UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 20-F

(Mark One)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

for the fiscal year ended December, 31 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

for the transition period from _____ to _____

OR

☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of event requiring this shell company report _____

Commission File Number: 001-39777

NANOBIOTIX S.A.

(Exact name of registrant as specified in its charter)

France
(Jurisdiction of incorporation or organization)

Nanobiotix S.A.
60 rue de Wattignies
75012 Paris, France
(Address of principal executive offices)

Mr. Bart van Rhijn
Chief Financial Officer
Nanobiotix S.A.
60 rue de Wattignies
75012 Paris, France
Tel: +33 (0)1 40 26 04 70, Fax: +33 (0)1 40 26 04 44
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
American depositary shares, each representing one ordinary share, nominal value €0.03 per share	**NBTX**	**The Nasdaq Stock Market LLC**
Ordinary shares, nominal value €0.03 per share*	*	**The Nasdaq Stock Market LLC***

*Not for trading, but only in connection with the registration of the American Depositary Shares.

Securities registered or to be registered pursuant to Section 12(g) of the Act.

None

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act.

None

Indicate the number of outstanding shares of each of the issuer's class of capital or common stock as of the close of the period covered by the annual report.

Ordinary shares, nominal value €0.03 per share: 34,825,872 as of December 31, 2021

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

If this report is an annual or transition report, indicate by check mark, if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes ☐ No ☒

Note – Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those Sections.

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, accelerated filer, a non-accelerated filer, or an emerging growth company. See definition of "large accelerated filer", "accelerated filer" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☒
Non-accelerated filer ☐	Emerging Growth Company ☒

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards † provided pursuant to Section 13(a) of the Exchange Act. ☐

† The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☐	International Financial Reporting Standards as issued by the International Accounting Standards Board ☒	Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow: Item 17 ☐ Item 18 ☐

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

(APPLICABLE ONLY TO ISSUERS INVOLVED IN BANKRUPTCY PROCEEDINGS DURING THE PAST FIVE YEARS) Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court.Yes ☐ No ☐

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INTRODUCTION

Unless otherwise indicated or the context otherwise requires, references in this Annual Report to "we," "our," "us," "Nanobiotix", the "Company", or the "Group" refer to Nanobiotix S.A. and its consolidated subsidiaries.

We were incorporated as a *société anonyme* on March 4, 2003. We are registered at the Paris *Registre du Commerce et des Sociétés* under the number 447 521 600 00034. Our principal executive offices are located at 60, rue de Wattignies, 75012 Paris, France, and our telephone number is +33 1 40 26 04 70. Our agent for service of process in the United States is our U.S. subsidiary, Nanobiotix Corporation located at 210 Broadway, Cambridge, Massachusetts 02139.

Our ordinary shares, nominal value €0.03 per share ("ordinary shares") began trading on the regulated market of Euronext in Paris in October 2012. Our American Depositary Shares, each representing one ordinary share, began trading on the Nasdaq Global Select Market on December 11, 2020. Throughout this Annual Report, references to ADSs mean American Depository Shares or ordinary shares represented by ADSs, as the case may be.

We maintain a website at *http://www.nanobiotix.com/en/*. The reference to our website is an inactive textual reference only and the information contained in, or that can be accessed through, our website or any other website cited in this Annual Report is not a part of this Annual Report.

Our audited consolidated financial statements have been prepared in accordance with International Financial Reporting Standards ("IFRS"), as issued by the International Accounting Standards Board ("IASB"). Our audited consolidated financial statements are presented in euros and, unless otherwise specified, all monetary amounts presented in this Annual Report are in euros. All references in this Annual Report to "$," "dollars" and "USD" mean U.S. dollars and all references to all references to "€" and "euros" mean euros.

Trademarks and Service Marks

We own various trademark registrations and applications, and unregistered trademarks and service marks. "Nanobiotix," "NBTX" (including, among others, referring to NBTXR3), the Nanobiotix logo and other trademarks or service marks of Nanobiotix S.A. appearing in this Annual Report are the property of Nanobiotix S.A. or its subsidiaries. Solely for convenience, the trademarks, service marks and trade names referred to in this Annual Report 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 this Annual Report 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains "forward-looking statements" within the meaning of applicable federal securities laws, including the Private Securities Litigation Reform Act of 1995. All statements other than present and historical facts and conditions contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, plans and our objectives for future operations, are forward-looking statements. When used in this Annual Report, the words "anticipate," "believe," "can," "could," "estimate," "expect," "intend," "is designed to," "may," "might," "plan," "potential," "predict," "objective," "shall," "should," "will," or the negative of these and similar expressions identify forward-looking statements. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified under "Item 3D. Risk Factors" in this Annual Report. These risks and uncertainties include factors relating to:

- our ability to successfully develop and commercialize NBTXR3;
- our ability to expand our product pipeline by developing and commercializing NBTXR3 in additional indications, including in combination with chemotherapies or I-O treatment;
- our ability to compete with institutions with greater financial resources and expertise in research and development, preclinical testing, clinical trials, manufacturing and marketing;
- the completion of applicable pre-marketing regulatory requirements and/or our ability to maintain regulatory approvals and certifications for our products and product candidates and the rate and degree of market acceptance of our product candidates, including NBTXR3;
- regulatory developments in the United States, the EU, and other countries;
- the effects of the COVID-19 pandemic on our business operations and clinical development timelines and plans;
- the initiation, timing, progress and results of our preclinical studies and clinical trials, including those trials to be conducted under our collaboration with MD Anderson;
- the expected timeline of our clinical trial completion, including our ability, and the ability of third party collaborators, to successfully conduct, supervise and monitor clinical trials for our product candidates;
- our ability to obtain raw resources and maintain and operate our facilities to manufacture our product candidates;
- our ability to manufacture, market and distribute our products upon successful completion of applicable pre-marketing regulatory requirements, specifically NBTXR3;
- our ability to achieve the commercialization goals for NBTXR3;
- our ability to enter into effective collaborations on attractive terms and to successfully resolve disputes, if any, under existing and future collaboration agreements;
- our ability to obtain funding for our operations;
- our ability to attract and retain key management and other qualified personnel;
- our global operations and exposure to global markets;
- our ability to protect and maintain our intellectual property rights, manufacturing know-how and proprietary technologies and our ability to operate our business without infringing upon the intellectual property rights and proprietary technologies of third parties;
- our ability to effectively deploy the proceeds from our Global Offering (as defined herein);
- future revenue, expenses, capital expenditures, capital requirements and performance of our publicly traded equity securities;
- our status as a foreign private issuer and emerging growth company and the reduced disclosure requirements associated with maintaining these statuses; and
- other risks and uncertainties, including those listed under "Item 3D. Risk Factors."

As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

You should read this Annual Report and the documents that we reference in this Annual Report and have filed as exhibits completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

Market, Industry and Other Data

Unless otherwise indicated, information contained in this Annual Report concerning our industry and the markets in which we operate, including our general expectations and market position, market opportunity and market size estimates, is based on information from independent industry analysts, third-party sources and management estimates. Management estimates are derived from publicly available information released by independent industry analysts and third-party sources, as well as data from our internal research, and are based on assumptions made by us based on such data and our knowledge of such industry and market, which we believe to be reasonable. In addition, while we believe the market opportunity information included in this Annual Report is generally reliable and is based on reasonable assumptions, such data involves risks and uncertainties and are subject to change based on various factors, including those discussed under “Item 3D. Risk Factors.”

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A.[Reserved]

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

Our business and our industry are subject to significant risks. You should carefully consider the risks and uncertainties described below, together with all of the other information in this Annual Report, including our audited consolidated financial statements and related notes. This Annual Report also includes forward-looking statements that involve risks and uncertainties. See “Special Note Regarding Forward-Looking Statements.” If any of the following risks are realized, our business, financial condition, operating results and prospects could be materially and adversely affected.

Summary of Key Risks

- Risks Related to Our Business
  - Our operating history, which has focused primarily on research and development and advancing the clinical trial program for NBTXR3, makes it difficult to assess our future prospects.
  - We have not generated significant revenues and have incurred significant operating losses since our inception. While the amount of our future net losses will depend, in part, on the amount of our future operating expenses and our ability to obtain funding, we anticipate that we will continue to incur significant losses for the foreseeable future.
  - Because each of our ongoing and contemplated clinical trials involves NBTXR3, we are heavily dependent on the successful development and commercialization of this lead product candidate.
  - We face significant competition in our discovery, development and commercialization activities from competitors who may have significantly greater resources than we do.
  - The extent to which the COVID-19 pandemic and resulting deterioration of worldwide economic conditions adversely impacts our business, financial condition, and operating results will depend on future developments, which are difficult to predict.
  - We will require additional funding, which may not be available on acceptable terms or at all, and certain financing instruments—such as the finance contract for the EIB loan (as defined herein)—may impose certain restrictions on the operation of our business.

- Risks Related to the Development of Our Product Candidates
  - Our product candidates must undergo clinical trials that are time-consuming and expensive, the outcomes of which are unpredictable and for which there is a high risk of failure, and which are susceptible under a variety of circumstances to additional costs, delays, suspensions and terminations.
  - We rely on third parties to assist in our discovery, development, commercialization and manufacturing of our product candidates and issues relating to such third parties, or their activities, could result in additional costs and delays and hinder our research, development and commercialization prospects.
  - In connection with collaboration agreements with third parties for the development and commercialization of our product candidates, we may be unable to identify suitable collaboration partners, and once a collaboration partner is secured, we have limited control over the attention that our commercialization partner devotes to our product candidates.

- Risks Related to Obtaining Regulatory Approval or Certification for Our Product Candidates
  - Our business is governed by a rigorous, complex and evolving regulatory framework, including stringent clinical trial regulations, pre-marketing regulatory requirements, pricing, reimbursement and cost-containment regulations, and rigorous ongoing regulation of approved products. This regulatory framework results in significant compliance costs, makes the development and approval of our product candidates time intensive and unpredictable, and may reduce the ultimate economic value and prospects for our product candidates.
  - A Fast Track or Breakthrough Therapy designation by the FDA may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive regulatory approval.

- Risks Related to the Production and Manufacturing of Our Product Candidates
  - Because we depend on third parties for the supply of various materials that are necessary to produce our product candidates for clinical trials, the loss of key suppliers, the unavailability of raw materials, or disruptions in manufacturing processes could increase production costs or result in delays in our product development.
  - Our and our subcontractors' manufacturing facilities are subject to significant government regulations and approvals and any compliance failures could lead to significant delays in the availability of products for commercial sale or clinical trials, may result in the termination of or a hold on a clinical trial, or may delay or prevent filing or approval of marketing applications or the completion of pre-marketing certification procedures, as applicable, for our products.

- Risks Related to the Commercialization of Our Product Candidates
  - Even if we successfully complete clinical trials for certain of our product candidates, those candidates may not be commercialized or achieve commercial success for a variety of reasons, including a lack of acceptance by the medical community, the imposition of post-marketing regulatory restrictions, the costs and burdens associated with post-marketing regulatory requirements, or unanticipated problems with our products following regulatory approval.
  - If we are unable to establish sales, marketing and distribution capabilities for our product candidates, we may not be successful in commercializing those product candidates if and when they are approved or duly CE marked.

- Risks Related to Human Capital Management
  - We may encounter difficulties in managing our development and expansion, including challenges associated with our ability to attract and retain executive management and supervisory board members as a U.S. public company.
  - Our business could be harmed if we lose key management personnel on whom we depend or if we cannot attract and retain other qualified personnel.
  - Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

- Risks Related to Operational Compliance and Risk Management
  - We use hazardous chemicals in our business, and any claims relating to improper handling, storage or disposal of these materials could be time-consuming and costly.
  - The risk of product liability claims is inherent in the development and commercialization of therapeutic products, and product liability or other lawsuits could divert management and financial resources, result in substantial liabilities and reduce the commercial potential of our product candidates.
  - We are subject to extensive healthcare laws and regulations impacting, among other things, our research and proposed sales, marketing and education programs of product candidates that successfully complete applicable pre-marketing regulatory requirements, and which may require substantial compliance efforts. Any regulatory compliance failures could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

- Risks Related to Intellectual Property
  - Because our commercial success depends, in part, on obtaining and maintaining proprietary rights to our and our licensors' intellectual property, our ability to compete may decline if we fail to obtain protection for our products, product candidates, processes and technologies or do not adequately protect our intellectual property.
  - Our competitive position may be adversely impacted as a result of a variety of factors, including potentially adverse determinations of complex legal and factual questions involved in patents and patent applications or insufficiently long patent lifespans in one or more jurisdictions where we obtain intellectual property protection.

- Because it is cost prohibitive to seek intellectual property protection on a global basis, our intellectual property protection in certain jurisdictions many not be as robust as in the United States, which may adversely impact our competitive position.
- Third parties may assert ownership or commercial rights to inventions we develop or otherwise regard as our own, or assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.
- A dispute concerning the infringement or misappropriation of our intellectual property rights or the intellectual property rights of others could be time-consuming and costly, and an unfavorable outcome could harm our business.

- Risks Related to the Ownership of Our Ordinary Shares and ADSs
  - We do not currently intend to pay dividends on our securities, and under French law may be limited in our ability to do so in the future.
  - Holders of ADSs will not be directly holding our ordinary shares and may be subject to limitations on the transfer of their ADSs and certain voting and withdrawal rights of the underlying ordinary shares as well as limitations on their ability to exercise preferential subscription rights or receive share dividends.
  - We are an emerging growth company and we cannot be certain if the reduced disclosure requirements applicable to us will make our ADSs less attractive to investors.
  - ADSs holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiffs in any such action.

- Risks Related to Our Status as a Non-U.S. Company
  - The rights of shareholders in companies subject to French corporate law differ in material respects from the rights of shareholders of corporations incorporated in the United States.
  - As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and the Nasdaq's corporate governance standards. We expect to follow certain home country practices in relation to certain corporate governance matters, which may afford less protection than would be provided if we fully complied with the Nasdaq requirements.
  - Our By-laws and French corporate law contain provisions that may delay or discourage a takeover attempt.
  - If we are determined to be a PFIC for any taxable year, there may be adverse U.S. federal income tax consequences to U.S. holders.
  - Our international operations may be exposed to foreign exchange risks, U.S. federal income tax risks, and additional risks, and our exposure to these risks will increase as our business continues to expand.

Risks Related to Our Business

Our operating history makes it difficult to assess our future prospects.

Our operating history has been focused primarily on research and development and the advancement of the clinical trial program for our lead product candidate, NBTXR3. A key element of our strategy is to use and expand our proprietary technology to continue to develop our 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, including STS, head and neck cancers, liver cancers, prostate cancer and rectal cancer. The nanotechnology underlying our product candidates, specifically the use of nano-sized radiation enhancers as a cancer treatment method, is novel.

Although in April 2019, we successfully completed the applicable conformity assessment procedure for affixing the CE marking to our NBTXR3 device for the treatment of locally advanced STS, enabling commercialization of the product in the European Union (the "EU") for such indication, we have not yet commercialized the product nor generated any revenues from the sale of any approved products and we may ultimately not be able to generate substantial revenue from the commercialization of approved products.

We have encountered, and will continue to encounter, risks and difficulties frequently encountered by growing companies in new and rapidly evolving fields, particularly as we seek to utilize nanotechnology to provide solutions to unmet therapeutic needs in oncology. Consequently, the ability to predict our future operating results or business prospects is more limited than if we had a portfolio of approved products on the market.

We may not be able to fully implement or execute on our commercial strategy or realize, in whole or in part or within our expected time frames, the anticipated benefits of our growth strategies. You should consider our business and prospects in light of the risks and difficulties we face as a growing company focused primarily on the development and advancement of clinical trials.

We have incurred significant losses and anticipate that we will continue to incur significant losses for the foreseeable future.

We have not generated significant revenues and have incurred significant operating losses since our inception. To date, our limited revenues and other income have been derived primarily from payments under our license and collaboration agreement with PharmaEngine, which terminated in March 2021 (see item 4B. Business overview - our collaboration agreements" for additional details), and research tax credits. We have not generated revenues to date from product sales or royalties, and we do not expect to generate significant revenues from product sales or royalties unless and until our product candidates are successfully commercialized following regulatory approval. We incurred net losses of €47.0 million for the year ended December 31, 2021. The amount of our future net losses will depend, in part, on the amount of our future operating expenses and the pace at which they are incurred and our ability to obtain funding through our commercialization activities, through equity or debt financings or through research grants or collaborative partnerships. As of December 31, 2021, our losses are primarily attributable to expenditures committed to developing our nanotechnology and our clinical and preclinical programs. We expect to continue to incur significant expenses and losses for the foreseeable future. We anticipate that such expenses and capital requirements will increase substantially as we:

- continue our preclinical and clinical programs currently in progress;
- expand the scope of our current clinical trials and commence new clinical trials to research new oncological applications for our nanotechnology;
- expand our manufacturing capabilities for the production of our product candidates and maintain compliance with applicable manufacturing regulatory requirements;
- seek regulatory and marketing approvals, or initiate the necessary conformity assessment procedures, as applicable, for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may successfully complete applicable pre-marketing regulatory requirements;
- advance our research and development efforts, which may include the acquisition of new technologies, products or licenses;
- maintain, protect and expand our intellectual property portfolio; and
- attract new and retain existing skilled personnel.

The net losses we incur may fluctuate significantly from year-to-year such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular period or periods, our operating results could be below the expectations of securities analysts or investors, which could cause the price of our ordinary shares and ADSs to decline.

We are heavily dependent on the successful development and commercialization of NBTXR3.

Our business and future success depends heavily on our ability to develop and commercialize our lead product candidate, NBTXR3, for indications for which there is an attractive market opportunity, and to satisfy the necessary regulatory requirements for its marketing and sale. Our development programs of NBTXR3 for the treatment of different cancer indications are at varying stages. Because each of our ongoing and contemplated trials involves NBTXR3, if one of these preclinical or clinical trials reveals safety and/or therapeutic efficacy issues, the validity of our nanotechnology platform itself could be questioned, which could potentially require additional time and investment in research and development to attempt to remedy the issues identified. The development of each application of NBTXR3 could subsequently be impacted, potentially having a significant negative impact on our business prospects, financial situation and anticipated growth.

Although we successfully completed the applicable conformity assessment procedure for affixing the CE marking to our NBTXR3 device for the treatment of locally advanced STS, enabling the commercialization of the product in the EU for such indication, NBTXR3 remains in clinical development for other indications, and we cannot be certain that NBTXR3 will receive regulatory approval or successfully complete the necessary conformity assessment procedures, as applicable, or be successfully commercialized, for any additional cancer indications, even if we successfully complete applicable pre-marketing regulatory requirements. Any failure or delay in the development or commercialization of NBTXR3 could have a material adverse effect on our business, financial condition and prospects.

We face competition and our competitors may have significantly greater financial, technical and other resources than we do, which may result in others discovering, developing, receiving approval for, or commercializing products before or more successfully than us.

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. Certain companies are developing treatments to increase sensitivities of tumors to radiation and other sources of energy. Like us, these companies are pursuing various technologies that involve substances that work to destroy tumor cells from the inside without causing additional damage to surrounding healthy tissues. Any product candidates that we 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. Similarly, our commercial opportunity could be reduced if we fail to protect or to enforce our intellectual property rights successfully against third parties who infringe our patents or our licensors' patents, or if competitors design around our patent claims or our licensors' patent claims to produce competitive products, product candidates, processes and technologies that fall outside of the scope of our or our licensors' patents. Our competitors may also successfully complete applicable pre-marketing regulatory requirements for their products more rapidly than us.

The extent to which the COVID-19 pandemic and resulting deterioration of worldwide economic conditions adversely impacts our business, financial condition, and operating results will depend on future developments, which are difficult to predict.

In December 2019, a new strain of coronavirus, SARS-CoV-2, identified as the cause of coronavirus disease 2019 (COVID-19), emerged. Since then, SARS-CoV-2 and the resulting disease COVID-19 has spread to many countries, including each of the countries in which our clinical trials are planned or ongoing.

As a result of the COVID-19 pandemic, governmental authorities have implemented and are continuing to implement numerous and rapidly evolving measures to try to contain the virus, such as travel bans and restrictions, limits on gatherings, quarantines, shelter-in-place orders, and business shutdowns. In response to the COVID-19 pandemic and in accordance with governmental orders, we have also modified our business practices and implemented proactive measures to protect the health and safety of employees, including restricting employee travel, requiring remote work arrangements for non-laboratory employees, implementing social distancing and enhanced sanitary measures in our facilities, and cancelling attendance at in-person events and conferences. Many of the suppliers and service providers on whom we rely have made similar modifications. There is no certainty that such measures will be sufficient to mitigate the risks posed by, or the impacts and disruptions of, the COVID-19 pandemic.

As a result of the COVID-19 pandemic, we have experienced, and expect to continue to experience, disruptions and adverse impacts to our business, including delays in certain clinical trial activities. Although the ultimate impact of the COVID-19 pandemic on our business is not determinable at this stage, the operational and functional impacts of the COVID-19 pandemic could be material, including:

- Disruptions, interruptions or delays of our clinical trial activities, whether conducted by us or in collaboration with our partners (such as MD Anderson), due in particular to delays or difficulties in recruiting patients, challenges from quarantines, site closures, supply chain interruptions, limitations or redirection of human or material resources normally allocated to these clinical trials, interruptions in data collection, monitoring and/or processing, more limited access to physicians, delays in receiving, or shortages of, the supplies and materials necessary for the performance of clinical trials, or travel restrictions imposed or recommended by local authorities;
- Changes in local regulations due to the measures taken in response to the COVID-19 pandemic, which could require us to modify the conditions of our clinical trials, potentially resulting in unforeseen costs or the interruption of our trials;
- Delays in obtaining from regulatory authorities the approvals required to launch our contemplated clinical trials, as well as delays in the necessary interactions with local authorities or other important organizations and third-party partners;
- 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; or
- Challenges 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.

While recruitment and monitoring in our clinical trials have slowed due to the pandemic and based on current circumstances, we expect that the receipt and reporting of data in head and neck cancer and immuno-oncology ("I-O") clinical trials that were underway prior to the pandemic will generally proceed as planned based on the number of patients that had already been recruited. We anticipate that, as a result of the disruptions of the COVID-19 pandemic, protocol development and review processes and enrollment in trials not yet in progress are likely to be

delayed or to progress more slowly than originally anticipated. Moreover, given recruitment barriers, we expect delays in launching these trials even after regulatory clearance to proceed is obtained.

The degree to which COVID-19 ultimately impacts our business will depend on future developments, which are highly uncertain and cannot be predicted, including, but not limited to, the severity, duration and geographic spread of the outbreak, potential resurgence events and the emergence of additional variant strains, the effectiveness of available vaccines (including with respect to emerging variants of COVID-19) and the effective distribution thereof, as well as the global, national and regional actions to contain the virus and address its impact. The resumption of normal business operations after interruptions caused by COVID-19 may be delayed or constrained by lingering effects of COVID-19 on us or our suppliers and third-party service providers, respectively. Even after the COVID-19 outbreak has subsided, we may experience material and adverse impacts as a result of the global economic impact of the COVID-19 outbreak.

