance with the professional standard applicable in France relating to the procedures performed by statutory auditors regarding the annual and consolidated financial statements prepared in the European single electronic format, that the preparation of the consolidated financial statements intended to be included in the annual financial report mentioned in Article L. 451-1-2, I of the French Monetary and Financial Code, prepared under the chairman's of the board responsibility, complies with the single electronic format defined in Commission Delegated Regulation (EU) No. 2019/815 of December 17, 2018. Regarding consolidated financial statements, our work includes verifying that the tagging thereof complies with the format defined in the above-mentioned regulation.

On the basis of our work, we conclude that the preparation of the consolidated financial statements intended to be included in the annual financial report complies, in all material respects, with the European single electronic format.

We have no responsibility to verify that the consolidated financial statements that will ultimately be included by your Company in the annual financial report filed with the AMF (*Autorité des marchés financiers)* agree with those on which we have performed our work.

- **Appointment of the Statutory Auditors**

We were appointed as statutory auditors of Nanobiotix by your Annual general meeting held on June 14, 2017 for GRANT THORNTON and May 4, 2012 for ERNST & YOUNG et Autres.

As at December 31, 2021, GRANT THORNTON was in the fifth year of total uninterrupted engagement and ERNST AND YOUNG et Autres in its tenth year, including nine years since the securities of the Company were admitted to trading on a regulated market.

Responsibilities of Management and Those Charged with Governance for the Consolidated Financial Statements

Management is responsible for the preparation and fair presentation of the consolidated financial statements in accordance with International Financial Reporting Standards as adopted by the European Union and for such internal control as Management determines is necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, Management is responsible for assessing the Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless it is expected to liquidate the Company or to cease operations.

The Audit Committee is responsible for monitoring the financial reporting process and the effectiveness of internal control and risk management systems and where applicable, its internal audit, regarding the accounting and financial reporting procedures.

The consolidated financial statements were approved by the Executive Board.

Statutory Auditors' Responsibilities for the Audit of the Consolidated Financial Statements

- **Objectives and audit approach**

Our role is to issue a report on the consolidated financial statements. Our objective is to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement. Reasonable assurance is a high level of assurance but is not a guarantee that an audit conducted in accordance with professional standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users made on the basis of these consolidated financial statements.

As specified in Article L. 823-10-1 of the French Commercial Code (*Code de commerce*), our statutory audit does not include assurance on the viability of the Company or the quality of management of the affairs of the Company.

As part of an audit conducted in accordance with professional standards applicable in France, the statutory auditor exercises professional judgment throughout the audit and furthermore:

- Identifies and assesses the risks of material misstatement of the consolidated financial statements, whether due to fraud or error, designs and performs audit procedures responsive to those risks, and obtains audit evidence considered to be sufficient and appropriate to provide a basis for his opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.

- Obtains an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal control.

- Evaluates the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by Management in the consolidated financial statements.

- Assesses the appropriateness of Management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Company's ability to continue as a going concern. This assessment is based on the audit evidence obtained up to the date of his audit report. However, future events or conditions may cause the Company to cease to continue as a going concern. If the statutory auditor concludes that a material uncertainty exists, there is a requirement to draw attention in the audit report to the related disclosures in the consolidated financial statements or, if such disclosures are not provided or inadequate, to modify the opinion expressed therein.

- Evaluates the overall presentation of the consolidated financial statements and assesses whether these statements represent the underlying transactions and events in a manner that achieves fair presentation.

- Obtains sufficient appropriate audit evidence regarding the financial information of the entities or business activities within the Group to express an opinion on the consolidated financial statements. The statutory auditor is responsible for the direction, supervision and performance of the audit of the consolidated financial statements and for the opinion expressed on these consolidated financial statements.

- **Report to the Audit Committee**

We submit to the Audit Committee a report which includes in particular a description of the scope of the audit and the audit program implemented, as well as the results of our audit. We also report significant deficiencies, if any, in internal control regarding the accounting and financial reporting procedures that we have identified.

Our report to the Audit Committee includes the risks of material misstatement that, in our professional judgment, were of most significance in the audit of the consolidated financial statements of the current period and which are therefore the key audit matters that we are required to describe in this report.
We also provide the Audit Committee with the declaration provided for in Article 6 of Regulation (EU) No. 537/2014, confirming our independence within the meaning of the rules applicable in France as set out in particular in Articles L. 822-10 to L. 822-14 of the French Commercial Code and in the French Code of Ethics for Statutory Auditors Where appropriate, we discuss with the Audit Committee the risks that may reasonably be thought to bear on our independence, and the related safeguards.

Neuilly-sur-Seine and Paris- La Défense, April 8, 2022

The Statutory Auditors
French original signed by

GRANT THORNTON	ERNST & YOUNG et Autres
French member of Grant Thornton International	
Samuel Clochard	Cédric Garcia

4.3. ANNUAL FINANCIAL STATEMENTS (STATUTORY ACCOUNTS) FOR THE FISCAL YEAR ENDED DECEMBER 31, 2021

4.3.1. Balance sheet

Assets

	12/31/2021			12/31/2020
(€K)	Gross	Amort. & Prov.	Net	
Concessions and patents	718	715	3	19
Other intangible asset	—	—	—	—
Intangible assets	**718**	**715**	**3**	**19**
Fixtures and buildings	3,318	1,641	1,678	1,992
Technical installations	2,072	1,595	477	561
Other fixed assets	935	826	108	182
Intangible assets in progress	98	—	98	1
Tangible assets	**6,423**	**4,061**	**2,361**	**2,737**
Other equity investments	4,052	—	4,052	4,052
Other financial fixed assets	600	12	587	656
Receivables from related interests	2,295	—	2,295	2,252
Financial assets	**6,946**	**12**	**6,934**	**6,960**
TOTAL	**14,087**	**4,789**	**9,298**	**9,716**
Advances and deposits paid on orders	3,291	—	3,291	805
Advances	**3,291**	**—**	3,291	**805**
Receivables and related accounts	—	—	—	72
Other current assets	5,304	189	5,115	3,432
Receivables	**5,304**	**189**	5,115	**3,504**
Investment securities	—	—	—	—
Available funds	82,372	—	82,372	118,420
Cash	**82,372**	**—**	**82,372**	**118,420**
Prepaid expenses	2,315	—	2,315	2,330
TOTAL	**93,281**	**189**	**93,093**	**125,060**
Translational adjustment - Assets	5	—	5	12
TOTAL ASSETS	**107,373**	**4,978**	**102,396**	**134,788**

Liabilities

(€K)	12/31/2021	12/31/2020
Share Capital	1,045	1,033
Premiums	255,781	255,751
Deferred losses	(182,504)	(146,784)
Profit (loss) for the year	(45,146)	(35,719)
SHAREHOLDERS' EQUITY	**29,177**	**74,280**
Provisions for liabilities	50	40
Provisions for risks	5	12
Provisions for contingencies	16	—
PROVISIONS	**71**	**52**
Miscellaneous loans and financial liabilities	43,985	45,725
Trade payables	7,715	8,852
Tax and social security liabilities	4,283	5,519
Other liabilities	432	350
Deferred income	16,518	—
LIABILITIES	**72,933**	**60,446**
Translation adjustment - Liabilities	215	9
TOTAL LIABILITIES	**102,396**	**134,788**

4.3.2. Income statement

(€K)	12/31/2021	12/31/2020
Sales of goods	5	—
Sales of services	120	231
Revenue	**125**	**231**
Stored production	—	—
Fixed asset production	—	—
Operating subsidy	—	—
Reversals of depreciation, amortization, provisions and transfers of expenses	463	130
Other income	194	134
TOTAL OPERATING INCOME	**783**	**496**
Purchase of goods	—	—
Changes in goods inventories	—	—
Purchases of raw materials and other supplies	542	265
Changes in inventory	—	—
Other purchases and external expenses	33,382	22,743
Taxes, duties and related payments	438	274
Salaries and wages	7,826	7,375
Social security expenses	3,609	3,274
Amortization	603	784
Depreciation	—	—
Provisions	15	52
Other charges	437	113
TOTAL OPERATING EXPENSES	**46,852**	**34,881**
OPERATING PROFIT (LOSS)	**(46,069)**	**(34,385)**
Financial income from equity investments	48	45
Other interest and similar income	13	92
Reversals of depreciation, provisions and transfers of financial expenses	7	16
Exchange rate gains	5,916	—
Net income from disposals of investment securities	52	134
TOTAL FINANCIAL INCOME	**6,036**	**287**
Amortization, depreciation and financial provisions	12	7
Interest and similar expenses	1,890	1,780
Exchange rate losses	—	1,414
Net expense on disposals of investment securities	117	115
TOTAL FINANCIAL EXPENSES	**2,020**	**3,316**
FINANCIAL PROFIT (LOSS)	**4,016**	**(3,028)**
CORE PRE-TAX LOSS	**(42,053)**	**(37,413)**
Exceptional income from management transactions	73	—
Exceptional income from equity transactions	1	—
Reversals of depreciation, provisions and transfers of exceptional expenses	—	—
TOTAL EXCEPTIONAL INCOME	**73**	**—**
Exceptional expenses on management transactions	5,422	164
Exceptional expenses on equity transactions	1	—
Amortization, depreciation and exceptional provisions	16	—
TOTAL EXCEPTIONAL EXPENSES	**5,439**	**164**
EXCEPTIONAL INCOME (LOSS)	**(5,366)**	**(164)**
Employee profit sharing	—	—
Tax credit	2,273	1,858
NET PROFIT & LOSS	**(45,146)**	**(35,719)**

4.3.3. Notes

Notes to the balance sheet, before distribution of the year's net profit, for a total of €102,396 thousand, and notes to the statement of income for the year presented in list form, showing revenue of €125 thousand and a loss of €45,146 thousand.

The accounting period lasts 12 months, covering the period from January 1, 2021 to December 31, 2021.

The notes and tables presented below are an integral part of the annual financial statements. The tables are presented in thousands of euros.

SIGNIFICANT EVENTS OF THE PERIOD

Nanobiotix and PharmaEngine mutually agree to terminate their collaboration

In March 2021, in light of disagreements over a number of issues with respect to the development of NBTXR3 in the Asia-Pacific region, Nanobiotix and PharmaEngine mutually agreed to terminate the licensing and collaboration agreement entered into in August 2012. Accordingly, on March 4, 2021, Nanobiotix and PharmaEngine entered into a termination and release agreement (the "Termination Agreement"). Under the Termination Agreement, Nanobiotix retained all rights to the development and commercialization of NBTXR3 in the Asia-Pacific region. Nanobiotix agreed to make total termination payments to PharmaEngine of up to $12.5 million in the aggregate as described below.

PharmaEngine was eligible for and received a $2.5 million payment following the announcement of Nanobiotix's collaboration with LianBio for the Asia-Pacific region. During the six months ended June 30, 2021, PharmaEngine also received $4.0 million in conjunction with the completion of various administrative steps in connection with the winding-up of the collaboration.

PharmaEngine will be eligible to receive an additional $1.0 million in administrative fees and a final payment of an additional $5.0 million upon a second regulatory approval of an NBTXR3-containing product in any jurisdiction of the world for any indication. PharmaEngine is entitled to receive a low-single digit tiered royalty based on net sales of NBTXR3 in the Asia-Pacific region for a 10-year period commencing on the corresponding first date of sales in the region. As of December 31, 2021, these future payments were not accrued because the triggering events have not occurred.

As part of the Termination Agreement, PharmaEngine re-assigned to Nanobiotix rights for the development, manufacture, commercialization and exploitation of NBTXR3 in the Asia-Pacific region, as well as all development data, regulatory materials, and all regulatory approvals that are in the name of PharmaEngine or its affiliates. Consequently, NBTXR3 clinical trials conducted by PharmaEngine in Asia are in the process of being concluded or terminated.

Nanobiotix and PharmaEngine also agreed to a mutual release of all claims against the other party and its respective affiliates.

Nanobiotix partners with LianBio for the development and commercialization of NBTXR3 in several oncology indications and in combination with several anti-cancer therapies, in China and other Asian markets

In May 2021, Nanobiotix entered into a partnership with LianBio, a biotechnology company dedicated to bringing paradigm-shifting medicines to patients in China and major Asian markets, to develop and commercialize Nanobiotix's lead product candidate, NBTXR3 into Greater China (mainland China, Hong Kong, Taiwan, and Macau), South Korea, Singapore and Thailand.

LianBio will collaborate in the development of NBTXR3 in Asia Pacific, and contribute to patient enrollment in five future global registrational studies across several tumor types and therapeutic combinations including immunotherapy. LianBio will also support the expansion of global phase III registrational study in head and neck cancer into Greater China with longer term strategic alignment across multiple tumor indications and therapeutic combinations.

Under the terms of the agreement, the Company received a $20 million upfront payment and is entitled to receive up to an aggregate of $220 million in potential contingent, development and commercialization milestone payments. The Company will also be eligible to receive tiered, low double-digit royalties based on net sales of NBTXR3 in the licensed territories. LianBio will fund all development and commercialization expenses in the collaboration territory, and the Company will continue to fund all development and commercialization expenses in all other geographies.

Nanobiotix announces the appointment of Dr. Gary Phillips as Chairman of the Supervisory Board

In May 2021, Dr. Gary Phillips was appointed Chairman of the Company's supervisory board of the Company ("the "Supervisory Board"). Dr Phillips succeeded Laurent Condomine, who retired from the Supervisory Board after 11 years of leadership.

Nanobiotix announces the appointment of Bart Van Rhijn as Chief Financial Officer and member of the executive board of the Company to support its international expansion

On June 1, 2021, the Company announced the appointment of Bart Van Rhijn, MBA, as Chief Financial Officer and member of the executive board of the Company (the "Executive Board"). Bart Van Rhijn brings proven capabilities in global financial management, business development and pharmaceutical commercialization as the Company prepares for the planned launch of its second clinical registration study for NBTXR3 in head and neck cancer (NANORAY-312), continued development in immunotherapy, and planned expansion across solid tumor types and therapeutic combinations. He succeeded Philippe Mauberna, who stepped down from his roles as Chief Financial Officer and Executive Board member after 8 years of service to the Company.

Nanobiotix opened a branch in Switzerland

On November 26, 2021, the Company opened a branch in Switzerland.

SUBSEQUENT EVENTS

Considerations arising from the Russia-Ukraine war

Russia launched in February 2022 the invasion of Ukraine, which, in addition to creating humanitarian concerns, may also impact the health care ecosystem in the form of delayed clinical trials. Clinical trial sites originally appointed in Russia and Ukraine for the clinical trial NANORAY-312 were not actively opened at the time of such conflict and, consequently, did not recruit patients. While backup options are being identified and the replacement of such sites by sites located in other countries is actively conducted by the Company, however it is currently impossible to excluded any delay in this clinical trial activity, even if no significant delay has been identified as of the date of issuance of this report.

ACCOUNTING RULES AND METHODS

Principle and General Conventions

The annual financial statements have been prepared and presented in accordance with the general rules applicable and in compliance with French accounting standards, including the ANC Regulation 2015-06 (GCA 2014) of November 23, 2015 and 2016-07 of November 4, 2016.

The general conventions were applied in compliance with the principle of prudence and in accordance with Articles 121-1 *et seq* of the French General Chart of Accounts:

- Fair view;
- Comparability of accounting periods and going concern;
- Fairness and truthfulness;
- Consistency of the accounting methods from one year another;
- Independence of the accounting periods; and
- Compliance with the general rules for preparing and presenting annual financial statements.

The historical cost method was used as the basis for measuring accounting items.

The going concern assumption was chosen by the Executive board for the following reasons:

- The Company's historical loss-making position is due to the innovative nature of the products it develops which involve research and development phases over several years;

- With cash and cash equivalents of €82,372 thousand as of December 31, 2021, as compared to €118,420 thousand as of December 31, 2020, the Company believes it has sufficient resources to continue operating for at least twelve months following the annual financial statements' publication.

Consistency of accounting methods

The valuation and presentation methods used for this accounting period are identical to those used for the previous period.

Revenue recognition: as part of a licensing agreement, the Company is required to defer recognition of a portion of the revenue regardless of the payments received.

NOTES TO THE STATEMENT OF FINANCIAL POSITION

Statement of tangible and intangible fixed assets

(€K)	Gross value at year opening	Increases Account to account transfer	Increases Acquisitions	Reductions Account to account transfer	Reductions Disposals	Gross value at year-end
Intangible assets - Software & Licenses	713	—	5	—	—	718
Intangible assets - Equity	—	—	—	—	—	—
Intangible assets in progress	—	—	—	—	—	—
General fixtures and fittings, buildings fitting out	3,313	—	5	—	—	3,318
Technical installations, equipment and industrial tooling	1,998	—	74	—	—	2,072
General fixtures and fittings, miscellaneous fitting out	79	—	—	—	—	79
Office and IT equipment, Furniture	859	—	32	—	35	855
Fixed assets in progress	1	—	98	1	—	98
Advances and deposits	—	—	—	—	—	—
TOTAL	**6,963**	**—**	**213**	**1**	**35**	**7,141**

The Company continued its investments during the financial year 2021 for €213 thousand mainly comprising:

- General fixtures and fittings (€5 thousand) ;
- Technical installations, equipment (€74 thousand) ;
- New software and computer licenses (€5 thousand) ;
- Purchase of computer hardware and miscellaneous equipment (€32 thousand) ; and
- Fixed assets in progress (€98 thousand).

Disposals during the financial year amounted to €35 thousand, corresponding to retired assets.

Research and Development Cost

Considering the risks and uncertainties associated with obtaining the market authorization for its product candidates, The Company believes that the technical feasibility of projects under development will only be established once regulatory authorizations have been obtained for the products' distribution. Therefore, the Company has expensed all of its research and development costs incurred in 2021 and during previous periods. It was decided not to capitalize research and development expenses.

Research and development expenses incurred for the financial year 2021 amount to €29,637 thousand.

Since the start of its clinical trials, Nanobiotix has incurred costs that have not yet been invoiced. As of December 31, 2021, these costs, estimated to €1,486 thousand, have therefore been accrued in accordance with the principles of caution and independence of accounting periods, and estimated for each study, on the basis of contracts signed with clinical research centers, taking into account the duration of treatment and the injection date of each patient. The total estimated amount for each study at December 31, 2021 has been reduced by the invoices received up to the year-end date.

Measurement of fixed assets

The gross value of tangible fixed assets corresponds to the recording value of goods in assets and liabilities including the expenses required to make the assets usable, but excluding the expenses incurred for their acquisition.

Measurement of intangible assets

Patents, concessions and other capitalized intangible assets were valued at their acquisition cost, excluding the expenses incurred for their acquisition.

Changes in amortization

The methods and depreciation periods used were as follows:

Category	Method	Period
Other intangible assets	Straight-line	1 to 5 years
General fixtures and fittings, buildings fitting out	Straight-line	5 to 10 years
Technical installations, equipment's and industrial tooling	Straight-line	3 to 10 years
General fixtures and fittings, fitting out	Straight-line	3 to 5 years
Office and IT equipment, furniture	Straight-line	1 to 10 years

Depreciation and Amortization

(€K)	Amount at fiscal Year Opening	Movement from item to item	Allocations over the financial year	Allocations Reversals	Amount at Year End
Intangible assets - Software & Licenses	694	—	21	—	715
General fixtures and fittings, buildings fitting out.	1,320	—	320	—	1,641
Technical installations, equipment and industrial tooling	1,438	—	157	—	1,595
General fixtures and fittings, fitting out	20	—	12	—	32
Office and IT equipment, furniture	736	—	93	34	794
TOTAL	**4,208**	**—**	**603**	**34**	**4,777**

Non-current financial assets

(€K)	Gross value at beginning of the year	Increases	Decreases	Gross Value at the end of the year
Deposits	377	2	—	379
Equity investments	4,052	—	—	4,052
Receivables from related interests	2,252	43	—	2,295
Non-equity securities	—	—	—	—
Treasury shares	182		59	123
Liquidity Account	104	—	6	97
TOTAL	**6,967**	**45**	**66**	**6,946**

Long-term investments

Equity investments and other long-term securities are measured at cost, excluding transaction costs.

In the event of the disposal of a set of securities of the same type providing the same rights, their cost is determined using the "first in, first out" method.

Where necessary, long-term investments are written down to take into account their fair value on the reporting date.

Nanobiotix holds 100% of Nanobiotix Corp., which has share capital of €3,001 thousand. This subsidiary reported a profit of €454 thousand in 2021.

Nanobiotix also holds 100% of Nanobiotix Spain S.L.U. and Nanobiotix Germany GmbH, which have share capital of, respectively, €3 thousand and €25 thousand.

Finally, Nanobiotix holds 100% of Curadigm SAS, incorporated on July 3, 2019, which had share capital amounts to €1,023 thousand as of December 31, 2021.

Under the liquidity contract put in place following the IPO, the Company holds 15,456 treasury shares for a value of €7.31 per share at December 31, 2021, i.e. a total value of €113 thousand. These shares were written down at the year-end and have a carrying amount in the financial statements of €111 thousand.

Changes in shareholders' equity

(€K)	Share Capital	Share Premium	Reserves	Accumulated deficit	Net Loss	TOTAL
December 31, 2020	1,033	255,735	16	(146,784)	(35,719)	**74,280**
Allocation of profit & loss N-1	—	—	—	(35,719)	35,719	—
Capital Increase	12	—	(12)	—	—	—
Allocation of free shares	—	(11)	11	—	—	—
Warrants subscription	—	43	—	—	—	**43**
Exercise of founder's warrants	—	—	—	—	—	—
Profit & Loss year N	—	—	—	—	(45,146)	**(45,146)**
December 31, 2021	**1,045**	**255,767**	**15**	**(182,504)**	**(45,146)**	**29,177**

As of December 31, 2021, the change in shareholders' equity includes:

- €35,719 thousand relating to the allocation of the loss for the previous year;
- €12 thousand relating to the capital increase through the allocation of free shares; and
- €43 thousand relating to share subscription of warrants.

Share capital

Categories of securities	Per value	At opening	Created	Repaid	At year-end
	€				
Normal Shares	**0.03**	**34,432,122**	**393,750**	**—**	**34,825,872**

Share subscription options

The Company issued the following plans: founders' warrant plans (BSPCE), warrant plans (BSA), share option plans (OSA) and free share plans (AGA).

Founders' warrants (BSPCE)

At a meeting of July 23, 2019, the Executive Board, which can, in its sole discretion, at any time during the acquisition period, decide that the holders do not have to remain in the Company anymore, decided to waive this condition that predefines the final acquisition of free shares and subscription of founders' warrants granted to some of Company's employees owning the founders 'warrants.