The impact of COVID-19 may also exacerbate other risks discussed in this Annual Report, any of which could have a material effect on us. This situation is changing rapidly and additional impacts may arise that we are not aware of currently.

Due to our limited resources and access to capital, our decisions to prioritize development of certain product candidates or certain indications to pursue with the product candidates that we are developing may adversely affect our business prospects.

Because we have limited resources and access to capital to fund our operations, we must decide which product candidates to pursue and the amount of resources to allocate to each. In addition, for product candidates under development, such as NBTXR3, we must decide for which indications we intend to develop the product candidate for treatment. As such, we are currently primarily focused on the development of NBTXR3, 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. Our decisions concerning the allocation of research, collaboration, management and financial resources toward particular product candidates, oncological indications or therapeutic areas may not lead to the development of viable commercial products and may divert resources away from other more promising opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties with respect to some of our product development programs may also prove not to be optimal and could cause us to miss valuable opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights. If we make incorrect determinations regarding the market potential of our product candidates or misread trends in the field of cancer treatment, our business prospects could be harmed.

We will require additional funding, which may not be available on acceptable terms or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

The process of developing our product candidates is expensive, lengthy and risky. We expect our research and development expenses to increase substantially as we continue to develop NBTXR3 through our clinical development programs and identify new product candidates for development. Further, as a result of our increasing commercialization efforts with respect to NBTXR3 and the costs of operating as a U.S. public company, our selling, general and administrative expenses will increase significantly in the next several years.

As of December 31, 2021, we had cash and cash equivalents of €83.9 million. We believe our cash and cash equivalents will be sufficient to fund our operations through the second quarter of 2023. However, in order to continue our ongoing research and development efforts, pursue regulatory approval and certification, and advance our commercialization efforts, we will require substantial additional funding. Also, our operating plan, including our product candidate development plans, may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other strategic alliances and licensing arrangements, or a combination of these approaches.

To the extent that we raise additional capital through the sale of additional equity or convertible securities, holders of our ordinary shares and ADSs will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our shareholders. Debt financing, if available, would result in increased fixed payment obligations and a portion of our operating cash flows, if any, being dedicated to the payment of principal and interest on such indebtedness. In addition, debt financing may involve agreements that include restrictive covenants that impose operating restrictions, such as restrictions on the incurrence of additional debt, the making of certain capital expenditures or the declaration of dividends. To the extent that we raise additional funds through arrangements with research and development partners or otherwise, we may be required to relinquish some of our technologies, product candidates or revenue streams, license our technologies or product candidates on unfavorable terms, or otherwise agree to terms unfavorable to us. Any additional fundraising efforts may divert our management's attention from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates.

In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of specific strategic considerations.

If we are unable to obtain funding on a timely basis, our growth prospects could be impaired, the price of our ordinary shares and ADSs may decline, and we may be required to, among other things:

- delay or reduce the number or extent of our preclinical and clinical trials or eliminate them entirely;
- grant licenses to our technology to collaborative partners or third parties; or
- enter into new collaboration agreements upon less favorable conditions than we would have been able to obtain under different circumstances.

Covenants in the Finance Contract governing the EIB loan impose restrictions on the operation of our business.

The Finance Contract governing our loan from the European Investment Bank, or EIB (the "EIB loan"), contains covenants that impose restrictions on the operation of our business. For example, without the approval of the EIB, the restrictions in the Finance Contract limit our and our subsidiaries' ability, among other things, to:

- dispose of any part of our business or assets outside of arm's-length ordinary course transactions;
- restructure or make substantial changes to the nature of our business;
- enter into certain merger or consolidation transactions;
- dispose of our shareholdings in our material subsidiaries;
- pursue acquisitions or investments;
- incur any indebtedness in excess of €1.0 million in the aggregate;
- provide guarantees in respect of liabilities or other obligations;
- engage in certain hedging activities;
- grant security over our assets;
- pay dividends or repurchase our shares; and
- impair our intellectual property rights.

As a result of these covenants and restrictions, we are limited in how we conduct our business. Although the restrictions in the Finance Contract contain several exceptions and carve-outs and may be waived by EIB, as a result of the restrictions we may be unable to raise additional financing or pursue new business opportunities that we believe would be beneficial to our business objectives.

Risks Related to the Development of Our Product Candidates

Our product candidates must undergo clinical trials that are time-consuming and expensive, the outcomes of which are unpredictable, and for which there is a high risk of failure. If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

In order to obtain requisite regulatory approvals and to successfully complete the necessary conformity assessment procedures, as applicable, we conduct preclinical and clinical programs for our product candidates with the goal of ultimately marketing therapeutic solutions to transform cancer treatments that utilize radiotherapy. NBTXR3, our lead product candidate, is currently being evaluated in a total of eight clinical trials worldwide as a potential treatment in various cancer indications. In January 2019 we announced a collaboration with MD Anderson which provides for approximately 340 patients to be enrolled across multiple clinical trials to be conducted in the United States to evaluate NBTXR3 across several cancer types. Because we are conducting clinical trials for NBTXR3 in multiple cancer indications, an unfavorable outcome in one or more trials may call into question the safety or efficacy in trials with respect to other cancer indications, and potentially undermine the validity of our nanotechnology platform.

Further, preclinical testing and clinical trials are long, expensive and unpredictable processes that can encounter extensive delays. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. For example, one patient who participated in our clinical trial evaluating NBTXR3 in patients with late-stage cancers died from his cancer before any observation of response to treatment. Although this death was determined to be unrelated to the treatment, such setbacks could cause delays in our clinical trials. It may take several years to complete the preclinical testing and clinical development necessary to commercialize a product candidate, and delays or failure can occur at any stage. The design of a clinical trial can determine whether its results will support approval and certification of a product, as applicable, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. An unfavorable outcome in one or more trials would be a major setback for our product candidates and for us. Due to our limited financial resources, an unfavorable outcome in one or more trials may require us to delay, reduce the scope of, or eliminate one or more product development programs, which could have a material adverse effect on our business and financial condition and on the value of our ordinary shares or ADSs.

In connection with clinical testing and trials, we face a number of risks, including risks that:

- a product candidate is ineffective, inferior to existing approved treatments, unacceptably toxic, or has 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 could invalidate the use of our product;
- the results may not confirm the positive results of earlier testing or trials;
- the independent data monitoring committee assigned to review our testing and trials could identify potential flaws in, or recommend against advancement of or adjustments to, any particular trial or trial design; and
- the results may not meet the level of statistical significance required by the FDA or other regulatory agencies to establish the safety and efficacy of our product candidates.

The 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 data; however, we may have different enrollment criteria in our future clinical trials and certain clinical trials have only yielded preliminary data. As a result, we may not observe similar results as in our prior clinical trials or in our preliminary data. Frequently, product candidates developed by pharmaceutical, biopharmaceutical and nanomedicine companies have shown promising results in preclinical studies or early clinical trials, but have subsequently suffered significant setbacks or failed in later clinical trials. Further, clinical trials of potential products often reveal that it is not possible or practical to continue development efforts for these product candidates.

We cannot guarantee that our current or future product development efforts will be successful, or completed within our anticipated time frames. If we do not successfully complete preclinical and clinical development, we will be unable to pursue required market authorization to market and sell our product candidates and generate revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before submitting marketing applications to the FDA, or initiating necessary conformity assessment procedures, as applicable. Although there are a large number of drugs and medical devices in development in Europe, the United States and other countries, only a small percentage result in the submission of a marketing application or the initiation of a conformity assessment procedure, even fewer are approved for commercialization, and only a small number achieve widespread physician and consumer acceptance following regulatory approval or successful completion of the conformity assessment procedure, as applicable. If our clinical trials are substantially delayed or fail to prove the safety and effectiveness of our product candidates in development, we may not successfully complete applicable pre-marketing regulatory requirements for any of these product candidates and our business and financial condition will be materially harmed.

Delays, suspensions and terminations in our clinical trials could result in increased costs to us and delay or prevent our ability to generate revenues.

Human clinical trials are very expensive, time-consuming, and difficult to design, implement and complete. Commencement of our clinical trials for our 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
- 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.

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

- lack of efficacy of product candidates during clinical trials;
- adverse events, safety issues or side effects relating to 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;
- the need to sequence and prioritize clinical trials as opposed to conducting them concomitantly in order to conserve resources;
- our inability to enter into collaborations relating to the development and commercialization of our product candidates;
- our failure to conduct clinical trials in accordance with regulatory requirements or clinical trial protocols;
- our 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 such manufacture;

- governmental or regulatory delays and changes in regulatory requirements or policy and 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 failure of patients to maintain contact after treatment;
- varying interpretations of our data by the Notified Body, FDA and 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 also ultimately lead to the denial of our marketing application or the failure to complete applicable pre-marketing regulatory requirements for NBTXR3, or our other product candidates. If we experience delays, suspensions or terminations in a clinical trial, the commercial prospects for the related product candidate will be harmed, and our ability to generate product revenues will be delayed or such revenues could be reduced or fail to materialize.

We rely on third parties to assist in our discovery and development activities, manufacture the nanoparticles used in our product candidates, and conduct our clinical trials and perform data collection and analysis, which could hinder our product development prospects or result in costs and delays that prevent us from successfully commercializing our product candidates.

We currently, and expect to continue to, depend on collaborations with public and private research institutions, including hospitals, clinics and cancer treatment centers, to conduct some of our development activities. If we are unable to enter into research collaborations with these institutions, or if any one of these institutions fails to work efficiently with us, the research, development or marketing of our product candidates planned as part of the collaboration could be delayed or cancelled. In the event a collaboration agreement is terminated or we become unable to renew the arrangement under acceptable conditions, our discovery and development activities may also be delayed.

Further, we depend on our production method, which we developed internally, for the manufacturing of nanoparticles. Although we have trained our third-party manufacturers in the application of our production method (and seek to maintain quality control through, among other things, implementation of a monitoring system), we do not control such third-party manufacturers' implementation of our production methods. In addition, we cannot provide any assurance that such third-party manufacturers will comply with all necessary safety protocols with respect to the implementation of our production method. Any interruption in the production of nanoparticles using the production method, including due to injuries or safety concerns from the implementation thereof, could significantly compromise our product development efforts.

We rely, or may rely, on medical institutions, clinical investigators and contract collaborators to carry out our clinical trials and to perform data collection and analysis. For example, under our primary collaboration agreement, two NBTXR3 clinical trials are currently being run by MD Anderson, and MD Anderson is expected to serve, pursuant to the terms of the MD Anderson Collaboration Agreement as the sponsor for the remaining several clinical trials we expect to launch as part of this collaboration.

Our clinical trials conducted in reliance on third parties may be delayed, suspended, or terminated if:

- the third parties do not devote a sufficient amount of time or effort to our activities or otherwise fail to successfully carry out their contractual duties or to meet regulatory obligations or expected deadlines;
- we replace a third party; or
- 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.

We rely on a number of third parties for the conduct of clinical trials and data collection and analysis. Third-party performance failures may increase our development costs, delay our ability to obtain regulatory approval or successfully complete pre-marketing certification procedures, and delay or prevent the commercialization of our product candidates. In addition, our third-party agreements usually contain a clause limiting such third party's liability, such that we may not be able to obtain full compensation for any losses we may incur in connection with the third party's performance failures. Ultimately, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of this responsibility. While we believe that in many cases there are alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without incurring delays or additional costs. Further, in the event of a default, bankruptcy or shutdown of, or a dispute with, a third party, we may be unable to enter into a new agreement with another third party on commercially acceptable terms.

We have entered, and may in the future enter, into collaboration agreements with third parties for the development and commercialization of our product candidates, which may affect our ability to generate revenues.

We have limited capabilities for product development and may seek to enter into collaborations with third parties for the development and potential commercialization of our product candidates. Should we seek to collaborate with a third party with respect to a prospective development program, we may not be able to locate a suitable collaborator and may not be able to enter into an agreement on commercially reasonable terms or at all. Even if we succeed in securing collaborators for the development and commercialization of our product candidates, such as our existing collaboration arrangements, we have limited control over the amount and timing that our collaborators may dedicate to the development or commercialization of our product candidates.

These collaborations pose a number of risks, including the following:

- collaborators may not have sufficient resources or decide not to devote the necessary resources due to internal constraints such as budget limitations, lack of human resources, or a change in strategic focus;
- collaborators may believe our intellectual property is not valid or is unenforceable or the product candidate infringes on the intellectual property rights of others;
- collaborators may dispute their responsibility to conduct development and commercialization activities pursuant to the applicable collaboration, including the payment of related costs or the division of any revenues;
- collaborators may decide to pursue a competitive product developed outside of the collaboration arrangement;
- collaborators may not be able to obtain, or believe they cannot obtain, the necessary regulatory approvals or certifications; or
- collaborators may delay the development or commercialization of our product candidates in favor of developing or commercializing another party's product candidate.

Thus, collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We also face competition in seeking out collaborators. If we are unable to secure new collaborations that achieve the collaborator's objectives and meet our expectations, we may be unable to advance our product candidates and may not generate meaningful revenues.

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.

Our collaboration agreements, and those we may enter into in the future, generally require that our collaboration partners use commercially reasonable efforts to advance the development and/or potential commercialization of our 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 us and our 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 our collaboration partner, which could limit the geographies in which we are able to effectively develop and commercialize our product candidates.

Early termination of any collaboration agreement could result in additional costs and the loss of potential revenue opportunities. For example, 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 License and Collaboration agreement that we entered into in August 2012. While we will retain all rights to the development and commercialization of NBTXR3 in the Asia Pacific region, pursuant to a Termination and Release Agreement, we agreed to make payments to PharmaEngine of up to $5 million in total upfront payments upon the completion of various administrative steps in connection with the winding-up of the collaboration, $7.5 million in future payments upon a second regulatory approval of NBTXR3 in any jurisdiction of the world for any indication and 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 commencing on the corresponding first date of sales in the region. In addition, unilateral 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 us to enter into a new agreement with another third party on commercially acceptable terms.

Risks Related to Obtaining Regulatory Approval or Certification for Our Product Candidates

Our business is governed by a rigorous, complex and evolving regulatory framework.

The development and commercialization of therapeutic solutions for cancer treatment are governed by a rigorous, complex and evolving global regulatory environment. Regulatory authorities, including the FDA in the United States, have imposed stringent requirements on the amount and types of data required to demonstrate the safety and efficacy of products prior to marketing and sale. Moreover, any products approved for commercialization are reassessed in terms of their patient risk/benefit ratio on a regular basis following initial approval or certification. The late discovery of issues or potential problems 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. Given that extensive global regulation has increased the cost of obtaining and maintaining the necessary marketing authorizations and the cost of successfully completing the necessary conformity assessment procedures, for therapeutic oncology solutions, and therefore may limit the economic value of a new product, the prospects for growth in this field, and for our product candidates, have been reduced.

In addition, clinical studies for our product candidates are subject to prior submission requirements to the relevant regulatory authorities of the countries in which the studies will be carried out. For example, in the United States, a clinical study may proceed once the FDA notifies the applicant that the study may proceed or after 30 days if the submission is not placed on hold by the FDA. A negative opinion from such a regulatory authority with respect to any of our clinical development programs could suspend or terminate such programs. Moreover, depending on the information provided to regulatory authorities during a clinical trial pursuant to ongoing reporting requirements, particularly about the occurrence of undesirable side effects, the regulatory authorities could decide to prematurely suspend or terminate the clinical trial.

NBTXR3 has been classified as a “Class III medical device” in the EU and as a “drug” in the United States. Independent certification organizations (“Notified Bodies”) designated by the national EU Member States, the FDA in the United States and comparable regulatory authorities in other jurisdictions must approve or certify the conformity of, as applicable, new drug or high risk medical device candidates before they can be commercialized, marketed, promoted or sold in those jurisdictions. We must provide these regulatory authorities with data from preclinical studies and clinical trials that demonstrate that our product candidates are safe and effective for a defined indication before they can be approved or certified for commercial distribution. We must provide data to ensure the strength, quality and purity of the substance and product. We must also assure the regulatory authorities that the characteristics and performance of the clinical batches will be replicated consistently in the commercial batches.

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.” If our product candidates were to be classified as drugs in the EU, their clinical development would become subject to a 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..

If our product candidates are not approved for marketing by applicable government authorities or we fail to complete other applicable pre-marketing regulatory requirements, we will be unable to commercialize them.

As of the date of this Annual Report, we are primarily focusing our development and planned commercialization efforts on the EU and the United States. Although we achieved a proof-of-concept in 2019 when 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, we are now prioritizing the development of NBTXR3 in the United States and the EU for the treatment of head and neck cancers. We cannot assure you that NBTXR3, or any of our future product candidates, will receive approval from the FDA or any other regulatory authority, or will successfully complete conformity assessment procedures in the EU. Our April 2019 CE marking for Hensify® does not provide any assurance that additional NBTXR3 product candidates will successfully complete similar regulatory procedures. Even if we successfully complete applicable pre-marketing regulatory requirements for any of our product candidates in a major market such as the United States or the EU, we may never obtain approval or commercialize our products in other major markets, due to varying approval procedures or otherwise, which would limit our ability to realize their full market potential.

Several factors will determine whether we receive FDA approval or whether we successfully complete the conformity assessment procedures in the EU, including, but not limited to:

- our ability to continue to develop our product candidates currently in preliminary clinical phases and to move our products currently in preclinical development phase to a clinical phase or from one clinical phase to the next;
- our ability, or the ability of a contracted third party, to successfully complete the clinical trials required by the set deadlines and with the human, technical and financial resources initially planned.

In the event that we do not successfully complete applicable pre-marketing regulatory requirements for our product candidates established by the applicable authorities or bodies in our target jurisdictions, we will be unable to commercialize such candidates.

Government restrictions on pricing and reimbursement, as well as other healthcare payor cost-containment initiatives, may negatively impact our ability to generate revenues even if we successfully complete applicable pre-marketing regulatory requirements to market a product.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products 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 therapeutic treatments they will cover and establish reimbursement levels. Assuming we obtain coverage 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 our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products and the treatment associated with use of our products. Therefore, coverage and adequate reimbursement is critical to new 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 particular therapeutic treatments. Increasingly, third-party payors are requiring that healthcare companies provide them with predetermined discounts from list prices as a condition of coverage, are deploying various techniques to leverage greater discounts in competitive classes, and are challenging the prices charged for therapeutic products. In addition, in the United States, federal programs impose penalties on drug manufacturers in the form of mandatory additional rebates and/or discounts if commercial prices increase at a rate greater than the Consumer Price Index-Urban, and these rebates and/or discounts, which can be substantial, may impact our ability to raise commercial prices. 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 will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

The continuing efforts of third-party payors to contain or reduce costs of healthcare may negatively affect our commercialization prospects, including:

- our ability to set a price we believe is fair for our products, if approved;
- our ability to obtain and maintain market acceptance by the medical community and patients;
- our ability to generate revenues and achieve profitability; and
- the availability of capital.

We cannot be sure that coverage and reimbursement will be available for any potential product candidate that we may commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we successfully complete applicable pre-marketing regulatory requirements. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we successfully complete applicable pre-marketing regulatory requirements.

In the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the “ACA”) has significantly impacted, and will continue to impact, 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 multiple challenges to certain aspects of the ACA and considerable uncertainty remains regarding the implementation and impact of the ACA. For example, tax reform legislation was enacted at the end of 2017 that eliminated the individual mandate—a tax penalty for individuals who did not maintain mandated health insurance coverage—beginning in 2019.

In addition to further legal review of the ACA, U.S. federal and state governments are continuing to focus on the cost of health coverage, health care and pharmaceuticals although future policy or the timing of any changes remains unclear, creating significant risks for the sector. At the federal level, legislation like the Bipartisan Budget Act of 2018 (“BBA”) amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, and also increased in 2019 the percentage by which a drug manufacturer must discount the cost of prescription drugs from 50 percent to 70 percent.

In addition, both the Budget Control Act of 2011 and the American Taxpayer Relief Act of 2012 (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. Federal regulatory reform intended to reduce costs of drugs furnished under Medicare and Medicare Advantage plans through utilization management tools, like step therapy, and to increase price transparency for such drugs through the prohibition of gag clauses in pharmacy contracts became effective on January 1, 2020. Since 2017, multiple states enacted and even more states have considered proposed legislation which will require price transparency and reporting of certain manufacturer information. This trend is anticipated to continue, where legislation is expected regarding pricing transparency, marketing, access to drugs and other measures related to pricing.

In November 2020, the U.S. Department of Health and Human Services, Office of Inspector General, finalized proposed modifications to the U.S. federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, will affect discounts paid by manufacturers to Medicare Part D plans and pharmacy benefit managers working with these organizations. The rule was challenged as arbitrary and capricious under the Administrative Procedure Act. In response, the government agreed to delay the effective date and evaluate the rule adopted by the previous administration. In the interim, the status quo has been restored. In addition to these, new legislative and/or administrative measures and other initiatives to control drug costs could harm our ability to market any product candidates and generate revenues.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product candidate. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. Additionally, the United States market has been further consolidated by key private payor organizations. For instance, CVS-Aetna and Cigna-ESI mergers highlight the role of integrated payor arrangements, including PBMs, which impacts product access and affordability. Such market consolidation may further impact market pricing in the future (three PBMs now cover over 75% of the market resulting in significant negotiating power for commercial and Medicare Part D plans). Both government and commercial payors are aggressively pursuing and implementing cost containment tools designed to lower plan-level net costs. Further, the United States Congress is expected to continue its focus on pharmaceutical pricing with bipartisan support. Additional legislative focus from state and federal bodies is anticipated. The potential implementation of further pricing practice scrutiny and related cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products. Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future.

In some foreign countries, the proposed pricing for a therapeutic product must be approved before it may be lawfully marketed. In addition, in some foreign markets, the pricing of therapeutic products is subject to government control and reimbursement may in some cases be unavailable. The requirements governing pricing of therapeutic products vary widely from country to country. For example, the EU provides options for its Member States to restrict the range of therapeutic products for which their national health insurance systems provide reimbursement and to control the prices of therapeutic products for human use. A Member State may approve a specific price for the therapeutic product, may refuse to reimburse a product at the price set by the manufacturer or may instead adopt a system of direct or indirect controls on the profitability of the company placing the therapeutic product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for therapeutic products will allow favorable reimbursement and pricing arrangements for NBTXR3 or any of our other product candidates that may be approved.

Historically, therapeutic products launched in the EU do not follow price structures of the United States and generally tend to have significantly lower prices.

The scope and nature of pricing controls vary country to country, but common themes include the following: reference pricing, systematic price reduction, formularies, volume limitations, patient copayment limitations, and generic substitution. In the United States and internationally, we believe that pricing pressures at multiple levels of government, including third party review of pricing practices, will continue and may increase, which may make it difficult for us to sell our potential product candidates that may be approved in the future at a price acceptable to us or any third parties with whom we may choose to collaborate.