	BSPCE 2012-2	**BSPCE 08-2013**	**BSPCE 09-2014**	**BSPCE 2015-1**	**BSPCE 2015-3**	**BSPCE 2016 Ordinary**	**BSPCE Performance 2016**	**BSPCE 2017 Ordinary**	**BSPCE 2017**
Date of the General Meeting granting the founders' warrants	May 4, 2012	Jun 28, 2013	Jun 18, 2014	Jun 18, 2014	Jun 18, 2014	Jun 25, 2015	Jun 25, 2015	Jun 23, 2016	Jun 23, 2016
Supervisory board grant date	Dec 18, 2012	Aug 28, 2013	Sep 16, 2014	Feb 10, 2015	Jun 10, 2015	Feb 2, 2016	Feb 2, 2016	Jan 7, 2017	Jan 7, 2017
Total number of authorized BSPCE	500,000	500,000	450,000	450,000	450,000	450,000	450,000	450,000	450,000
Total number of granted BSPCE	100,000	50,000	97,200	71,650	53,050	126,400	129,250	117,650	80,000
Total number of shares that may be subscribed	100,000	50,000	97,200	71,650	53,050	126,400	129,250	117,650	80,000
the number of which may be subscribed or purchased by corporate officers:	—	—	21,000	24,000	—	23,500	23,500	26,400	32,000
Of which Laurent LEVY	—	—	21,000	24,000	—	23,500	23,500	26,400	32,000
Number of non-officer beneficiaries (on issue)	2	1	30	13	42	43	50	42	3
Start date of exercise of BSPCE	Dec 18, 2012	Aug 28, 2013	Sep 16, 2015	Feb 10, 2016	Jun 10, 2016	Feb 2, 2017	Feb 2, 2016	Jan 8, 2018	Jan 7, 2017
Expiration date of BSPCE	Dec 18, 2022	Aug 28, 2023	Sep 16, 2024	Feb 10, 2025	Jun 10, 2025	Feb 2, 2026	Feb 2, 2026	Jan 7, 2027	Jan 7, 2027
Strike price of BSPCE	€6.63	€5.92	€18.68	€18.57	€20.28	€14.46	€14.46	€15.93	€15.93
Number of shares subscribed	—	—	—	—	—	333	—	—	—
Total number of cancelled or null and void BSPCE	0	0	11,050	3,200	22,700	25,500	28,976	18,150	0
Total number of remaining BSPCE	100,000	50,000	86,150	68,450	30,350	100,567	100,274	99,500	80,000
Total number of shares that may be subscribed	100,000	50,000	86,150	68,450	30,350	100,567	38,170	99,500	80,000
Total number of shares that may be subscribed upon exercise of all outstanding founder's warrants (assuming that all conditions for exercising said founders' warrants are met)	100,000	50,000	86,150	68,450	30,350	100,567	100,274	99,500	80,000

Warrants (BSA)

At a meeting on April 20, 2021, the Executive Board, acting pursuant to the delegation granted by the Company's shareholders' meeting held on November 30, 2020 granted 48,103 warrants to members and observers of the Supervisory Board, each entitling its holder to subscribe one ordinary share, each with a par value of €0.03 and at a price of €13.47 (share premium included). The designated warrants included 18,103 warrants that were issued in replacement of certain 2016 ordinary warrants that became null on February 2, 2021. The subscription period is open from the date of the meeting of the Executive Board until September 30, 2021, inclusive. As of December 31, 2021, 14,431 warrants have been subscribed by their beneficiaries.

The warrants can be exercised at any time during a 10-year period, subject to the satisfaction of the following conditions:

- the subscription by the relevant beneficiary of his/her warrant;
- the relevant holder has attended at least 75% of the Supervisory Board meetings held during the twelve months preceding the exercise of the warrants or, as the case may be, the date the holder ceases to be part of the Group; and
- the recommended dose for two out of the three patient cohorts enrolled in the study 1100 has been determined in order to define the next steps of the immuno-oncology development plan.

It is being specified that (i) the Executive Board, with the prior approval of the Supervisory Board, shall acknowledge the satisfaction of such condition and (ii) such condition shall automatically be waived in the event of a change of control.

At the same meeting, the Executive Board, acting pursuant to the above mentioned delegation, also granted 30,000 warrants to a consultant of the Company, each warrant giving its holder the right to subscribe one ordinary share, each with a par value of €0.03 and at a price of €13.64 (share premium included) at any time during a ten-year period subject to (i) the subscription by such consultant of the warrants and (ii) the drafting by such consultant of a Chemistry, Manufacturing, Control (CMC) risk assessment report. The corresponding subscription period has been fixed from the date of the meeting of the Executive Board until July 20, 2021 inclusive. As of December 31, 2021, no warrants have been subscribed by the beneficiary. In addition, as of December 31, 2021 the report is not prepared yet. Therefore, the warrants are not vested yet.

At a meeting on March 17, 2020, the Executive Board, acting pursuant to the delegation granted by the thirty-fourth resolution of the annual shareholders' meeting dated April 11, 2019 and following the approval granted by the Supervisory Board on March 13, 2020, granted 18,000 warrants to members of the Supervisory Board, each entitling the holder to subscribe to a defined number of ordinary shares with a par value of €0.03, at a price of €6.59. The holders subscribed to the warrants prior to the end of the subscription period on September 30, 2020.

	BSA 04-12	BSA 2013	BSA 2014	BSA 2015-1	BSA 2015-2 (a)	BSA 2015-2 (b)	BSA 2016 Ordinary	BSA 2016 Performance	BSA 2016-2
Date of the General Meeting granting the warrants	May 4, 2012	May 4, 2012	Jun 18, 2014	Jun 18, 2014	Jun 18, 2014	Jun 25, 2015	Jun 25, 2015	Jun 25, 2015	Jun 23, 2016
Supervisory Board Grant Date	May 4, 2012	Apr 10, 2013	Sep 16, 2014	Feb 10, 2015	Jun 25, 2015	Jun 25, 2015	Feb 2, 2016	Feb 2, 2016	Nov 3, 2016
Total number of authorized BSA	200,000	200,000	100,000	100,000	100,000	100,000	100,000	100,000	100,000
Total number of granted BSA	52,500	10,000	14,000	26,000	64,000	6,000	18,103	18,105	8,000
Total number of shares that may be subscribed	52,500	10,000	14,000	26,000	64,000	6,000	18,103	18,105	8,000
the number of which may be subscribed or purchased by corporate officers:	22,500	—	8,000	15,000	—	—	11,072	11,073	—
Of which Anne-Marie GRAFFIN	—	—	—	5,000	—	—	2,000	2,000	—
Of which Enno SPILLNER	—	—	—	3,000	—	—	1,500	1,500	—
Of which Alain HERRERA	—	—	4,000	5,000	—	—	4,327	4,327	—
Of which Gary PHILLIPS	—	—	—	—	—	—	—	—	—
Of which Christophe DOUAT (observer)	22,500	—	4,000	2,000	—	—	3,245	3,246	—
Number of non-officer beneficiaries (on issue)	1	1	1	2	1	1	1	1	2
Start date of exercise of BSA	10/23/2013	4/30/2014	9/16/2014	2/10/2015	6/25/2015	6/25/2015	2/2/2016	2/2/2016	11/3/2016
Expiration date of BSA	05/04/2022	04/10/2023	09/16/2024	02/10/2025	06/25/2025	06/25/2020	02/02/2021	02/02/2021	11/03/2021
Issue price of BSA	€0.60	€2.50	€4.87	€4.87	€5.00	€2.80	€1.67	€1.67	€2.03
Strike price of BSA	€6.00	€6.37	€17.67	€17.67	€19.54	€19.54	€13.74	€13.74	€15.01
Number of BSA subscribed	22,500	—	—	—	—	—	—	—	—
Total number of cancelled or null and void BSA	—	4,000	4,000	5,000	—	6,000	18,103	18,105	8,000
Total number of remaining BSA	30,000	6,000	10,000	21,000	64,000	—	—	—	—
Total number of shares that may be subscribed	30,000	6,000	—	—	—	—	—	—	—
Total number of shares that may be subscribed upon exercise of all outstanding warrants (assuming that all conditions for exercising said warrants are met)	30,000	6,000	10,000	21,000	64,000	—	—	—	—

	BSA 2017	BSA 2018	BSA 2018-1	BSA 2018-2	BSA 2019-1	BSA 2020	BSA 2021 (a)	BSA 2021 (b)
Date of the General Meeting granting the warrants	Jun 23, 2016	Jun 14, 2017	Jun 14, 2017	May 23, 2018	May 23, 2018	Apr 11, 2019	Nov 30, 2020	Nov 30, 2020
Supervisory Board Grant Date	Jan 7, 2017	Mar 6, 2018	Mar 6, 2018	Jul 27, 2018	Mar 29, 2019	Mar 17, 2020	Apr 20, 2021	Apr 20, 2021
Total number of authorized BSA	100,000	116,000	116,000	140,000	140,000	500,000	650,000	650,000
Total number of granted BSA	18,000	18,000	10,000	5,820	18,000	18,000	48,103	30,000
Total number of shares that may be subscribed	18,000	18,000	10,000	5,820	18,000	18,000	48,103	30,000
the number of which may be subscribed or purchased by corporate officers:	13,280	12,700	—	—	12,700	14,024	—	—
Of which Anne-Marie GRAFFIN	3,820	2,900	—	—	2,900	3,843	—	—
Of which Enno SPILLNER	3,820	4,000	—	—	4,000	3,829	—	—
Of which Alain HERRERA	2,820	2,900	—	—	2,900	3,195	—	—
Of which Gary PHILLIPS	—	—	—	—	—	—	—	—
Of which Christophe DOUAT (observer)	2,820	2,900	—	—	2,900	3,157	—	—
Number of non-officer beneficiaries (on issue)	1	1	1	1	1	1	1	1
Start date of exercise of BSA	01/07/2017	03/06/2018	03/06/2018	07/27/2018	03/29/2019	03/17/2020	04/20/2021	04/20/2021
Expiration date of BSA	01/07/2022	03/06/2023	03/06/2023	07/27/2028	03/29/2029	03/17/2030	04/20/2031	04/20/2031
Issue price of BSA	€2.26	€1.62	€1.62	€2.36	€1.15	€0.29	€2.95	€0.68
Strike price of BSA	€15.76	€13.55	€13.55	€16.10	€11.66	€6.59	€13.47	€13.64
Number of BSA subscribed	—	—	—	—	—	—	—	—
Total number of cancelled or null and void BSA	—	—	—	—	—	—	33,672	—
Total number of remaining BSA	18,000	18,000	10,000	5,820	18,000	18,000	14,431	30,000
Total number of shares that may be subscribed	—	—	—	—	—	—	—	—
Total number of shares that may be subscribed upon exercise of all outstanding warrants (assuming that all conditions for exercising said warrants are met)	18,000	18,000	10,000	5,820	18,000	18,000	14,431	30,000

Stock options (OSA)

At a meeting on April 20, 2021, the Executive Board, acting pursuant to delegations granted by the Company's shareholders' meeting held on November 30, 2020, granted to certain employees of the Group and members of the Executive Board 571,200 stock options (including 143,200 stock options and 428,000 performance stock options), each giving its holder the right to subscribe one ordinary share, each with a par value of €0.03 and at a price of €13.74 (share premium included). Such stock options are governed by the 2020 stock option plan adopted by the Executive Board on February 9, 2021 and approved by the Company's annual shareholders' meeting held on April 28, 2021 (the "2020 Stock Option Plan").

The ordinary stock options are exercisable as follows:

- up to one-third of the ordinary stock options as from April 20, 2022;
- an additional one-third of the ordinary stock options as from April 20, 2023,
- the balance, i.e., one-third of the ordinary stock options as from April 20, 2024, subject to, for each increment, a continued service condition, and in any case,
- no later than 10 years after the date of grant, it being specified that stock options which have not been exercised by the end of this ten-year period will be forfeited by law.

The performance stock options may be exercised under the following conditions:

- 10% of the stock options may be exercised when the market price of the Company's shares on the regulated market of Euronext in Paris reaches €24.00,
- an additional 10% of the stock options may be exercised when the market price of the Company's shares on the regulated market of Euronext in Paris reaches €30.00,
- an additional 40% of the stock options may be exercised when the market price of the Company's shares on the regulated market of Euronext in Paris reaches €40.00,
- an additional 40% of the stock options may be exercised when the market price of the Company's shares on the regulated market of Euronext in Paris reaches €60.00, and

- at the latest within 10 years of the date of grant, it being specified that stock options which have not been exercised by the end of this 10-year period will be forfeited by law.

It being specified that (i) among such performance stock options that may be exercised, and subject to, for each increment, a continued service condition, their holders may only exercise (x) up to 10% of such performance stock options as from April 20, 2022, (y) an additional 30% of such performance stock options as from April 20, 2023, and (z) the balance, i.e., 60% of such performance stock options as from April 20, 2024, and (ii) such additional vesting condition shall be automatically waived in the event of a change of control.

The number of ordinary and performance stock options that may be exercised under the above exercise schedules would always be rounded down to the nearest whole number.

At a meeting on June 21, 2021, the Executive Board, acting pursuant to the delegation granted by the shareholders' meeting held on November 30, 2020 granted 60,000 ordinary stock options to Bart Van Rhijn following his entry into the Company and his appointment as a Member of the Executive Board. Such stock options are governed by the 2020 Stock Option Plan. Acting pursuant to a delegation granted by the Company's annual shareholders' meeting held on April 28, 2021, it also decided to adopt the 2021 stock option plan and to grant to Bart Van Rhijn 60,000 performance stock options governed by such plan. Each of such 120,000 stock options (whether ordinary and performance) gives it holders the right to subscribe one ordinary share, each with a par value of €0.03 and at a price of €12.99 (share premium included).

The exercise conditions of the 143,200 ordinary stock options and 428,000 performance stock options granted on April 20, 2021 described above shall apply mutatis mutandis to these 60,000 ordinary stock options and 60,000 performance stock options respectively, save for the anniversary date which shall be June 30 rather than April 20. In addition, in accordance with French regulation, the exercise of the above stock options (whether ordinary and performance) are subject to an additional performance condition as soon as they are granted to a member of the Executive Board: determination of the recommended dose for two of the three patient cohorts enrolled in the NBTXR3-1100 clinical study, in order to be able to define the next stage of the development plan in immuno-oncology.

At a meeting on March 11, 2020, the Executive Board adopted the 2019 Stock Option Plan and, acting pursuant to the authorization granted by the thirty-second resolution of the annual shareholders' meeting dated April 11, 2019, granted 407,972 stock options (the "OSA 2020"), 300,000 of which to members of the Executive Board and Alain Dostie and the remaining 107,972 to employees of the Company, under such 2019 Stock Option Plan. Each OSA 2020 entitles its holder to subscribe one ordinary share of the Company with a par value of €0.03, at an exercise price of €6.25 (issue premium included).

The OSA 2020 may be exercised as follows:

- up to one-third of the OSA 2020 as from March 11, 2021;
- an additional one-third of the OSA 2020 as from March 11, 2022; and

- the balance, i.e., one-third of the OSA 2020 as from March 11, 2023, subject to, for each increment, a continued service condition.

In addition, the Executive Board decided that the exercise of the OSA 2020 granted to members of the Executive Board and Alain Dostie would also be subject to the achievement of positive results in the 1100 study in 2020. The satisfaction of this performance condition was acknowledged by the Executive Board, with the approval of the supervisory board, on March 17, 2021.

	OSA 2016-1 Performance	OSA 2016-2	OSA 2017 Performance	OSA 2018	OSA 2019-1	OSA 2019 LLY	OSA 2020	OSA 2021-04 Ordinary	OSA 2021-04 Performance	OSA 2021-06 Performance	OSA 2021-06 Ordinary
Date of the general meeting granting the stock option plan	Jun 25, 2015	Jun 23, 2016	Jun 23, 2016	Jun 14, 2017	May 23, 2018	Apr 11, 2019	Apr 11, 2019	Nov 30, 2020	Nov 30, 2020	Nov 30, 2020	Apr 28, 2021
Date granted by the Supervisory board	Feb 2, 2016	Nov 3, 2016	Jan 7, 2017	Mar 6, 2018	Mar 29, 2019	Oct 24, 2019	Mar 11, 2020	Apr 20, 2021	Apr 20, 2021	Jun 21, 2021	Jun 21, 2021
Total number of authorized OSA	450,000	450,000	450,000	526,800	648,000	500,000	500,000	850,000	1,000,000	1,000,000	850,000
Total number of granted OSA	6,400	4,000	3,500	62,000	37,500	500,000	407,972	143,200	428,000	60,000	60,000
Total number of shares that may be subscribed	6,400	4,000	3,500	62,000	37,500	500,000	407,972	143,200	428,000	60,000	60,000
The number of which may be subscribed or purchased by Corporate officers:	—	—	—	—	—	500,000	180,000	—	240,000	60,000	60,000
Of which Laurent LEVY	—	—	—	—	—	500,000	120,000	—	180,000	—	—
Of which Anne-Juliette HERMANT	—	—	—	—	—	—	60,000	—	60,000	—	—
Of which Bart VAN RHIJN	—	—	—	—	—	—	—	—	—	60,000	60,000
Number of non-officers beneficiaries (on issue)	2	1	2	5	12	—	104	13	14	—	—
Exercise date	02/02/2017	11/03/2017	01/08/2018	03/07/2019	03/30/2021	10/24/2019	03/11/2021	04/20/2022	04/20/2022	06/21/2022	06/21/2022
Expiration date	02/02/2026	11/03/2026	01/07/2027	03/06/2028	03/29/2029	10/24/2029	03/11/2030	04/20/2031	04/20/2031	06/21/2031	06/21/2031
Strike price	€13.05	€14.26	€14.97	€12.87	€11.08	€6.41	€6.25	€13.74	€13.74	€12.99	€12.99
Number of shares subscribed	—	—	—	—	—	—	—	—	—	—	—
Total number of cancelled or null and void OSA	6,000	—	3,000	10,000	9,250	—	20,516	50,000	30,000	—	—
Total number of remaining OSA	400	4,000	500	52,000	28,250	500,000	387,456	93,200	398,000	60,000	60,000
Total number of shares that may be subscribed	120	4,000	500	52,000	19,165	—	122,738	—	—	—	—
Total number of shares that may be subscribed upon exercise of all outstanding stock options (assuming that all conditions for exercising said warrants are met)	400	4,000	500	52,000	28,250	500,000	387,456	93,200	398,000	60,000	60,000

Free shares (AGA)

At a meeting on April 20, 2021, the Executive Board, acting pursuant to the authorization granted by Company's shareholders' meeting on November 30, 2020, granted 362,515 free shares, each with a par value of €0.03 to certain employees of the Group and members of the Executive Board. Such free shares will be subject to a one-year holding period starting at the end of the two-year acquisition period, i.e. starting on April 20, 2021. Such free shares are governed by the 2020 free share plan adopted by the Executive Board on February 9, 2021.

Furthermore, the final vesting of the free shares granted to members of the Executive Board is conditioned upon the determination of the recommended dose for two out of the three patient cohorts enrolled in the NBTXR3-1100 clinical study in order to define the next steps of the development plan in immuno-oncology.

At a meeting on March 11, 2020, the Executive Board, acting pursuant to the authorization granted by the thirty-third resolution of the annual shareholders' meeting dated April 11, 2019, granted 50,000 free shares (the "AGA 2020") with a par value of €0.03 to Anne-Juliette Hermant, a member of the Executive Board.

In addition to the acquisition and holding conditions detailed below, the acquisition of the AGA 2020 granted to Anne-Juliette Hermant is conditioned upon the achievement of positive results in Study 1100 in 2020. The satisfaction of this performance condition was acknowledged by the Executive Board, with the approval of the Supervisory Board, on March 17, 2021.

	AGA 2018-1	AGA 2018-2	AGA 2019-1	AGA 2020	AGA 2021
General Meeting date(s)	June 14, 2017	May 23, 2018	May 23, 2018	April 11, 2019	November 30, 2020
Date granted by the Executive Board	March 6, 2018	July 27, 2018	March 29, 2019	March 11, 2020	April 20, 2021
Total number of authorized AGA	526,800	648,000	648,000	650,000	850,000
Total number of granted AGA	396,250	6,000	438,250	50,000	362,515
Total number of shares that may be subscribed	396,250	6,000	438,250	50,000	362,515
the number of which may be subscribed or purchased by Corporate officers:	77,500	—	150,000	50,000	270,000
Of which Laurent LEVY	77,500	—	150,000	—	180,000
Of which Anne-Juliette HERMANT	—	—	—	50,000	90,000
Number of non-officer beneficiaries (on issue)	78	1	80	—	79
Start date of exercise of AGA	March 6, 2018	July 27, 2018	March 29, 2019	March 11, 2020	April 20, 2021
Expiration date of AGA	*(1)*	July 27, 2020	*(2)*	March 11, 2022	April 20, 2023
Number of shares subscribed	340,583	6,000	369,250	—	—
Total number of canceled or null and void AGA	55,667	—	69,000	—	2,003
Total number of remaining AGA	—	—	—	50,000	360,512
Total number of shares that may be subscribed	—	—	—	50,000	360,512
Duration of the retention period	*(1)*	1 year	*(2)*	1 year	1 year

(1) AGA 2018-1 - conditions of presence and retention of 2 years+1 for French residents or (3+0) for foreign tax residents as of March 6, 2020 (end of the 2-year presence period).

(2) AGA 2019-1 - condition of presence and retention of 2 years + 1 and to make the definitive vesting of the free shares granted to Anne-Juliette Hermant subject to the achievement of the following performance condition: positive results in the study 1100 in 2020

As of December 31, 2021, the social contribution due in respect of the allocation of free shares to Company employees was valued at €362 thousands. This valuation is based on a total valuation of the shares granted amounting to €14,792 thousands, spread over the acquisition period.

Provisions

Provisions for liabilities and charges (€K)	**At the beginning of year**	**Increases**	**Decreases Amounts used**	**Decreases Amounts not used**	**At the end of the year-end**
Currency exchange losses	12	5	12	—	5
Provision for charges	40	10	—	—	50
Tax provision	—	16	—	—	16
TOTAL	**52**	**31**	**12**	**—**	**71**

Provisions for amortization and depreciation (€K)	**At the beginning of year**	**Increases**	**Decrease paid**	**Decrease Not paid**	**At the end of the year-end**
For other financial assets	7	12	7	—	12
For partners' current accounts	189	—	—	—	189
SUBTOTAL	**196**	**12**	**7**	**—**	**201**
TOTAL	**248**	**43**	**19**	**—**	**272**
Of which allocations and operating provisions	—	31	12	—	—
Of which allocations and financial provisions	—	12	7	—	—

The Company recorded a provision for charges of €10 thousand in 2021 relating to a litigation with an employee.

A provision for foreign exchange losses in the amount of 5 K€ has been recorded at December 31, 2021.

At December 31, 2021, a provision for taxes of €16,000 has been recorded. This provision relates to the CET rebate for 2018 and 2019.

Receivables and Liabilities' terms

Receivables (€K)	**Gross amount**	**1 year at most**	**Over 1 year**
Receivables from related interests	2,295	—	2,295
Other non-current financial assets	600	220	379
Receivables from suppliers	3,291	3,291	—
Social security and other social organizations	19	19	—
Income tax	2,273	2,273	—
Value added tax	935	935	—
Miscellaneous government and other public authorities	71	71	—
Group and partners	2,007	—	2,007
Prepaid expenses	2,315	2,315	—
TOTAL	**13,804**	**9,123**	**4,681**
Amount of loans granted during the financial year	—		
Amount of repayments received during the financial year	—		

The research tax credit in respect of 2021 was €2,273 thousand versus €1,858 thousand in respect of 2020.

The Company obtained the refund of the 2020 research tax credit in November 2021.

As of December 31, 2021, the Company books prepaid expenses related to the invoices received for €965 thousand under the MD Anderson agreement. The amount is determined on the basis of patients enrolled. The first enrolments started during the second semester of 2020.

Payables (€K)	**Gross amount**	**1 year at most**	**1 to 5 years**	**Over 5 years**
Loans and liabilities and credits	43,985	7,581	36,404	—
Accounts payable	7,715	7,715	—	—
Amounts due to and from employees	1,531	1,531	—	—
Social security and other social organizations	2,542	2,542	—	—
Value added tax	107	107	—	—
Other taxes and related items	103	103	—	—
Group and partners	32	32	—	—
Other liabilities	400	400	—	—
Deferred income	16,518	—	—	16,518
TOTAL	**72,933**	**20,011**	**36,404**	**16,518**
Loans taken out during the financial year	—			
Loans repaid during the financial year	—			

In July 2013, Bpifrance granted the Company funding for a maximum amount of €2,795 thousand to open a new indication for the NBTXR3 product: primary and secondary liver cancer, via one of its strategic industrial innovation (*Innovation Stratégique Industrielle*, ISI) programs, to accelerate the clinical and industrial development of its NBTXR3 product for this new indication. The funding includes a repayable advance for a maximum of €2,451 thousand (for which repayment is planned between 2022 and 2024) and a subsidy for a maximum of €344 thousand.