Even if we successfully complete applicable pre-marketing regulatory requirements for the commercialization of our product candidates, the terms of approvals or certifications and ongoing regulation of our products may limit how we market our products, which could materially impair our ability to generate revenues.

Even if we successfully complete 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. For instance, a regulatory approval may limit the indicated uses for which we can market a product or the patient population that may utilize the product.

These restrictions could make it more difficult to market the product effectively. Accordingly, assuming we successfully complete applicable pre-marketing regulatory requirements for the commercialization of any of our product candidates, we will continue to expend time, money and effort in all areas of regulatory compliance.

A Fast Track designation by the FDA may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive regulatory approval.

In February 2020, the FDA granted Fast Track designation for 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. If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for that condition, the product sponsor may apply for FDA Fast Track designation. The FDA has broad discretion whether or not to grant this designation. Even though we have received Fast Track designation for NBTXR3, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw a Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Many products that have received Fast Track designation have failed to obtain approval from the FDA.

A Breakthrough Therapy designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive regulatory approval.

We do not currently have Breakthrough Therapy designation for any of our product candidates but may seek it in the future. A Breakthrough Therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for development.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe, after completing early clinical trials, that one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead decide not to grant that designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as Breakthrough Therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

Risks Related to the Production and Manufacturing of Our Product Candidates

We may not have access to the raw materials and other components necessary for the manufacturing of our product candidates.

We are dependent on third parties for the supply of various materials that are necessary to produce our product candidates for clinical trials. See “Item 4B. Business Overview—Manufacturing.” Although we have entered into agreements related to the supply of the raw materials used in the manufacturing of our nanoparticles, the supply could be reduced or interrupted at any time. In such case, we may not be able to find other suppliers of acceptable materials in appropriate quantities at an acceptable cost. If we lose key suppliers or the supply of materials is diminished or discontinued, or in the event of a major or international crisis impacting mining or the extraction of minerals in certain regions, we may not be able to continue to develop, manufacture and market our product candidates or products 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 our ability to complete trials and commercialize our products in a cost-effective and timely manner. If we encounter difficulties in the supply of these materials, chemicals or other necessary products, or if we were not able to maintain our supply agreements or establish new supply agreements in the future, or incur increased production costs as a result of any of the foregoing, our product development and our business prospects could be significantly compromised.

In November 2017, we opened a new facility to expand our manufacturing capabilities, increase production capacity of NBTXR3 for our clinical trial needs and prepare for potential commercialization. This new facility is located in the Villejuif BioPark, a scientific research and innovation center just outside of Paris, France. We expect that the facility will expand in due course our production capacity with the aim to produce NBTXR3 for our ongoing clinical trials and our initial commercial phase. However, we have not yet manufactured significant doses of NBTXR3 at this scale and may never be successful in developing manufacturing capabilities sufficient to meet our clinical trial needs. Moreover, we may have more limited access to raw materials and other components necessary for the manufacturing of our product candidates than third-party manufacturers, who may have more established relationships with suppliers, greater financial resources than us, and/or the ability to leverage purchasing scale for more efficient pricing of raw materials. Our manufacturing facilities could be affected by cost-overruns, unexpected delays, equipment failures, labor shortages, natural disasters, power failures, regulatory issues and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

Our manufacturing facilities as well as our subcontractor's manufacturing facilities are subject to significant government regulations and approvals. If we or our third-party manufacturers fail to comply with these regulations or maintain these approvals, our business will be materially harmed.

We contract the production of NBTXR3 for use in clinical trials to high-precision manufacturing partners. In addition, in 2017 we expanded our own manufacturing capabilities by opening an internal research and innovation center facility just outside of Paris, France. We and our third-party manufacturers are subject to ongoing regulation and periodic inspection by the national competent authorities of the EU Member States, FDA and other regulatory bodies to ensure current Good Manufacturing Practices ("cGMP") and international organization for standards ("ISO") compliance, as applicable. Any failure to follow and document our or their adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical trials, may result in the termination of or a hold on a clinical trial, or may delay or prevent filing or approval of marketing applications or the completion of pre-marketing certification procedures, as applicable, for our products. Failure to comply with applicable regulations could also result in the FDA or other applicable regulatory authorities taking, or causing to be taken, various actions, including:

- levying fines and other civil penalties;
- imposing consent decrees or injunctions;
- requiring us to suspend or put on hold one or more of our clinical trials;
- suspending or withdrawing regulatory approvals or certifications;
- delaying or refusing to approve pending applications or supplements to approved applications;
- requiring us to suspend manufacturing activities or product sales, imports or exports;
- requiring us to communicate with physicians, hospitals and other stakeholders about concerns related to actual or potential safety, efficacy, and other issues involving our products;
- ordering or requiring product recalls or seizing products;
- imposing operating restrictions; and
- seeking criminal prosecutions.

Any of the foregoing actions could be detrimental to our reputation, business, financial condition or operating results. Furthermore, our key suppliers may not continue to be in compliance with all applicable regulatory requirements, which could result in our failure to produce our products on a timely basis and in the required quantities, if at all. In addition, before any products would be considered for marketing in the United States, the EU or elsewhere, our suppliers will have to pass an audit by the applicable regulatory agencies. We are dependent on our suppliers' cooperation and ability to pass such audits, and the audits and any audit remediation may be costly. Failure to pass such audits by us or any of our suppliers would affect our ability to commercialize our product candidates in the United States, the EU or elsewhere.

Risks Related to the Commercialization of Our Product Candidates

The commercial success of our products is not guaranteed.

To date, we have the right to CE mark, and therefore to commercialize only one of our product candidates, Hensify®, the brand name for NBTXR3 for the treatment of locally advanced STS. This does not mean any of our other product candidates will receive approval for commercialization or that Hensify® will receive approval for commercialization in any other jurisdictions. In addition, even though we received approval for Hensify® and even if we receive additional approvals to commercialize any of our product candidates in the EU, the United States or elsewhere, we will need to gain the approval of the medical community, care prescribers and third party payors in order to achieve commercial success. Despite the fact that we have successfully completed all the regulatory steps allowing us to commercialize Hensify® in the EU, we have not yet undertaken any commercialization activities. Following evaluation of the results from Study 102 and NANORAY-312, we intend to undertake a strategic review and to determine where we believe we are best positioned to pursue commercialization, including our commercialization strategy with respect to Hensify®.

Even if the medical community accepts a product as safe and efficacious for its indicated use, physicians may choose to restrict the use of the product if we are unable to demonstrate that, based on experience, clinical data, side-effect profiles and other factors, our product is preferable to any alternative treatment methods. We cannot

predict the degree of market acceptance of any product candidate that successfully completes applicable pre-marketing regulatory requirements, which will depend on a number of factors, including, but not limited to:

- the perceived therapeutic benefit of the product by care prescribers;
- the potential occurrence of unanticipated or harmful side effects;
- the ease of integration of the product in current care/treatment processes;
- the advantages and disadvantages of the product compared to existing or alternative treatments;
- the ability of physicians to correctly and effectively administer our product to patients;
- the cost of treatment, and coverage and reimbursement policies of third-party payors, including government payors, pertaining to the product;
- our ability to educate the medical community about the safety and effectiveness of the product;
- support from the medical community in the oncology field; and
- the development of one or more competing products for the same oncological indication, including therapies with a mode of action similar to that of NBTXR3.

Even if our products are able to improve current therapeutic responses, poor market penetration, resulting from one or more of the factors listed above, could have a negative impact on our business prospects. Other product solutions which directly or indirectly compete with our products could also hinder our development efforts or render our products obsolete. Similarly, to the extent a cancer treatment method is shown to be more effective than, or were to displace, radiotherapy, our business would be adversely affected. Despite our best efforts, we cannot guarantee that the clinical development of our product candidates will result in successful completion of applicable pre-marketing regulatory requirements for commercialization, or that even if we do complete such requirements, that our products will be accepted by the market and experience commercial success.

Even if we successfully complete clinical trials of our product candidates, those candidates may not be commercialized successfully for other reasons.

Even if we successfully complete clinical trials for one or more of our product candidates and complete relevant regulatory requirements, those candidates may not be commercialized for other reasons, including:

- failing to receive regulatory clearances required to market them as drugs or medical devices, as applicable;
- being subject to proprietary rights held by others;
- failing to obtain clearance from regulatory authorities for the manufacturing of our products;
- being difficult or expensive to manufacture on a commercial scale;
- having adverse side effects that make their use less desirable;
- failing to compete effectively with products or treatments commercialized by competitors;
- failing to show that the long-term benefits of our products exceed their risks;
- changes to our overall development priorities; or
- shifting our commercialization strategy based upon our view that the market no longer supports commercialization of a particular product candidate or for a particular indication.

Any of our product candidates for which we obtain authorization for commercialization could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products following approval.

Any of our product candidates for which we successfully complete applicable pre-marketing regulatory requirements for commercialization, such as CE marking for NBTXR3 for the treatment of locally advanced STS in the EU, as well as the manufacturing processes, post-approval studies and measures, and labeling and promotional activities for such products, among other things, will be subject to continual requirements of and review by the Notified Body and national competent authorities of EU Member States, FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if we successfully complete applicable pre-marketing regulatory requirements for a product candidate, the resulting approval or certification, as applicable, may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including an FDA requirement to implement a risk evaluation and mitigation strategy to ensure that the benefits of a drug product outweigh its risks.

The FDA, and other regulatory bodies, may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product, such as long term observational studies. The FDA and other U.S. agencies, including the U.S. Department of Justice, closely regulate and monitor the post-approval marketing and promotion of therapeutic products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The national competent authorities of EU Member States and FDA impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not limit the marketing of any of our product candidates to their approved indications, we may be subject to warnings or enforcement action for off-label marketing. Similarly, we cannot promote our products before completion of applicable pre-marketing regulatory requirements. Violation of the

U.S. Federal Food, Drug and Cosmetic Act, and other related statutes, may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

If we are unable to establish sales, marketing and distribution capabilities for our product candidates, whether it be an internal infrastructure or an arrangement with a commercial partner, we may not be successful in commercializing those product candidates if and when they are approved or duly CE marked.

We do not currently have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of drug or medical device products. We are currently prioritizing the development of NBTXR3 in the United States and the EU for the treatment of head and neck cancers while also evaluating NBTXR3 in the treatment of various other indications and building out a robust immuno-oncology program. At such time as we pursue commercial sales with respect to an approved product candidate, we will have to quickly transition some of our resources and attention to marketing and developing a sales force, either internally or in coordination with strategic partners. We may enter into arrangements with partners for future marketing needs with respect to certain of our products, while also implementing our own sales and marketing organization with respect to other products. Such partners may not attain goals specified in agreements we enter into with them (including, for example, goals related to the timing of product commercialization, amount of sales and payment of milestones and royalties). There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize products on our own include:

- our inability to recruit, train, manage, motivate and retain adequate numbers of effective sales and marketing personnel;
- the failure of an adequate number of physicians to adopt any future products as part of treatment; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and enter into arrangements with third parties to perform these services, our revenue and our profitability, if any, are likely to be lower than if we were to sell, market and distribute any products that we develop ourselves.

Risks Related to Human Capital Management

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of December 31, 2021, we had 100 full-time employees and we expect to increase our number of employees and expand the scope and location of our operations. To manage our anticipated development, expansion and incurrence of additional expenses, including the development and potential commercialization of our product candidates, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Members of our management team may need to divert a disproportionate amount of their attention away from their day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

We depend on key management personnel and attracting and retaining other qualified personnel, and our business could be harmed if we lose key management personnel or cannot attract and retain other qualified personnel.

Our success depends to a significant degree upon the technical skills and continued service of certain members of our management team, particularly Laurent Levy, Ph.D., our Chairman of the Executive Board. The loss of the services of any member of our management team could have a material adverse effect on us.

Our success will also depend upon our ability to attract and retain additional qualified management, regulatory, technical, 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 our business. We compete for such personnel against numerous companies, including larger, more established companies with significantly greater

financial resources than we possess. In addition, failure to succeed in our product candidates' development may make it more challenging to recruit and retain qualified personnel. There can be no assurance that we will be successful in attracting or retaining such personnel and the failure to do so could have a material adverse effect on our business, financial condition and results of operations.

Being a public company requires significant resources and management attention and may affect our ability to attract and retain executive management and qualified supervisory board members.

As a public company in both the United States and France, we incur significant legal, accounting and other compliance expenses. In the United States, we are subject to the Exchange Act, including the reporting requirements thereunder, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, certain Nasdaq corporate governance requirements and other applicable securities laws, rules and regulations. Compliance with these laws, rules and regulations will increase our legal and financial compliance costs, make some activities more difficult, time-consuming or costly and increase demand on our systems and resources, particularly after we are no longer an emerging growth company.
Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting, and will, in the future, be required to provide an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include this attestation report on internal control over financial reporting issued by our independent registered public accounting firm. When our independent registered public accounting firm is required to undertake an assessment of our internal control over financial reporting, the cost of complying with Section 404 will significantly increase and management's attention may be diverted from other business concerns, which could adversely affect our business and results of operations. We may need to hire more employees in the future or engage outside consultants to comply with these requirements, which will further increase our costs and expenses. If we fail to implement the requirements of Section 404 in the required timeframe, we may be subject to sanctions or investigations by regulatory authorities, including the SEC and Nasdaq. Furthermore, if we are unable to conclude that our internal control over financial reporting is effective, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our ADSs could decline, and we could be subject to sanctions or investigations by regulatory authorities. Failure to implement or maintain effective internal control systems required of public companies could also restrict our future access to the capital markets. In addition, enhanced legal and regulatory regimes and heightened standards relating to corporate governance and disclosure for public companies result in increased legal and financial compliance costs and make some activities more time consuming.

Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with legal requirements or the requirements of the CMS, national competent authorities of EU Member States, FDA and other government regulators, provide accurate information to applicable government authorities, comply with fraud and abuse and other healthcare laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation.

We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of 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 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 our operations, any of which could substantially disrupt our operations.

Risks Related to Operational Compliance and Risk Management

We use hazardous chemicals in our business. Any claims relating to improper handling, storage or disposal of these materials could be time-consuming and costly.

Our research and development processes involve the controlled storage, handling, use and processing of hazardous materials (notably radioactive substances), including toxins and chemical agents. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed any insurance coverage and our total assets. EU and U.S. federal, state, local or other foreign laws and regulations govern the use, manufacture, storage, handling and disposal of these hazardous materials and specified waste products, as well as the discharge of pollutants into the environment and human health and safety matters. Compliance with environmental laws and regulations may be expensive and may impair our research and development efforts. If we fail to comply with these requirements, we could incur substantial costs, including civil or criminal fines and penalties, clean-up costs or capital expenditures for control equipment or operational changes necessary to achieve and maintain compliance.

In addition, we cannot predict the impact on our business of new or amended environmental laws or regulations or any changes in the way existing and future laws and regulations are interpreted and enforced.

Product liability and other lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of our product candidates.

The risk that we may be sued on product liability claims is inherent in the development and commercialization of therapeutic products. Side effects of, manufacturing defects in, or improper physician administration of, products that we develop could result in the deterioration of a patient's condition, injury or even death. For example, our liability could be sought after by patients participating in clinical trials due to unexpected side effects resulting from the administration of our products. Once a product successfully completes applicable pre-marketing regulatory requirements and is commercialized, the likelihood of product liability lawsuits increases. Criminal or civil proceedings might be filed against us by patients, physicians, regulatory authorities, pharmaceutical companies and any other third party using or marketing our products. These actions could include claims resulting from acts by our collaboration partners, potential licensees and subcontractors, over which we have little or no control. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and may be forced to limit or forgo further commercialization of the affected products. Any such adverse outcomes in future legal proceedings could also damage our market reputation which could in turn have an adverse effect on our ability to commercialize our products successfully.

We maintain product liability insurance coverage for our clinical trials at levels which we believe are appropriate for our clinical trials. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. In addition, in the future, we may not be able to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product or other legal or administrative liability claims by us or our collaboration partners, licensees or subcontractors, which could prevent or inhibit the commercial production and sale of any of our product candidates that complete applicable pre-marketing regulatory requirements.

We are subject to healthcare laws and regulations which may require substantial compliance efforts and could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings, among other penalties.

Healthcare providers, physicians and others will play a primary role in the recommendation, and the incorporation into treatment regimes, of our products, if approved and duly CE-marked. Our business operations in the United States and our arrangements with clinical investigators, healthcare providers, consultants, third-party payors and patients expose us to broadly applicable federal and state fraud and abuse and other healthcare laws. These laws may impact, among other things, our research, proposed sales, marketing and education programs of our product candidates that successfully complete applicable pre-marketing regulatory requirements. Restrictions under applicable U.S. federal, state and foreign healthcare laws and regulations include, 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 wilfully soliciting, offering, receiving or providing remuneration, 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;

- the U.S. federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created additional federal criminal statutes which prohibits, 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 clearing houses, 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;
- the laws and regulations relating to the protection of personal data, and in particular Regulation (EU) 2016/679 of April 27, 2016, or the General Data Protection Regulation ("GDPR"), which imposes strict requirements on activities that involve the processing of "personal data" (i.e., any information relating to an identified or identifiable natural person), as well as any national implementing law. For example, the GDPR requires the following non-exhaustive requirements: data processing activities must be justified by a legal basis, data subjects must be informed of the characteristics of the processing of their personal data, adequate security measures must be implemented, contractual relationships with data processors and transfers of personal data outside of the EU must be formalized and performed in compliance with data protection rules, data controllers must hold and maintain up to date records of data processing activities, data privacy impact assessments must be performed under certain circumstances, and personal data breaches must be notified. In 2019, a GDPR gap analysis was carried out by external experts on our behalf and we are in the process of implementing the most critical actions suggested to us to be taken;
- 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 that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our 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 our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we 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 our operations, any of which could substantially disrupt our operations. If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Risks Related to Intellectual Property

Our ability to compete may decline if we do not adequately protect our intellectual property proprietary rights.

Our commercial success depends, in part, on obtaining and maintaining proprietary rights to our and our licensors' intellectual property as well as successfully defending these rights against third-party challenges. We will only be able to protect our products, product candidates, processes and technologies from unauthorized use by third parties to the extent that valid and enforceable patents, or effectively protected trade secrets, cover them. Our ability to obtain patent protection for our products, product candidates, processes and technologies is uncertain due to a number of factors, including:

- we or our licensors may not have been the first to invent the technology covered by our or their pending patent applications or issued patents;
- we cannot be certain that we or our licensors were the first to file patent applications covering our 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;
- others may independently develop identical, similar or alternative products, product candidates, processes and technologies;
- the disclosures in our patent applications or our licensors' patent applications may not be sufficient to meet the statutory requirements for patentability;
- any or all of our pending patent applications or our licensors' pending patent applications may not result in issued patents;
- we or our licensors may not seek or obtain patent protection in countries or jurisdictions that may eventually provide us a significant business opportunity;
- any patents issued to us or our 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 our patent claims or our licensors' patent claims being narrowed, invalidated or held unenforceable;
- our or our licensors' products, product candidates, processes and technologies may not be patentable;
- others may design around our patent claims or our licensors' patent claims to produce competitive products, product candidates, processes and technologies that fall outside of the scope of our patents or our licensors' patents;
- others may identify prior art or other bases upon which to challenge and ultimately invalidate our or our licensors' patents or otherwise render them unenforceable; and
- our employees may claim intellectual property rights over, or demand remuneration with respect to, inventions they helped to develop.

Even if we have or obtain patents covering our products, product candidates, processes and technologies, we may still be barred from making, using and selling our products, product candidates, processes and technologies because of the patent rights of others. Others may have filed, and in the future may file, patent applications covering products, product candidates, processes or technologies that are similar or identical to ours. Numerous U.S. and foreign issued patents and pending patent applications owned by others exist in the cancer treatment field in which we are developing products.

These could materially affect our ability to develop and commercialize our product candidates or sell our products if approved. Because patent applications can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents that our products, product candidates, processes or technologies may infringe. These patent applications may have priority over patent applications filed by us or our licensors. Patent applications in France are only published 18 months after their priority date. In the United States, some patent applications are not published until the grant of the patent itself.

Obtaining and maintaining a patent portfolio entails significant expense and resources. Part of the expense includes periodic maintenance fees, renewal fees, annuity fees, various other governmental fees on patents and/or applications due over the course of several stages over the lifetime of patents and/or applications, as well as the cost associated with complying with numerous procedural provisions during the patent application process. We or our licensors may or may not choose to pursue or maintain protection for particular inventions. In addition, there are situations in which failure to make certain payments or noncompliance with certain requirements in the patent process can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we choose to forgo patent protection or allow a patent application or patent to lapse purposefully or inadvertently, our competitive position could suffer.

Legal actions to enforce our patent rights can be expensive and may involve the diversion of significant management time. In addition, these legal actions could be unsuccessful and could also result in the invalidation of our patents or a finding that they are unenforceable. We may or may not choose to pursue litigation or other actions against those that have infringed on our patents, or used them without authorization, due to the associated expense and time commitment of monitoring these activities. If we fail to protect or to enforce our intellectual property rights successfully, our competitive position could suffer, which could harm our results of operations.

In addition to patent protection, because we operate in the highly technical field of the development of therapies using nanotechnology, we rely in part on trade secret protection in order to protect our proprietary technology and processes. However, trade secrets are difficult to protect. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. We enter into non-disclosure agreements with our employees, consultants, outside collaborators, sponsored researchers and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may be breached or held unenforceable and may not effectively assign intellectual property rights to us. In particular, such parties may enter into other agreements with third parties and we would have no control over such contractual relationships and how they protect our confidential information.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not provide adequate protection for our proprietary information. For example, our security measures may not prevent an employee or consultant with authorized access from misappropriating our trade secrets and providing them to a competitor, and the recourse we have available against such misconduct may not provide an adequate remedy to protect our interests fully. 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. In addition, courts outside the United States may be less willing to protect trade secrets.

Furthermore, our proprietary information may be independently developed by others in a manner that could prevent legal recourse by us.

If any of our confidential or proprietary information, including our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed and our business could be materially and adversely affected.

Patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our competitive position.

The patent positions of companies developing oncology therapeutic solutions, including pharmaceutical and nanomedicine companies and other actors in our fields of business, can be highly uncertain and typically involve complex scientific, legal and factual analyses. In particular, the interpretation and breadth of claims allowed in some patents covering therapeutic compositions may be uncertain and difficult to determine, and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. The standards of the United States Patent and Trademark Office (the "USPTO") and foreign patent offices are sometimes uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated, narrowed or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, and U.S. patents may be subject to reexamination proceedings, post-grant review, *inter partes* review, or other administrative proceedings in the USPTO. Foreign patents as well may be subject to opposition or comparable proceedings in corresponding foreign patent offices. Challenges to our patents and patent applications or our licensors' patents and patent applications, if successful, may result in the denial of our patent applications or our licensors' patent applications or the loss or reduction in their scope. In addition, such interference, reexamination, post-grant review, *inter partes* review, opposition proceedings and other administrative proceedings may be costly and involve the diversion of significant management time. Accordingly, rights under any of our patents or our licensors' patents may not provide us with sufficient protection against competitive products or processes and any loss, denial or reduction in scope of any of such patents and patent applications may have a material adverse effect on our business.