As of December 31, 2021, the repayable advance shown as a liability under the heading "borrowings and miscellaneous financial debt" amounts to €2,083 thousand (repayment of which is scheduled between 2022 and 2025).

In July 2016, Nanobiotix obtained an interest-free loan in the amount of €2,000 thousand from BPI France to fund the Phase II/III clinical trial on soft tissue sarcoma.

As of December 31, 2021, €500 thousand had been repaid.

The financing agreement with the EIB, signed in July 2018, allows the Company to borrow up to EUR 40 million in three tranches to finance its NBTXR3-related research, development and innovation activities in various therapeutic indications, subject to the achievement of a set of agreed performance criteria.

This agreement is divided into three tranches:

- A first tranche of €16.0 million, received in October 2018, subject to a fixed interest rate of 6% and to be repaid in a single installment within five years of its receipt;
- A second tranche of €14.0 million, received in March 2019, subject to a fixed interest rate of 5% and to be repaid over five years starting two years after it was obtained (see note 12); and
- A final tranche of €10.0 million, subject to a fixed interest rate of 4%, to be repaid over five years starting one year after it is obtained. The deadline for requesting this third tranche, initially

scheduled as of July 26, 2020, was delayed by 12 months to July 31, 2021. As the conditions have not been met by July 31, 2021, the Company will not request the final tranche of the EIB loan.

As part of this financing agreement, the Company also signed a "royalties agreement" whereby it has agreed to pay the EIB an additional fee based on the consolidated forecasted sales in the six years as of January 1, 2021.

Nanobiotix obtained a €10 million loan under the government-guaranteed loan program to support innovation, broken down as follows:

- €5.0 million received in June 2020 from HSBC (interest-free, repayable in June 2026);
- €5.0 million received in July 2020 from BPI (fixed rate of 2.25%, repayable quarterly in arrears until July 31, 2026).

Long-term accounts receivable

Loans, deposits and other receivables were booked at par value.

Long-term accounts receivables were amortized via provisions to take into account their present value at the close of the accounting period.

Valuation of receivables and liabilities

Receivables and liabilities are booked at par value.

Patient treatment costs were not yet fully invoiced at the time the 2021 annual financial statements were finalized. They were estimated based on the number of patients treated over the past accounting period and provisions were made in accordance with the caution principles and the separation of accounting periods.

Impairment of receivables

Where applicable, receivables are written down via impairment provisions to take into account any collection difficulties they may potentially face.

The receivable of €2,295 thousand for the American subsidiary was not written down despite the net negative position of the subsidiary, given the prospects for collection.

At December 31, 2021, an impairment provision of €189 thousand was recognized against partners' current accounts. This impairment provision concerns the receivable relating to the Group's Spanish subsidiary, Nanobiotix Spain S.L.U.

Available funds in euros

The funds available in cash or at the bank are valued at their par value.

Trade and other receivables

Receivables (€K)	**Amount**
Social security charges - accrued income	2
State - other receivables	71
Total	**72**

Accrued liabilities

Amount of accrued liabilities included in the following balance sheet items (€K)	**Amount**
Miscellaneous loans and financial liabilities	43,985
Accounts payables and related accounts	7,715
Tax and social security liabilities	4,283
Total	**55,983**

Prepaid expenses and deferred income

Prepaid expenses (€K)	**Amount**
Prepaid expenses	2,315
Total	**2,315**

As of December 31, 2021, prepaid expenses mainly relate to:

- research agreements related to MD Anderson agreement (see Note 4.3 – Collaboration Agreement with the University of Texas MD Anderson Cancer Center) for €1.0 million, and
- insurance related to the Directors & Officers for €0.6 million.

Deferred income (€K)	**Amount**
Deferred income	16,518
Total	**16,518**

In May 2021, Nanobiotix announced a partnership with LianBio a biotechnology company dedicated to bringing paradigm-shifting medicines to patients in China and major Asian markets, to develop and commercialize NBTXR3 into Greater China (mainland China, Hong Kong, Taiwan, and Macau), South Korea, Singapore and Thailand.

As of December 31, 2021, a non-refundable upfront payment of $20 million (€16.5 million) has been collected by the Company at the signature of the LianBio Agreement. The Company's obligation to LianBio under this agreement relates to the granting of the distribution license associated with the commitment to exclusively supply the licensed products. The Company's obligation to grant the license cannot be dissociated from its obligation to supply the products, which will only become effective when a marketing authorization is obtained and therefore the right for LianBio to market the products according to the terms of the agreement in Greater China, South Korea, Singapore and Thailand.

Thus, it is only when this authorization is obtained and LianBio begins to commercialize the licensed product in Greater China, South Korea, Singapore and Thailand that the Company will begin to fulfill its obligations and that the revenues related to the initial payment will begin to be earned.

Items related to several balance sheet items

Balance sheet items (€K)	**Amount**
Investment in subsidiaries	4,052
Loan to Nanobiotix Corp.	2,295
Current account - Nanobiotix Corp.	449
Current account - Nanobiotix S.L.U.	189
Current account - Nanobiotix GmbH	(32)
Current account - Curadigm SAS	1,354
Current account - Swiss branch	14

NOTES TO THE INCOME STATEMENT

Revenue

(€K)	Geographic area			
	EU	**France**	**Export**	**Total**
Services	14	105	5	**125**
Other sales	—	—	—	—
Total Revenue	**14**	**105**	**5**	**125**

The Company's revenue results mainly from the re-invoicing of subsidiaries and the sales of associated services in the context of technology transfers.

Revenue corresponds to the fair value of the consideration received, or to be received, for licenses and services sold by the Company. Revenue is recorded net of value added tax, rebates and discounts.

The Company recognizes income when the amount can be reliably valued, when it is probable that the future economic benefits will benefit the Company and that specific criteria have been met for the Company's business.

The Company also invoices services to its four subsidiaries (Nanobiotix Corp, Nanobiotix Spain S.L.U, Nanobiotix Germany GmbH and Curadigm SAS) under services contracts.

Compensation of executives and related parties

(€K)	**Amount**
Company executive and management	1,245
Supervisory fees:	
- Director fees	375
- Consulting fees	—
Total	**1,620**

Average headcount

Average headcount	
Managers	65
Supervisors and technicians	10
Total	**75**

This headcount corresponds to the average number of employees over the accounting period, bound to the Company by an employment agreement. It is equal to the arithmetic average of headcount on the last day of each calendar quarter. It does not include part-time employees.

Independent Auditors' fees

Total Independent auditors' fees in 2021 were as follows:

- €762 thousand for the statutory audit;
- €148 thousand for audit-related services.

COMMITMENTS AND OTHER FINANCIAL INFORMATION

Off-balance sheet commitments related the EIB loan

In the event the EIB loan is repaid early, or in the event of a change of control after repayment of the loan, the amount of royalties due will be equal to the net present value of the royalties as determined by an independent expert, such amount not to be less than €35.0 million.

The EIB finance contract contains covenants that impose restrictions on the operation of the Company's business but no financial covenants that the Company is required to comply with.

Off-balance sheet commitments related the MD Anderson agreement

In January 2019, the Company and the University of Texas MD Anderson Cancer Center, world prominent center of research, education, prevention and care for cancer patients announced a large-scale research collaboration.

The collaboration will initially support nine new Phase I/II clinical trials with Nanobiotix's first-in-class agent NBTXR3 for use in treating six cancer types – head and neck, pancreatic, thoracic, lung, gastrointestinal and genitourinary cancers – involving around 340 patients.

As part of the funding for this collaboration, Nanobiotix is committed to pay approximately $11 million for those clinical trials during the collaboration and made an initial $1.0 million payment at the commencement of the collaboration and a second $1.0 million payment on February 3, 2020. Additional payments will be made in the six months following a patient enrollment, and expense is recorded in the statement of consolidated operations during the course of the collaboration on the basis of patients enrolled during the relevant period, with the balance payable upon enrollment of the final patient for all studies. Nanobiotix may also be required to pay an additional one-time milestone payment upon (i) grant of the first regulatory approval by the Food and Drug Administration in the United States and (ii) the date on which a specified number of patients have been enrolled in the clinical trials. The milestone payment increases on an annual basis ranging from $2.2 million to $16.4 million. The amount will be determined on the basis of patients enrolled in the nine clinical trials at the date of FDA registration.

This number increases every year and varies between $2.2 million (if it had been payable in 2020) and $16.4 million (if payable in 2030).

As of December 31, 2021, €1.8 million have already been invoiced since the beginning of the collaboration and €1.0 million remain in prepaid expenses. An additional payment will also occur in the event of a successful first registration of NBTXR3 with the FDA.

Financial commitments

Commitments given

Commitments given (€K)	**Amount**
Lease for headquarters – Wattignies Rent excluding rental charges (from 7/1/2017 to 6/30/2026)	3,662
Operating lease – Villejuif Rent excluding rental charges (from 6/30/2021 to 6/29/2030)	3,197
Total	**6,859**

Commitments received

In July 2018, the European Investment Bank (EIB) granted Nanobiotix a fixed-rate loan of €40,000 thousand, split into three tranches. The first tranche of €16,000 thousand was drawn down in October 2018. The principal plus accrued interest will be repaid in a single installment in 2023. A second tranche of €14,000 thousand was drawn down in March 2019 and will be repaid in full between 2019 and 2024. The third tranche of €10,000 thousand may be drawn down by Nanobiotix subject to meeting certain performance conditions. The deadline for requesting this third tranche, initially scheduled as of July 26, 2020, was delayed by 12 months to July 31, 2021. As the conditions have not been met by July 31, 2021, the Company will not request the final tranche of the EIB loan.

Pension and retirement commitments

The Company has not signed any specific commitments for pension obligations. Pensions committed are therefore limited to contractual retirement benefits. The collective agreement is the French collective agreement for the manufacture and sale of pharmaceutical products (*"Convention Collective Pharmacie"*).

No provisions for charges related to pension have been recognized for this accounting period.

As of December 31, 2021, the Company's off-balance sheet commitment was €318 thousand, calculated with the following assumptions:

Assessment date	12/31/2021	12/31/2020
Retirement assumptions	*Management: Age 66* *Non-management: Age 64*	*Management: Age 66* *Non-management: Age 64*
Social security contribution rate	42.01%	44%
Discount rate	0.98%	0.33%
Mortality tables	Regulatory table INSEE 2015 -2017	Regulatory table INSEE 2014 -2016
Salary increase rate (including inflation)	Executive: 3% Non-Executive: 2.5%	Executive: 3% Non-Executive: 2.5%
Staff turnover	Constant average rate of 5.86%	Constant average rate of 5.86%
Duration	20 years	17 years

List of subsidiaries and equity investments

Nanobiotix SA has four wholly owned subsidiaries:

- Nanobiotix Corp., wholly owned, with headquarters at 245 Main street, CIC, 3rd floor, Cambridge, Massachusetts, United States.
- Nanobiotix Spain, S.L.U., wholly owned, with headquarters are located at 37, Pas Recoletos 28 004, Madrid, Spain.
- Nanobiotix Germany GmbH, wholly owned, with headquarters at Prinzregentenstraße 11, 80538 Munich, Germany.
- Curadigm SAS, wholly owned, whose registered office is located at 60 rue de Wattignies, 75012 Paris.

Subsidiaries (€K)	Share capital	Shareholders' equity other than share capital	Share held (%)	Gross carrying value of the securities held	Loans and advances granted by the Parent Company, not yet repaid	Current account with the parent company	Revenue excluding taxes for the past year	2021 Net Profit & Loss
Nanobiotix Corp.	1	(1,346)	100%	3,001	2,295	449	—	454
Nanobiotix S.L.U.	3	(164)	100%	3	—	189	—	—
Nanobiotix GmbH	25	11	100%	25	—	(32)	—	4
Curadigm SAS	1,023	(531)	100%	1,023	—	1,354	—	(790)

4.4. STATUTORY AUDITOR'S REPORT ON THE 2021 COMPANY'S ANNUAL FINANCIAL STATEMENTS

GRANT THORNTON
French member of Grant Thornton International

ERNST & YOUNG et Autres

This is a translation into English of the statutory auditors' report on the financial statements of the Company issued in French and it is provided solely for the convenience of English-speaking users. This statutory auditors' report includes information required by European regulations and French law, such as information about the appointment of the statutory auditors or verification of the management report and other documents provided to the shareholders. This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.

Nanobiotix
Year ended December 31, 2021

Statutory auditors' report on the financial statements

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S.A. au capital de € 2 297 184
632 013 843 R.C.S. Nanterre

Commissaire aux Comptes
Membre de la compagnie
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Commissaire aux Comptes
Membre de la compagnie
régionale de Versailles et du Centre

Nanobiotix
Year ended December 31, 2021

Statutory auditors' report on the financial statements

To the Annual General Meeting of Nanobiotix,

Opinion

In compliance with the engagement entrusted to us by your Annual General Meeting, we have audited the accompanying financial statements of Nanobiotix for the year ended December 31, 2021.

In our opinion, the financial statements give a true and fair view of the assets and liabilities and of the financial position of the Company as at December 31, 2021 and of the results of its operations for the year then ended in accordance with French accounting principles.

The audit opinion expressed above is consistent with our report to the Audit Committee.

Basis for Opinion

- **Audit Framework**

We conducted our audit in accordance with professional standards applicable in France. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Our responsibilities under those standards are further described in the *Statutory Auditors' Responsibilities for the Audit of the Financial Statements* section of our report.

- **Independence**

We conducted our audit engagement in compliance with the independence requirements of the French Commercial Code (Code de commerce) and the French Code of Ethics for Statutory Auditors (Code de déontologie de la profession de commissaire aux comptes) for the period from January 1, 2021 to the date of our report, and specifically we did not provide any prohibited non-audit services referred to in Article 5(1) of Regulation (EU) No. 537/2014.

Justification of Assessments - Key Audit Matters

Due to the global crisis related to the COVID-19 pandemic, the financial statements for this period have been prepared and audited under special circumstances. Indeed, this crisis and the exceptional measures taken in the context of the health emergency have had numerous consequences for companies, particularly on their operations and their financing, and have led to greater uncertainties regarding their future prospects. Some of these measures, such as travel restrictions and remote working, have also had an impact on companies' internal organization and on the performance of audits.

It is in this complex, evolving context that, in accordance with the requirements of Articles L. 823-9 and R. 823-7 of the French Commercial Code relating to the justification of our assessments, we inform you of the key audit matters relating to risks of material misstatement that, in our professional judgment, were of most significance in our audit of the financial statements of the current period, as well as how we addressed those risks.

These matters were addressed in the context of our audit of the financial statements as a whole and in forming our opinion thereon, and we do not provide a separate opinion on specific items of the financial statements.

- **Recognition of the revenue from the licensing, development and marketing agreement signed with the company LianBio Oncology Limited in 2021**

Risk identified	Our response
The “Differed revenues” paragraph to the financial statements sets out that your Company signed in 2021 a license, development, and commercialization agreement with LianBio, specialized in biotechnology, that comprises the licensing of rights to technology, research and development programs, participation in the funding of the clinical trials and the exclusive right to buy and sell the licensed products in its territory. Under this license, development and commercialization agreement, your Company received a M$20 non-refundable upfront payment. Your Company evaluated this agreement to determine whether this non-refundable upfront payment constitutes a revenue to differ at year end. Based on its analysis, your Company determined that this non-refundable upfront payment constitutes a revenue to be differed until the occurrence of the first sales of the licensed product. Given the complexity of determining if the conditions requiring deferral of revenue were satisfied, requiring Management’s judgement, we considered the estimation of the revenue recognition as a key audit matter.	Our audit procedures mainly consisted in: • reading the license, development, and commercialization agreement signed in 2021; • familiarizing ourselves with internal control procedures implemented to analyze the license, development, and commercialization agreement and to determine the related accounting treatment; • analyzing the accounting note prepared by Management and its counsels documenting identification and the achievement of the services related to this agreement.

- **Estimation of invoices not received relating to expenses incurred for the performance of clinical trials**

Risk identified	Our response
In the context of the development of its products, your Company carried out clinical trials (phase II/III) in collaboration with contract research organizations. The "Research and development costs" paragraph to the financial statements sets out the method applied to determine an estimation of the costs incurred in that respect according to the to progress of the clinical studies. At year-end, Management estimates the costs not yet invoiced, for each study, taking into account the duration of the treatment as well as each patient's injection date, and records such estimate as accrued expenses for the financial year. The identification of all the clinical trials on-going at year-end, the actual costs incurred and the correct estimate of the accruals at year end constitute a risk. A misstatement would lead to an improper estimate of the amount presented in the "Other purchases and external expenses" the income statement item. Given the complexity of determining the key assumptions used to determine the research and development expenses, and their estimation method at year end requiring Management's judgement, we considered the estimation of the clinical trial accrued expenses incurred as a key audit matter.	Our audit procedures mainly consisted in assessing the valuation and the factors underlying the assumptions used by Management to determine the amount of accrued expenses. In this context, we have: • familiarized ourselves with internal control procedures implemented to identify and estimate the costs to be recognized as accruals at year end; • tested key controls set up regarding the number of patients injected over the year, the update of the average cost per patient based on contracts entered into with clinical trial centers, and the clearance of the provision; • read the significant contracts entered into with clinical trial centers; • analyzed the information drawn up by Management documenting the cost per patient of the trials performed; • tested the invoices billed by the contract research organizations during the subsequent period to assess the consistency of the management's estimate; • reconciled the number of patients recruited and the treatment start dates declared by the clinical trial centers with the number of patients and the treatment dates taken into account to calculate the accrual.

- **Investments in subsidiaries and related receivables valuation**

Risk identified	Our response
The net book value of investments in subsidiaries and related receivables in the balance sheet is MEUR 6,3, i.e. 5% of the total assets. As disclosed in Note "Non-equity securities" to the financial statements, they are valued at their acquisition price. A depreciation is recorded when the present value at the close of the accounting period is higher than the value in use determined based on the valuation of the subsidiaries which is based on cash flow forecasts. We considered the valuation of investments in subsidiaries and related receivables as a key audit matter due to its importance in the balance sheet and the significance of Management's judgements, namely in determining cash flow assumptions used to determine the value in use.	Our assessment of the valuation of investment in subsidiaries and related receivables is based on the process used by the Company to determine the value in use of the investment in subsidiaries. Our audit procedures mainly consisted in: • obtaining the relevant subsidiaries' cash flow forecasts and comparing these forecasts with the corporate business plan approved by Management; • analyzing the appropriateness of the assumptions used with the historical performance of the Company and challenging, per management inquiry, the projected growth of revenue; • performing sensitivity tests on key assumptions used by Management; • including valuation experts in our audit team to assist us in assessing the discount rate based on market benchmarks.

Specific verifications

We have also performed, in accordance with professional standards applicable in France, the specific verifications required by laws and regulations.

- **Information given in the management report and in the other documents with respect to the financial position and the financial statements provided to the shareholders**

We have no matters to report as to the fair presentation and the consistency with the financial statements of the information given in the Executive board's management report and in the other documents with respect to the financial position and the financial statements provided to the shareholders.

We attest the fair presentation and the consistency with the financial statements of the information relating to payment deadlines mentioned in Article D. 441-6 of the French Commercial Code *(Code de commerce).*

- **Report on Corporate Governance**

We attest that the Supervisory Board's Report on Corporate Governance sets out the information required by Articles L. 225-37-4, L. 22-10-10 and L. 22-10-9 of the French Commercial Code *(Code de commerce).*

Concerning the information given in accordance with the requirements of Article L. 22-10-9 of the French Commercial Code *(Code de commerce)* relating to the remuneration and benefits received by, or allocated to the directors and any other commitments made in their favor, we have verified its consistency with the financial statements, or with the underlying information used to prepare these

financial statements and, where applicable, with the information obtained by your Company from companies controlled thereby, included in the consolidation scope. Based on these procedures, we attest the accuracy and fair presentation of this information.

With respect to the information relating to items that your Company considered likely to have an impact in the event of a takeover bid or exchange offer, provided pursuant to Article L. 22-10-11 of the French Commercial Code (*Code de commerce*, we have agreed this information to the source documents communicated to us. Based on these procedures, we have no observations to make on this information.

- **Other information**

In accordance with French law, we have verified that the required information concerning the purchase of investments and controlling interests and the identity of the shareholders and holders of voting rights has been properly disclosed in the management report.

Report on Other Legal and Regulatory Requirements

- **Format of preparation of the financial statements intended to be included in the annual financial report**

We have also verified, in accordance with the professional standard applicable in France relating to the procedures performed by statutory auditors regarding the annual prepared in the European single electronic format, that the preparation of the financial statements intended to be included in the annual financial report mentioned in Article L. 451-1-2, I of the French Monetary and Financial Code (*Code monétaire et financier*), prepared under the Chairman of the Executive Board's responsibility, complies with the single electronic format defined in Commission Delegated Regulation (EU) No. 2019/815 of December 17, 2018.

On the basis of our work, we conclude that the preparation of the financial statements intended to be included in the annual financial report complies, in all material respects, with the European single electronic format.

We have no responsibility to verify that the financial statements that will ultimately be included by your Company in the annual financial report filed with the AMF (*Autorité des marchés financiers)* agree with those on which we have performed our work.

- **Appointment of the Statutory Auditors**

We were appointed as statutory auditors of Nanobiotix by your Annual General Meeting held on June 14, 2017 for GRANT THORNTON and May 4, 2012 for ERNST & YOUNG et Autres.

As at December 31, 2021, GRANT THORNTON was in the fifth year of total uninterrupted engagement and ERNST & YOUNG et Autres in its tenth year, including nine years since the securities of the Company were admitted to trading on a regulated market.

Responsibilities of Management and Those Charged with Governance for the Financial Statements

Management is responsible for the preparation and fair presentation of the financial statements in accordance with French accounting principles and for such internal control as Management determines is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, Management is responsible for assessing the Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless it is expected to liquidate the Company or to cease operations.

The Audit Committee is responsible for monitoring the financial reporting process and the effectiveness of internal control and risk management systems and where applicable, its internal audit, regarding the accounting and financial reporting procedures.

The financial statements were approved by the Executive Board.

Statutory Auditors' Responsibilities for the Audit of the Financial Statements

- **Objectives and audit approach**

Our role is to issue a report on the financial statements. Our objective is to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement. Reasonable assurance is a high level of assurance but is not a guarantee that an audit conducted in accordance with professional standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users made on the basis of these financial statements.

As specified in Article L. 823-10-1 of the French Commercial Code *(Code de commerce)*, our statutory audit does not include assurance on the viability of the Company or the quality of management of the affairs of the Company.

As part of an audit conducted in accordance with professional standards applicable in France, the statutory auditor exercises professional judgment throughout the audit and furthermore:

- Identifies and assesses the risks of material misstatement of the financial statements, whether due to fraud or error, designs and performs audit procedures responsive to those risks, and obtains audit evidence considered to be sufficient and appropriate to provide a basis for his opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.

- Obtains an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal control.

- Evaluates the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by Management in the financial statements.

- Assesses the appropriateness of Management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Company's ability to continue as a going concern. This assessment is based on the audit evidence obtained up to the date of his audit report. However, future events or conditions may cause the Company to cease to continue as a going concern. If the statutory auditor concludes that a material uncertainty exists, there is a requirement to draw attention in the audit report to the related disclosures in the financial statements or, if such disclosures are not provided or inadequate, to modify the opinion expressed therein.

- Evaluates the overall presentation of the financial statements and assesses whether these statements represent the underlying transactions and events in a manner that achieves fair presentation.

▪ **Report to the Audit Committee**

We submit to the Audit Committee a report which includes in particular a description of the scope of the audit and the audit program implemented, as well as the results of our audit. We also report significant deficiencies, if any, in internal control regarding the accounting and financial reporting procedures that we have identified.

Our report to the Audit Committee includes the risks of material misstatement that, in our professional judgment, were of most significance in the audit of the financial statements of the current period and which are therefore the key audit matters that we are required to describe in this report.