Furthermore, even if not challenged, our patents and patent applications or our licensors' patents and patent applications may not adequately protect our product candidates, processes or technologies or prevent others from designing their products or technology to avoid being covered by our patent claims or our licensors' patent claims. If the breadth or strength of protection provided by the patents we own or license with respect to our products, product candidates, processes or technologies is threatened, it could dissuade companies from partnering with us to develop, and could threaten our ability to successfully commercialize, our product candidates, processes and technologies. Furthermore, for U.S. patent applications in which claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO in order to determine who was the first to invent any of the subject matter covered by such patent claims.

In addition, changes in, or different interpretations of, patent laws in the United States and other countries may permit others to use our discoveries or to develop and commercialize our products, product candidates, processes and technologies without providing any notice or compensation to us, or may limit the scope of patent protection that we or our licensors are able to obtain. The laws of some countries do not protect intellectual property rights to the

same extent as U.S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights.

If we or our licensors fail to obtain and maintain patent protection and trade secret protection of our products, product candidates, processes and technologies, we could lose our competitive advantage and competition we face would increase, potentially reducing revenues and having a material adverse effect on our business.

The lives of our patents may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. Individual patent terms extend for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. In the United States, the natural expiration of a patent is generally 20 years after its first effective filing date. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of legal remedies in a particular country, and the validity and enforceability of the patent. If we or our licensors do not have sufficient patent life to protect our products, processes and technologies, our business and results of operations will be adversely affected.

If we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced, possibly materially.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on our products, product candidates, processes and technologies in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. Competitors may use our technologies in jurisdictions where we or our licensors do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we or our licensors have patent protection, but where the ability to enforce our or our licensors' patent rights is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent such competition. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as the federal and state laws in the United States. Patent protection must be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we and our licensors may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries. In addition, the legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to novel therapeutic products or techniques, and the requirements for patentability differ, in varying degrees, from country to country, and the laws of some foreign countries do not protect intellectual property rights, including trade secrets, to the same extent as federal and state laws of the United States. As a result, many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. Such issues may make it difficult for us to stop the infringement, misappropriation or other violation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities.

Accordingly, our and our licensors' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. Similarly, if our trade secrets are disclosed in a foreign jurisdiction, competitors worldwide could have access to our proprietary information and we may be without satisfactory recourse. Such disclosure could have a material adverse effect on our business.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

Furthermore, proceedings to enforce our licensors' and our patent rights and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our or our licensors' patents at risk of being invalidated or interpreted narrowly, could put our or our licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded to us, if any, may not be commercially meaningful, while the damages and other remedies we may be ordered to pay such third parties may be significant. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of intellectual property.

Accordingly, our licensors' and our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Third parties may assert ownership or commercial rights to inventions we develop or otherwise regard as our own.

Third parties may in the future make claims challenging the inventorship or ownership of our or our licensors' intellectual property. We have written agreements with collaborators that provide for the ownership of intellectual property arising from our collaborations. These agreements provide that we must 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. In some instances, there may not be adequate written provisions to address clearly the resolution of intellectual property rights that may arise from a collaboration. If we cannot successfully negotiate sufficient ownership and commercial rights to the inventions that result from our use of a third-party collaborator's materials where required, or if disputes otherwise arise with respect to the intellectual property developed through a collaboration, we may be limited in our ability to capitalize on the full market potential of these inventions. In addition, we may face claims by third parties that our agreements with employees, contractors or consultants obligating them to assign intellectual property to us are ineffective, or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and could interfere with our ability to capture the full commercial value of such inventions. Litigation may be necessary to resolve an ownership dispute, and if we are not successful, we may be precluded from using certain intellectual property and associated products, product candidates, processes and technologies, or may lose our rights in that intellectual property. Either outcome could have an adverse impact on our business.

Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

We currently employ, and in the future may employ, individuals who were previously employed at universities or other biotechnology, pharmaceutical or nanomedicine companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or damage our reputation. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

A dispute concerning the infringement or misappropriation of our intellectual property rights or the intellectual property rights of others could be time-consuming and costly, and an unfavorable outcome could harm our business.

There is significant litigation in the fields of pharmaceutical and medical device development regarding patent and other intellectual property rights. While we are not currently subject to any pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our products, product candidates, processes, technologies or activities infringe the intellectual property rights of others.

If our development activities are found to infringe any such patents, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from using the patented drugs or compositions. In addition, we may need to resort to litigation to enforce a patent issued to us, to protect our trade secrets, or to determine the scope and validity of third-party proprietary rights. If we initiate or threaten patent infringement litigation, such action could provoke third parties to assert claims against us or our licensors or could put our patents at risk of being

invalidated or interpreted narrowly. From time to time, we may hire scientific personnel or consultants formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject to allegations of trade secret misappropriation or other similar claims as a result of prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We may not be able to afford the costs of litigation. Any adverse ruling or perception of an adverse ruling in defending ourselves against these claims could have a negative impact on our cash position. Any legal action against us or our collaborators could lead to:

- payment of damages, potentially treble damages, if we are found to have wilfully infringed a party's patent rights;
- injunctive or other equitable relief that may effectively block our ability to further develop, commercialize, and sell products; or
- us or our collaborators having to enter into license arrangements that may not be available on commercially acceptable terms, if at all.

Any of these outcomes could hurt our cash position and financial condition and our ability to develop and commercialize our product candidates.

If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names and trademarks, which we need to build name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Ownership of Our Ordinary Shares and ADSs

The market price of our equity securities may be volatile or may decline regardless of our operating performance.

The trading price of our ADSs may fluctuate substantially. The trading price of our ADSs depends on a number of factors, including those described in this "Item 3D. Risk Factors", many of which are beyond our control. Such fluctuations in the market price and demand for our ordinary shares or ADSs may occur regardless of, and unrelated to, our actual operating performance, which may limit or prevent holders from readily selling their securities and may otherwise negatively affect the liquidity of our ordinary shares or ADSs. In addition, pharmaceutical, biotechnology and nanomedicine companies, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies.

We do not currently intend to pay dividends on our securities. In addition, French law may limit the amount of dividends we are able to distribute.

We have never declared or paid any cash dividends on our ordinary shares and do not currently intend to do so for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, holders of our ordinary shares are not likely to receive any dividends on such ordinary shares or ADSs for the foreseeable future, and the success of an investment in ordinary shares or ADSs will depend upon any future appreciation in its value. Consequently, investors may need to sell all or part of their holdings of ordinary shares or ADSs after price appreciation, which may never occur, as the only way to realize any future gains on their investment. There is no guarantee that the ordinary shares or ADSs will appreciate in value or even maintain the price at which our shareholders have purchased them. Investors seeking cash dividends should not purchase our ADSs or ordinary shares.

Further, under French law, the determination of whether we have been sufficiently profitable to pay dividends is made on the basis of our statutory financial statements prepared and presented in accordance with accounting standards applicable in France. In addition, payment of dividends may subject us to additional taxes under French law. See "Item 10B. Memorandum and Articles of Association" for further details on the limitations on our ability to declare and pay dividends. Therefore, we may be more restricted in our ability to declare dividends than companies not based in France.

In addition, exchange rate fluctuations may affect the amount of euros that we are able to distribute, and the amount in U.S. dollars that our shareholders receive upon the payment of cash dividends or other distributions we declare and pay in euros, if any. These factors could harm the value of the ADSs.

Future sales of ordinary shares or ADSs by existing shareholders could depress the market price of our ADSs and ordinary shares.

We believe that additional capital may be needed to continue our planned operations, including conducting our planned clinical trials, manufacturing and commercialization efforts, expanded research and development activities and costs associated with operating as a public company. Sales of additional ordinary shares or ADSs by us, or the perception that these sales could occur, could cause the market price of our ADSs to decline.

If our existing shareholders sell, or indicate an intent to sell, substantial amounts of ordinary shares or ADSs, the trading price of our ADSs and ordinary shares could decline significantly. In addition, such secondary sales may impair our ability to raise capital through the sale of additional equity securities.

As of December 31, 2021, we had 34,825,872 ordinary shares outstanding. Outstanding shares held by our affiliates, including our supervisory board members and executive board members, may be publicly sold in accordance with the requirements of Rule 144 under the Securities Act, including the volume and manner of sale requirements of that rule. All outstanding ADSs held by non-affiliates may be resold without restriction.

Holders of our ADSs may not be able to exercise their right to vote the ordinary shares underlying their ADSs.

Holders of ADSs may exercise voting rights with respect to the ordinary shares represented by the ADSs only in accordance with the provisions of the deposit agreement and not as a direct shareholder. The deposit agreement provides that, upon receipt of notice of any meeting of holders of our ordinary shares, the depositary will fix a record date for the determination of ADS holders who shall be entitled to give instructions for the exercise of voting rights. Upon timely receipt of notice from us, if we so request, the depositary shall distribute to the holders as of the record date (1) the notice of the meeting or solicitation of consent or proxy sent by us and (2) a statement as to the manner in which instructions may be given by the holders.

Holders of ADSs may instruct the depositary of their ADSs to vote the ordinary shares underlying their ADSs. Otherwise, Holders of ADSs will not be able to exercise voting rights, unless they withdraw the ordinary shares underlying the ADSs they hold. However, a holder of ADSs may not know about the meeting far enough in advance to withdraw those ordinary shares. If we ask for a holder of ADSs' instructions, the depositary, upon timely notice from us, will notify him or her of the upcoming vote and arrange to deliver our voting materials to him or her. We cannot guarantee to any holder of ADSs that he or she will receive the voting materials in time to ensure that he or she can instruct the depositary to vote his or her ordinary shares or to withdraw his or her ordinary shares so that he or she can vote them. If the depositary does not receive timely voting instructions from a holder of ADSs, it may give a proxy to a person designated by us to vote the ordinary shares underlying his or her ADSs. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. This means that a holder of ADSs may not be able to exercise his or her right to vote, and there may be nothing he or she can do if the ordinary shares underlying his or her ADSs are not voted as he or she requested.

Holders of ADSs will not be directly holding our ordinary shares.

A holder of ADSs will not be treated as one of our shareholders and will not have direct shareholder rights. French law governs our shareholder rights. The depositary, through the custodian or the custodian's nominee, will be the holder of the ordinary shares underlying ADSs held by holders of ADSs. Holders of ADSs will have ADS holder rights. Among other things, ADS holder rights do not provide for double voting rights, which otherwise would be available to holders of ordinary shares held in a shareholders' name for a period of at least two years. The deposit agreement among us, the depositary and holders of ADSs, and all other persons directly and indirectly holding ADSs, sets out ADS holder rights, as well as the rights and obligations of us and the depositary.

The right as a holder of ADSs to participate in any future preferential subscription rights or to elect to receive dividends in shares may be limited, which may cause dilution to the holdings of holders of ADSs.

According to French law, if we issue additional securities for cash, current shareholders will have preferential subscription rights for these securities on a pro rata basis unless they waive those rights at an extraordinary meeting of our shareholders (by a two-thirds majority vote) or individually by each shareholder. However, our ADS holders in the United States will not be entitled to exercise or sell such rights unless we register the rights and the securities to which the rights relate under the Securities Act or an exemption from the registration requirements is available. In addition, the deposit agreement provides that the depositary will not make rights available to holders of ADSs in the United States unless the distribution to ADS holders of both the rights and any related securities are either registered under the Securities Act or exempted from registration under the Securities Act. Further, if we offer holders of our ordinary shares the option to receive dividends in either cash or shares, under the deposit agreement the depositary may require satisfactory assurances from us that extending the offer to holders of ADSs does not require registration of any securities under the Securities Act before making the option available to holders of ADSs. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. Accordingly, ADS holders may be unable to participate in our rights offerings or to elect to receive dividends in shares and may experience dilution in their holdings. In addition, if the depositary is

unable to sell rights that are not exercised or not distributed or if the sale is not lawful or reasonably practicable, it will allow the rights to lapse, in which case holders of our ADSs will receive no value for these rights.

Holders of ADSs in the United States may be subject to limitations on the transfer of their ADSs and the withdrawal of the underlying ordinary shares.

ADSs, which may be evidenced by American Depositary Receipts ("ADRs"), are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, or for any other reason subject to a holder of ADSs' right to cancel his or her ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or we are paying a dividend on our ordinary shares. In addition, a holder of ADSs may not be able to cancel his or her ADSs and withdraw the underlying ordinary shares when he or she owes money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities.

We are an emerging growth company and we cannot be certain if the reduced disclosure requirements applicable to us will make our ADSs less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. As an emerging growth company, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, and exemptions from the requirements of holding a non-binding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our ADSs less attractive because we rely on these exemptions. If some investors find our ADSs less attractive as a result, there may be a less active trading market for our ADSs and the price of our ADSs may be more volatile. We intend to take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) December 31, 2025; (iii) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous three years; and (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. Once we cease to be an emerging growth company, we may continue to avail ourselves of the accommodations available to us as a foreign private issuer for so long as we qualify as such.

We previously identified a material weakness in our internal control over financial reporting. We may identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal control over financial reporting, and as a result, investor confidence in us and the value of our common stock could be materially and adversely affected.

As a public company in the United States, we are required to establish and maintain internal control over financial reporting. Pursuant to Section 404(a) of the Sarbanes-Oxley Act we are required to furnish a report by our management that assesses our internal control over financial reporting as of year-end in our Annual Reports on Form 20-F, commencing with an initial report as of December 31, 2021, which is included in this Annual Report.

Prior to the issuance of our interim financial statements as of and for the six months ended June 30, 2021, a deficiency, which constituted a material weakness in our 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 our annual or interim financial statements will not be prevented or detected on a timely basis. A material adjustment was made to our 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 our clinical trials. Specifically, we 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 our interim financial statements. This material weakness did not result in material adjustments, or restatements, of our audited consolidated financial statements or disclosures for any prior period previously reported by us.

During the year ended December 31, 2021, we remediated the identified material weakness in internal control over financial reporting identified above. Under the supervision of management and the oversight of our Audit Committee, Under supervision of management and the oversight of our Audit Committee, the Company increased its internal control personnel, strengthened the necessary skills for employees involved in internal control over financial reporting, implemented a more robust data collection system and enhanced reporting processes, including more

detailed accounting analyses at time of contract execution next to engaging independent specialists to modernize and perform certain internal control functions.

If we are unable to maintain an effective system of internal control over financial reporting, the reliability of our financial reporting, investor confidence in us and the value of our common stock could be materially and adversely affected. In addition, we may discover other control deficiencies in the future, and we cannot assure you that we will not have a material weakness in future periods.

ADSs holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiffs in any such action.

The deposit agreement governing the ADSs representing our ordinary shares provides that, to the fullest extent permitted by law, ADS holders, including holders who acquire ADSs in the secondary market, waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to our shares, the ADSs or the deposit agreement, including any claim under the U.S. federal securities laws.

If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable based on the facts and circumstances of that case in accordance with the applicable state and federal law. To our knowledge, the enforceability of a contractual pre-dispute jury trial waiver in connection with claims arising under the federal securities laws has not been finally adjudicated by the United States Supreme Court. However, we believe that a contractual pre-dispute jury trial waiver provision is generally enforceable, including under the laws of the State of New York, which govern the deposit agreement, by a federal or state court in the City of New York, which has non-exclusive jurisdiction over matters arising under the deposit agreement. In determining whether to enforce a contractual pre-dispute jury trial waiver provision, courts will generally consider whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. We believe that this is the case with respect to the deposit agreement and the ADSs. It is advisable that holders of our ADSs consult legal counsel regarding the jury waiver provision before acquiring ADSs and thereby entering into the deposit agreement.

If holders of our ADSs or any other beneficial owners of ADSs bring a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under federal securities laws, they may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us and the depositary. If a lawsuit is brought against either or both of us and the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different outcomes than a trial by jury would have, including results that could be less favorable to the plaintiffs in any such action.

Nevertheless, if this jury trial waiver provision is not permitted by applicable law, an action could proceed under the terms of the deposit agreement with a jury trial. No condition, stipulation or provision of the deposit agreement or ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

Risks Related to Our Status as a Non-U.S. Company

The rights of shareholders in companies subject to French corporate law differ in material respects from the rights of shareholders of corporations incorporated in the United States.

We are a French company with limited liability. Our corporate affairs are governed by our By-laws and by the laws governing companies incorporated in France. The rights of shareholders and the responsibilities of members of our executive board and supervisory board are in many ways different from the rights and obligations of shareholders in companies governed by the laws of U.S. jurisdictions. For example, in the performance of its duties, our executive board and supervisory board are required by French law to consider the interests of our company, its shareholders, its employees and other stakeholders, rather than solely our shareholders and/or creditors. It is possible that some of these parties will have interests that are different from, or in addition to, the interests of our shareholders or holders of ADSs.

Further, in accordance with French law, double voting rights automatically attach to each ordinary share of companies listed on a regulated market (such as the regulated market of Euronext in Paris, where our ordinary shares are listed) that is held of record in the name of the same shareholder for a period of at least two years, except as otherwise set forth in a company's by-laws. Our By-laws currently do not exclude such double voting rights. See "Item 6C—Board Practices—Corporate Governance Practices" and "Item 10B. Memorandum and Articles of Association." Ordinary shares held in the form of ADSs are not be eligible for double voting rights.

U.S. investors may have difficulty enforcing civil liabilities against our company and supervisory board and senior management and the experts named in this Annual Report.

Certain members of our executive board, supervisory board and senior management and certain experts named in this Annual Report are non-residents of the United States, and all or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible to serve process on such persons or us in the United States or to enforce judgments obtained in U.S. courts against them or us based on civil liability provisions of the securities laws of the United States. Additionally, it may be difficult to assert U.S.

securities law claims in actions originally instituted outside of the United States. Foreign courts may refuse to hear a U.S. securities law claim because foreign courts may not be the most appropriate forums in which to bring such a claim. Even if a foreign court agrees to hear a claim, it may determine that the law of the jurisdiction in which the foreign court resides, and not U.S. law, is applicable to the claim. Further, if U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact, which can be a time-consuming and costly process, and certain matters of procedure would still be governed by the law of the jurisdiction in which the foreign court resides. In particular, there is some doubt as to whether French courts would recognize and enforce certain civil liabilities under U.S. securities laws in original actions or judgments of U.S. courts based upon these civil liability provisions. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in France. An award for monetary damages under the U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered but is intended to punish the defendant. French law provides that a shareholder, or a group of shareholders, may initiate a legal action to seek indemnification from the directors of a corporation in the corporation's interest if it fails to bring such legal action itself. If so, any damages awarded by the court are paid to the corporation and any legal fees relating to such action may be borne by the relevant shareholder or the group of shareholders.

The enforceability of any judgment in France will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and France do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

Our By-laws and French corporate law contain provisions that may delay or discourage a takeover attempt.

Provisions contained in our By-laws and French corporate law could make it more difficult for a third party to acquire us, even if doing so might be beneficial to our shareholders. In addition, provisions of French law and our By-laws impose various procedural and other requirements, which could make it more difficult for shareholders to effect certain corporate actions. These provisions include the following:

- provisions of French law allowing the owner of 90% of the share capital or voting rights of a public company to force out the minority shareholders following a tender offer made to all shareholders are only applicable to companies listed on a regulated market or a multilateral trading facility in a Member State of the EU or in a state party of the European Economic Area Agreement, including the main French stock exchange, and will therefore be applicable to us only if we continue to dual-list in France;
- a merger (i.e., in a French law context, a stock-for-stock exchange after which our company would be dissolved without being liquidated into the acquiring entity and our shareholders would become shareholders of the acquiring entity) of our company into a company incorporated in the EU would require the approval of our executive board as well as a two-thirds majority of the votes cast by the shareholders present, represented by proxy or voting by mail at the relevant meeting;
- a merger of our Company into a company incorporated outside of the EU would require the unanimous approval of our shareholders;
- under French law, a cash merger is treated as a share purchase and would require the consent of each participating shareholder;
- our shareholders have granted and may grant in the future to our executive board broad authorizations to increase our share capital or to issue additional ordinary shares or other securities (for example, warrants) to our shareholders, the public or qualified investors, including as a possible defense following the launching of a tender offer for our shares;
- our shareholders have preferential subscription rights proportional to their shareholding in our company on the issuance by us of any additional shares or securities giving right, immediately or in the future, to new shares for cash or a set-off of cash debts, which rights may only be waived by the extraordinary shareholders' general meeting (by a two-thirds majority vote) of our shareholders or on an individual basis by each shareholder;
- our supervisory board has the right to appoint new members to fill a vacancy created by the resignation or death of a member, subject to the approval by the shareholders of such appointment at the next shareholders' meeting, which prevents shareholders from having the sole right to fill vacancies on our supervisory board;
- the members of our executive board are appointed by our supervisory board and can be removed either by our supervisory board or by the shareholders' general meeting;
- our supervisory board can only be convened by its chairman, by its vice-president, by any two members acting jointly, or, on a reasoned request (e.g. when no board meeting has been held for more than two consecutive months), by (1) members representing at least one-third of the total number of members of our supervisory board or (2) a member of the executive board;
- our supervisory board's meetings can only be regularly held if at least half of its members attend either physically or by way of videoconference or teleconference, enabling the members' identification and ensuring their effective participation in the supervisory board's decisions;
- our ordinary shares are nominative or bearer, if the legislation so permits, according to the shareholder's choice;
- under French law, (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 may have to file a declaration for statistical purposes with the Bank of France (Banque de France) within 20 business days following the date of certain direct foreign investments in us, including any purchase of our ADSs. In

particular, such filings are required in connection with investments exceeding €15,000,000 that lead to the acquisition of at least 10% of our share capital or voting rights or cross such 10% threshold. See "Item 10B. Memorandum and Articles of Association;"
- under French law, certain investments in any entity governed by French law relating to certain strategic industries (such as research and development in biotechnologies and activities relating to public health) and activities by individuals or entities not French, not resident in France or controlled by entities not French or not resident in France are subject to prior authorization of the Ministry of Economy; see "Item 10B. Memorandum and Articles of Association;"
- approval of at least a majority of the votes cast by shareholders present, represented by a proxy, or voting by mail at the relevant ordinary shareholders' general meeting is required to remove members of the supervisory board with or without cause;
- advance notice is required for nominations to the members of the supervisory board or for proposing matters to be acted upon at a shareholders' meeting, except that a vote to remove and replace a member of our supervisory board can be proposed at any shareholders' meeting without notice;
- pursuant to French law, our By-laws, including the sections relating to the number of our supervisory board's members and election and removal of a member of the supervisory board from office, may only be modified by a resolution adopted by a two-thirds majority vote of our shareholders present, represented by a proxy or voting by mail at the meeting;
- in the event where certain ownership thresholds would be crossed, a number of disclosures should be made by the relevant shareholder and can impose certain obligations; see "Item 10B. Memorandum and Articles of Association;" and
- transfers of shares shall comply with applicable insider trading rules and regulations, and in particular with the Market Abuse Directive and Regulation dated April 16, 2014.