We also provide the Audit Committee with the declaration provided for in Article 6 of Regulation (EU) No. 537/2014, confirming our independence within the meaning of the rules applicable in France as set out in particular in Articles L. 822-10 to L. 822-14 of the French Commercial Code *(Code de commerce)* and in the French Code of Ethics for Statutory Auditors *(Code de déontologie de la profession de commissaire aux comptes)*. Where appropriate, we discuss with the Audit Committee the risks that may reasonably be thought to bear on our independence, and the related safeguards.

Neuilly-sur-Seine and Paris-La Défense, April 8, 2022

The Statutory Auditors
French original signed by

GRANT THORNTON
French member of Grant Thornton International

Samuel Clochard

ERNST & YOUNG et Autres

Cédric Garcia

5. COMPANY AND CAPITAL INFORMATION

5.1. REGISTERED CAPITAL

5.1.1. Amount of the share capital

As of the date of the Universal Registration Document, the share capital of the Company amounted to €1,046,276.16 divided into 34,875,872 ordinary shares fully subscribed and paid with a nominal value of €0.03 per share.

As of December 31, 2021, the share capital amounted to €1,044,776.16 divided into 34,825,872 ordinary shares fully subscribed and paid with a nominal value of €0.03 per share.

5.1.2. Non-equity securities

None.

5.1.3. Acquisition by the Company of its own shares

5.1.3.1. Share redemption program

The Company's ordinary shareholders' meeting dated April 28, 2021 authorized, for a duration eighteen months, the Executive Board to implement a share buy-back program (*programme de rachat d'actions*) in compliance with article L. 22-10-62 et seq. of the French Commercial Code and European Regulation n 596/2014 on Market Abuse (MAR) and market practices accepted by the *Autorité des marchés financiers*. The main terms of this authorization are as follows:

Maximum number of shares that can be redeemed: 10% of the number of shares comprising the share capital at any time, being specified that (i) when shares are acquired for the purpose of promoting the liquidity of the Company's shares, the number of shares taken into account for the calculation of this limit corresponds to the number of shares purchased less the number of shares resold during the duration of the authorization, and (ii) when they are acquired with a view to hold them and subsequently delivering them in payment or exchange in connection with a merger, split or contribution in kind, the number of shares acquired shall not exceed 5% of the total number of shares.

Share redemption objectives:

- Ensuring the liquidity of the Company's shares under a liquidity contract with an investment service provider;
- Respecting obligations related to stock-options programs, free shares plans, employee saving plans or other equity allowances to employees and officers of the Company or related companies;
- Delivering shares following the exercise of rights attached to securities giving access to capital;
- Acquiring shares with a view to retaining them and subsequently using them as payment or exchange in connection with potential external growth transactions, in compliance in particular with stock market regulations ; or
- Cancel all or part of the shares so redeemed as part of a share capital reduction.

Maximum purchase price: €60 per share, excluding fees and commissions and adjustments taking into account equity transactions, if any; Maximum amount of funds that may be invested in the redemption of shares: €20,000,000. Shares thus redeemed may be cancelled. As of the date of the Universal Registration Document, this share buy-back program was used exclusively in the context of a liquidity contract entered into on October 23, 2012 with Gilbert Dupont as amended on November 30, 2018 – see below.

5.1.3.2. Liquidity contract with Gilbert Dupont

The aforementioned liquidity contract entered into for a period of one year, renewable annually by tacit agreement, relates to the Company's shares listed on Compartment B of the regulated market of Euronext in Paris. Upon signing the liquidity contract, an amount of €300,000 was allocated to the liquidity account. As of the date of the Universal Registration Document, the resources that appear on the liquidity account set up under this contract represented €178,708.50 and 15,456 shares of the Company, corresponding to less than 0.1% of its share capital.

5.1.3.3. Employee equity allocations

During the financing year ended on December 31, 2021, the Company did not redeem any of its own shares in view of allocating them to its employees in connection with a stock-option program, free share plan, employee saving plan or other equity allocations to employees and officers of the Company or related companies.

A report of all the transactions carried out between December 31, 2020 and December 31, 2021 under the share buy-back program is as follows:

	From December 31, 2020 to December 31, 2021
Number of securities purchased	543,595
Average price	€11.62
Volume traded for purchase	6,343,850

Number of securities sold	542,422
Average price	€11.74
Volume traded for sale	6,349,161

	Situation as of February 28, 2022
Number of shares held	15,072
Portfolio book value	102,852
Portfolio market value	106,182

The treasury shares are accounted for in fixed assets and reduced equity (see note 7 to the consolidated financial statements for the financial year ended December 31, 2021 prepared under IFRS, in Section 4.1 of the Universal Registration Document).

5.1.4. Securities giving access to share capital

As of the date of the Universal Registration Document, there are four different types of securities and other valid instruments entitling their holders to a stake in the Company's share capital (founders' warrants, warrants, stock options and free shares). The amounts and characteristics of these instruments are summarized below.

5.1.4.1. Founders' warrants (bons de souscription de parts de créateur d'entreprise or BSPCE)

Term of the BSPCEs

The term of each BSPCE is 10 years from the date of grant by the Executive Board. Any BSPCEs not exercised by this date will automatically lapse. In addition, unless otherwise decided by the Executive Board and the Supervisory Board, BSPCEs may be exercised by their holders or assigns six months from (i) the death or disability of the holder or (ii) the termination of the holder from employment or corporate office within the Group, failing which the BSPCEs will lapse.
By way of exception, the Executive Board decided to lift, for three of our employees and for Bernd Muehlenweg and Philippe Mauberna, former members of the executive board, the continued service condition, and, where applicable for Bernd Muehlenweg, the performance conditions to which the exercise of certain BSPCEs was subject, notwithstanding the termination of their employment agreement and/or corporate office.

Change of control

In the event of a change of control of the Company, unless otherwise decided by the Executive Board and Supervisory Board, the right of holders to exercise outstanding BSPCEs will be accelerated so that all of such shares may be exercised with effect on the day of the change of control. Any BSPCE not exercised for any reason on or prior to the day of the change of control will automatically lapse after this date.

	BSPCE 2012-2	BSPCE 08-2013	BSPCE 09-2014	BSPCE 2015-1	BSPCE 2015-3
Date of the shareholders' meeting	**5/4/2012**	**6/28/2013**	**6/18/2014**	**6/18/2014**	**6/18/2014**
Date of grant by the Executive Board	**12/18/2012**	**8/28/2013**	**9/16/2014**	**2/10/2015**	**6/10/2015**
Total number of BSPCEs authorized	500,000	500,000	450,000	450,000	450,000
Total number of BSPCEs granted	100,000	50,000	97,200	71,650	53,050
Total number of shares to which the BSPCE were likely to give right on the date of their grant	100,000	50,000	97,200	71,650	53,050
the number of which that may be subscribed by corporate officers:	0	0	21,000	24,000	0
including Laurent LEVY	0	0	21,000	24,000	0
Number of beneficiaries who are not corporate officers	2	1	30	13	42
Starting date for the exercise of the BSPCE	12/18/12	08/28/13	09/16/15	02/10/16	06/10/16
BSPCE expiry date	12/18/22	08/28/23	09/16/24	02/10/25	06/10/25
BSPCE exercise price	€6.63	€5.92	€18.68	€18.57	€20.28
Terms of exercise [3]	(1)	(1)	(1)	(1)	(1)
Number of shares subscribed as of the date of the Universal Registration Document	0	0	0	0	0
Total number of BSPCEs lapsed or cancelled as of the date of the Universal Registration Document	0	0	11,050	3,200	22,700
Total number of BSPCEs outstanding as of the date of the Universal Registration Document	100,000	50,000	86,150	68,450	30,350
Total number of shares available for subscription as of the date of the Universal Registration Document	100,000	50,000	86,150	68,450	30,350
Maximum total number of shares that may be subscribed for upon exercise of all outstanding BSPCEs (assuming that all the conditions for the exercise of said BSPCEs are met)	100,000	50,000	86,150	68,450	30,350

	BSPCE 2016 Ordinary	BSPCE 2016 Performance	BSPCE 2017 Ordinary	BSPCE 2017
Date of the shareholders' meeting	**06/25/15**	**06/25/15**	**06/23/16**	**06/23/16**
Date of grant by the Executive Board	**02/02/16**	**02/02/16**	**01/07/17**	**01/07/17**
Total number of BSPCEs authorized	450,000	450,000	450,000	450,000
Total number of BSPCEs granted	126,400	129,250	117,650	80,000
Total number of shares to which the BSPCE were likely to give right on the date of their grant	126,400	129,250	117,650	80,000
the number of which that may be subscribed by corporate officers:	23,500	23,500	26,400	32,000
including Laurent LEVY	23,500	23,500	26,400	32,000
Number of beneficiaries who are not corporate officers	43	50	42	3
Starting date for the exercise of the BSPCE	02/02/17	02/02/16	01/08/18	01/07/17
BSPCE expiry date	02/02/26	02/02/26	01/07/27	01/07/27
BSPCE exercise price	€14.46	€14.46	€15.93	€15.93
Terms of exercise [3]	(1)	(2)	(1)	(1)
Number of shares subscribed as of the date of the Universal Registration Document	333	0	0	0
Total number of BSPCEs lapsed or cancelled as of the date of the Universal Registration Document	25,500	28,976	18,150	0
Total number of BSPCEs outstanding as of the date of the Universal Registration Document	100,567	100,274	99,500	80,000
Total number of shares available for subscription as of the date of the Universal Registration Document	100,567	38,170	99,500	80,000
Maximum total number of shares that may be subscribed for upon exercise of all outstanding BSPCEs (assuming that all the conditions for the exercise of said BSPCEs are met)	100,567	100,274	99,500	80,000

(1) As of the date of the Universal Registration Document, all BSPCEs may be exercised.

(2) The BSPCE 2016 Performance may be exercised from their date of grant, subject to reaching the following thresholds:

- *up to 15% of the BSPCE 2016 Performance may be exercised if the number of patients under treatment is at least equal to 200,*
- *additional 15% of the BSPCE 2016 Performance may be exercised if the number of patients under treatment is at least equal to 300,*
- *additional 30% of the BSPCE 2016 Performance may be exercised if the number of patients under treatment is at least equal to 400, and*
- *the balance, i.e. 40% of the BSPCE 2016 Performance, may be exercised if the number of patients under treatment is at least equal to 500.*

As of the date of the Universal Registration Document, 30% of the BSPCE 2016 Performance could be exercised. On July 23, 2019, the Executive Board decided to lift, for Mr. Bernd Muehlenweg (a member of the Executive Board until June 20, 2019), the performance conditions to which the exercise of his BSPCE 2016 Performance was subject, notwithstanding the termination of his employment agreement and his corporate office within the Company. Accordingly, all of Mr. Bernd Muehlenweg's BSPCE 2016 Performance may be exercised.

(3) See also the paragraphs "Term of issue of the BSPCE" and "Change of control" above.

5.1.4.2. Warrants (bons de souscription d'actions or BSAs)

Term of issue of the BSAs

The term of warrants granted is 10 years from the date of grant by the Executive Board, except for the warrants granted on March 6, 2018, the term of which is five years from the date of grant by the Executive Board.

In addition, unless otherwise decided by the Supervisory Board and the Executive Board, the BSA 2017 must be exercised within six months from (i) the death or disability of the holder or (i) the termination of the holder from employment or corporate office within the Group, failing which the BSAs will lapse.

Change of control

In the event of a change of control of the Company, unless otherwise decided by the Executive Board and Supervisory Board, the right of holders to exercise outstanding BSA 2015-1 and BSAs issued from January 7, 2017 onwards will be accelerated so that all of such warrants may be exercised with effect on the day of the change of control (subject, if applicable, to continued service in the Group). Any BSAs not exercised for any reason on or prior to the day of the change of control will automatically lapse after this date. Holders of BSA 2015-2(a) may similarly exercise all or part of their BSA 2015-2(a) in the event of a change of control of the Company.

	BSA 04-12	BSA 2013	BSA 2014	BSA 2015-1	BSA 2015-2 (a)	BSA 2017	BSA 2018
Date of the shareholders' meeting	**05/04/12**	**05/04/12**	**06/18/14**	**06/18/14**	**06/18/14**	**06/23/16**	**06/14/17**
Date of grant by the Executive Board	**05/04/12**	**04/10/13**	**09/16/14**	**02/10/15**	**06/25/15**	**01/07/17**	**03/06/18**
Maximum number of BSAs authorized	200,000	200,000	100,000	100,000	100,000	100,000	116,000
Total number of BSAs granted	52,500	10,000	14,000	26,000	64,000	18,000	18,000
Number of shares to which the BSA were likely to give right on the date of their grant	52,500	10,000	14,000	26,000	64,000	18,000	18,000
including the total number of shares that may subscribed by the corporate officers of the Company	22,500	—	8,000	15,000	—	13,280	12,700
Relevant officers:							
Anne-Marie GRAFFIN	—	—	—	5,000	—	3,820	2,900
Enno SPILLNER	—	—	—	3,000	—	3,820	4,000
Alain HERRERA	—	—	4,000	5,000	—	2,820	2,900
Gary PHILLIPS	—	—	—	—	—	—	—
Christophe DOUAT (observer)	22,500	—	4,000	2,000	—	2,820	2,900
Number of beneficiaries who are not corporate officers	1	1	1	2	1	1	1
Starting date for the exercise of the BSA	10/23/13	04/30/14	09/16/14	02/10/15	06/25/15	01/07/17	03/06/18
BSA expiry date (6)	05/04/22	04/10/23	09/16/24	02/10/25	06/25/25	01/07/22	03/06/23
BSA issue price	€0.60	€2.50	€4.87	€4.87	€5.00	€2.26	€1.62
Exercise price per BSA	€6.00	€6.37	€17.67	€17.67	€19.54	€15.76	€13.55
Terms of exercise	(1)	(1)	(2)	(2)	(3)	(2)	(2)
Number of shares subscribed as of the date of the Universal Registration Document	22,500	—	—	—	—	—	—
Total number of forfeited or cancelled BSAs as of the date of the Universal Registration Document	—	4,000	4,000	5,000	—	18,000	0
Total number of BSAs outstanding as of the date of the Universal Registration Document	30,000	6,000	10,000	21,000	64,000	—	18,000
Total number of shares available for subscription as of the date of the Universal Registration Document (considering the conditions of exercise of the BSAs)	30,000	6,000	—	—	—	—	—
Maximum total number of shares that may be subscribed for upon exercise of all outstanding BSAs (assuming that all the conditions for the exercise of said BSAs are met)	30,000	6,000	10,000	21,000	64,000	—	18,000

	BSA 2018-1	BSA 2018-2	BSA 2019-1	BSA 2020	BSA 2021-1	BSA 2021-2
Date of the shareholders' meeting	**06/14/17**	**05/23/18**	**05/23/18**	**04/11/19**	**11/30/20**	**11/30/20**
Date of grant by the Executive Board	**03/06/18**	**07/27/18**	**03/29/19**	**03/17/20**	**04/20/21**	**04/20/21**
Maximum number of BSAs authorized	116,000	140,000	140,000	500,000	650,000	650,000
Total number of BSAs granted	10,000	5,820	18,000	18,000	48,103	30,000
Number of shares to which the BSA were likely to give right on the date of their grant	10,000	5,820	18,000	18,000	48,103	30,000
including the total number of shares that may subscribed by the corporate officers of the Company	—	—	12,700	14,024	—	—
Relevant officers:						
Anne-Marie GRAFFIN	—	—	2,900	3,843	—	—
Enno SPILLNER	—	—	4,000	3,829	—	—
Alain HERRERA	—	—	2,900	3,195	—	—
Gary PHILLIPS	—	—	—	—	—	—
Christophe DOUAT (observer)	—	—	2,900	3,157	—	—
Number of beneficiaries who are not corporate officers	1	1	1	1	1	1
Starting date for the exercise of the BSA	03/06/18	07/27/18	03/29/19	03/17/20	04/20/21	04/20/21
BSA expiry date (6)	03/06/23	07/27/28	03/29/29	03/17/30	04/20/31	04/20/31
BSA issue price	€1.62	€2.36	€1.15	€0.29	€2.95	€0.68
Exercise price per BSA	€13.55	€16.10	€11.66	€6.59	€13.47	€13.64
Terms of exercise	(4)	(4)	(2)	(2)	(5)	(6)
Number of shares subscribed as of the date of the Universal Registration Document	—	—	—	—	—	—
Total number of forfeited or cancelled BSAs as of the date of the Universal Registration Document	—	—	—	—	33,672	—
Total number of BSAs outstanding as of the date of the Universal Registration Document	10,000	5,820	18,000	18,000	14,431	30,000
Total number of shares available for subscription as of the date of the Universal Registration Document (considering the conditions of exercise of the BSAs)	—	—	—	—	—	—
Maximum total number of shares that may be subscribed for upon exercise of all outstanding BSAs (assuming that all the conditions for the exercise of said BSAs are met)	10,000	5,820	18,000	18,000	14,431	30,000

(1) As of the date of the Universal Registration Document, all of the BSAs may be exercised, provided that, on the day the BSA is exercised, the relevant holder, when a Supervisory Board member, has attended at least 75% of the Supervisory Board meetings held during the period preceding the exercise of the warrants or, as the case may be, the date the holder ceases to be part of the Group.

(2) As of the date of the Universal Registration Document, all of the BSAs may be exercised, provided that, on the day the BSA is exercised, (i) the relevant holder, when a Supervisory Board member, has attended at least 75% of the Supervisory Board meetings held during the period preceding the exercise of the warrants or, as the case may be, the date the holder ceases to be part of the Group (ii) the market value of a Nanobiotix share shall be at least equal to €40.

(3) As of the date of the Universal Registration Document, all of the BSAs may be exercised, provided that on the day the BSA is exercised, the market value of a Nanobiotix share shall be at least equal to €50.

(4) As of the date of the Universal Registration Document, all BSAs may be exercised, provided that on the day the BSA is exercised, the market value of a Nanobiotix share shall be at least equal to €40.

(5) As of the date of the Universal Registration Document, all outstanding BSAs may be exercised, provided that, on the day the BSA is exercised, (i) the relevant holder has attended at least 75% of the Supervisory Board meetings held during the 12-months preceding the exercise of the warrants or, as the case may be, the date the holder ceases to be part of the Group, and (ii) the recommended dose for two out of the three patient cohorts enrolled in Study 1100 has been determined in order to define the next steps of the immuno-oncology development plan, it being specified that (i) the Executive Board, with the prior approval of the Supervisory Board, shall acknowledge the satisfaction of such condition and (ii) such condition shall automatically be waived in the event of a change of control.

(6) As of the date of the Universal Registration Document, all BSAs may be exercised, subject to the satisfaction of a performance condition to be acknowledged by the Executive Board, with the prior approval of the Supervisory Board.

(7) See also the "Term of issue of the BSAs" and "Change of control" paragraphs above.

5.1.4.3. Stock options (Options or OSAs)

Term of issue of the Options

The term of the Options is 10 years from the date of grant by the Executive Board. Unless otherwise decided by the Executive Board and the Supervisory Board, the Options may be exercised by their holders or assigns six months from (i) the death or disability of the holder or (ii) the termination of the holder from employment or corporate office within the Group, failing which the Options will lapse (in the specific case of termination, this period is reduced to three (3) months for Group employees having their tax residence in the United States of America and benefiting from incentive stock options).

By way of exception, the Executive Board decided to lift, for two of our employees and Philippe Mauberna, a former member of the Executive Board, the continued service condition to which the exercise of their Options is subject, notwithstanding the termination of their corporate office and/or employment agreement. The Executive Board also decided to extend the exercise period of the vested stock options of an employee having left the Group by two years. In addition, the Executive Board decided to accelerate, as from June 30, 2021, the vesting of the OSA 2020 Philippe Mauberna holds, enabling him to exercise all of them, in the context of his departure from the Company.

Change of control

In the event of a change of control of the Company, unless otherwise decided by the Executive Board and Supervisory Board, the right of holders to exercise the outstanding Options will be accelerated so that all of such shares may be exercised with effect on the day of the change of control. Any Options not exercised for any reason on or prior to the day of the change of control will automatically lapse after this date.

	OSA 2016-1 Performance	OSA 2016-2	OSA 2017 Ordinary	OSA 2018	OSA 2019-1	OSA 2019 LLY
Date of the shareholders' meeting	**06/25/15**	**06/23/16**	**06/23/16**	**06/14/17**	**05/23/18**	**04/11/19**
Date of grant by the Executive Board	**02/02/16**	**11/03/16**	**01/07/17**	**03/06/18**	**03/29/19**	**10/24/19**
Total number of OSAs authorized	450,000	450,000	450,000	526,800	648,000	500,000
Total number of OSAs granted	6,400	4,000	3,500	62,000	37,500	500,000
Total number of shares to which the OSAs were likely to give right on the date of their grant	6,400	4,000	3,500	62,000	37,500	500,000
including the number that may be subscribed or purchased by corporate officers:	—	—	—	—	—	500,000
including Laurent Levy	—	—	—	—	—	500,000
including Bart Van Rhijn	—	—	—	—	—	—
including Anne-Juliette Hermant	—	—	—	—	—	—
Number of beneficiaries who are not corporate officers	2	1	2	5	12	—
Starting date for the exercise of the OSA	02/02/17	11/03/17	01/08/18	03/07/19	03/30/21	10/24/19
OSA expiry date	02/02/26	11/03/26	01/07/27	03/06/28	03/29/29	10/24/29
Exercise price per OSA	€13.05	€14.26	€14.97	€12.87	€11.08	€6.41
Terms of exercise [8]	(1)	(2)	(3)	(4)	(5)	(6)
Number of shares subscribed as of the date of the Universal Registration Document	—	—	—	—	—	—
Total number of lapsed or cancelled OSAs as of the date of the Universal Registration Document	6,000	—	3,000	10,000	10,084	—
Total number of OSAs outstanding as of the date of the Universal Registration Document	400	4,000	500	52,000	27,416	500,000
Maximum number of shares available for subscription as of the date of the Universal Registration Document (given the vesting conditions of the OSAs)	120	4,000	500	52,000	27,416	—
Maximum total number of shares that may be subscribed for upon exercise of all outstanding OSAs (assuming that all the conditions for the exercise of said OSAs are met)	400	4,000	500	52,000	27,416	500,000

	OSA 2020	OSA 2021-04 Ordinary	OSA 2021-04 Performance	OSA 2021-06 Performance	OSA 2021-06 Ordinary
Date of the shareholders' meeting	**04/11/19**	**11/30/20**	**11/30/20**	**11/30/20**	**04/28/21**
Date of grant by the Executive Board	**03/11/20**	**04/20/21**	**04/20/21**	**06/21/21**	**06/21/21**
Total number of OSAs authorized	500,000	850,000	1,000,000	1,000,000	850,000
Total number of OSAs granted	407,972	143,200	428,000	60,000	60,000
Total number of shares to which the OSAs were likely to give right on the date of their grant	407,972	143,200	428,000	60,000	60,000
including the number that may be subscribed or purchased by corporate officers:	180,000	—	240,000	60,000	60,000
including Laurent Levy	120,000	—	180,000	—	—
including Bart Van Rhijn	—	—	—	60,000	60,000
including Anne-Juliette Hermant	60,000	—	60,000	—	—
Number of beneficiaries who are not corporate officers	104	13	14	—	—
Starting date for the exercise of the OSA	03/11/21	04/20/22	04/20/22	06/21/22	06/21/22
OSA expiry date	03/11/30	04/20/31	04/20/31	06/21/31	06/21/31
Exercise price per OSA	€6.25	€13.74	€13.74	€12.99	€12.99
Terms of exercise [8]	(7)	(8)	(9)	(10)	(11)
Number of shares subscribed as of the date of the Universal Registration Document	—	—	—	—	—
Total number of lapsed or cancelled OSAs as of the date of the Universal Registration Document	22,217	99,000	60,000	—	—
Total number of OSAs outstanding as of the date of the Universal Registration Document	385,755	44,200	368,000	60,000	60,000
Maximum number of shares available for subscription as of the date of the Universal Registration Document (given the vesting conditions of the OSAs)	279,656	—	—	—	—
Maximum total number of shares that may be subscribed for upon exercise of all outstanding OSAs (assuming that all the conditions for the exercise of said OSAs are met)	385,755	44,200	368,000	60,000	60,000

(1) The OSA 2016-1 Performance may be exercised under the following conditions:

- *up to 15% of the OSA 2016-1 Performance may be exercised if the number of patients under treatment is at least equal to 200,*
- *an additional 15% of the OSA 2016-1 Performance may be exercised if the number of patients under treatment is at least equal to 300,*
- *an additional 30% of the OSA 2016-1 Performance may be exercised if the number of patients under treatment is at least equal to 400, and*
- *the balance, i.e. 40% of the OSA 2016-1 Performance, may be exercised if the number of patients under treatment is at least equal to 500.*

As of the date of the Universal Registration Document, 30% of the OSA 2016-1 Performance may be exercised.

(2) As of the date of the Universal Registration Document, all of the OSA 2016-2 may be exercised.

(3) As of the date of the Universal Registration Document, all of the OSA 2017 Ordinary may be exercised.

(4) As of the date of the Universal Registration Document, all of the OSA 2018 may be exercised, it being specified that the exercise of any OSA 2018 remains subject to the ongoing presence of the beneficiary within the Group (except for one employee).

(5) As of the date of the Universal Registration Document, all of the OSA 2019-1 may be exercised, it being specified that, the exercise of any OSA 2019-1 remains subject to the ongoing presence of the beneficiary within the Group.

(6) The OSA LLY 2019 may be exercised under the following conditions:

- *10% of the OSA LLY 2019 may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €24,*
- *An additional 10% of the OSA LLY 2019 may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €30,*
- *An additional 40% of the OSA LLY 2019 may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €40,*
- *An additional 40% of the OSA LLY 2019 may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €60.*

(7) As of the date of the Universal Registration Document, two-thirds of the OSA 2020 may be exercised and the balance, i.e., one-third of the OSA 2020, may be exercised as from March 11, 2023, subject to each increment of the ongoing presence of the beneficiary within the Group. The exercise of the OSA 2020 granted to members of the Executive Board and Alain Dostie, an employee, is also subject to the achievement of positive results in the 1100 study in 2020. The satisfaction of this performance condition was acknowledged by the Executive Board, with the approval of the Supervisory Board, on March 17, 2021.

By way of exception, on April 6, 2021, the Executive Board decided to accelerate the vesting of the 60,000 OSA 2020 granted to Philippe Mauberna, a former member of the Executive Board, effective June 30, 2021, enabling him to exercise all of them.

(8) As of the date of the Universal Registration Document, none of the OSA 2021-04 Ordinary may be exercised. The OSA 2021-04 Ordinary may be exercised as follows:

- *up to one-third of the OSA 2021-04 Ordinary as from April 20, 2022;*
- *an additional one-third of the OSA 2021-04 Ordinary as from April 20, 2023; and*
- *the balance, i.e., one-third of the OSA 2021-04 Ordinary as from April 20, 2024,*

subject to, for each increment, a continued service condition. In addition, the exercise of the OSA 2021-04 Ordinary granted to members of the Executive Board is subject to the determination of the recommended dose for two of the three patient cohorts enrolled in the NBTXR3-1100 clinical study, in order to be able to define the next stage of the development plan in immuno-oncology before April 20, 2022. The satisfaction of this performance condition shall be acknowledged by the Executive Board with the approval of the Supervisory Board.

(9) The OSA 2021-04 Performance may be exercised under the following conditions:

- *10% of the OSA 2021-04 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €24;*
- *an additional 10% of the OSA 2021-04 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €30;*
- *an additional 40% of the OSA 2021-04 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €40;*
- *an additional 40% of the OSA 2021-04 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €60;*

it being specified that (i) among such OSA 2021-04 Performance that may be exercised, and subject to, for each increment, a continued service condition, their holders may only exercise (x) up to 10% of such OSA 2021-04 Performance as from April 20, 2022, (y) an additional 30% of such OSA 2021-04 Performance as from April 20, 2023, and (z) the balance, i.e., 60% of such OSA 2021-04 Performance as from April 20, 2024 and (ii) such additional vesting condition shall be automatically waived in the event of a change of control. In addition, the exercise of the OSA 2021-04 Performance granted to members of the Executive Board is subject to the determination of the recommended dose for two of the three patient cohorts enrolled in the NBTXR3-1100 clinical study, in order to be able to define the next stage of the development plan in immuno-oncology before April 20, 2022. The satisfaction of this performance condition shall be acknowledged by the Executive Board with the approval of the Supervisory Board.

(10) The OSA 2021-06 Performance may be exercised under the following conditions:

- *10% of the OSA 2021-06 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €24;*
- *an additional 10% of the OSA 2021-06 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €30;*
- *an additional 40% of the OSA 2021-06 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €40; and*
- *an additional 40% of the OSA 2021-06 Performance may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext in Paris reaches €60,*

it being specified that (i) among such OSA 2021-06 Performance that may be exercised, and subject to, for each increment, a continued service condition, their holders may only exercise (x) up to 10% of such OSA 2021-06 Performance as from June 21, 2022, (y) an additional 30% of such OSA 2021-06 Performance as from June 21, 2023 and (z) the balance, i.e., 60% of such OSA 2021-06 Performance as from June 21, 2024 and (ii) such additional vesting condition shall be automatically waived in the event of a change of control. The exercise of the OSA 2021-06 Performance is also subject to the determination of the recommended dose for two of the three patient cohorts enrolled in the NBTXR3-1100 clinical study, in order to be able to define the next stage of the development plan in immuno-oncology before June 21, 2022. The satisfaction of this performance condition shall be acknowledged by the Executive Board with the approval of the Supervisory Board.

(11) As of the date of the Universal Registration Document, none of the OSA 2021-06 Ordinary may be exercised. The OSA 2021-06 Ordinary may be exercised as follows:

- *up to one-third of the OSA 2021-06 Ordinary as from June 21, 2022;*
- *an additional one-third of the OSA 2021-06 Ordinary as from June 21, 2023; and*
- *the balance, i.e., one-third of the OSA 2021-06 Ordinary as from June 21, 2024,*

subject to, for each increment, a continued service condition. The exercise of the OSA 2021-06 Ordinary is also subject to the determination of the recommended dose for two of the three patient cohorts enrolled in the NBTXR3-1100 clinical study, in order to be able to define the next stage of the development plan in immuno-oncology before June 21, 2022.

(12) See also the "Term of Issue of the OSAs" and "Change of control" paragraphs above.

5.1.4.4. Free shares (attribution d'actions gratuites or AGA)

Continued service condition

The AGA 2020 and the AGA 2021 are subject to continued service within the Group during the acquisition period (*période d'acquisition*, at the end of which the AGA will be definitively acquired) (i.e., for the AGA 2020, until March 11, 2022, and, for the AGA 2021, until April 20, 2023), it being specified that, failing such continued service, the beneficiary definitively and irrevocably loses his or her right to acquire the relevant AGA 2020 or AGA 2021.

Furthermore, in the event of disability or death of a beneficiary before the end of the acquisition period, the relevant free shares shall be definitely acquired at, respectively, the date of disability or the date of the request of allocation made by his or her beneficiary in the framework of the inheritance, provided that such request is made within six months from the date of death.

Change of control

In the event of a change of control of the Company, unless otherwise decided by the Executive Board and Supervisory Board, all of the AGAs shall be completely and definitely acquired:

1. For French tax residents, (i) if the change of control of the Company occurs before or on the first anniversary date of the grant, on the first anniversary date of the grant and (ii) if the change of control occurs after the first anniversary of grant, on the date of the change of control, it being specified that, in both cases, the relevant free shares will then be subject to a holding period until the second anniversary of the grant.
2. For foreign tax residents, if the change of control occurs before the second anniversary of the grant, on the first anniversary of the grant, it being specified that the relevant free shares will then be subject to a year-long holding period as from their date of acquisition.

	AGA 2020	AGA 2021
Date of the shareholders' meeting	**04/11/19**	**11/30/20**
Date of grant by the Executive Board	**03/11/20**	**04/20/21**
Total number of AGAs authorized	650,000	850,000
Total number of AGAs granted	50,000	362,515
Total number of shares to which the AGAs were likely to give right on the	50,000	362,515
including the number that can be subscribed by corporate officers:	50,000	270,000
including Laurent Levy	—	180,000
including Anne-Juliette Hermant	50,000	90,000
including Bart van Rhijn	—	—
Number of beneficiaries who are not corporate officers	—	79
Starting date of the exercise of the AGA	03/11/20	04/20/21
Date of acquisition (end of the	03/11/22	04/20/23
Terms of acquisition [7]	(1)	(2)
Number of shares subscribed as of the date of the Universal Registration	50,000	—
Total number of AGAs lapsed or cancelled as of the date of the Universal	—	3,003
Total number of AGAs outstanding as of the date of the Universal Registration	—	359,312
Total number of shares that may be	—	359,312
Duration of the holding period [6]	1 year	1 year

(1) The acquisition of the AGA 2020 granted to a member of the Executive Board is subject to the achievement of positive results in the 1100 study in 2020. The satisfaction of this performance condition was acknowledged by the Executive Board, with the approval of the Supervisory Board, on March 17, 2021. Furthermore, the AGA 2020 will be subject to a one-year holding period starting at the end of the two-year acquisition period, i.e. starting March 11, 2022.

(2) The AGA 2021 granted to members of the Executive Board are conditioned upon the determination of the recommended dose for two out of the three patient cohorts enrolled in the NBTXR-1100 clinical study in order to define the next steps of the immuno-oncology development plan before April 20, 2022.] The satisfaction of this condition must be acknowledged by the Executive Board, with the prior approval of the Supervisory Board, before April 20, 2023. Furthermore, the AGA 2021 will be subject to a one-year holding period starting at the end of the two-year acquisition period, i.e. starting April 20, 2023.

(3) See also the "Continued service condition" and "Change of control" paragraphs above.

5.1.4.5. Summary of the dilutive instruments

As of the date of the Universal Registration Document, the full exercise of all granted and outstanding instruments entitling their holders to a stake in the Company's share capital (assuming all the terms of exercise or acquisition of said instruments were fulfilled) would result in the subscription of 2,881,997 new ordinary shares, consisting of:

- 715,291 BSPCEs, the exercise of which would lead to the creation of 715,291 new ordinary shares;
- 245,251 BSAs, the exercise of which would lead to the creation of 304,923 new ordinary shares;
- 1,502,271 Options, the exercise of which would lead to the creation of 1,502,271 new shares;
- 359,512 AGAs, the acquisition of which would lead to the creation of 359,512 new ordinary shares.

	No. of securities	**Terms**		**Potential dilution**
Dilutive securities not linked to stock market price evolution	**1,715,074**			
BSAs	***66,000***	**—**		***0.19%***
BSCPEs	***715,291***	**—**		***2.01%***
OSAs	***574,271***	**—**		***1.62%***
AGAs	***359,512***	**—**		***1.02%***
Dilutive securities linked to stock market price evolution[(1)]	**1,107,251**		*Cumulative no. of exercisable securities*	*Cumulative potential dilution*
2014 BSAs	*10,000*	*if stock market price ≥ €40*	*10,000*	0.03%
2015-1 BSAs	*21,000*	*if stock market price ≥ €40*	*31,000*	0.09%
2015-2 (a) BSAs	*64,000*	*if stock market price ≥ €50*	*95,000*	0.27%
2018 BSAs	*18,000*	*if stock market price ≥ €40*	*113,000*	0.32%
2018-1 BSAs	*10,000*	*if stock market price ≥ €40*	*123,000*	0.35%
2018-2 BSAs	*5,820*	*if stock market price ≥ €40*	*128,820*	0.37%
2019-1 BSAs	*18,000*	*if stock market price ≥ €40*	*146,820*	0.42%
2019 LLY OSAs	*500,000*	*if stock market price ≥ €24*	*646,820*	1.83%
2020 BSAs	*18,000*	*if stock market price ≥ €40*	*664,820*	1.91%
2021-1 BSAs	*14,431*	*if stock market price ≥ €40*	*679,251*	1.95%
2021-04 Performance OSAs	*368,000*	*if stock market price ≥ €24*	*1,047,251*	2.97%
2021-06 Performance OSAs	*60,000*	*if stock market price ≥ €24*	*1,107,251*	3.17%
Maximum theoretical potential dilution based on current capital				***8.01%***

(1) For more information on such securities, in particular their exercise conditions, see Sections 5.1.4.2 and 5.1.4.3 of the Universal Registration Document.

This figure above represents a maximum potential dilution of 8.01% on a non-diluted share capital basis and 7.92% on a non-diluted voting right basis as of the date of the Universal Registration Document, and 7.57% and 7.34%, respectively, on a fully diluted basis, it being specified that the exercise of a significant share of said dilutive instruments (i.e., 39.59%) is conditioned on the Company's share price as of its exercise date.

5.1.5. Authorized share capital

Shareholders' meeting held on April 28, 2021

As of the date of the Universal Registration Document, all of the authorizations and delegations granted by the shareholders' meeting held on April 28, 2021 are valid.

Combined Shareholders' Meeting of April 28, 2021	Term of Validity/ Expiry	Limit (nominal value)	Methods for determining price	Dates and terms of use by the Executive Board
Authorization to the Executive Board to execute a buyback of Company stock (fifteenth resolution)	18 months	10% of the share capital	See [a]	See section 5.1.3 of the Universal Registration Document.
Delegation of authority to the Executive Board to increase the Company's share capital by issuing ordinary shares or any securities giving immediate or long-term access to the Company's share capital, while preserving the shareholders' preferential subscription rights (seventeenth resolution)	26 months	€625,000 [b][c]	-	The Executive Board did not use this delegation during the past financial year.
Delegation of authority to the Executive Board to increase the Company's share capital by issuing ordinary shares, or any securities giving immediate or long-term access to the Company's share capital, through a public offering excluding the public offerings referred to in paragraph 1° of article L. 422-1 of the French Monetary and Financial code, without shareholders' preferential subscription rights, as well as the ability to institute a right of priority (eighteenth resolution)	26 months	€625,000 [b][c]	See [d]	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board to increase the Company's share capital by way of issuing of ordinary shares and/or of any security giving immediate or long-term access to the share capital, through a public offering referred to in paragraph 1° of article L. 422-1 of the French Monetary and Financial code, without shareholders' preferential subscription rights (nineteenth resolution)	26 months	€260,000 [b] up to 20% of the Company's share capital over a 12-month period [c]	See [d]	The Executive Board did not use this delegation during the past financial year.
Authorization to be granted to the Executive Board, in the event of issuance of shares or any securities granting access to capital with removal of the shareholders' preferential subscription right, to set the issue price within the limit of 10% of the capital and within the limit set by the general meeting of shareholders (twentieth resolution)	26 months	up to the limit of 10% of the share capital as existing on the date of the operation considered per 12-month period	See [e]	The Executive Board did not use this delegation during the past financial year.

Delegation of authority to the Executive Board to increase the Company's share capital by issuing ordinary shares, or any securities, for the benefit of a category of persons meeting specific characteristics, without shareholders' preferential subscription rights, in the context of the implementation of an equity or bond financing, (including, if applicable, an "At-the-market" or "ATM" program) (twenty-first resolution)	18 months	€208,000 in the event of a share capital increase [(b)(c)]	See [(f)]	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board in order to increase the Company's share capital by way of issuing of ordinary shares or of any security giving access to the share capital with removal of the shareholders' preferential subscription right to the benefit of a first determined category of persons who meet certain criteria, i.e. investors with experience in the healthcare or biotechnology sector; credit institution, investment services provider or member of an investment syndicate guaranteeing the issue (twenty-second resolution)	18 months	€625,000 [(b)]	See [(f)]	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board in order to increase the Company's share capital by way of issuing of ordinary shares or of any security giving access to the share capital with removal of the shareholders' preferential subscription right to the benefit of a second determined category of persons who meet certain criteria, i.e. industrial companies, institutions or entities active in the health or biotechnology sector (twenty-third resolution)	18 months	€625,000 [(b)]	See [(f)]	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board in order to increase the number of securities to be issued as a result of a share capital increase with or without preferential subscription right performed under the aforementioned delegations (twenty-fourth resolution)	26 months	within the limit of 15% of the issuance [(b) (g)]	Same price as the issuance	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board in order to issue ordinary shares and securities granting access to the share capital, in the event of a public offer including an exchange component initiated by the Company (twenty-fifth resolution)	26 months	€516,000 [(b)(c)]	-	The Executive Board did not use this delegation during the past financial year.

Delegation to be granted to the Executive Board to increase the Company's share capital, within the limits of 10% of the share capital, to remunerate in-kind contributions of ordinary shares or of any security giving access to the capital stock of third-party companies, outside of the context of a public exchange offer (twenty-sixth resolution)	26 months	up to the limit of 10% of the share capital as existing on the date of the operation considered [(b)(c)]	-	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board to increase the Company's share capital by incorporation of premiums, reserves, profits or other items (twenty-eight resolution)	26 months	€25,000	-	The Executive Board did not use this delegation during the past financial year.
Authorization to be granted to the Executive Board to grant stock-option or stock-purchase for shares (OSAs) of the Company (twenty-ninth resolution)	38 months	850,000 shares [(i)]	See [(h)]	The Executive Board used this delegation on June 21, 2021, granting 60,000 stock options to Bart Van Rhijn, a member of the Executive Board.
Authorization to be granted to the Executive Board to grant free existing shares or shares (AGAs) to be issued, pursuant to articles L.225-197-1 et seq. of the French Commercial Code (thirtieth resolution)	38 months	850,000 shares [(i)]	-	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board in order to issue and to grant warrants (BSAs) in favor of a range of persons satisfying determined characteristics (i) of members and non-voting members of the Company's Supervisory Board serving on the date of grant of the warrants who are neither employees nor legal officers of the Company or of one of its subsidiaries, (iii) of individuals persons bound by a service or consultancy contract with the Company, or (iii) of members of any committee that the Executive Board has or would have implemented neither employees nor legal officers of the Company or of one of its subsidiaries (twenty-first resolution)	18 months	850,000 shares [(i)]	See [(j)]	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board to increase the Company's share capital by way of issuing of ordinary shares or of any security giving access to the share capital for the benefit of employees who are members of a company savings plan(s) (*plan d'épargne d'entreprise*) (twenty-fifth resolution)	18 months	€20,000 [(k)]	See [(l)]	The Executive Board did not use this delegation during the past financial year.

(a) The maximum purchase price per share (excluding costs and commissions) is set at €60.00, with an overall maximum ceiling of €20,000,000, it being specified that this purchase price will be subject to any adjustments that may be necessary so as to take into account share capital transactions that occur during the authorization's validity period.

(b) These amounts are not cumulative. The maximum ceiling authorized by the shareholders' meeting for capital increases in nominal terms is fixed at €625,000 set by the twenty-seventh resolution.

(c) The global amount of issues of debt securities against the Company giving access to the Company's capital cannot, for its part, exceed €150,000,000, it being specified that such limit does not apply to the debt securities referred to in Articles L. 228-40, L. 228-36-A and L. 228-92 al. 3 of the French Commercial Code if the issue has been decided or authorized by the Executive Board in

accordance with Article L. 228-40 of the French Commercial Code, or, in other cases, under the terms that the Company would determine in accordance with the provisions of Article L. 228-36-A of the French Commercial Code.

(d) The issue price of shares will be at least equal to the weighted average price by volume during the last three trading sessions on the regulated market of Euronext in Paris preceding the beginning of the offer within the meaning of the regulation (EU) 2017-1129, reduced, where appropriate by a maximum discount of 10%, it being specified that the issue price of securities giving access to capital will be that of the sum immediately received by the Company, increased, where necessary, by that which may be subsequently received by the Company for each share issued as a result of the issue of these securities, at least equal to the issue price defined in the last preceding sentence.

(e) The issue price of the ordinary shares and/or securities giving immediate or future access to the capital issued shall be determined according to the following methods:

(f) the issue price of ordinary shares will be at least equal to the volume weighted average price during the last three trading sessions on the regulated market of Euronext in Paris prior to pricing, possibly reduced by a maximum discount of 15% and corrected in the event of differences in dividend eligibility dates, under no circumstances can it be lower than the nominal value of a Company share on the issue date of the shares concerned,

(g) the issue price of securities giving access to the capital will be the sum immediately received by the Company, increased, where appropriate, by that likely to be subsequently received by it, or, for each share issued as a result of the issue of these securities, at least equal to the issue price defined in the above paragraph.

(h) The issue price of shares will be at least equal to the volume weighted average price during the last three trading sessions on the regulated market of Euronext in Paris prior to pricing, reduced, where appropriate by a maximum discount of 15% and corrected in the event of differences in dividend eligibility dates, it being specified that the issue price of securities giving access to capital will be that of the sum immediately received by the Company, increased, where necessary, by that which may be subsequently received by the Company for each share issued as a result of the issue of these securities, at least equal to the issue price defined in the last preceding sentence.

(i) 15% or any other percentage that may have been determined by the regulations in force.

(j) The purchase or subscription price per share will be determined by the Executive Board on the day when the option is granted within the legal limits; this price cannot fall below ninety five per cent (95%) of the average price listed during the 20 trading sessions on the regulated market of Euronext in Paris prior to the day of the Executive Board's decision to allocate the options, rounded up to the nearest euro cent, nor in the case of purchase options, 80% of the average purchase price of treasury shares, rounded up to the nearest euro cent.

(k) These amounts are not cumulative; the maximum accumulated number authorized by the shareholders' meeting likely to result from the exercise of stock options and warrants and the allocation of free shares is 850,000 shares.

(l) The issue price of a warrant will be determined by the Executive Board on the date on which the warrants are allocated, based on the characteristics of the warrants and at least equal to 5% of the volume weighted average price over the last five (5) trading sessions on the regulated market of Euronext in Paris preceding the allocation of said warrants by the Executive Board.

(m) The global amount of issues of securities representing claims against the Company giving access to the Company's capital cannot exceed €850,000.

(n) The issue price of the shares or securities granting access to the share capital will be determined by the Executive Board in accordance with the provisions of Article L. 3332-19 of the French Labor Code and may not be higher than the average price listed during the 20 trading sessions on the regulated market of Euronext on Paris prior to the day of the Executive Board's decision setting the opening date of the subscription period, nor fall lower than 20% of said average, or 30% of said average when the lock-up period provided for in the plan, pursuant to Articles L. 3332-25 and L. 3332-26 of the French Commercial Code is equal to or higher than 10 years.

Shareholders' meeting held on November 30, 2020.

As of the date of the Universal Registration Document, all of the authorizations and delegations granted by the shareholders' meeting held on November 30, 2020 were cancelled and replaced by granted by the shareholders' meeting held on April 28, 2021, except for the authorization granted in its 15th resolution.

Extraordinary Shareholders' Meeting of November 30, 2020	Term of Validity/ Expiry	Limit (nominal value)	Methods for determining price	Dates and terms of use by the Executive Board
Delegation of authority to the Executive Board to increase the Company's share capital by issuing ordinary shares, or any securities giving immediate or long-term access to the Company's share capital, while preserving the shareholders' preferential subscription rights (First resolution)	26 months	€625,000 [(a)(b)]	-	The Executive Board did not use this delegation during the past financial year.