Our business may be exposed to foreign exchange risks.

We incur some of our expenses, and may in the future derive revenues, in currencies other than the euro. In particular, as we expand our operations and continue to conduct clinical trials in the United States, we will continue to incur expenses in U.S. dollars. As a result, we may be exposed to foreign currency exchange risk as our results of operations and cash flows would be subject to fluctuations in foreign currency exchange rates. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the euro.

Therefore, for example, an increase in the value of the euro against the U.S. dollar could have a negative impact on our revenue and earnings growth as U.S. dollar revenue and earnings, if any, are translated into euros at a reduced value. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows. Our ADSs are quoted in U.S. dollars on the Nasdaq Global Select Market, while our ordinary shares trade in euros on the regulated market of Euronext in Paris. Our financial statements are prepared in euros. Therefore, fluctuations in the exchange rate between the euro and the U.S. dollar will also affect, among other matters, the value of our ordinary shares and ADSs.

Our international operations involve additional risks, and our exposure to these risks will increase as our business continues to expand.

We operate in a number of jurisdictions and intend to continue to expand our global presence. To date, we have focused our development and planned commercialization efforts on the EU and the United States, and to a lesser extent, Asia. International operations are subject to the legal, political, regulatory, and social requirements and economic conditions in the jurisdictions in which they are conducted. Risks inherent to international operations include, but are not limited to:

- currency exchange restrictions or costs and exchange rate fluctuations;
- exposure to local or regional economic or political instability, war or other armed conflicts, such as the Russian invasion of Ukraine that commenced in February 2022, and other threatened or actual acts of terrorism and security concerns in general;
- compliance with various laws and regulatory requirements relating to anti-corruption, antitrust or competition, economic sanctions, data content, data protection and privacy, employment and labor laws and health and safety;
- difficulties in attracting and retaining qualified employees in certain international markets, as well as managing staffing and operations due to increased complexity, distance, time zones, language and cultural differences;
- difficulty in enforcing agreements, judgments, and arbitration awards in various legal systems; and
- inability to obtain, maintain or enforce our intellectual property rights.

We believe that our overall success as a global business depends on our ability to succeed in different legal, regulatory, economic, social, and political situations and conditions. We may not be able to develop and implement effective policies and strategies in each jurisdiction where we may conduct operations or do business in the future.

As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and are permitted to file less information with the SEC than a U.S. company. This may limit the information available to holders of ADSs and ordinary shares.

We are a foreign private issuer, as defined in the SEC's rules and regulations and, consequently, we are not subject to all of the disclosure requirements applicable to public companies organized within the United States. For example, we are exempt from certain rules under the Exchange Act that regulate disclosure obligations and procedural requirements related to the solicitation of proxies, consents or authorizations applicable to a security registered under the Exchange Act, including the U.S. proxy rules under Section 14 of the Exchange Act. In addition, our executive board members and supervisory board members are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and related rules with respect to their purchases and sales of our securities. Moreover, while we currently make annual and semi-annual filings with respect to our listing on the regulated market of Euronext in Paris and expect to file financial reports on an annual basis with the SEC and furnish semi-annual financial information with the SEC, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. public companies and will not be required to file quarterly reports on Form 10-Q or current report on Form 8-K under the Exchange Act. Accordingly, there will be less publicly available information concerning our company than there would be if we were not a foreign private issuer.

As a foreign private issuer, we are permitted and we expect to follow certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq's corporate governance standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with the Nasdaq corporate governance standards.

As a foreign private issuer listed on the Nasdaq Global Select Market, we will be subject to Nasdaq's corporate governance standards. However, Nasdaq rules provide that foreign private issuers are permitted to follow home country corporate governance practices in lieu of Nasdaq's corporate governance standards as long as notification is provided to Nasdaq of the intention to take advantage of such exemptions. Certain corporate governance practices in France, which is our home country, may differ significantly from Nasdaq corporate governance standards. Other than as set forth in this Annual Report, we currently intend to comply with the corporate governance listing standards of Nasdaq to the extent possible under French law. However, we may choose to change such practices to follow additional French home country practices in the future.

As a result of the accommodations for foreign private issuers, our shareholders may be afforded less protection than they otherwise would have under Nasdaq's corporate governance standards applicable to U.S. domestic issuers. For an overview of our corporate governance practices, see "Item 6C. Board Practices - Corporate Governance Practices."

We may lose our foreign private issuer status in the future, which could result in significant additional cost and expense.

While we currently qualify as a foreign private issuer, the determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter and, accordingly, the next determination will be made with respect to us on June 30, 2022. In the future, we would lose our foreign private issuer status if we fail to meet the requirements necessary to maintain our foreign private issuer status as of the relevant determination date. For example, if more than 50% of our securities are held by U.S. residents and more than 50% of our executive board members or supervisory board members are residents or citizens of the United States, we could lose our foreign private issuer status. As of December 31, 2021, approximately 19% of our outstanding ordinary shares are held by U.S. residents.

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly more than costs we incur as a foreign private issuer. If we are not a foreign private issuer, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive in certain respects than the forms available to a foreign private issuer. We would be required under current SEC rules to prepare our financial statements in accordance with U.S. GAAP, rather than IFRS, and modify certain of our policies to comply with corporate governance practices associated with U.S. domestic issuers. Such conversion of our financial statements to U.S. GAAP would involve significant time and cost. In addition, we may lose our ability to rely upon exemptions from certain corporate governance requirements on U.S. stock exchanges that are available to foreign private issuers such as the ones described under "Item 6. Directors, Senior Management and Employees - C. Board Practices - Corporate Governance Practices" and exemptions from procedural requirements related to the solicitation of proxies.

Although not free from doubt, we do not believe that we were a "passive foreign investment company" ("PFIC") for U.S. federal income tax purposes for the taxable year ended December 31, 2021. However, it is not yet known whether we will be a PFIC for the taxable year ending December 31, 2022 or in subsequent taxable years. If we are determined to be a PFIC for any taxable year, there may be adverse U.S. federal income tax consequences to U.S. holders (as defined in the section of this Annual Report titled "Item 10E. Taxation—Material U.S. Federal Income Tax Considerations").

A non-U.S. corporation will be considered a PFIC for any taxable year if either (1) at least 75% of its gross income for such year is passive income or (2) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during such year) is attributable to assets that produce or are held for the production of passive income.

Passive income for this purpose generally includes, among other things, dividends, interest, rents, royalties, gains from commodities and securities transactions, and gains from assets that produce passive income. In determining whether a foreign corporation is a PFIC, a pro rata portion of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account. Although not free from doubt, we do not believe that we were a PFIC for the taxable year ended December 31, 2021. However, it is not yet known whether we will be a PFIC for the taxable year ending December 31, 2022 or in subsequent taxable years. The determination of PFIC status is fact-specific, and a separate determination must be made each taxable year as to whether we are a PFIC (after the close of each such taxable year). Our status as a PFIC depends on the composition of our income (including whether reimbursements of certain refundable research tax credits will constitute gross income for purposes of the PFIC income test) and the composition and value of our assets. The value of our assets may be determined in large part by reference to the market value of the ADSs and our ordinary shares, which may fluctuate substantially. Our status as a PFIC may also depend in part upon how quickly we utilize the cash proceeds from our U.S. Offering (and the cash proceeds from other fund-raising activities) in our business.

If we are a PFIC for any taxable year during which a U.S. holder holds ADSs, the U.S. holder may be subject to adverse tax consequences, including (1) the treatment of all or a portion of any gain on disposition as ordinary income, (2) the application of an interest charge with respect to such gain and certain dividends and (3) compliance with certain reporting requirements. Each U.S. holder is strongly urged to consult its tax advisor regarding these issues and any available elections to mitigate such tax consequences. See "Item 10E. Taxation—Material U.S. Federal Income Tax Considerations."

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

Pursuant to the provisions of the French Monetary and Financial Code (code monétaire et financier), any investment by any non-French citizen, any French citizen not residing in France, any non-French entity or any French entity controlled by one of the aforementioned persons or entities 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, in each case, conducting activities in certain strategic industries, such as activities essential to protecting public health as well as biotechnology-related research and development activities, i.e. the industry in which we operate, is subject to the prior authorization of the French Ministry of Economy, which authorization may be conditioned on certain undertakings.

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.

On November 5, 2020, the French Ministry of Economy informed us that our activities are subject to the above described foreign investment control regime. Therefore, any investor meeting the above criteria willing to acquire all or part of our business with the effect of crossing the applicable share capital thresholds set forth by the French Monetary and Financial Code will have to request this prior governmental authorization before acquiring our ordinary shares or ADSs.

We cannot guarantee that such investor will obtain the necessary authorization in due time. The authorization may also be granted subject to conditions that deter a potential purchaser. The existence of such conditions to an investment in our securities could have a negative impact on our ability to raise the funds necessary to our development. In addition, failure to comply with such measures could result in significant consequences for the investor (including the investment to be deemed null and void). 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 "Item 10B. Memorandum and Articles of Association."

General Risk Factors

We must maintain effective internal control over financial reporting, and if we are unable to do so, the accuracy and timeliness of our financial reporting may be adversely affected, which could hurt our business, lessen investor confidence and depress the market price of our securities.

We must maintain effective internal control over financial reporting in order to accurately and timely report our results of operations and financial condition. In addition, as a U.S. public company, the Sarbanes-Oxley Act requires, among other things, that we assess the effectiveness of our disclosure controls and procedures and the effectiveness of our internal control over financial reporting at the end of each fiscal year. Pursuant to Section 404(a) of the Sarbanes-Oxley Act, we are required to furnish an annual report by our management on our internal control over financial reporting, commencing with this Annual Report for the year ended December 31, 2021. The rules governing the standards that must be met for our management to assess our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act are complex and require significant documentation, testing and possible remediation. These stringent standards require that our audit and finance committee be advised and regularly updated on management's review of internal control over financial reporting.

Our compliance with applicable provisions of Section 404 requires that we incur substantial accounting expense and expend significant management attention and time on compliance-related issues as we implement additional corporate governance practices and comply with reporting requirements. In addition, our independent registered public accounting firm will be required to attest to the effectiveness of our internal controls over financial reporting beginning with our annual report following the date on which we are no longer an emerging growth company, which may extend until December 31, 2025.

If we fail to staff our accounting and finance function adequately or maintain internal control over financial reporting adequate to meet the requirements of the Sarbanes-Oxley Act, our business and reputation may be harmed. Moreover, if we are not able to comply with the applicable requirements of Section 404 in a timely manner, we may be subject to sanctions or investigations by regulatory authorities, including the SEC and Nasdaq. Furthermore, if we are unable to conclude that our internal control over financial reporting is effective or if deficiencies in our internal control over financial reporting that are deemed to be material weaknesses are identified, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our ADSs could decline, and we could be subject to sanctions or investigations by the SEC, Nasdaq or other regulatory authorities. Failure to implement or maintain effective internal control systems required of public companies could also restrict our access to the capital markets. The occurrence of any of the foregoing would also require additional financial and management resources.

Our internal computer systems, or those of our third-party subcontractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our operations.

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, malware, unauthorized access, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. If such an event were to occur and cause interruptions in our systems, it could result in a material disruption of our operations. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval, certification and commercialization efforts and significantly increase our costs to recover or reproduce the lost data. In addition, system redundancy may be ineffective or inadequate, and our disaster recovery planning may not be sufficient to cover all eventualities. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities, damage to our reputation, and the further development of our product candidates could be delayed. In addition, we may not have adequate insurance coverage to compensate for any losses associated with such events.

Use of social media by third parties may materially and adversely impact our reputation.

There has been a marked increase in the use of social media platforms and similar devices, including weblogs (blogs), social media websites and other forms of Internet-based communications which allow individual access to a broad audience of interested persons. The medical community and care prescribers may value any such readily available information concerning our products or product candidates and may act on such information without further investigation, authentication and without regard to its accuracy. Social media platforms and devices immediately publish the content their subscribers and participants post, often without filters or checks on accuracy of the content posted.

The opportunity for dissemination of information, including inaccurate information, is virtually limitless. Information concerning or affecting us, including information regarding our products, product candidates or proprietary nanotechnology, may be posted by third parties on such platforms and devices at any time. Information posted may be inaccurate and adverse to us, and it may harm our business or reputation. The harm may be immediate without affording us an opportunity for redress or correction. Further, such inaccurate information may require us to engage in a defensive media campaign, which may divert our management's attention or result in an increase in our

expenses. Such platforms also could be used for the dissemination of trade secret information or compromise of other valuable company assets, any of which could harm our business.

We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.

We may decide to acquire companies or technologies facilitating access to, or enabling us to access, new therapeutic solutions, new research projects, or new geographical areas, or enabling us to express synergies with our existing operations. If such acquisitions were to become necessary or attractive in the future, we may not be able to identify appropriate targets or make acquisitions under satisfactory conditions, in particular, satisfactory price conditions. In addition, we may be unable to obtain the financing for these acquisitions on favorable terms, which could require us to finance these acquisitions using our existing cash resources that could have been allocated to other purposes, including existing business activities. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure holders of our ordinary shares and ADSs that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

ITEM 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

Our legal and commercial name is Nanobiotix S.A. We were incorporated as a *société anonyme* under the laws of the French Republic on March 4, 2003 for a period of 99 years. We are registered at the Paris *Registre du Commerce et des Sociétés* under the number 447 521 600. Our principal executive offices are located at 60, rue de Wattignies, 75012 Paris, France, and our telephone number is +33 1 40 26 04 70. Our agent for service of process in the United States is our U.S. subsidiary, Nanobiotix Corporation, located at 210 Broadway, Cambridge, Massachusetts 02139. Our ordinary shares began trading on the regulated market of Euronext in Paris in October 2012. Our ADSs began trading on the Nasdaq Global Select Market on December 11, 2020.

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 we are a pioneer and leader in the field of nanomedicine. We have built an integrated, multidisciplinary team that combines expertise in physics, biology and medicine. Our corporate headquarters and manufacturing facilities are located in Paris, France, with U.S. operations in New York City, New York and Cambridge, Massachusetts.

Our capital expenditures and additions to intangible assets for the years ended December 31, 2019, 2020 and 2021 together amounted to €0.9 million, €0.08 million and €1.6 million, respectively. These expenditures primarily consisted of the manufacturing line implementation and offices expansion. We expect our capital expenditures to increase in absolute terms in the near term as we continue to advance our research and development programs and grow our operations. We anticipate our capital expenditure in 2022 to be financed from our cash and cash equivalents on hand. Primarily, these capital expenditures will be made in France, where our research and development facilities are currently located.

The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC at *http://www.sec.gov*. We also maintain a website at *http://www.nanobiotix.com/en/*. The reference to our website is an inactive textual reference only and the information contained in, or that can be accessed through, our website or any other website cited in this Annual Report is not a part of this Annual Report.

B. Business 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 "—Our Clinical Programs—Locally Advanced Head and Neck Cancers—Dose Expansion Results." 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 2021 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 "Business—Our Clinical Programs—HNSCC, Lung Metastasis or Liver Metastasis" 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. 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 "Business—Our Collaboration Agreements—PharmaEngine" 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 this Annual Report 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".

Our Strategy

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 "Business—Our Clinical Programs —Locally Advanced Head and Neck Cancers—Dose Expansion Results." 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 "Business—Our Clinical Programs—HNSCC, Lung Metastasis or Liver Metastasis" 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 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.

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.

NBTXR3: Addressing the challenges of radiotherapy and I-O

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.

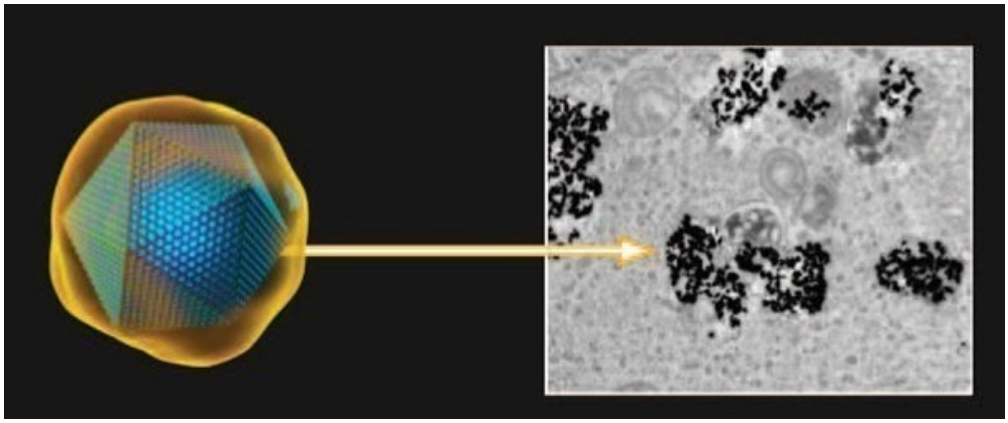
Our NBTXR3 technology

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.

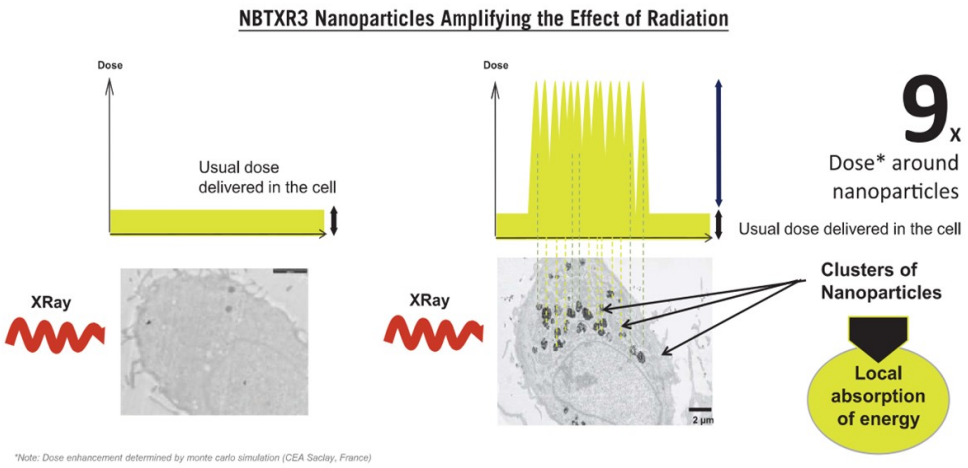
Clustered 50 nm Nanoparticles in Cytoplasm



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.

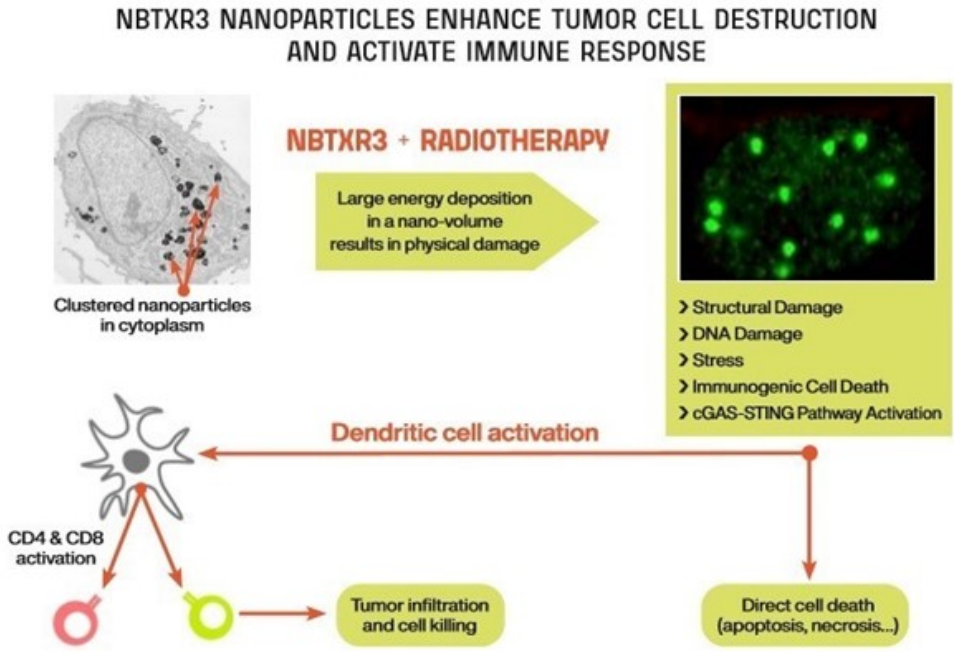
Stage 3: Subsequent Action in the Cells

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.



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.

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 “Business—Our Collaboration Agreements—Other Collaborations—NBTXR3 Clinical Collaboration with MD Anderson” 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 “Our Collaboration Agreements” 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.

Locally advanced soft tissue sarcoma

Background and Opportunity

Soft tissue sarcomas (“STSs”) 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.