Extraordinary Shareholders' Meeting of November 30, 2020	Term of Validity/ Expiry	Limit (nominal value)	Methods for determining price	Dates and terms of use by the Executive Board
Delegation of authority to the Executive Board to increase the Company's share capital by issuing ordinary shares, or any securities giving immediate or long-term access to the Company's share capital, through a public offering, without shareholders' preferential subscription rights, as well as the ability to institute a right of priority (Second resolution)	26 months	€625,000 [(a)(b)]	See [(c)]	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board to increase the Company's share capital by way of issuing of ordinary shares and/or of any security giving immediate or long-term access to the share capital with removal of the shareholders' preferential subscription right in the framework of an offering made to the benefit of qualified investors or to a restricted circle of investors mentioned at the II of article L. 411-2 of the French Monetary and Financial Code (Third resolution)	26 months	€260,000 [(a)] up to 20% of the Company's share capital over a 12-month period (b)	See [(c)]	
Authorization to be granted to the Executive Board, in the event of issuance of shares or any securities granting access to capital with removal of the shareholders' preferential subscription right, to set the issue price within the limit of 10% of the capital and within the limit set by the general meeting of shareholders (Fourth resolution)	26 months	up to the limit of 10% of the share capital as existing on the date of the operation considered per 12-month period	See [(d)]	The Executive Board did not use this delegation during the past financial year.
Delegation of authority to the Executive Board to increase the Company's share capital by issuing ordinary shares, or any securities, for the benefit of a category of persons, without shareholders' preferential subscription rights, in the context of equity or bond financing (Fifth resolution)	18 months	€156,000 in the event of a share capital increase [(a)(b)]	See [(e)]	The Executive Board did not use this delegation during the past financial year.

Extraordinary Shareholders' Meeting of November 30, 2020	Term of Validity/ Expiry	Limit (nominal value)	Methods for determining price	Dates and terms of use by the Executive Board
Delegation to be granted to the Executive Board in order to increase the Company's share capital by way of issuing of ordinary shares or of any security giving access to the share capital with removal of the shareholders' preferential subscription right to the benefit of a determined category of persons who meet certain criteria (Sixth resolution)	18 months	€625,000 [(a)]	See [(e)]	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board in order to increase the number of securities to be issued as a result of a share capital increase with or without preferential subscription right performed under the aforementioned delegations (Seventh resolution)	26 months	within the limit of 15% of the issuance [(a) (f)]	Same price as the issuance	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board in order to issue ordinary shares and securities granting access to the share capital, in the event of a public offer including an exchange component initiated by the Company (Eighth resolution)	26 months	€260,000 [(a)(b)]	-	The Executive Board did not use this delegation during the past financial year.
Delegation to be granted to the Executive Board to increase the Company's share capital, within the limits of 10% of the share capital, to remunerate in-kind contributions of ordinary shares or of any security giving access to the capital stock of third-party companies, outside of the context of a public exchange offer (Ninth resolution)	26 months	up to the limit of 10% of the share capital as existing on the date of the operation considered [(a)(b)]	-	The Executive Board did not use this delegation during the past financial year.
First authorization to be granted to the Executive Board to grant stock-option or stock-purchase for shares (OSAs) of the Company (Eleventh resolution)	38 months	600,000 shares, increased to 850,000 shares in the event of completion of the Company's initial public offering on the Nasdaq [(h)]	See [(g)]	The Executive Board used this delegation on April 20, 2021, granting 143,200 stock options to employees of the Group.
Authorization to be granted to the Executive Board to grant free existing shares or shares (AGAs) to be issued, pursuant to articles L.225-197-1 et seq. of the French Commercial Code (Twelfth resolution)	38 months	600,000 shares, increased to 850,000 shares in the event of completion of the Company's initial public offering on the Nasdaq [(h)]	-	The Executive Board used this delegation on April 20, 2021, granting 92,515 free shares to employees of the Group and 270,000 free shares to members of the Executive Board.

Extraordinary Shareholders' Meeting of November 30, 2020	Term of Validity/ Expiry	Limit (nominal value)	Methods for determining price	Dates and terms of use by the Executive Board
Delegation to be granted to the Executive Board in order to issue and to grant warrants (BSAs) in favor of a range of persons satisfying determined characteristics (i) of members and non-voting members of the Company's Supervisory Board serving on the date of grant of the warrants who are neither employees nor legal officers of the Company or of one of its subsidiaries, (iii) of individuals persons bound by a service or consultancy contract with the Company, or (iii) of members of any committee that the Executive Board has or would have implemented neither employees nor legal officers of the Company or of one of its subsidiaries (Thirtheenth resolution)	18 months	600,000 shares, increased to 650,000 shares in the event of completion of the Company's initial public offering on the Nasdaq [(h)]	See [(i)]	The Executive Board used this delegation on April 20, 2021, granting 48,103 warrants to members of the Supervisory Board and 30,000 warrants to a consultant.
Second authorization to be granted to the Executive Board to grant stock-option or stock-purchase for shares (OSAs) of the Company (Fifteenth resolution)	38 months	1,000,000 shares in the event of completion of the Company's initial public offering on the Nasdaq[(j)]	See [(g)]	The Executive Board used this delegation twice: once on April 20, 2021, granting 188,000 stock options to employees of the Group and 240,000 stock options to members of the Executive Board, and a second time on June 21, 2021, granting 60,000 stock options to Bart Van Rhijn, a member of the Executive Board.
Delegation to be granted to the Executive Board to increase the Company's share capital by way of issuing of ordinary shares or of any security giving access to the share capital for the benefit of employees who are members of a company savings plan(s) (*plan d'épargne d'entreprise*) (Sixteenth resolution)	18 months	€20,000 [(k)]	See [(l)]	The Executive Board did not use this delegation during the past financial year.

(a) These amounts are not cumulative. The maximum ceiling authorized by the shareholders' meeting for capital increases in nominal terms is fixed at €625,000 set by the tenth resolution.

(b) The global amount of issues of debt securities against the Company giving access to the Company's capital cannot, for its part, exceed €150,000,000, it being specified that such limit does not apply to the debt securities referred to in Articles L. 228-40, L. 228-36-A and L. 228-92 al. 3 of the French Commercial Code if the issue has been decided or authorized by the Executive Board in accordance with Article L. 228-40 of the French Commercial Code, or, in other cases, under the terms that the Company would determine in accordance with the provisions of Article L. 228-36-A of the French Commercial Code.

(c) The issue price of shares will be at least equal to the weighted average price by volume during the last three trading sessions preceding the beginning of the offer within the meaning of the regulation (EU) 2017-1129, reduced, where appropriate by a maximum discount of 10%, it being specified that the issue price of securities giving access to capital will be that of the sum immediately received by the Company, increased, where necessary, by that which may be subsequently received by the Company for each share issued as a result of the issue of these securities, at least equal to the issue price defined in the last preceding sentence.

(d) The issue price of the ordinary shares and/or securities giving immediate or future access to the capital issued shall be determined according to the following methods:

- the issue price of ordinary shares will be at least equal to the volume weighted average price during the last three trading sessions prior to pricing, possibly reduced by a maximum discount of 15% and corrected in the event of

differences in dividend eligibility dates, under no circumstances can it be lower than the nominal value of a Company share on the issue date of the shares concerned,
- the issue price of securities giving access to the capital will be the sum immediately received by the Company, increased, where appropriate, by that likely to be subsequently received by it, or, for each share issued as a result of the issue of these securities, at least equal to the issue price defined in the above paragraph.

(e) The issue price of shares will be at least equal to the volume weighted average price during the last three trading sessions prior to pricing, reduced, where appropriate by a maximum discount of 15% and corrected in the event of differences in dividend eligibility dates, it being specified that the issue price of securities giving access to capital will be that of the sum immediately received by the Company, increased, where necessary, by that which may be subsequently received by the Company for each share issued as a result of the issue of these securities, at least equal to the issue price defined in the last preceding sentence.

(f) 15% or any other percentage that may have been determined by the regulations in force.

(g) The purchase or subscription price per share will be determined by the Executive Board on the day when the option is granted within the legal limits; this price cannot fall below ninety five per cent (95%) of the average price listed during the 20 trading sessions prior to the day of the Executive Board's decision to allocate the options, rounded up to the nearest euro cent, nor in the case of purchase options, 80% of the average purchase price of treasury shares, rounded up to the nearest euro cent.

(h) These amounts are not cumulative; the maximum accumulated number authorized by the shareholders' meeting likely to result from the exercise of stock options and warrants and the allocation of free shares is 600,000 shares, increased to 850,000 shares in the event of completion of the Company's initial public offering on the Nasdaq.

(i) The issue price of a warrant will be determined by the Executive Board on the date on which the warrants are allocated, based on the characteristics of the warrants and at least equal to 5% of the volume weighted average price over the last five (5) trading sessions on said market or stock exchange preceding the allocation of said warrants by the Executive Board.

(j) The OSAs granted under this authorization will be exercisable under the following conditions:
- 10% of the OSAs may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext Paris reaches €24,
- An additional 10% of the OSAs may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext Paris reaches €30,
- An additional 40% of the OSAs may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext Paris reaches €40,
- The balance, i.e. 40% of the OSAs, may be exercised when the market value of a Nanobiotix share on the regulated market of Euronext Paris reaches €60.

(k) The global amount of issues of securities representing claims against the Company giving access to the Company's capital cannot exceed €1,000,000.

(l) The issue price of the shares or securities granting access to the share capital will be determined by the Executive Board in accordance with the provisions of Article L. 3332-19 of the French Labor Code and may not be higher than the average price listed during the 20 trading sessions prior to the day of the Executive Board's decision setting the opening date of the subscription period, nor fall lower than 20% of said average, or 30% of said average when the lock-up period provided for in the plan, pursuant to Articles L. 3332-25 and L. 3332-26 of the French Commercial Code is equal to or higher than 10 years.

5.1.6. Information on the capital of any member of the Group who is the subject of an option or of a conditional or unconditional agreement to put it under option

To the Company's knowledge, there is no put or call option or other commitments in favor of shareholders of the Company or granted by these shareholders in relation to the Company's shares.

5.1.7. History of share capital

5.1.7.1. Evolution of capital in the last three years

Date	Nature of operations	Capital	Issue Premium	Number of shares created	Number of Shares making up the capital	Nominal value	Share capital
	Balance as of December 31, 2018				**19 633 373**	**€0.03**	**€589,001.19**
04/09/2019	Issuance of new shares payable in cash (capital increase)	€76,999.98	€29,439,659.02	2,566,666	22 200 039	€0.03	€666,001.17
04/25/2019	Exercise of BSPCE 2012-1	€4,800.00	€955,200.00	160,000	22 360 039	€0.03	€670,801.17
07/17/2019	Exercise of BSPCE 04-2013	€1,650.00	€344,850.00	55,000	22 415 039	€0.03	€672,451.17
	Balance as of December 31, 2019				**22,415,039**	**€0.03**	**€672,451.17**
03/06/2020	Definitive acquisition of AGA 2018-1	€9,482.49	€0.00	316,083	22,731,122	€0.03	€681,933.66
07/27/2020	Definitive acquisition of AGA 2018-2	€180.00	€0.00	6,000	22,737,122	€0.03	€682,113.66
07/30/2020	Issuance of new shares payable in cash (capital increase)	€99,000	€20,031,000	3,300,000	26,037,122	€0.03	€781,113.66
12/15/2020	Issuance of new shares payable in cash (capital increase)	€219,000	€81,103,000	7,300,000	33,337,122	€0.03	€1,000,113.66
12/18/2020	Issuance of new shares payable in cash (capital increase)	€32,850	€12,165,450	1,095,000	34,432,122	€0.03	€1,032,963.66
	Balance as of December 31, 2020				**34,432,122**	**€0.03**	**€1,032,963.66**
03/06/2021	Definitive acquisition of AGA 2018-1	€735.00	€0.00	24,500	34,456,622	€0.03	€1,033,698.66
03/29/2021	Definitive acquisition of AGA 2019-1	€11,077.50	€0.00	369,250	34,825,872	€0.03	€1,044,776.16
	Balance as of December 31, 2021				**34,825,872**	**€0.03**	**€1,044,776.16**

On March 11, 2022, the share capital of the Company was increased by a nominal amount of €1,500, through the issuance of 50,000 new ordinary shares with a nominal value of €0.03 each, increasing the Company's share capital from €1,044,776.16 to €1,046,276.16, as a result of the definitive acquisition of 50,000 AGA 2020. Such acquisition was acknowledged by the Executive Board on March 11, 2022.
For more information on the AGA 2020, see Section 5.1.4.4. of the Universal Registration Document.

5.1.7.2. Evolution of the share capital and voting rights in the last three financial years

The allocation of the Company's share capital and voting rights as of December 31, 2019, 2020 and 2021 was, to the Company's knowledge, as follows:

	Share capital											
	As at Dec 31, 2021				As at Dec 31, 2020				As at Dec 31, 2019			
	Number of shares	Number of voting rights	% of share capital	% of voting rights	Number of shares	Number of voting rights	% of share capital	% of voting rights	Number of shares	Number of voting rights	% of share capital	% of voting rights
Institutional investors	18,019,273	18,019,273	51.74%	50.07%	18,981,392	18,978,441	55.13%	53.57%	7,583,156	7,583,156	33.83%	32.44%
Invus	*3,069,034*	*3,069,034*	*8.81%*	*8.53%*	*2,132,478*	*2,132,478*	*6.12%*	*5.72%*				
Caisse des Dépôts et Consignation	*1,921,722*	*1,921,722*	*5.52%*	*5.34%*								
Baillie Gifford	*1,809,326*	*1,809,326*	*5.20%*	*5.03%*	*2,109,836*	*2,109,836*	*6.06%*	*5.66%*				
Amiral Gestion	*1,750,624*	*1,750,624*	*5.03%*	*4.86%*								
Family offices	139,697	139,697	0.40%	0.39%	298,388	297,590	0.87%	0.84%	793,325	847,145	3.54%	3.62%
Total Financial investors	**18,158,970**	**18,158,970**	**52.14%**	**50.46%**	**19,279,780**	**19,276,031**	**55.99%**	**54.41%**	**8,376,481**	**8,430,301**	**37.37%**	**36.07%**
Laurent LEVY	959,060	1,690,620	2.75%	4.70%	809,060	1,381,667	2.35%	3.90%	731,560	1,303,120	3.26%	5.57%
Bart VAN RHIJN	—	—	0.00%	0.00%	—	—	0.00%	0.00%	—	—	0.00%	0.00%
Anne-Juliette HERMANT	—	—	0.00%	0.00%	—	—	0.00%	0.00%	—	—	0.00%	0.00%
OTHER MANAGERS AND EMPLOYEES	358,818	451,136	1.03%	1.25%	553,764	980,940	1.61%	2.77%	248,513	434,731	1.11%	1.86%
Total Management and employees	**1,317,878**	**2,141,756**	**3.78%**	**5.95%**	**1,412,824**	**2,412,604**	**4.10%**	**6.81%**	**980,073**	**1,737,851**	**4.37%**	**7.43%**
Other	**15,333,568**	**15,687,207**	**44.03%**	**43.59%**	**13,726,548**	**13,725,763**	**39.87%**	**38.74%**	**13,042,762**	**13,191,092**	**58.19%**	**56.43%**
Treasury shares	**15,456**	**—**	**0.04%**	**0.00%**	**12,970**	**—**	**0.04%**	**0.00%**	**15,723**	**—**	**0.07%**	**0.00%**
TOTAL	**34,825,872**	**35,987,933**	**100%**	**100%**	**34,432,122**	**35,414,397**	**100%**	**100%**	**22,415,039**	**23,374,967**	**100%**	**100%**

	Share capital on a fully diluted basis											
	As at Dec 31, 2021				As at Dec 31, 2020				As at Dec 31, 2019			
	Number of shares	Number of voting rights	% of share capital	% of voting rights	Number of shares	Number of voting rights	% of share capital	% of voting rights	Number of shares	Number of voting rights	% of share capital	% of voting rights
Institutional investors	18,019,273	18,019,273	47.67%	46.25%	18,981,392	18,978,441	51.51%	50.17%	7,583,156	7,583,156	30.64%	29.49%
Invus	*3,069,034*	*3,069,034*	8.12%	7.88%	*2,132,478*	*2,132,478*	5.80%	5.44%				
Caisse des Dépôts et Consignation	*1,921,722*	*1,921,722*	5.08%	4.93%								
Baillie Gifford	*1,809,326*	*1,809,326*	4.79%	4.64%	*2,109,836*	*2,109,836*	5.73%	5.38%				
Amiral Gestion	*1,750,624*	*1,750,624*	4.63%	4.49%								
Family offices	139,697	139,697	0.37%	0.36%	298,388	297,590	0.81%	0.79%	793,325	847,145	3.20%	3.29%
Total Financial investors	**18,158,970**	**18,158,970**	**48.04%**	**46.61%**	**19,279,780**	**19,276,031**	**52.32%**	**50.96%**	**8,376,481**	**8,430,301**	**33.84%**	**32.79%**
Laurent LEVY	2,089,460	2,821,020	5.53%	7.24%	1,889,460	2,462,067	5.13%	6.51%	1,609,460	2,181,020	6.50%	8.48%
Bart VAN RHIJN	120,000	120,000	0.32%	0.31%			0.00%	0.00%			0.00%	0.00%
Anne-Juliette HERMANT	260,000	260,000	0.69%	0.67%	110,000	110,000	0.30%	0.29%	—	—	0.00%	0.00%
OTHER MANAGERS AND EMPLOYEES	1,821,278	1,913,596	4.82%	4.91%	1,519,818	1,946,990	4.12%	5.15%	1,374,606	1,560,824	5.55%	6.07%
Total Management and employees	**4,290,738**	**5,114,616**	**11.35%**	**13.13%**	**3,827,478**	**4,827,258**	**10.39%**	**12.76%**	**3,232,266**	**3,990,044**	**13.06%**	**15.52%**
Other	**15,333,568**	**15,687,207**	**40.57%**	**40.26%**	**13,726,548**	**13,725,763**	**37.25%**	**36.28%**	**13,128,582**	**13,276,912**	**53.04%**	**51.64%**
Treasury shares	**15,456**	**—**	**0.04%**	**0.00%**	**12,970**	**—**	**0.04%**	**0.00%**	**15,723**	**—**	**0.06%**	**0.00%**
TOTAL	**37,798,732**	**38,960,793**	**100%**	**100%**	**36,846,776**	**37,829,052**	**100%**	**100%**	**24,753,052**	**25,712,980**	**100%**	**100%**

Since December 31, 2020, the AMF has received the following threshold crossing statements:

- By letter received by the AMF on July 23, 2021, Amiral Gestion stated that (i) on July 1st, 2021, it had crossed the threshold of 5% of the voting rights of Company and that it held, on behalf of the funds it manages, 1,756,430 Nanobiotix shares, representing 5.10% of the capital and 4.93% of the voting rights, and (ii) on July 22, 2021, it had crossed the threshold of 5% of the capital of Company and that it held, on behalf of the funds it manages, 1,716,128 Nanobiotix of, representing 4.98% of the capital and 4.82% of the voting rights.

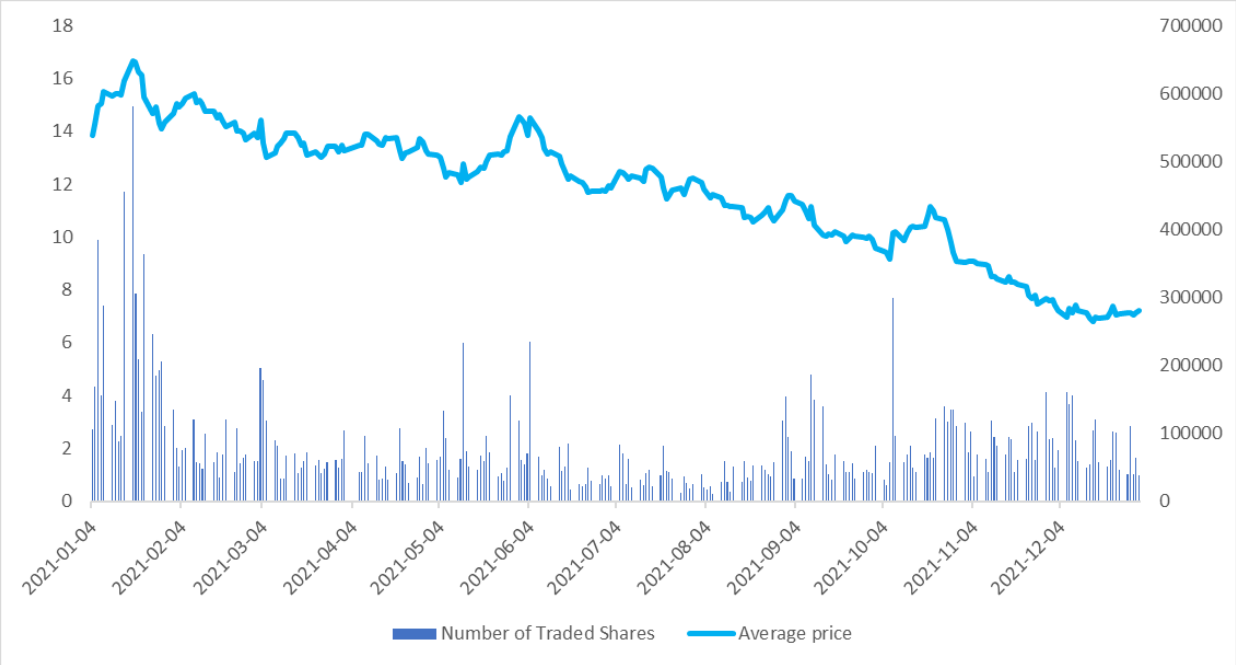
The Company is aware of the following threshold crossings since December 31, 2020:

- Invus crossed the threshold of 5% of the capital and the voting rights of Company and held, as of December 31, 2021, to the Company's knowledge, 3,069,034 shares of Nanobiotix, representing 8.81% of the capital and 8.53% of the voting rights of the Company.
- Baillie Gifford crossed the threshold of 5% of the capital and the voting rights of Company and held, as of December 31, 2021, to the Company's knowledge, 1,818,586 shares of Nanobiotix, representing 5.22% of the capital and 5.05% of the voting rights of the Company.
- Caisse des Dépots et des Consignations crossed the threshold of 5% of the capital of Company and held, as of December 31, 2021, to the Company's knowledge, 1,921,722 shares of Nanobiotix, representing 5.52% of the capital and 5.34% of the voting rights of the Company.
- Amiral Gestion crossed the threshold of 5% of the capital of Company and held, as of December 31, 2021, to the Company's knowledge, 1,750,624 shares of Nanobiotix, representing 5.03% of the capital and 4.86% of the voting rights of the Company.

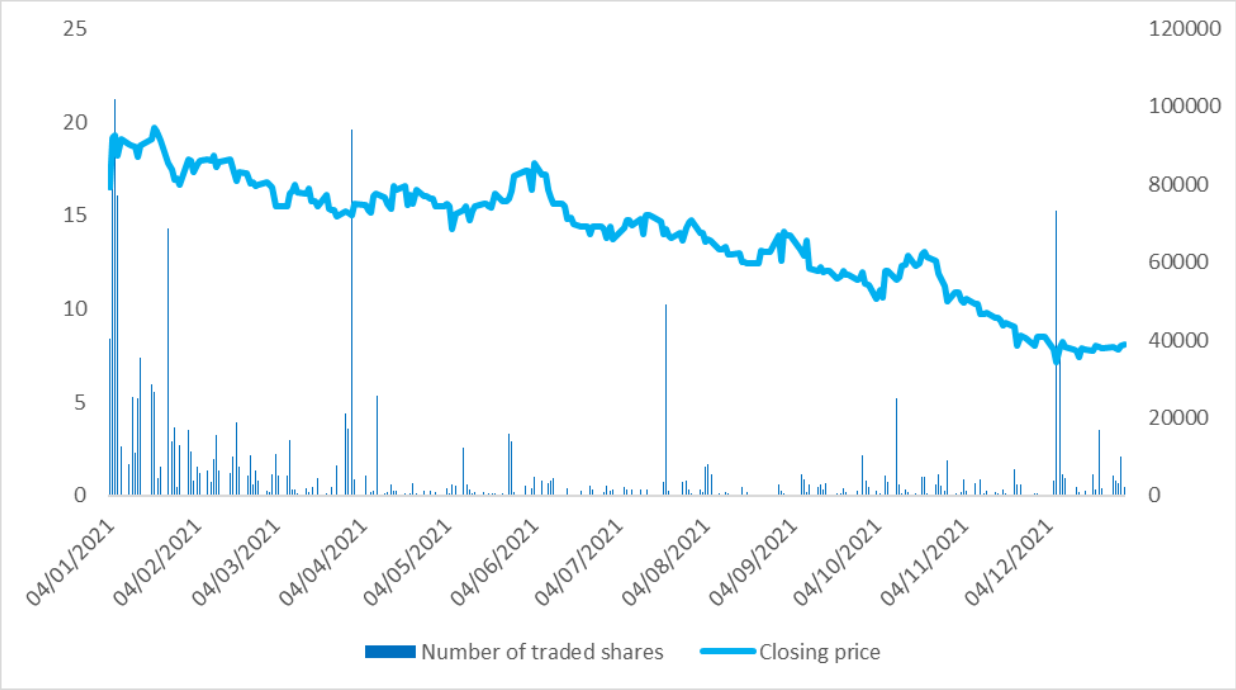
The Company is not aware of any other threshold crossing between December 31, 2021 and the date of the Universal Registration Document.

5.1.7.3. Stock Information

The Company's securities were admitted to trading on the regulated market of Euronext in Paris (compartment C) on October 29, 2012 under ISIN No. FR 0011341205. In January 2015, the Company announced the transfer of its share from Compartment C to Compartment B of the regulated market of Euronext in Paris given the progress of its market capitalization in 2014. The stock market trajectory for the share on the regulated market of Euronext in Paris throughout 2021 was as follows:



The Company's securities were admitted to trading on the Nasdaq Global Select Market on December 11, 2021 under the ticker symbol "NBTX.". The stock market trajectory for the share on the Nasdaq Global Select Market in 2021 was as follows:



5.2. MAJOR SHAREHOLDERS

5.2.1. Allocation of capital and voting rights as of the date of the Universal Registration Document

To the Company's knowledge, the allocation of capital and voting rights (taking into account the cancellation of voting rights attached to the treasury shares) as of the date of the Universal Registration Document is as follows:

	Non-diluted basis				Fully diluted basis			
	Share capital				Share capital			
	Number of shares	**Number of voting rights**	**% of share capital**	**% of voting rights**	**Number of shares**	**Number of voting rights**	**% of share capital**	**% of voting rights**
Institutional investors	18,019,273	18,019,273	51.67 %	49.63 %	18,019,273	18,019,273	47.80 %	46.19 %
Invus	*3,069,034*	*3,069,034*	*8.80 %*	*8.45 %*	*3,069,034*	*3,069,034*	*8.14 %*	*7.87 %*
Caisse des Dépôts et Consignation	*1,921,722*	*1,921,722*	*5.51 %*	*5.29 %*	*1,921,722*	*1,921,722*	*5.10 %*	*4.93 %*
Baillie Gifford	*1,809,326*	*1,809,326*	*5.19 %*	*4.98 %*	*1,809,326*	*1,809,326*	*4.80 %*	*4.64 %*
Amiral Gestion	*1,750,624*	*1,750,624*	*5.02 %*	*4.82 %*	*1,750,624*	*1,750,624*	*4.64 %*	*4.49 %*
Family offices	139,697	139,697	0.40 %	0.38 %	139,697	139,697	0.37 %	0.36 %
Total Financial investors	**18,158,970**	**18,158,970**	**52.07 %**	**50.02 %**	**18,158,970**	**18,158,970**	**48.17 %**	**46.54 %**
Laurent LEVY	959,060	1,768,120	2.75 %	4.87 %	2,089,460	2,821,020	5.54 %	7.23 %
Anne-Juliette HERMANT	50,000	50,000	0.14 %	0.14 %	260,000	260,000	0.69 %	0.67 %
Bart VAN RHIJN	0	0	— %	— %	120,000	120,000		
OTHER MANAGERS AND EMPLOYEES	351,319	546,388	1.03 %	1.25 %	1,713,244	1,872,733	4.54 %	4.80 %
Total Management and employees	**1,360,379**	**2,364,508**	**3.90 %**	**6.51 %**	**4,182,704**	**5,073,753**	**11.10 %**	**13.00 %**
Other	**15,343,566**	**15,781,388**	**43.99 %**	**43.47 %**	**15,343,566**	**15,781,388**	**40.70 %**	**40.45 %**
Treasury shares	**12,957**	**0**	**0.04 %**	**— %**	**12,957**	**-**	**0.03 %**	**— %**
TOTAL	**34,875,872**	**36,304,866**	**100.00 %**	**100.00 %**	**37,698,197**	**39,014,111**	**100.00 %**	**100.00 %**

5.2.2. Significant shareholders not represented on the Executive Board and Supervisory Board

To the Company's knowledge, the following shareholders hold more than 5% of the Company's share capital or voting rights and are not represented to one of its boards:

- Baillie Gifford & Co., and
- Invus Public Equities, L.P.
- Caisse des Dépôts et des Consignations
- Amiral Gestion

See Section 5.2.1 of the Universal Registration Document for more details on these shareholders.

The Company is not aware of any other shareholders holding more than 5% of the Company's share capital or voting rights that is not represented to one of its boards.

5.2.3. Shareholders' voting rights

At the date of the Universal Registration Document, each shareholder is entitled to one vote per share. However, a double voting right is attached to each registered share, which is held in the name of the same shareholder for at least two years. It is specified that American Depositary Shares are not eligible for double voting rights.

In addition, in the event of a capital increase by incorporation of reserves, profits or share premiums, double voting rights may be conferred, as soon as they are issued, on registered shares allocated free of charge to a shareholder on the basis of existing shares for which this right is granted.

Double voting rights will be stripped automatically from all shares converted to bearer shares or transferred to another shareholder, unless the transfer is the result of an inheritance, the liquidation of community property between spouses or an *inter vivos* gift made by a shareholder to his or her spouse or a relative in the line of succession, or as a result of a transfer resulting from a merger or demerger of a corporate shareholder.

5.2.4. Control of the Company

As of the date of the Universal Registration Document, no shareholder controls the Company within the meaning of article L. 233-3 of the French Commercial Code.
Accordingly, except for the presence of independent members within the Supervisory Board and the regulated convention procedure, the Company has not implemented measures to ensure that its eventual control is not exercised improperly.

5.2.5. Agreements that may result in a change of control

To the best of the knowledge of the Company, there is no agreement whose implementation could result in a change in control of the Company.

5.2.6. Pledges and collaterals

To the knowledge of the Company, none of its shares have been pledged.

5.3. MEMORANDUM AND BYLAWS

5.3.1. Corporate purpose (article 3 of the Company's bylaws)

Our corporate purpose, either directly or indirectly, in particular through the intermediary of subsidiaries or holdings, in France and abroad, is:

- The research and development in natural and physical sciences;
- The filing, study, acquisition, granting of any patents, licenses, methods, trademarks and protection of specialized knowledge connected or relating in any way to the fields or technologies covering our corporate purpose;
- The design, development, production, marketing, importation, exportation and exploitation by any means of drugs, pharmaceutical specialties, medical devices and other health possessions;
- The creation, acquisition, rental, lease-management of all business assets or facilities (*fonds de commerce*), lease, installation, operation of all establishments (*fonds de commerce*) factories and workshops, relating to any of the specified activities;
- The participation in any transactions that may relate to our corporate purpose by creating new companies, subscribing or purchasing securities or corporate rights, merging or otherwise; and
- More generally, all financial, commercial, industrial transactions and transactions involving real estate or movable properties relating directly or indirectly to any of the aforementioned corporate purposes or any similar or related purpose, in order to promote their development or extension.

5.3.2. Provisions enabling a change of control to be delayed, postponed or prevented

No particular provisions of the Company's bylaws or regulations could have the effect of delaying, deferring or preventing a change of control. To the best of the Company's knowledge, there is no action in concert between the Company's shareholders.

5.3.3. Special provisions governing changes in capital

No particular provisions of the Company's bylaws govern its changes in capital.

5.4. INFORMATION AND HISTORY OF THE LEGAL LIFE OF THE COMPANY OVER THE FINANCIAL YEAR

5.4.1. Corporate name of the Company

The Company's name is Nanobiotix.

5.4.2. Place of registration and registration number

The Company was registered with the Paris Trade and Companies Register on March 4, 2003 under number 447 521 600. The Company's LEI number is 969500667RSYIH8YL895.

5.4.3. Date of incorporation and term

The Company was incorporated for a term of 99 years ending March 4, 2102, subject to early dissolution or extension.

5.4.4. Company headquarters, legal form, legislation governing its activities

Initially incorporated as a limited liability company (*société à responsabilité limitée*), the Company was transformed into a limited company (*société anonyme*) with an Executive Board and a supervisory board by a decision of the general meeting of shareholders convened on May 27, 2004. The Company,

governed by French law, is mainly subject, for its operation, to the provisions of Articles L. 225-1 and L. 22-10-1 et seq. of the French Code of Commerce.
The Company's registered office is located at 60, rue de Wattignies, 75012 Paris, France. Company contact information is:
Phone: + 33 (0) 1 40 26 04 70
Fax: + 33 (0) 1 40 26 62 72
Website: www.nanobiotix.com
Email: contact@nanobiotix.com

The information appearing on the Company's website is not part of the Universal Registration Document unless such information is expressly incorporated by reference.

5.5. INFORMATION ABOUT THE SUBSIDIARIES

Nanobiotix Corp., a company established under the laws of the state of Delaware, incorporated in September 2014, is located in the Boston, Massachusetts, area, the world center for Life Sciences. Its capital is $3,560,660, wholly owned by Nanobiotix SA. Based within the Massachusetts Life Sciences Center, which is recognized worldwide for the number and quality of academic centers and biopharmaceutical companies located there, Nanobiotix Corp. develops part of the Company's business in the United States so as to provide with access to know-how and the expertise of the highest-level research.

Nanobiotix Corp. reported profits of €454 thousand in 2021 and €56 thousand in 2020.

Nanobiotix Spain, S.L.U., a company established under the laws of Spain, incorporated in December 2017, is wholly owned by Nanobiotix SA. Its registered office is 37, Pas Recoletos 28004, Madrid. Its share capital is €3,000. The corporate accounts of Nanobiotix Spain show a profit of €5 thousand for the financial year ending December 31, 2020 and a loss of €0 thousand in 2021.

Nanobiotix Germany GmbH, a company established under the laws of Germany, incorporated in October 2017, is wholly owned by Nanobiotix SA. Its registered office is Prinzregentenstraße 11, 80538 München. Its share capital is €25,000. The corporate accounts of Nanobiotix Germany show a profit of €13 thousand for the financial year ending December 31, 2020 and a profit of €4 thousand in 2021. In addition, the Company has a secondary establishment at 1 Mail du Professeur Georges Mate -Villejuif Biopark-94800 Villejuif.

Curadigm, a wholly owned subsidiary of Nanobiotix, was incorporated on July 9, 2018. The company operates in France and in the United States with headquarters located in Paris, 60 rue de Wattignies 75012, at Nanobiotix S.A.'s premises. Its net loss after tax amounted to €1,044 thousand for the financial year ending December 31, 2020 and €790 thousand in 2021. Curadigm SAS has itself a wholly owned subsidiary Curadigm Corp. a company established under the laws of the state of Delaware, United States. Its registered office is located in the Boston, Massachusetts, area and the company operates in Nanobiotix Corp. premises in Boston.

The Curadigm platform is being developed for use across multiple therapeutic classes to utilize biocompatible nanoparticles to transiently occupy the pathways responsible for therapeutic clearance and hepatic toxicity. Curadigm Nanoprimer technology aims to prime the body to receive various therapeutics and could reshape the balance between efficacy and toxicity for patients by increasing drug bioavailability while decreasing unintended off-target effects, specifically liver & spleen toxicities. Curadigm is dedicated to advancing therapeutic development based on the deep understanding of how drugs interact with the body, to impact both known and novel drugs across multiple clinical indications.

Nanobiotix also created a Swiss branch (*succursale*) registered on November 18, 2021, with offices located in Lausanne, c/o Berney et Associés SA, succursale de Lausanne, Rue Etraz 4, 1003 Lausanne, Switzerland.

5.6. REGULATED AGREEMENTS

5.6.1. Related-party agreements

Related-party transactions entered into during the financial years ending December 31, 2020 and December 31, 2021 are mentioned in the auditors' report on the regulated agreements in Section 5.6.3 of the Universal Registration Document, as well as in Note 23 to the consolidated financial statements for the financial year ending December 31, 2021, prepared under IFRS, in Section 4.1. of the Universal Registration Document. Since the drafting of the Auditor's Special Report for the 2021 financial year (see paragraph 5.6.3.1. below), no new related-party agreements have been entered into by the Company.

5.6.2. Severance pay and employment agreements

Termination arrangement

On May 27, 2004, our Supervisory Board approved terms for severance pay to be awarded to our Chairman of our Executive Board, Dr. Levy. The terms provide that Dr. Levy is entitled to severance pay in either of the following circumstances:

(i) dismissal or non-renewal of Executive Board membership for any reason other than gross negligence or willful misconduct ("faute lourde," as defined under French case law); or

(ii) resignation within six months following a change of control (within the meaning of Article L. 233-3 of the French Commercial Code) due to a significant reduction in duties and responsibilities or compensation (including fixed compensation, benefits in kind, variable compensation or severance pay) or transfer of workplace to another country, in each case, without consent.

In such circumstance, as applicable, Dr. Levy is entitled to severance pay in an amount not to exceed the annual gross compensation (fixed and variable) he received during the year preceding departure.

The payment of severance is subject to calculation of the ''average achievement rate,'' which is based on specified performance objectives and is used to calculate the variable compensation received by the payee during the three years preceding departure. If the average achievement rate is less than 50%, no severance is payable, and if the average achievement rate falls between 50% and 100%, severance is payable in full. Any such payment shall include legal indemnities, but exclude compensation due under any non-compete arrangements, subject to certain limitations.

However, the severance to be paid, together with compensation under any non-compete arrangements that is separately due, may not exceed twice the annual gross compensation received by the payee during the year of resignation, dismissal or non-renewal of Executive Board membership.

For the avoidance of doubt, no severance payment will be payable if, following resignation, dismissal or non-renewal of Executive Board membership, Dr. Levy becomes an employee and his duties, responsibilities or compensation have not been reduced nor has he been required to transfer his workplace to another country, in each case, without consent.

Employment agreements

On April 1, 2019 the Company entered into a permanent employment agreement (*contrat à durée indéterminée*) with our Chief People Officer and member of our Executive Board, Anne-Juliette Hermant. Anne-Juliette Herman's role and responsibilities include: developing, revising, and maintaining agency Human Resource policies; providing support to the CEO and CFO on the leadership team to determine and implement long-term objectives and strategies in order to meet organizational goals with a focus on programmatic implementation; developing and improving processes to build more efficient program structures and systems, including decision-making processes and workplan monitoring; recruiting, developing and retaining high-performing team members, providing clarity around roles; developing and motivating staff while facilitating effective team dynamics; promoting team members' personal and professional development and managing all HR functions, including payroll.

Under this employment agreement, Anne-Juliette Hermant is entitled to an annual base salary of €180,000 in 2019 and variable compensation in an amount up to 50% of the annual base salary, depending on the achievement of specified performance objectives. The agreement provides for a 12-month non-compete period following the termination of employment. Anne-Juliette Hermant is entitled to monthly compensation during the non-compete period of 66% of her annual base salary. Further, the agreement provides for an exclusivity undertaking during the term of the agreement, and a confidentiality undertaking for the term of the agreement 10 years thereafter. This employment agreement may be terminated by both Anne-Juliette Hermant and the Company under the conditions provided for by regulation and the collective labour agreement applicable to the employee and subject to a 3-month prior notice.

On May 11, 2021, Nanobiotix Corp. entered into an employment agreement with Bart Van Rhijn, effective June 1, 2021. Under the employment agreement, Bart Van Rhijn is entitled to an annual base salary of $380,000 and variable compensation in an amount up to 50% of the annual base salary, depending on the achievement of specified performance objectives. The agreement provides for a 12-month non-compete period following the termination of employment. Bart Van Rhijn is entitled to compensation during the non-compete period at a rate equal to 80% of his annual base salary. Further, the agreement provides for an exclusivity undertaking during the term of the agreement, and a confidentiality undertaking for the term of the agreement and at all times thereafter. This employment agreement may be terminated by both Bart Van Rhijn subject to a two-week notice period and by Nanobiotix Corp. with or without prior notice.

5.6.3. Special report of the statutory auditors on regulated agreements and commitments

5.6.3.1. Special report of the statutory auditors for financial year 2021

GRANT THORNTON
French member of Grant Thornton International

ERNST & YOUNG et Autres

This is a translation into English of a report issued in French and it is provided solely for the convenience of English-speaking users. This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.

Nanobiotix
Annual General Meeting held to approve the financial statements for the year ended December 31, 2021

Statutory auditors' report on related party agreements

GRANT THORNTON
French member of Grant Thornton International
29, rue du Pont
CS 20070
92200 Neuilly-sur-Seine
S.A.S. au capital de € 2 297 184
632 013 843 R.C.S. Nanterre

Commissaire aux Comptes
Membre de la compagnie
régionale de Versailles et du Centre

ERNST & YOUNG et Autres
Tour First
TSA 14444
92037 Paris-La Défense cedex
S.A.S. à capital variable
438 476 913 R.C.S. Nanterre

Commissaire aux Comptes
Membre de la compagnie
régionale de Versailles et du Centre

Nanobiotix
Annual General Meeting held to approve the financial statements for the year ended December 31, 2021

Statutory auditors' report on related party agreements

To the Annual General Meeting of Nanobiotix,

In our capacity as statutory auditors of your Company, we hereby present to you our report on related party agreements.

We are required to inform you, on the basis of the information provided to us, of the terms and conditions of those agreements indicated to us, or that we may have identified in the performance of our engagement, as well as the reasons justifying why they benefit the Company. We are not required to give our opinion as to whether they are beneficial or appropriate or to ascertain the existence of other agreements. It is your responsibility, in accordance with Article R. 225-58 of the French Commercial Code *(Code de commerce)*, to assess the relevance of these agreements prior to their approval.

We are also required, where applicable, to inform you in accordance with Article R. 225-58 of the French Commercial Code *(Code de commerce)* of the continuation of the implementation, during the year ended December 31, 2021, of the agreements previously approved by the Annual General Meeting.

We performed those procedures which we deemed necessary in compliance with professional guidance issued by the French Institute of Statutory Auditors (*Compagnie nationale des commissaires aux comptes*) relating to this type of engagement.

Agreements submitted for approval to the Annual General Meeting

We hereby inform you that we have not been notified of any agreements authorized and concluded during the year ended December 31, 2021, to be submitted to the Annual General Meeting for approval in accordance with Article R. 225-86 of the French Commercial Code *(Code de commerce).*

Agreements previously approved by the Annual General Meeting

We hereby inform you that we have not been notified of any agreements previously approved by the Annual General Meeting whose implementation continued during the year ended December 31, 2021.

Neuilly-sur-Seine and Paris-La Défense, April 8, 2022

The Statutory Auditors
French original signed by

GRANT THORNTON	ERNST & YOUNG et Autres
French member of Grant Thornton International	
Samuel Clochard	Cédric Garcia

5.7. EMPLOYEES

5.7.1. Human Resources

5.7.1.1. Workforce

At the end of the financial years under review, the Company's average number of employees, excluding trainees, evolved as follows:

Membership at cloture	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2015**
Business Development	3	2	1	1	2	2	1
General Management	3	4	4	5	4	2	3
Finance, Administration, HR, Communication	21	18	24	21	16	11	11
Medical Affairs	7	4	8	9	12	0	0
Research/Discovery	11	8	7	13	13	16	15
Clinical Development, Regulatory Affairs, Production & Quality	49	46	58	53	38	30	29
Corporate Development	0	0	0	0	0	3	1
Curadigm	6	6	8				
TOTAL	**100**	**88**	**110**	**102**	**85**	**64**	**60**
Nanobiotix SA	76	70	85	89	75	61	59
Nanobiotix Corp.	16	12	16	10	9	3	1
Nanobiotix S.L.U.	0	0	0	1	1	0	0
Nanobiotix Gmbh	1	0	2	2	0	0	0
Swiss Branch	1	NA					
Curadigm	6	6	7				
TOTAL	**100**	**88**	**110**	**102**	**85**	**64**	**60**

5.7.1.2. Financial instruments providing access to the Company's capital allocated or granted to the first ten employees who are not corporate officers of the Company, awarded and exercised or subscribed by them during the financial year ended December 31, 2021

	Total number of free shares awarded and stock options granted – shares subscribed or purchased	Weighted Average Price Per Share	OSA 2021-04 Ordinary	OSA 2021-04 Performance	AGA 2021	AGA 2018-1	AGA 2019-1
Number of financial instruments granted during the financial year by the Company to the ten employees who are not corporate officers of the Company and whose number of financial instruments is the highest (aggregate information)	194,000	13.74	44,200	122,000	63,000	—	—
Number of financial instruments exercised and/or definitely acquired by the ten Company employees, of which the number of financial instruments thus exercised and/or acquired is the highest (aggregate information)	104,250	—	—	—	—	18,500	87,750

5.7.2. Employee share ownership

As of December 31, 2021, the participation of the Company's employees in the company's share capital, calculated in accordance with the provisions of Article L. 225-102 of the French Commercial Code (i.e. as part of collective management), was 0%. To the Company's knowledge, the direct participation of the Company's employees (excluding members of the Executive Board) on that date was approximately 1.75%.

6. FURTHER INFORMATION

6.1. PERSON RESPONSIBLE FOR THE UNIVERSAL REGISTRATION DOCUMENT

Mr. Laurent LEVY, Chairman of the Executive Board of Nanobiotix SA.

6.1.1. Statement by the person responsible for the Universal Registration Document

"I certify that the information contained in the Universal Registration Document is, to the best of my knowledge, in accordance with the facts and contains no omission likely to affect its import.

I certify that, to the best of my knowledge, the financial statements have been prepared in accordance with the applicable accounting standards and give a true and fair view of the assets, liabilities, financial position and results of the company and of all the companies included in the consolidation, and that the management report, which is detailed in the cross-reference table in section 6.5 of the Universal Registration Document presents a true and fair view of the development of the business, the results of operations and the financial position of the company and of all the companies included in the consolidation and describes the main risks and uncertainties they face."

Paris, April 8, 2022,
LAURENT LEVY
Chairman of the Executive Board

6.1.2. Person responsible for the financial information

Laurent LEVY	**Bart Van Rhijn**
Chairman of the Executive Board	CFO
Address: 60, rue de Wattignies, 75012 Paris	Address: 60, rue de Wattignies, 75012 Paris
Phone: + 33 (0) 1 40 26 04 70	Phone: + 33 (0) 1 40 26 04 70
Fax: + 33 (0) 1 40 26 62 72	Fax: + 33 (0) 1 40 26 62 72
Mail: contact@nanobiotix.com	Mail: contact@nanobiotix.com

6.2. STATUTORY AUDITORS

6.2.1. Statutory Auditors

ERNST & YOUNG et Autres represented by Cédric Garcia
Paris La Défense 1 Place des Saisons 92400 Courbevoie.
Member of the *Compagnie régionale des commissaires aux comptes de Versailles et du Centre* (Regional Company of the Auditors of Versailles et du Centre).