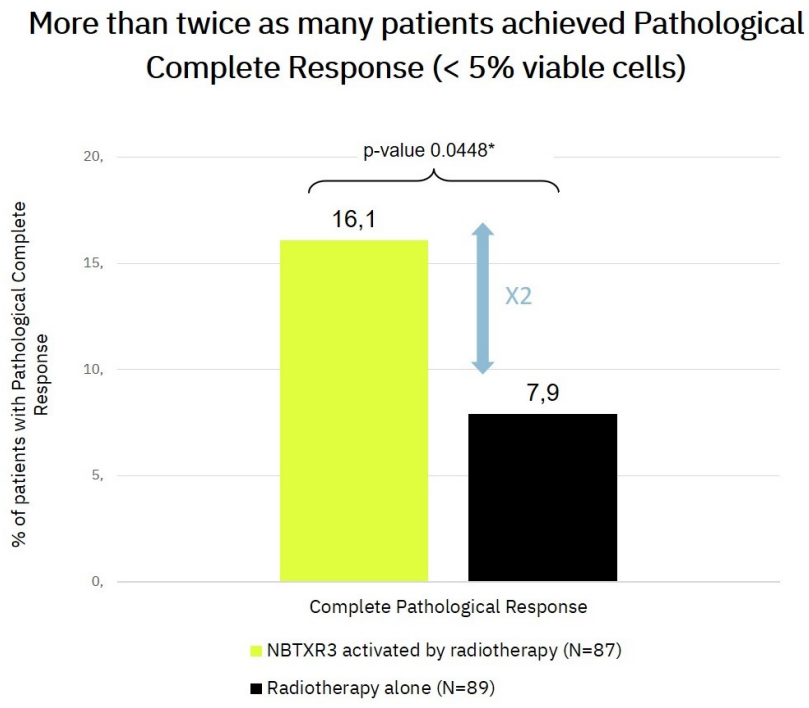
The primary endpoint of the Phase II/III trial was an increase in the pathological complete response rate of intratumoral injection of NBTXR3 activated by external beam radiation therapy ("**EBRT**"), as compared against EBRT alone. The primary endpoint was evaluated, in accordance with European Organisation 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

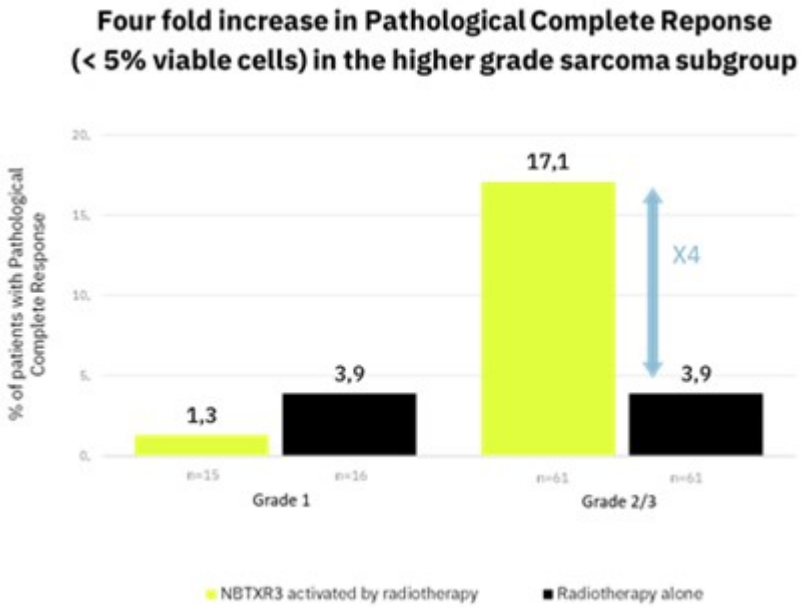
Pathological complete response rate

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 Annual Report 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 α threshold of 0.04575*



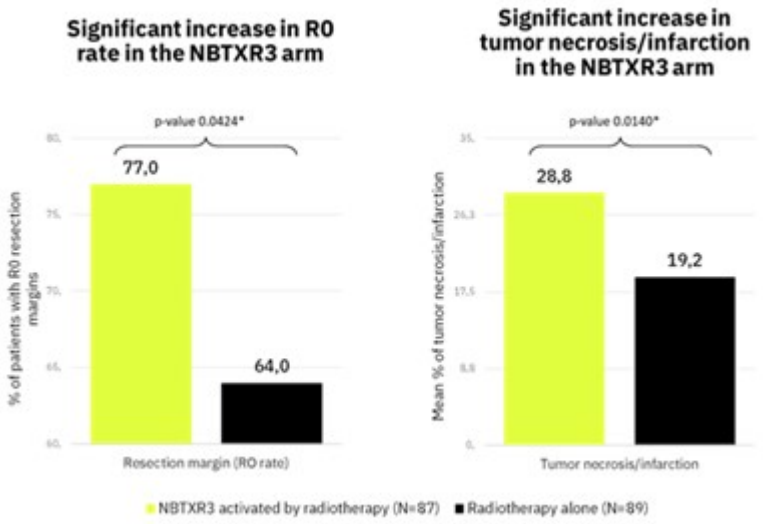
Patients in the NBTXR3 arm were more likely to have a pathological response (not limited to a complete response). The portion of patients with pathological “nearly” complete response (defined as less than 7% of residual viable cancer cells in the tumor) and pathological response with 10% or less of residual 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.

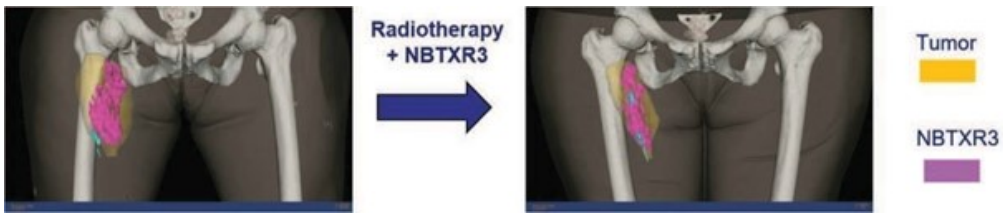
Phase I Trial Design

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.



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					
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					
2 (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 the 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.

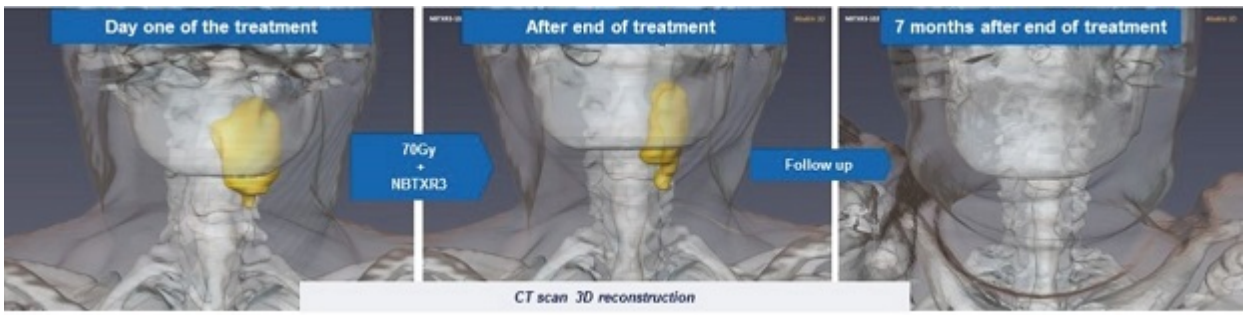
The secondary endpoints of both phases were to evaluate the safety and tolerability of NBTXR3, to evaluate the overall response rate and the complete response rate (based on the RECIST 1.1) of NBTXR3, to evaluate the local and general PFS, assess the feasibility of local administration by intratumoral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

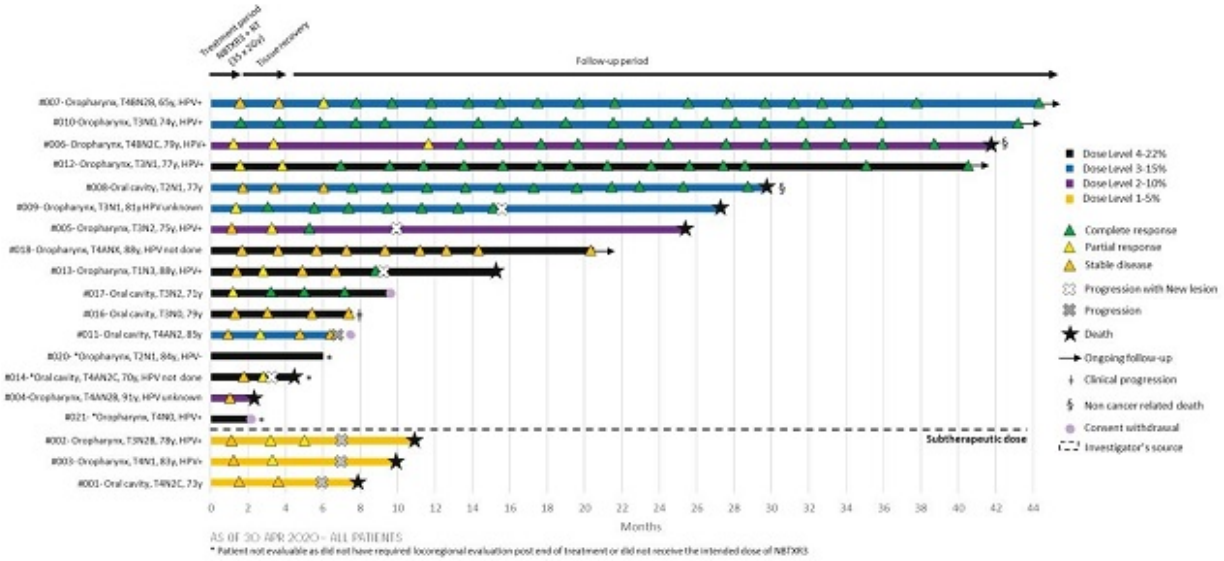
The following graphic depicts shrinkage of the tumor in a representative patient in the trial over time following treatment. The tumor continued to shrink after the end of treatment, with the patient achieving a complete response at seven months.



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. Overall complete response (including non-injected lesions) was observed in five of the 16 patients, or 31%, and objective response rate was observed 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

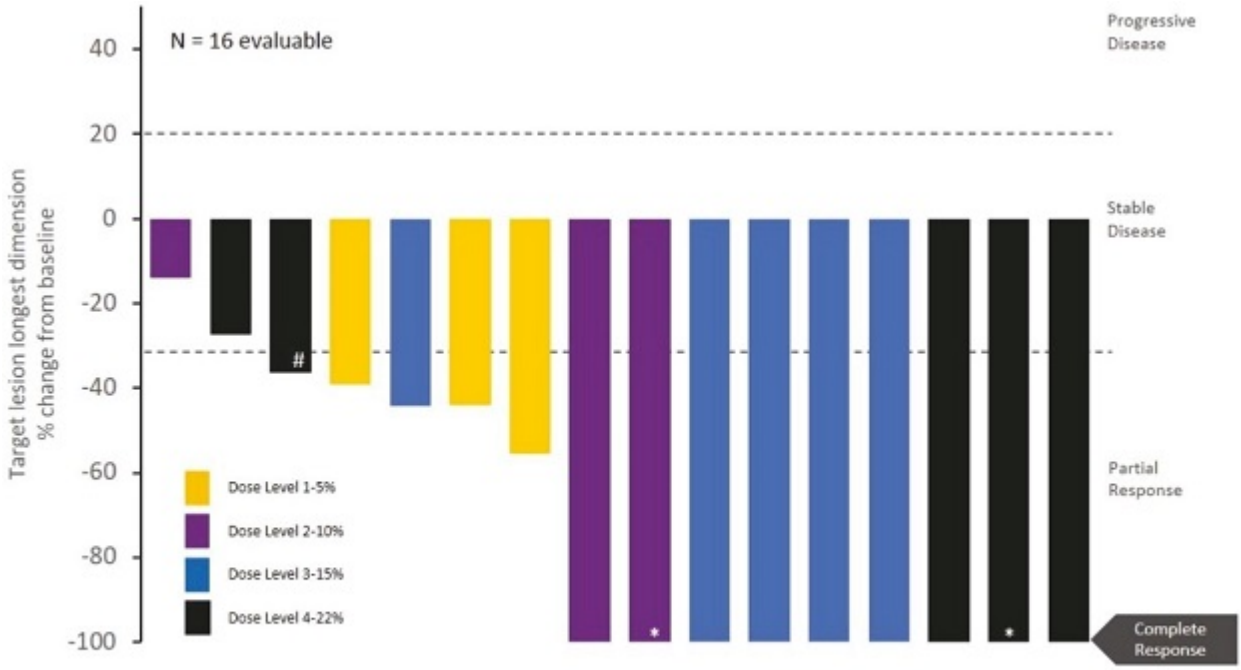
follow-up data of the 19 treated patients at the various NBTXR3 dose levels as of the end of April 2020, including the type of cancer, tumor grade, age and human papilloma virus status for each patient.

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



The following chart shows the best observed response from baseline of each of the 16 evaluable patients.

Patients' Best Response in Study 102 Escalation Locally Advanced Head and Neck Cancers Trial



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.

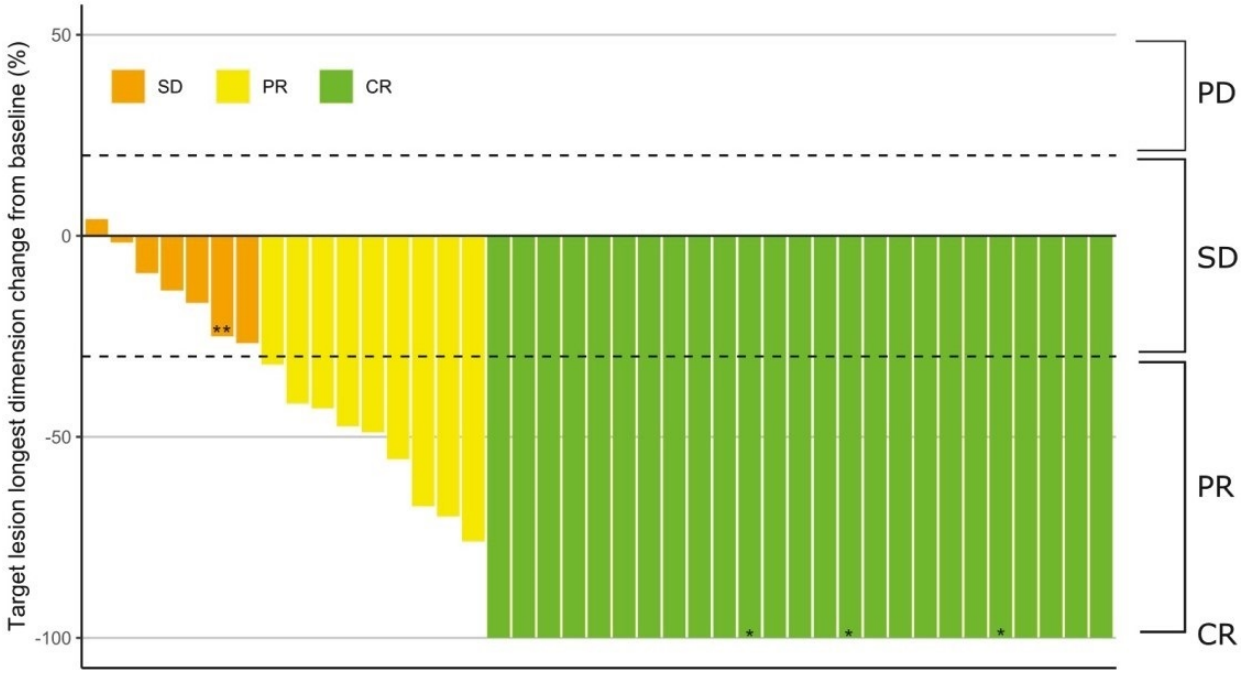
In head and neck cancer, an mCCI ≥ 4 is correlated with higher risk of death relative to the broader population.
In the Study 102 Expansion “all patients treated” population (54 patients, including 13 non-evaluable patients), mOS was 14.1 months, and median PFS was 9.4 months. Among the “all patients 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.

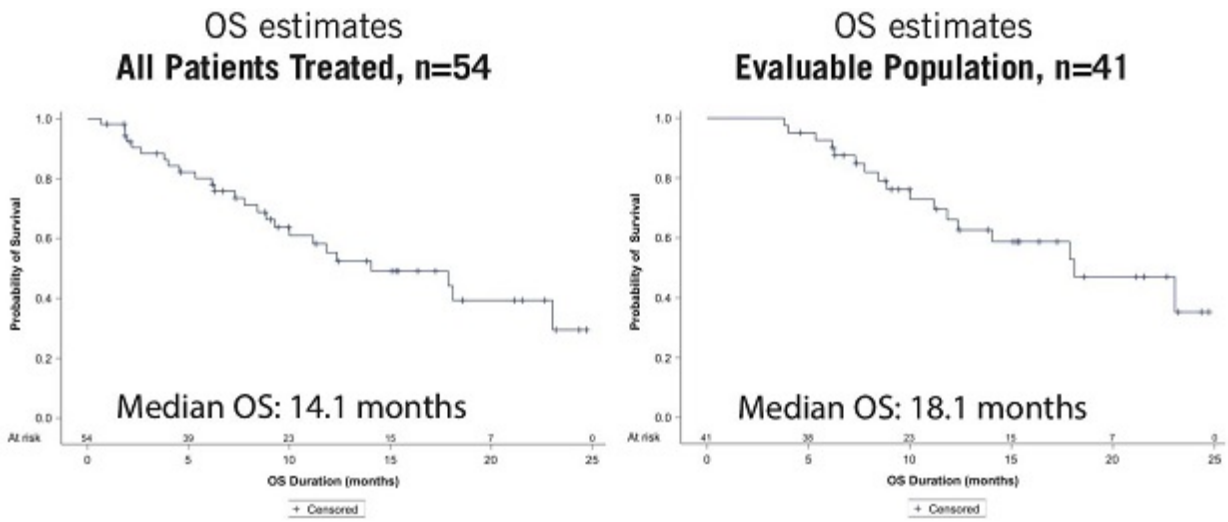
Patients' Best Observed Target Lesion Response by RECIST 1.1 as per Investigator Assessment in Study 102 Expansion Locally Advanced Head and Neck Cancers Trial (Evaluable Population: N=41)



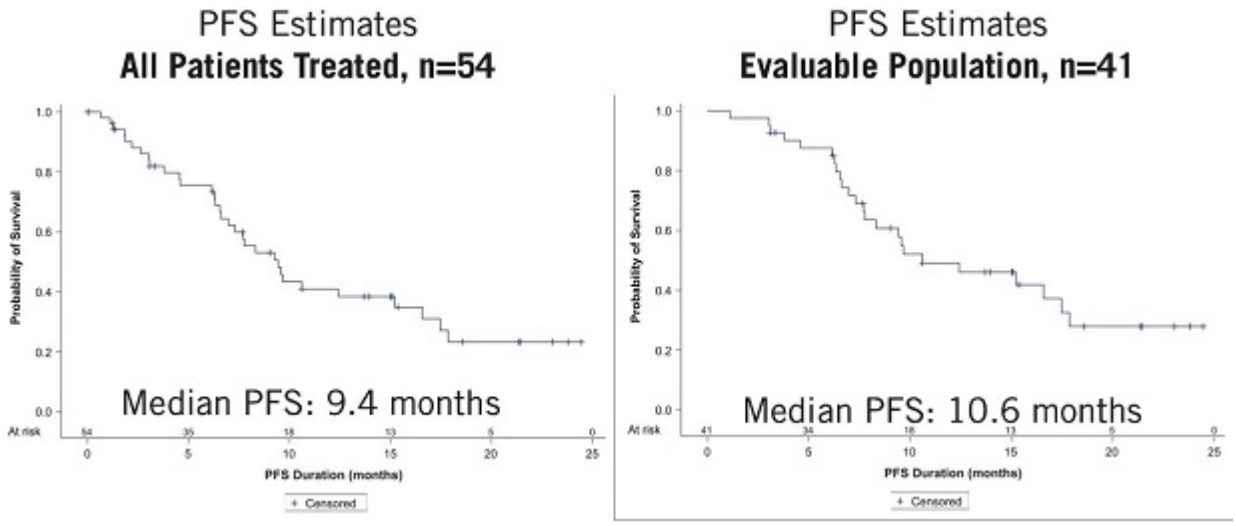
* unconfirmed complete response
** CR as per investigator

The 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

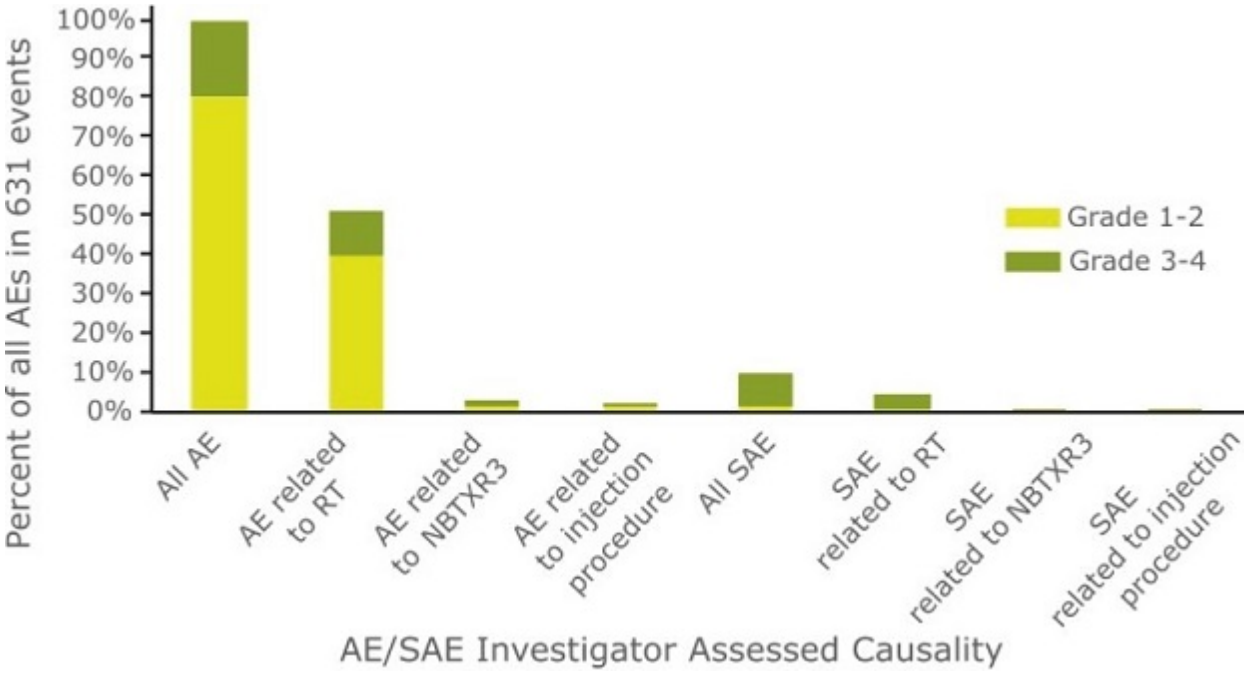


Kaplan Meier Curve of Progression Free Survival in Study 102 Expansion Locally Advanced Head and Neck Cancers Trial



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 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.

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

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.

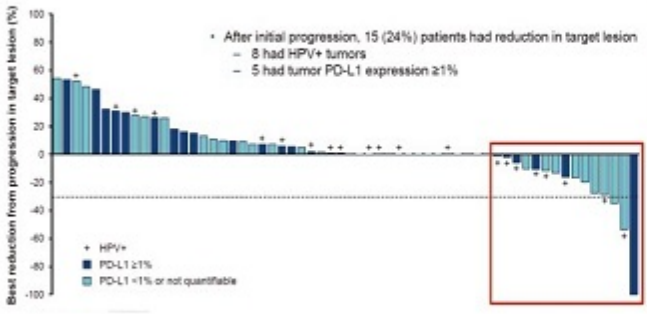
Cancer immunotherapy is becoming a major treatment paradigm for a variety of cancers. Although immunotherapy, especially the use of immune checkpoint inhibitors, has achieved clinical success, most cancer patients present resistance to I-O treatments. In fact, published scientific data shows that only 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)

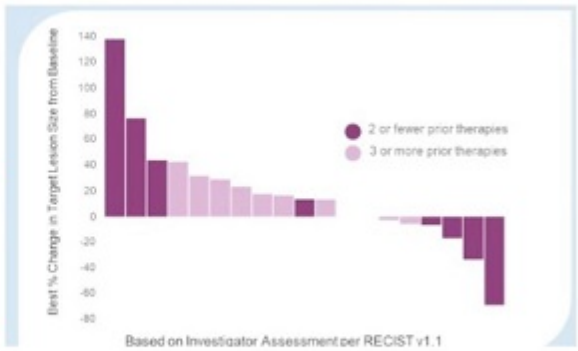
PD-1 Non-Responders ("NR") Trials

Nivolumab
CHECKMATE 141 – Anti-PD-1 NR



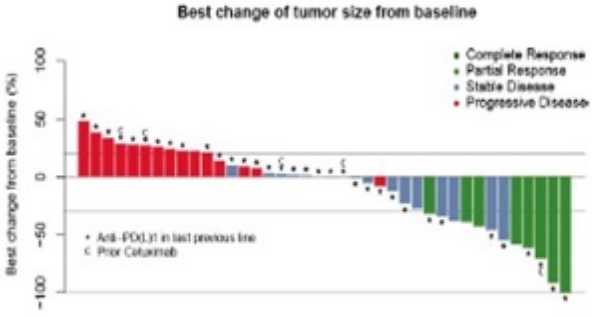
Source: Haddad R, et al., "Treatment Beyond Progression With Nivolumab in Patients With Recurrent or Metastatic (R/M) Squamous Cell Carcinoma of the Head and Neck (SCCHN) in the Phase 3 Checkmate 141 Study: A Biomarker Analysis and Updated Clinical Outcomes." European Society for Medical Oncology, September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

Eganelisib + Nivo
MARIO 1 – CPI NR



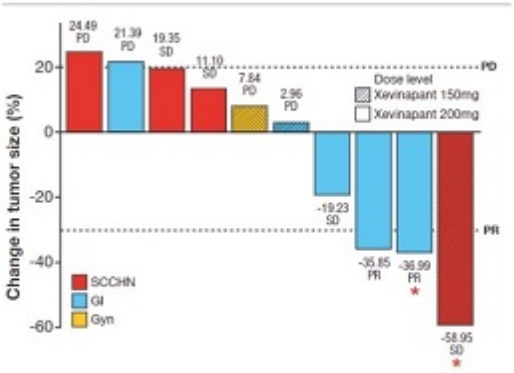
Source: Cohen E, Postow M, Sullivan R, et al., "352 Updated clinical data from the squamous cell carcinoma of the head and neck (SCCHN) expansion cohort of an ongoing Ph1/1b Study of eganelisib (formerly IPI-549) in combination with nivolumab." Journal for ImmunoTherapy of Cancer, December 10, 2020.

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.

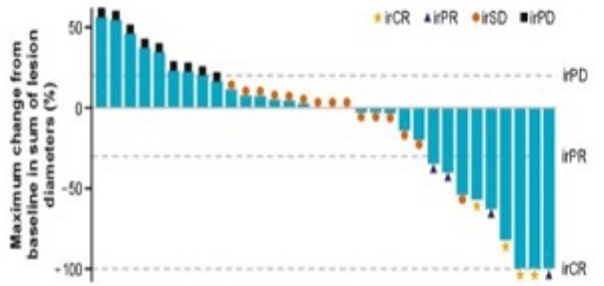
Debio + Anti-PD-1
previous Anti-PD-1



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.

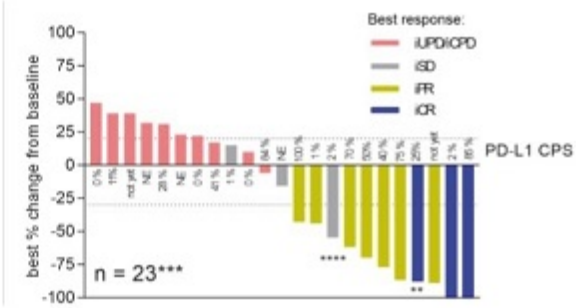
PD-1 Naïve Trials

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



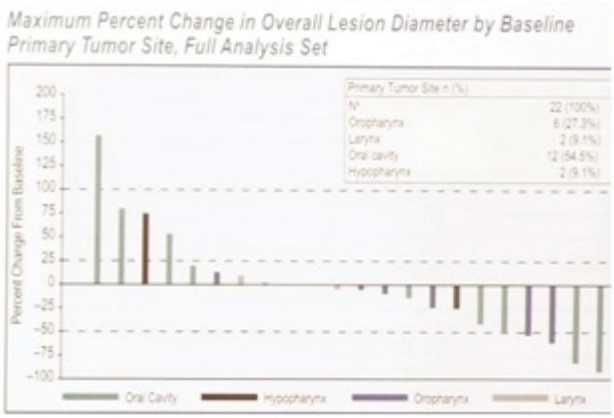
Source: Angevin E, et al. "Updated analysis of the inducible T-cell co-stimulatory receptor (ICOS) agonist, GSK3359609 (GSK609), combination with pembrolizumab (PE) in patients (pts) with anti-PD-1/L1 treatment-naive head and neck squamous cell carcinoma (HNSCC)." Journal of Clinical Oncology, May 25, 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 in combination with anti-PD-1 checkpoint inhibitors in patients with R/M HNSCC or with lung or liver metastases from any primary cancer eligible for 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.

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 nonresponsive to an anti-PD-1 therapy ("HNSCC Cohort"),
- patients with lung metastases from any primary cancer eligible for anti-PD-1 therapy ("Lung Cohort") or
- patients with 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 signaling 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).

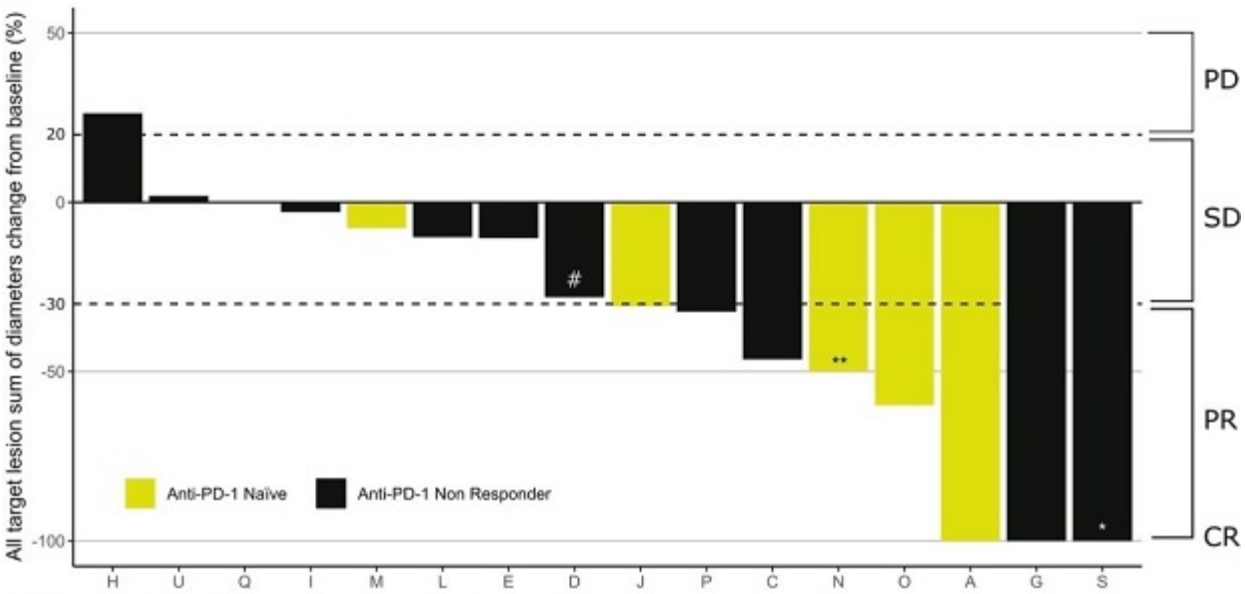
The updated results suggest that NBTXR3 administration has been feasible and well-tolerated in all patients currently enrolled in Study 1100. Through the cut-off date, six SAEs were observed which were identified as related to NBTXR3 or the injection procedure in 4 patients, and which included facial 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: aCR 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

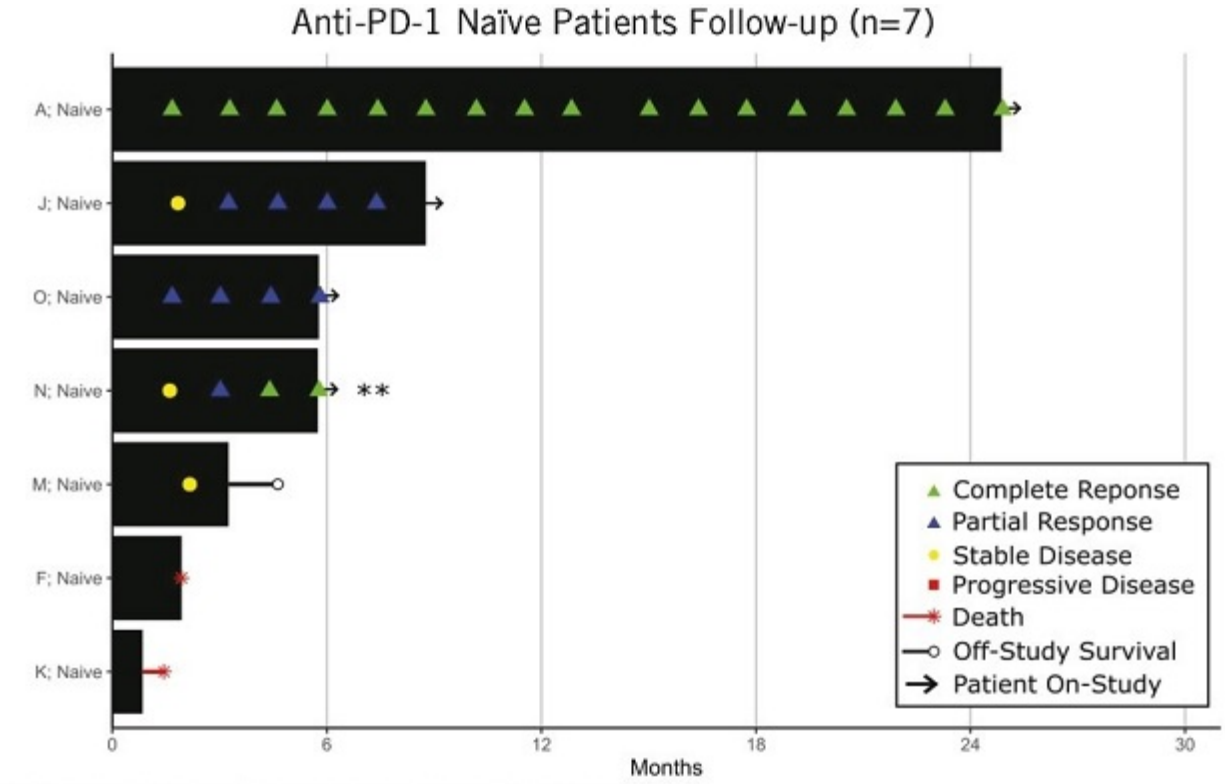
In addition, for three patients who exhibited prior resistance to anti-PD-1, a potential abscopal effect was observed. Specifically, improved control of the disease was observed in two patients (I and L) with highly progressive disease (PD on anti-PD-1 within six months of therapy), where both patients 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.

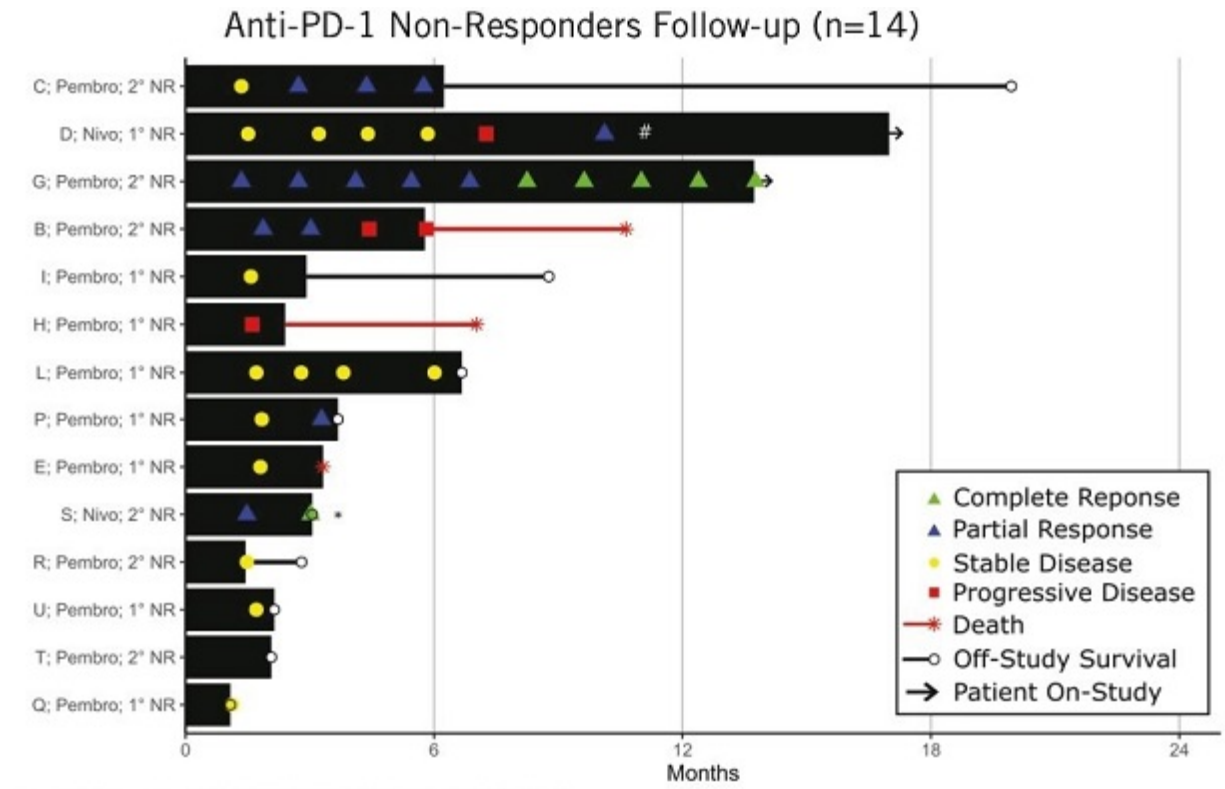
The charts below present preliminary response data for Study 1100 in the "all patients treated" population, which comprises 21 patients, including 5 non-evaluable patients.

All Target Lesions Response per Investigator Assessment Based on RECIST 1.1

(All Patients Treated: n=21)



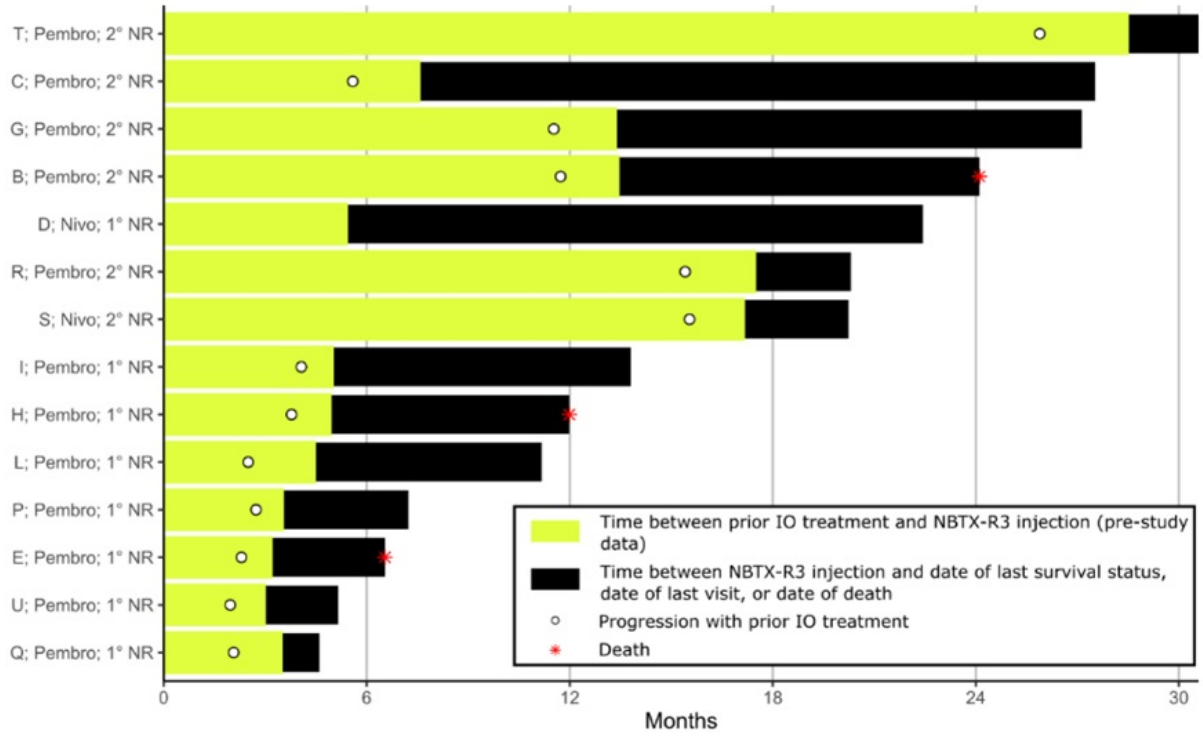
** Patient N: Lymph node size is 8mm; complete response as per RECIST 1.1



Patient D: pCR based on biopsy sample located in the target lesion
* Patient S: Patient with unconfirmed complete response

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.

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.

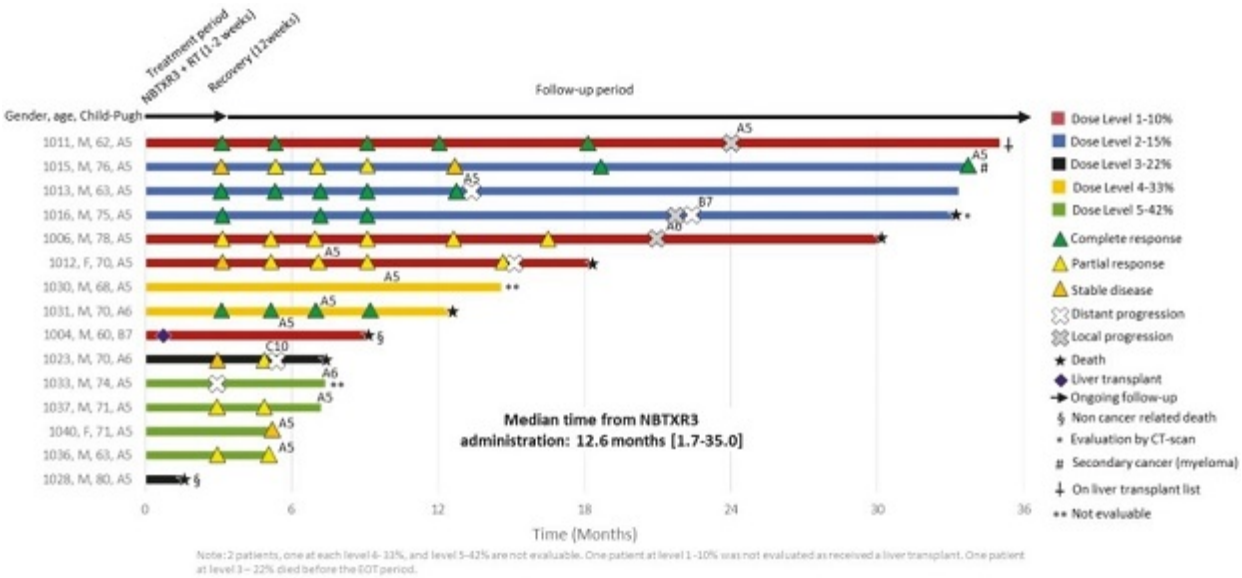
Results

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.

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.

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.

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.

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.

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 "—Our Collaboration Agreements—PharmaEngine" below for additional information).

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.

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.

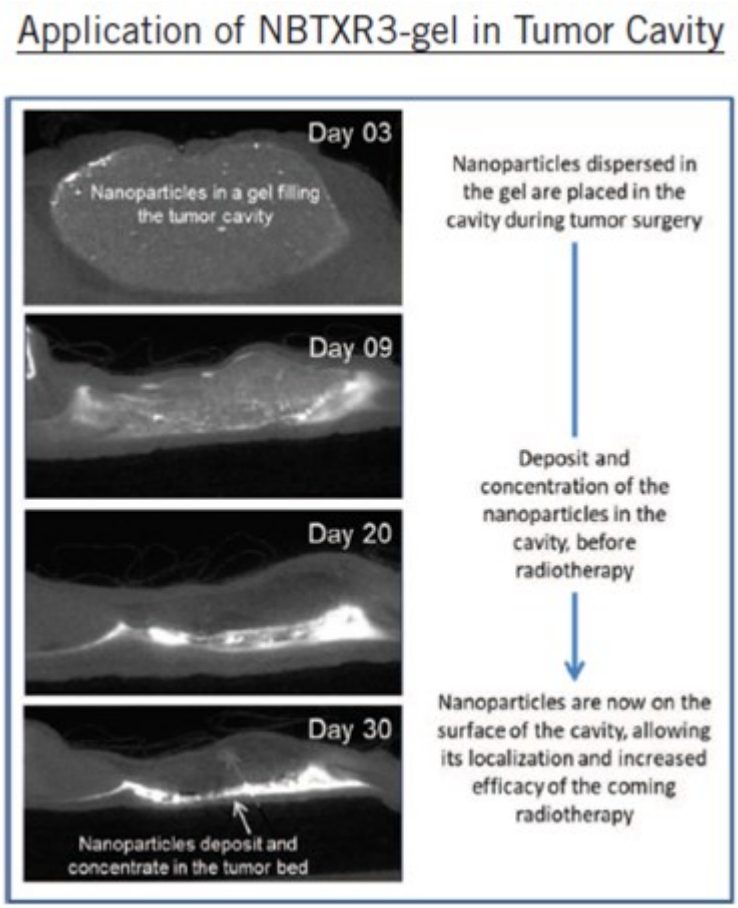
Results

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 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.

Our Preclinical Program for 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.



This unique product candidate has dual aims: 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.

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.

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.

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.

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.

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.
		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.

Our collaboration agreements

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.

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

On December 21, 2018, we entered into a strategic collaboration agreement with MD Anderson, which was amended and restated in January 2020 and subsequently amended in June 2021. Pursuant to the MD Anderson Collaboration Agreement, we and MD Anderson established a large-scale, comprehensive NBTXR3 clinical collaboration to improve the efficacy of radiotherapy for certain types of cancer. The collaboration initially is expected to support multiple clinical trials conducted by MD Anderson, as sponsor, with NBTXR3 for use in treating several cancer types. We expect to enroll approximately 340 patients across these clinical trials.

Obligations of the Parties

Under the MD Anderson Collaboration Agreement, MD Anderson will provide all necessary personnel, equipment, supplies, facilities and resources for each trial, and we will provide batches of NBTXR3 to be used in the trials. In addition, we have committed to provide financing of approximately $11.0 million for clinical trials during the collaboration. We 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 are processed semi-annually 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.

We are also required to make an additional one-time milestone payment upon (i) the first regulatory approval granted by the FDA for NBTXR3 and (ii) the date on which a specified number of patients have been enrolled in the clinical trials in the United States. The milestone payments increase on an annual basis ranging from $2.2 million to $16.4 million. Accordingly, depending on when the requisite conditions are satisfied, we could be required to pay up to $16.4 million in such milestone payment if the conditions were not satisfied until 2030.