ERNST & YOUNG's term as the statutory auditor was renewed by the shareholders' meeting convened on May 23, 2018 for a period of six financial years expiring at the end of the shareholders' meeting called to settle on approve the accounts for the financial year ended December 31, 2023.

GRANT THORNTON represented by Samuel Clochard
29 rue du Pont 92200 Neuilly sur Seine.
Member of the *Compagnie régionale des commissaires aux comptes de Versailles et du Centre* (Regional Company of the Auditors of Versailles et du Centre).

Grant Thornton was appointed as the statutory auditor by the shareholders' meeting convened on May 23, 2018 for a period of six financial years expiring at the end of the shareholders' meeting called to settle on approve the accounts for the financial year ended December 31, 2023.

6.2.2. Statement on the fees paid to the statutory auditors

The fees paid to the statutory auditors in the year ended December 31, 2021 appear in Note 24 of the Exhibits to the consolidated financial statements for the financial year ended December 31, 2021, prepared under IFRS in Section 4.1 of the Universal Registration Document.

6.3. INFORMATION FROM THIRD PARTIES, STATEMENTS BY EXPERTS AND DECLARATION OF INTERESTS

None.

6.4. PUBLICLY AVAILABLE DOCUMENTS

Copies of the Universal Registration Document are available at no charge at the Company's headquarters, 60, rue de Wattignies, 75012 Paris, France. The Universal Registration Document can also be found on the Company's website (www.nanobiotix.com) and on the AMF website (www.amf-france.org). The bylaws, minutes of shareholders' meetings and other corporate documents of the Company, as well as the historical financial information and any evaluation or statement made by an expert at the request of the Company that must be made available to shareholders in accordance with applicable law may be found at no cost to the Company's registered office. Hard-copies of these documents can also be requested by the Company.

Furthermore, in accordance with article 221-3 of the General Regulations of the French Financial Markets Authority (*Règlement général de l'Autorité des Marchés Financiers*), the regulatory information within the meaning of article 221-1 of said General Regulations is available on the Company's website (www.nanobiotix.com), as well as the last updated version of the Company's bylaws.

It is specified that the Universal Registration Document was drafted based on Annex I and II of the Delegated Regulation (EU) 2019/980 dated March 14, 2019.

6.5. CROSS-REFERENCE TABLE

The following cross-reference table allows to identify, in the Universal Registration Document, the information required by Annex I and Annex II of the Delegated Regulation (EU) 2019/980 dated March 14, 2019.

	Annual Financial Report Cross-Reference Table		
	Annual Financial Report	**Chapter(s) / Section(s)**	**Page**
1	Statement of the persons responsible	6.1.1	384
2	Annual financial statements (statutory accounts)- French GAAP	4.3	308
3	Consolidated financial statements – IFRS	4.1	224
4	Management Report	See index below	
5	Report on corporate governance	See index below	
6	Information related to the share buybacks	5.1.3	344
6	Statement of statutory auditors' fees	6.2.2	385
7	Report of the statutory auditors on the annual financial statements and on the consolidated financial statements	4.4 and 4.2 respectively	336, 299

	Management Report Cross-Reference Table		
	Management Report	**Chapter(s) / Section(s)**	**Page**
1	Activity and financial position of the Company during the past year	1.4	122
2	Progress made and difficulties encountered	1.3	42
3	Main risks and uncertainties - Use of financial instruments	1.5	135
4	Group's research and development activity	1.3.1 and 1.3.12	42, 86
5	Foreseeable evolution of the situation of the Company and of the Group - Future prospects	1.4.2	126
6	Significant events since the end of the financial year	1.1.3, 1.2	30, 31
7	Non-tax deductible expenses	1.4.7	134
8	Net income for the year and proposed allocation of net income	1.4.1	122
9	Dividends distributed over the last three financial years	1.4.6	134
10	Transactions in securities carried out by managers and persons mentioned in Article L. 621-18-2 of the French Monetary and Financial Code on the Company's securities during the financial year	2.2.4	180
11	State of equity holdings and/or controlling interests in companies having their registered office in France	5.5	376
12	Activities of subsidiaries and controlled companies	5.5	376
13	Branches	1.2.2.3.1	39
14	Risk management and internal control procedures implemented by the Company	2.4	194
15	Description and management of environmental and climate risks	1.5 and 3	135, 203
16	Potential Capital	5.1.5	359
17	Adjustments in the event of the issue of securities giving access to capital	N/A	
18	Changes in the ownership structure of the capital during the financial year	5.1.7	367
19	Information relating to the allocation of capital and treasury shares - Share buyback program - Share price volatility risk	5.1.3	344
20	Employee shareholding	5.7.2	383
21	Information relating to the grant of stock-options and allocation of free shares	5.1.4.3 and 5.1.4.4	352, 356
22	Extra-financial performance statement	N/A	
23	Tables of results over the past five years	1.4.7	134
24	Report on Corporate Governance	See index below	

	Corporate Government Report Cross-Reference Table		
	Report on corporate governance		**Page**
1	List of all offices and positions held in any company by each of the officers during the financial year	2.1.2	160
2	Composition, work preparation and organization conditions for the Supervisory Board	2.1.3, 2.1.5	162, 165
3	Limitations placed by the Supervisory Board on the Executive Board's powers	2.1.5	165
4	Reference to a Corporate Governance Code and application of the "comply or explain" principle	2.3	192
5	Compensation policy for corporate officers	2.2.8	182
6	Compensation and benefits of any kind paid during the financial year or allocated for the financial year to each corporate officer	2.2.2	173
7	Ratio of fixed and variable compensation	2.2.3	179
8	Commitments of any kind made by the Company for the benefit of its corporate officers, corresponding to compensation, indemnities or benefits due or likely to be due as a result of the acceptance, termination or change in their duties or subsequent to the performance thereof	5.6.2	377

	Corporate Government Report Cross-Reference Table		
	Report on corporate governance		**Page**
9	Compensation paid or granted by a company included in the scope of consolidation within the meaning of Article L. 233-16 of the French Commercial Code	2.2.8	182
10	Ratios between the level of compensation of each executive director and the average and median compensation of the Company's employees	2.2.3	179
11	Annual evolution of the compensation, Company performance, average compensation of the Company's employees and the aforementioned ratios over the last five financial years	2.2.3	173
12	Statement of how the total compensation complies with the adopted compensation policy, including how it contributes to the long-term performance of the Company and how the performance criteria have been implemented	2.2.9.6	191
13	Manner in which the vote of the last ordinary shareholders' meeting of the Company provided for in II of article L. 22-10-34 of the French Commercial Code was taken into account	2.2.9.5	191
14	Any deviations or waivers from the compensation policy implementation procedure	2.2.9.6	191
15	Enforcement of the provisions of Article L. 225-45 of the Commercial Code	N/A	
16	Agreements entered into between a member of the Executive Board or significant shareholder and a subsidiary	2.1.6.3 and 5.6	170, 377
17	Specific procedures relating to the participation of shareholders in the shareholders' meeting	5.2.3	374
18	Summary table of valid delegations of authority granted by the Company's shareholders' meeting with respect to capital increases	5.1.5	359
20	Description of the diversity policy	N/A	
21	Procedure for evaluating standard agreements - Implementation	2.1.7	171
22	Information likely to have an impact in the event of a public offer	2.5	201

	Universal Registration Document Table of concordance		
	Annexes I and II of the Delegated Regulation No. 2019/980 of the European Commission dated March 14, 2019	**Chapter(s) / Section(s)**	**Page**
1.	**PERSONS RESPONSIBLE, THIRD PARTY INFORMATION, EXPERTS' REPORTS AND COMPETENT AUTHORITY APPROVAL**	**6**	**384**
1.1.	Persons responsible for the information contained in the registration document	6.1	384
1.2.	Declaration of persons responsible for the information contained in the registration document	6.1.1	384
1.3.	Expert's statement or report	N/A	
1.4.	Statements regarding third-party information	6.3	385
1.5.	Statement with prior approval by the competent authority	Front page	
2.	**STATUTORY AUDITORS**	**6.2**	**384**
2.1.	Name and address of the Company's statutory auditors	6.1	384
2.2.	Statutory auditors having resigned, dismissed or not reappointed during the relevant period	N/A	
3.	**RISK FACTORS**	**1.5**	**135**
4.	**INFORMATION ABOUT THE COMPANY**	**1.2, 5.4**	**31, 375**
4.1.	Corporate name and trade name	5.4.1	375
4.2.	Place and number of incorporation, and legal entity identifier ("LEI")	5.4.2	375
4.3.	Date of incorporation and term	5.4.3	375
4.4.	Registered office, legal form, jurisdiction, country of origin, address and phone number of registered office and website	5.4.4	375
5.	**BUSINESS OVERVIEW**	**1.3**	**42**

	Universal Registration Document Table of concordance		
	Annexes I and II of the Delegated Regulation No. 2019/980 of the European Commission dated March 14, 2019	**Chapter(s) / Section(s)**	**Page**
5.1.	Principal activities	1.2.1, 1.3.1	31, 42
5.1.1.	*Nature of the operations and principal activities*	*1.3.1*	*42*
5.1.2.	*Significant new products and/or services*	*N/A*	
5.2.	Principal markets	1.3	42
5.3.	Important events in the development of business	1.2	31
5.4.	Strategy and objectives	1.3.1	42
5.5.	Information regarding the extent to which the company is dependent, on patents or licenses, industrial, commercial or financial contracts or new manufacturing processes	1.5	135
5.6.	Basis for any statements made by the Company regarding its competitive position	1.3.1, 1.3.11	42, 86
5.7.	Investments	1.2.4	41
5.7.1.	*Material investments made during the three last financial years*	*1.2.4*	41
5.7.2.	*Material investments in progress or for which firm commitments have already been made*	*1.2.4*	41
5.7.3.	*Joint ventures and undertakings in which the Company holds a proportion of the capital likely to have significant effect on the assessment of its own assets and liabilities, financial position or profits and losses*	*1.2.4*	41
5.7.4.	*Environmental issues that may affect the Company's utilization of the tangible fixed assets*	*N/A*	
6.	**ORGANIZATIONAL STRUCTURE**	**1.2.2**	**34**
6.1.	Brief description of the Group	1.2.2	**34**
6.2.	List of the significant subsidiaries	5.5	376
7.	**OPERATING AND FINANCIAL REVIEW**		
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7.1.1.	*Company's development and performance, financial condition, changes in financial condition for the last three financial years*		
7.1.2.	*Company's likely future development and activities in the field of research and development*		
7.2.	Operating results	1.4.1	122
7.2.1.	*Significant factors, including unusual or infrequent events or new development materially impacting the Group's operating income*	*1.4.5*	133
7.2.2.	*Reasons for material changes in the Group's net sales or revenues*	*1.4.5*	133
8.	**CAPITAL RESOURCES**	**1.4.4**	**130**
8.1.	Information concerning the Company's capital resources	1.4.4	**130**
8.2.	Sources, amounts and narrative description of the Company's cash flows	1.4.2.2	126
8.3.	Information on the borrowing requirements and funding structure of the Company	1.4.2.4	127
8.4.	Information regarding any restrictions on the use of capital resources that have materially affected, or could materially affect, directly or indirectly, the Company's operations	1.4.4	**130**
8.5.	Information regarding the anticipated sources of funds needed to fulfil commitments referred to in item 5.7.2	1.4.4	**130**
9.	**REGULATORY ENVIRONMENT**	**1.3.17**	**107**
10.	**TREND INFORMATION**	**1.4.3**	**130**
10.1.	Most significant recent trends and any significant change in the financial performance of the Group since the end of the last financial year	1.1.3	30
10.2.	Information on any known trends, uncertainties, demands, commitments or events that are reasonably likely to have a material effect on the Company's prospects	1.4.3.4	130
11.	**PROFIT FORECASTS OR ESTIMATES**	**1.4.3.3**	**130**

	Universal Registration Document Table of concordance		
	Annexes I and II of the Delegated Regulation No. 2019/980 of the European Commission dated March 14, 2019	**Chapter(s) / Section(s)**	**Page**
11.1.	Published profit forecasts or estimate	1.4.3.3	**130**
11.2.	Statement on the principal assumptions upon which the Company has based its forecast or estimate	N/A	
11.3.	Statement of comparability with the historical financial information and compliance with the Company's accounting policies	N/A	
12.	**ADMINISTRATIVE, MANAGEMENT, AND SUPERVISORY BODIES AND SENIOR MANAGEMENT**	**2.1**	**158**
12.1.	Information in relation to members of the administrative, management, and supervisory bodies	2.1	**158**
12.2.	Administrative, management and supervisory bodies and senior management conflicts of interests	2.1.6	170
13.	**COMPENSATION AND BENEFITS**	**2.2**	**171**
13.1.	Amount of compensation paid and benefits in kind granted by the Group	2.2.1, 2.2.2	172, 173
13.2.	Total amounts set aside or accrued by the Company or its subsidiaries to provide pension, retirement or similar benefit	2.2.5	181
14.	**BOARD PRACTICES**		
14.1.	Date of expiration of the current terms of office and period during which the person has served in that office	2.1.1	158
14.2.	Information about members of the administrative, management or supervisory bodies' service contracts with the Company or any of its subsidiaries providing for benefits upon termination of employment	2.2.2, 5.6.2	173, 377
14.3.	Information about the Company's specialized committees	2.1.5	165
14.4.	Corporate governance	2.3	192
14.5.	Potential material impacts on the corporate governance	2.5	201
15.	**EMPLOYEES**	**5.7**	**382**
15.1.	Number of employees	5.7.1.1	382
15.2.	Shareholdings and stock options of any person referred to in item 12.1	2.2.7, 5.1.4	182, 345
15.3.	Arrangement for involving the employees in the capital of the Company	5.7.2	383
16.	**PRINCIPAL SHAREHOLDERS**	**5.2**	**373**
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GLOSSARY

Abscopal effect: the abscopal effect (from the Latin *ab-* "distant" and the Greek *skopos* "target", literally "far from the target") is the effect caused by irradiation on tissues far from the irradiated site. In the field of cancerology, the term refers to the anti-tumor effect caused by radiotherapy outside the field of irradiation (i.e. the regression of distant metastases after irradiation of the primary tumor).

Adrenal gland: gland above the kidney.

Adverse Effect: incident or risk of incident involving a device or a drug that has resulted in or could result in death or any deterioration of the health of a patient, a user or a third party.

AMM (Marketing Authorization): administrative authorization which is pre-requisite to the sale of drugs, both in human and veterinary medicine. It is granted in the European Union by the European Medicines Agency and the United States by the Food and Drug Administration (FDA).

ANSM: the *Agence Nationale de Sécurité du Médicament et des Produits de Santé* replaced the *Agence Française de Sécurité Sanitaire du Médicament et des Produits de Santé* (AFSSMPS) on May 1st, 2012 at, overtaking its missions, rights and obligations. The ANSM has two main missions: providing equitable access to innovation for all patients; and ensuring the safety of health products throughout their life cycle, from the initial trials to post-marketing surveillance. It is responsible in particular for issuing marketing authorizations, withdrawing or suspending said marketing authorizations and approving clinical trials.

CE Branding: in force since 1993, the CE marking shows the conformity of a product to the Community requirements incumbent on the manufacturer of the product. It must be affixed before a product is placed on the European market. It gives the products in question freedom of circulation throughout the European Union.

Clearance: ability of a tissue, organ or body to remove a given substance.

Contract Manufacturing Organization (CMO): contract research companies to which the pharmaceutical/cosmetic industry may subcontract the planning, completion and follow-up of preclinical research studies and/or clinical trials as well as large scale production of drugs.

Contract Research Organization (CRO): contract research companies to which the pharmaceutical/ cosmetic industry may subcontract the planning, completion and follow-up of preclinical research studies and/or clinical trials.

Covalent Link: chemical bond in which each of the atoms bound together pools an electron from one of its outer layers to form an electron doublet linking the two atoms. It is one of the forces that produces the mutual attraction between atoms.

Cytotoxicity: the property of a chemical or biological agent to alter cells, possibly to the point of destruction.

Drug: any substance or composition presented as having curative or preventive properties with regard to human or animal diseases, as well as any substance or composition that may be used in or administered to humans, in order to establish a medical diagnosis or to restore, correct or modify their physiological functions by exerting a pharmacological, immunological or metabolic action (Article L5111-1 of the French Public Health Code).

Electron: one of the fundamental constituents of matter, negatively charged. It can be emitted by devices called particle accelerators for use in radiation therapy.

EMA (European Medicines Agency): based in Amsterdam, this decentralized body of the European Union is responsible for the protection and promotion public and animal health through the evaluation and supervision of medicinal products for human and veterinary use. The EMA is responsible for the scientific evaluation of applications for European marketing authorization for medicinal products (centralized procedure). When the centralized procedure is used, companies file a single application for marketing authorization to the EMA.

Federal Drug Administration (FDA): U.S. Food and Drug Administration. This body is tasked, among other things, with authorizing the sale of medicines in the United States.

GCP (Good Clinical Practice): set of measures ensuring quality of clinical trials.

Genotoxicity: the ability to alter genes.

GMED: French Notified Body for Medical Devices.

GMP (Good Manufacturing Practices): part of the pharmaceutical quality assurance which ensures that drugs are manufactured and controlled consistently, according to quality standards adapted to the intended use and in compliance with the specifications of these drugs.

Gray: X-ray dose unit, abbreviated as Gy. Of the name of an English radiobiologist Stephan Gray.

Hepatocellular carcinoma: cancer that develops from liver cells called hepatocytes. It is also referred to as HCC or hepatocarcinoma.

ICH: the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use is an international structure that brings together regulatory authorities and representatives from the pharmaceutical industry in Europe, Japan and the United States to discuss the scientific and technical aspects of drug registration. The mission of ICH is to achieve data and regulatory harmonization and thus ensure the safety, quality and effectiveness of drugs developed and recorded by the different participating countries.

Immune checkpoint inhibitor: tumor cells sometimes develop the ability to escape immune system control and thus being attacked and destroyed by the immune system. For this, the tumor triggers very precise mechanisms that make immune cells (i.e. T cells) ineffective. The body is then unable to adequately respond to fight the cancer cells. Key elements of these mechanisms, called immune checkpoints (CTLA-4, PD-1, PD-L1, among others) may be blocked by treatments called “immune checkpoint inhibitors.” Blocking these receptors reactivates the immune system so that it can fight more effectively tumor cells.

Immune System: the body's complex defense system against diseases; one of the properties of the immune system is its ability to recognize substances foreign to the body and to trigger defense measures, such as antibody synthesis.

Immunogenicity: the potential of an antigen to induce an immune response.

Immuno-Oncology (“IO”): a medical approach aimed at restoring or stimulating the patient’s immune system (e.g., the patient's natural defenses, white blood cells and T-cells) to help the body’s natural defense cells recognize and destroy cancer cells.

Immunotherapy: a therapy that acts primarily on the patient's immune system to make it capable of detecting and destroying cancer cells. Specific immunotherapy involves making tumor cells more recognizable by the immune system or stimulating certain immune cells to make them more effective.

It is based on monoclonal antibodies, including immune checkpoint inhibitors or bispecific antibodies but also adoptive cell transfer or anti-tumor vaccination.

Incidence: the frequency with which a pathology is detected in a population.

Irradiation Field: area of the body on which radiation is projected during radiation therapy.

La Fayette, we are here: La Fayette, nous voilà.

LEEM: professional organization that federates and represents the pharmaceutical companies present in France. It promotes collective approaches to progress, quality and enhancement of the sector.

Lethal Energy: deadly energy.

Dose Limiting Toxicity (DLT): dose for a given medication at which toxicity appears. This dose is used to define the therapeutic dose that will necessarily be below DLT.

Local Treatment: treatment that consists of acting directly on the tumor or the area where it is located. The goal of this type of treatment is to eliminate all cancer cells in that area. Surgery and radiotherapy are local cancer treatments. It is also called locoregional treatment.

Lymph node: small bulge on the lymphatic vessel pathway. Often arranged in chains or clusters, the lymph nodes are either on the superficial (in the neck, armpit, groin), or deep (in the abdomen, chest). They play an essential role in protecting the body against infection or cancer cells. They normally measure less than 1 centimeter in diameter. Adenopathy is the abnormal size of a lymph node. An enlarged lymph node may be related to something other than cancer.

Materio-vigilance: Monitoring of incidents that may occur in the use of medical devices, monitoring of incidents or risks of incidents resulting from their use of medical devices after they made available on the market. Specific procedures must ensure the quality of their supply, storage, commissioning or dispensing, the maintenance of their performance and safety level, their prescription and, finally, the training of those who have to use them.

Medical Device: any instrument, apparatus, equipment, material, product, with the exception of products of human origin, or other material used alone or in combination, including the accessories and software involved in its operation, intended by the manufacturer to be used in humans for medical purposes and the primary action of which is not obtained by pharmacological, immunological or metabolic means, but the function of which can be assisted by such means.

Metastasis: spread of cancer cells from one part of the body to others.

MRI (Magnetic Resonance Imaging): cross-sectional images in different planes based on the magnetic properties of the tissues, which allows a three-dimensional reconstruction of the analyzed structure.

Neoadjuvant treatment: treatment that precedes the main treatment. Most often, the purpose of neoadjuvant therapy is to reduce the size of the tumor before surgery or radiotherapy, which makes treatment easier. Chemotherapy, radiation therapy, or hormone therapy can be neoadjuvant therapies.

Oncology: medical speciality that focuses on cancer.

Principal investigator: person who leads and monitors the conduct of the research and ensures the coordination with any investigators who are at different sites (multicenter trials).

Protocol: Detailed plan of a scientific or medical experiment, treatment or procedure. The protocol of a clinical study describes what is being done, how it is being done and why.

Radiation oncologist: a doctor specializing in the treatment of cancer by radiotherapy. Radiation therapy involves exposing the tumor, and sometimes some of the lymph nodes connected to the affected organ, to radiation in order to destroy the cancer cells. In collaboration with a specialized team that includes a physicist and a dosimetrist, the radiotherapist calculates the dose of radiation needed to treat the patient and plans radiation therapy sessions. These will be carried out by a radiotherapy technician. Regular check-ups enable the radiotherapist to ensure that the treatment is going well and to prescribe medication to treat any adverse events.

Radiation therapy: treatment of cancer with radiation that destroys cancer cells or stops their growth. Unlike chemotherapy, which acts on cancer cells throughout the body, radiation therapy is a local treatment, like surgery. The rays themselves are not painful, but they can cause adverse events, sometimes several weeks after radiation therapy.

Randomization: process of randomly assigning patients to different groups to compare different treatments.

Standard of care: treatment (or other intervention) commonly used and considered effective based on previous clinical studies. It is the best-known treatment.

Response Evaluation Criteria in Solid Tumors (RECIST 1.1): the response evaluation criteria in solid tumors have defined a simple, single-dimensional evaluation method to provide standardized and simplified criteria that allows comparison between clinical trials. They have become the most widely accepted criteria for response assessment in clinical trials in most solid tumors.

Risk to benefit ratio: this term describes the theoretical relationship between the benefits expected from the treatment and the potential risk of adverse events from that treatment.

Sarcoma: type of cancer that develop in connective tissue (tissue that supports, wraps, protects or fills other organs in the body: bone, muscle, fat, vessels, etc.).

Solid tumor: an abnormal mass of tissue that usually does not contain a cyst or fluid. Solid tumors can be benign (non-cancerous) or malignant (cancerous).

Toxicity: adverse effects related to the administration of a treatment. Toxicity is graded on a scale of 0 to 4.

Tumorectomy: a surgery that removes a tumor and a small part of the surrounding tissue, while preserving the organ on which it grew.

USD: US Dollars.

Vigilance: the monitoring of all adverse events during a clinical trial.

X-ray: a ray of invisible light. X-rays pass through materials and are more or less stopped depending on the components they encounter. The passing rays can be detected, allowing body imaging. Depending on their power, they are used to perform medical imaging examinations (radiology) or treat patients (radiotherapy). X-rays are also called X-photons.

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