The protocol, schedule, monitoring, termination and replacement of each clinical trial will be determined by mutual agreement between MD Anderson and us, and MD Anderson has granted us certain audit and information rights in connection with the clinical trials.

Intellectual Property

We have granted MD Anderson a non-exclusive license with respect to NBTXR3 for the conduct of the clinical trials governed by the MD Anderson Collaboration Agreement. We will be the exclusive owner of any right, title or other interest in and to any and all inventions or discoveries made in a trial that incorporates NBTXR3 or any formulation relating to NBTXR3 (though we have agreed to grant MD Anderson a non-exclusive, perpetual irrevocable license to use any such inventions for academic or non-profit research purposes). Other inventions and discoveries made in the course of a trial will be the property of the inventor, Nanobiotix or MD Anderson, as the case may be. Should MD Anderson obtain ownership of any such other invention or discovery, they have agreed to grant us a non-exclusive, royalty-free license, as well as an exclusive option to negotiate an exclusive, royalty-bearing license within a specified time period. Further, we and MD Anderson will be co-owners of the data and clinical results related to the trials, with MD Anderson's use of such data limited to academic or non-profit research purposes. MD Anderson possesses a first right to publish and/or publicly disclose data and results of collaboration trials.

Term and Termination

The MD Anderson Collaboration Agreement will remain in effect until the later of five years or the duration of the clinical trials. Either party may terminate the agreement if the other party commits a material breach that is not cured pursuant to the terms of the agreement within 30 days of notification of the breach. Either party may also terminate a clinical trial in the event of a material breach of the other party's obligations, due to health/safety issues related to NBTXR3 or the clinical trial's procedures, or if the parties are unable to agree on the designation of the principal investigator or if the principal investigator does not accept the terms of the trial protocol. Termination of the MD Anderson Collaboration Agreement does not affect the conduct of ongoing clinical trials (other than with respect to a termination of a specific trial, as described in the preceding sentence). A clinical trial is automatically terminated in the event of a withdrawal or rejection of requisite regulatory approvals.

LianBio

On May 11, 2021, we 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—Mainland China, Macau, Hong Kong, Thailand, Taiwan, South Korea and Singapore (collectively, the "Territory"). We have 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 we will conclude. We are 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 our 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 our 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 us as a result. Otherwise, LianBio will fund all development and commercialization expenses in the Territory, and we 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, we and LianBio have agreed to provide each other with rights to access all clinical efficacy and safety data. For additional registrational trials, we 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, we received a non-refundable upfront payment from LianBio of $20.0 million in June 2021.

We are also eligible to receive up to an aggregate of $220 million in potential contingent, development and commercialization milestone payments. We 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 us, and will meet on a regular basis to provide oversight and facilitate information sharing between LianBio and us. 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 us. In the event such senior officers cannot reach an agreement on the matters at hand within a set timeframe, LianBio and we 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.

We retain the first right to prosecute, maintain and defend, at our expense, all of our licensed patents in the Territory. In the event that we elect not to prosecute or maintain any such patent in the Territory or not to defend a patent in the Territory, we have 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, our intellectual property against infringement in the Territory, except where we are enforcing such intellectual property both within and outside the Territory against such infringement. In the event that LianBio elects not to enforce our intellectual property against infringement in the Territory, it has agreed to notify us, and we will have the right to enforce such intellectual property at our expense.

We and LianBio have agreed to customary confidentiality obligations with respect to trade secrets and confidential or proprietary information disclosed in connection with our respective performance under the LianBio Agreement, subject to customary exceptions. We and LianBio have agreed to provide customary indemnification to one another for claims relating to our 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.

Intellectual Property

We and LianBio retain ownership of our 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 us 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 us together, such invention and any related patents will be jointly owned by LianBio and us. 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 us, 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 us, subject to a specified notice period. We may terminate the agreement under certain circumstances in connection with a change of control of LianBio. We 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 our patents, subject to certain limited exceptions.

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

PharmaEngine

In August 2012, we 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 us based on the achievement of development and commercialization milestones for NBTXR3. We 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, we and PharmaEngine mutually agreed to terminate the agreement. Accordingly, on March 4, 2021, we and PharmaEngine entered into a Termination and Release Agreement. Under the termination agreement we will retain all rights to the development and commercialization of NBTXR3 in the Asia Pacific region. We have 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 us following the announcement of our collaboration with LianBio for the Asia-Pacific region. During the six months ended June 30, 2021, PharmaEngine also received $4.0 million from us 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 us 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 us 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 us 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.

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

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.

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.

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 remuneration, 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.

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 EU, 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 EU 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 a 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 regards 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 this Annual Report, 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, in addition to 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).

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.

C. Organizational Structure

Nanobiotix S.A. is a *société anonyme* organized under the laws of the French Republic.

The following chart shows our organizational structure as of December 31, 2021:

Subsidiary Name	Jurisdiction of Organization	Ownership & Voting Interest Held by Nanobiotix S.A.
Nanobiotix Corp.	Delaware	100% (held directly)
Nanobiotix Germany GmbH	Germany	100% (held directly)
Nanobiotix Spain S.L.U	Spain	100% (held directly)
Curadigm S.A.S.	France	100% (held directly)
Curadigm Corp.	Delaware	100% (held indirectly through Curadigm S.A.S.)

Nanobiotix also has a Swiss branch (succursale) in Lausanne (Switzerland).

D. Property, Plant and Equipment

Our corporate headquarters is located in Paris, France, where we lease approximately 2,622 square meters of office space. The lease of our Paris headquarters continues through June 30, 2027. Our headquarters, located at 60 rue Wattignies in the 12th arrondissement of Paris, for which we signed a lease on July 1, 2017 for a term of 10 years and an amendment pursuant to which we leased additional space, with retroactive effect from January 1, 2019.

Our approximately 1,195 square meter manufacturing facility is located in the Villejuif BioPark, a scientific research and innovation center just outside of Paris, France. The lease for the facility began on July 1, 2017 for a term of nine years, expiring on June 30, 2029. The facility, which we opened in November 2017, expanded our potential production capacity with the aim to produce NBTXR3 for our current and contemplated clinical trials and the initial commercial phase. We have designed our manufacturing process to implement in a timely manner further set-up of in-house additional production lines.

We also rent office space in New York City, New York and rent office space for Nanobiotix Corp., our wholly owned U.S. subsidiary, in Cambridge, Massachusetts, in each case on a month-to-month basis.

We have no lease commitments with respect to our foreign subsidiaries, other than lease contracts for vehicles in the United States and Germany.

We believe that our existing facilities are adequate for our near-term needs, and we believe that suitable additional or alternative office and manufacturing space will be available as required in the future on commercially reasonable terms.

ITEM 4a. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

Unless otherwise indicated or the context otherwise requires, references in this Operating and Financial Review and Prospects to "Nanobiotix," or the "Company" refer to Nanobiotix S.A. and its consolidated subsidiaries. All references to "$," "dollars" and "USD" mean U.S. dollars and all references to all references to "€" and "euros" mean euros.

You should read the following discussion of our operating and financial review and prospects in conjunction with our audited consolidated financial statements and the related notes thereto included elsewhere in this Annual report. In addition to historical information, the following discussion and analysis contains forward-looking statements that reflect our current plans,estimates, expectations and beliefs and involve risks and uncertainties. Our actual results and the timing of events could differ materially from those anticipated in the forward-looking statements as a result of various factors. Factors that could cause or contribute to these differences include, but are not limited to, those discussed below and elsewhere in this Annual Report, particularly in sections titled "Risk Factors" and "Special Note Regarding Forward-Looking Statements."

Financial Overview

The following selected statement of consolidated operations data for the years ended December 31, 2021, 2020 and 2019 and the selected statement of consolidated financial position data as of December 31, 2021 and December 31, 2020 have been derived from our audited consolidated financial statements included elsewhere in this Annual Report. Our audited consolidated financial statements have been prepared in accordance with IFRS, as issued by the IASB.

The following summary consolidated financial data for the periods and as of the dates indicated are qualified by reference to, and should be read in conjunction with, our consolidated financial statements and related notes beginning on page F-1 of this Annual Report, as well as the sections titled "Operating And Financial Review And Prospects" included elsewhere in this Annual Report.

Our historical results for any prior period do not necessarily indicate our results to be expected for any future period.

	For the year ended December 31,		
(in thousands of Euros)	**2021**	**2020**	**2019**
Statement of consolidated operations data:			
Revenues	10	50	68
Other income	2,637	2,462	2,473
Total revenues and other income	**2,647**	**2,512**	**2,541**
Research and development expenses	(30,378)	(24,330)	(30,411)
Selling, general and administrative expenses	(19,434)	(14,611)	(18,909)
Other operating income and expenses	(5,414)	—	—
Total operating expenses	**(55,226)**	**(38,941)**	**(49,320)**
Operating income (loss)	**(52,579)**	**(36,428)**	**(46,779)**
Financial income	6,360	201	837
Financial expenses	(780)	2,646	(4,970)
Financial income (loss)	**5,580**	**2,847**	**(4,133)**
Income tax	(5)	(9)	(3)
Net loss for the period	**(47,003)**	**(33,590)**	**(50,915)**
Basic loss per share (euros/share)	**(1.35)**	**(1.38)**	**(2.35)**
Diluted loss per share (euros/share)	**(1.35)**	**(1.38)**	**(2.35)**

	As of December 31,	
(in thousands of Euros)	**2021**	**2020**
Statement of consolidated financial position data:		
Cash and cash equivalents	83,921	119,151
Total assets	101,769	134,030
Total shareholders' equity	26,790	70,468
Total non-current liabilities	38,134	44,522
Total current liabilities	36,845	19,041

Operation 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.

As of December 31, 2021, NBTXR3 has been administered to approximately 300 patients. Given our 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 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 we are 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 our unique expertise in nanotechnology will provide us with opportunities to expand our product pipeline and to advance the development of our product candidates, either on our 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.

As of December 31, 2021, we had cash and cash equivalents of €83.9 million. See "—Liquidity and Capital Resources" below for additional information. For the years ended December 31, 2021 and 2020, we had *de minimis* revenue. We have not generated significant revenues to date from product sales or royalties, and we do not expect to generate significant revenues from product sales or royalties unless and until our product candidates are approved for marketing and are successfully commercialized. Historically, we have financed our operations and growth through issuances of new shares, refunds of research tax credits, conditional advances and grants awarded by governmental agencies, as well as bank loans from time to time. From our inception in 2003 through December 31, 2021, we have received more than €324.4 million in financing in the form of external fundraising, loans and repayable advances. See ''—Liquidity and Capital Resources'' below for additional information.

Since our inception, we have recorded operating losses every year, due primarily to research and development expenses incurred in connection with our efforts to advance our development program for NBTXR3. Our net losses were €47.0 million, €33.6 million and €50.9 million for the years ended December 31, 2021, 2020 and 2019, respectively. Our net losses may fluctuate significantly from year to year, depending on the timing of our clinical trials and our expenditures on other research and development activities. We anticipate that our expenses and capital requirements will increase substantially in connection with our ongoing activities, as we:

- advance our ongoing clinical trials of NBTXR3;
- initiate and conduct additional planned clinical trials of NBTXR3;
- continue the research and development of other product candidates or other applications of NBTXR3;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- scale-up our manufacturing capabilities to support the launch of additional clinical trials and the commercialization of our product candidates, if approved;
- establish a sales and marketing infrastructure for the commercialization of our product candidates, if approved;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts.

Until such time that we can generate substantial revenue from product sales, we expect to finance these expenses and our operating activities through our existing liquidity. If we are unable to generate revenue from product sales in accordance with our expected timeframes and in the amounts we expect, or if we otherwise need additional capital to fund our operating activities, we will need to raise additional capital through the issuance of shares, through other equity or debt financings or through collaborations or partnerships with other companies. We may be unable to raise additional funds or enter into such arrangements when needed on favorable terms, or at all, which would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our development programs or commercialization efforts or grant to others rights to develop or market product candidates that we would otherwise prefer to develop and market ourselves. Failure to secure adequate funding could cause us to cease operations, in part or in full.

Although it is difficult to predict future liquidity requirements, we expect that our existing cash and cash equivalents as of December 31, 2021 will be sufficient to fund our current operations through the second quarter of 2023. However, this estimate is based on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. In any event, we will need additional capital to pursue preclinical and clinical activities, obtain regulatory approval for, and to commercialize our product candidates. Our ability to successfully transition to profitability will be dependent upon achieving a level of revenues adequate to support our cost structure. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

We operate in a single operating segment for accounting purposes. The audited 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 January 1, 2021. The audited consolidated financial statements are also compliant with IFRS as adopted by the EU.

COVID-19 Update

As previously reported, while implementing health and safety measures, we have continued to advance our research and development programs. As we continue to actively advance our clinical programs, we remain in close contact with our principal investigators and clinical sites and are assessing the impact of COVID-19 on the expected development timelines and costs of our clinical trials.

In light of the severity and duration of the COVID-19 pandemic, the focus of healthcare providers and hospitals on addressing COVID-19, and consistent with the FDA’s updated industry guidance for conducting clinical trials issued on March 18, 2020, we have experienced delays in the enrollment of patients and collection of results from our trials and our preclinical studies. In addition, the ability to conduct patient follow-up is expected to be impacted by the COVID-19 pandemic.

The exact timing of delays and overall impact of the COVID-19 pandemic to our business, preclinical studies, clinical trials and manufacturing facility is currently unknown, and we are monitoring the pandemic as it continues to rapidly evolve. The overall impact to our business will be dependent on future developments, which are highly uncertain and difficult to predict. See Part II, Item 3D. “Risk Factor” of this Annual Report.

Financial Operations Overview

Revenues and Other Income

Revenues

Our limited revenues during the years ended December 31, 2021, 2020 and 2019 have been derived mainly from the charging-back of external contract research organization costs that we incurred on behalf of PharmaEngine in connection with development support received as part of our license and collaboration agreement with PharmaEngine. In March 2021, we entered into a Termination and Release agreement, pursuant to which we and PharmaEngine agreed to discontinue our collaboration.

Other Income

Our other income consists of grants and subsidies from government agencies and refundable research tax credits.

Grants and Subsidies

We have received various grants and other assistance from the government of France and French public authorities, including through Bpifrance (formerly OSEO Innovation), since our inception. The funds are intended to finance our operations or specific projects. Grants and subsidies are recognized in income as the corresponding expenses are incurred and independently of cash flows received.

Research Tax Credits

The French tax authorities grant a research tax credit (*Crédit d'Impôt Recherche*) 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 in France (or, since January 1, 2005, other countries in the EU or the European Economic Area that have signed a tax treaty with France containing an administrative assistance clause) receive a tax credit that may be used for the payment of their income tax due for the fiscal year in which the expenditures were incurred and during the three fiscal years thereafter. If taxes due are not sufficient to cover the full amount of the tax credit at the end of the three-year period, the difference is repaid in cash to the company by the French tax authorities.

The main characteristics of the research tax credits are as follows:

- the research tax credits result in a cash inflow to us from the tax authorities, either through an offset against the payment of corporate tax or through a direct payment to us for the portion that remains unused;
- our income tax liability does not limit the amount of the research tax credit, as a company that does not pay any income tax can request direct cash payment of the research tax credit; and
- the research tax credit is not included in the determination of income tax.

We apply for the research tax credit for research expenses incurred in each fiscal year and recognize the amounts claimed in the same fiscal year. We have concluded that the research tax credits meet the definition of a government grant as defined in IAS 20, Accounting for Government Grants and Disclosure of Government Assistance, and, as a result, it has been classified as "Other income" within operating income in our statements of consolidated operations.

Operating Expenses

Our operating expenses are primarily incurred for research and development and selling, general and administrative purposes, for the most part in France.

Research and Development Expenses

Research and development activities are central to our business. Since our inception, most of our resources have been allocated to research and development. These expenses include:

- sub-contracting, collaboration and consultant expenses that primarily consist of the cost of third-party contractors, such as contract research organizations that conduct our non-clinical studies and clinical trials;
- employee-related costs for employees in research and development functions;
- expenses relating to preclinical studies and clinical trials for NBTXR3;
- manufacturing costs for production of NBTXR3 to support clinical development;
- certain intellectual property expenses;
- expenses relating to regulatory affairs; and
- expenses relating to the implementation of our quality assurance system.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we advance the clinical development of NBTXR3.

We cannot determine with certainty the duration and completion costs of the current or planned future clinical trials of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may not succeed in achieving regulatory approval for any particular product candidate. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress and expense of our ongoing and planned preclinical studies, clinical trials and other research and development activities;
- clinical trial and early-stage results;
- the terms and timing of regulatory approvals;
- the expense of filing patent applications and maintaining and enforcing patents and other intellectual property rights and defending against claims or infringements raised by third parties; and
- the ability to market, commercialize and achieve market acceptance for NBTXR3 or any other product candidate that we may develop in the future.

A change in the outcome of any of these variables with respect to the development of NBTXR3 or any other product candidate that we develop could mean a significant change in the costs and timing associated with the development of NBTXR3 or such other product candidates. For example, if the FDA or other comparable regulatory authority were to require us to conduct preclinical studies and clinical trials beyond those which we currently anticipate will be required for the completion of clinical development, or if we experience significant delays in enrollment in any clinical trials, we could be required to spend significant additional financial resources and time on clinical development.

Selling, General and Administrative (SG&A) Expenses

SG&A expenses mainly comprise administrative payroll costs, overhead costs relating to our headquarters in Paris, and costs such as accounting, legal, human resources, communications and market access activities.

We anticipate that our SG&A expenses will increase in the future as we increase our headcount to support the expected growth in our research and development activities and the potential commercialization of NBTXR3. We also anticipate increased expenses associated with being a public company in the United States following our initial public offering in December 2020, including costs related to audit, legal, regulatory and tax-related services associated with maintaining compliance with Nasdaq listing and SEC requirements, director and officer insurance premiums, and investor relations costs. In particular, we will need to incur additional accounting expenses to comply with the Sarbanes-Oxley Act of 2002 in the United States, which will require us to test the effectiveness of our internal controls over financial reporting.

Other Operating Income (Loss)

Other operating income (loss) relates to payments totalling $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.

Net Financial Income (Loss)

Net financial income (loss) comprises mainly interest income on short-term bank deposits, interest costs primarily on the EIB loan, foreign exchange gains and losses and, since January 1, 2019, the interest costs on leases related to the application of IFRS 16. See Note 12 of our audited consolidated financial statements for additional details regarding the IFRS 16 lease liabilities.

Critical Accounting Policies and Estimates

Some of the accounting methods and policies used in preparing our financial statements under IFRS are based on complex and subjective assessments by our management or on estimates based on past experience and assumptions deemed realistic and reasonable based on the circumstances concerned. The actual value of our assets, liabilities and shareholders' equity and of our losses could differ from the value derived from these estimates if conditions changed and these changes had an impact on the assumptions adopted. We believe that the most significant management judgments and assumptions in the preparation of our financial statements are named below. For further details, see Notes to our consolidated financial statements. Each of the following is incorporated by reference here:

- Revenue Recognition - license and collaboration agreement with PharmaEngine (see Notes 4.1 and 15)
- Share-Based Payments (see Notes 3.2 and 17)
- Clinical Trial Accruals (see Notes 3.2 and 13.1)
- Fair Value of Financial Liabilities – EIB Loan and associated royalty agreement (see Notes 4.2 and 12).

A. Operating results

We have one operating segment, which is the research and development of product candidates that use proprietary nanotechnology to transform cancer treatment.

Comparison of the years ended as of December 31, 2021, 2020 and 2019

Our results of operations for the years ended as of December 31, 2021, 2020 and 2019 are summarized in the table below:

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Revenues and other income			
Revenues	10	50	68
Other income	2,637	2,462	2,473
Total revenues and other income	**2,647**	**2,512**	**2,541**
Research and development expenses	(30,378)	(24,330)	(30,411)
Selling, general and administrative expenses	(19,434)	(14,611)	(18,909)
Other operating income and expenses	(5,414)	—	—
Total operating expenses	**(55,226)**	**(38,941)**	**(49,320)**
Operating income (loss)	**(52,579)**	**(36,428)**	**(46,779)**
Financial income	6,360	201	837
Financial expenses	(780)	2,646	(4,970)
Financial income (loss)	**5,580**	**2,847**	**(4,133)**
Income tax	(5)	(9)	(3)
Net loss for the period	**(47,003)**	**(33,590)**	**(50,915)**

Revenues and Other Income

Revenues and other income increased by 135 thousand, or 5%, from €2.5 million for the years ended December 31, 2020 to €2.6 million for the year ended December 31, 2021. For the years ended December 31, 2020 and 2019, the revenues and other income were stable at €2.5 million.

The components of our revenues and other income are set forth in the table below:

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Services	5	50	40
Other sales	5	—	28
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	**2,637**	**2,462**	**2,473**
Total revenues and other income	**2,647**	**2,512**	**2,541**

Revenues

All of our revenues for the years ended December 31, 2021, 2020 and 2019 were derived from the chargeback of external contract research organization costs in connection with development support provided to PharmaEngine as part of our license and collaboration agreement.

Other income

Other income remained relatively stable between the year ended December 31, 2021 and the year ended December 31, 2020. The research tax credit increased by €563 thousand from €1.9 million for the year ended December 31, 2020 to €2.5 million for the year ended December 31, 2021, mainly due to an increase in eligible expenditures.
The decrease of €400 thousand in subsidies, from €526 thousand for the year ended December 31, 2020 to €126 thousand for the year ended December 31, 2021, is mainly due to the €312 thousand provided by the French State as part of the ‘‘partial unemployment measure’’ in 2020 (see below).

The decrease in other income for the year ended December 31, 2020 was primarily attributable to the amounts provided by the French State as part of the ‘‘partial unemployment measure’’, a national plan allowing companies facing economic challenges posed by the COVID-19 pandemic to receive approximately 84% of specific employees’ net salaries from the French State. These subsidies were granted to us and to our subsidiary Curadigm and amounted to €312 thousand. Subsidies also included the Deep Tech Funding (defined below), €187 thousand of which was recognized as other income in the year ended December 31, 2020.

Subsidies increased by €506 thousand from 2019 to 2020, amounting to €526 thousand for the year ended December 31, 2020.

Research and Development Expenses

Research and development expenses for the years ended December 31, 2021, 2020 and 2019 are summarized below:

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Purchases, sub-contracting and other expenses	(19,562)	(12,734)	(16,804)
Payroll costs (including share-based payments)	(9,605)	(10,306)	(11,980)
Depreciation, amortization and provision expenses	(1,211)	(1,290)	(1,627)
Total research and development expenses	**(30,378)**	**(24,330)**	**(30,411)**

The total amount of expenses incurred with respect to research and development activities increased by €6.1 million, or 25.0%, 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; and
- a decrease of €0.7 million, 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 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 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.

Selling, General and Administrative ("SG&A") Expenses

SG&A expenses for the years ended December 31, 2021, 2020 and 2019 are summarized below:

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Purchases, fees and other expenses	(9,638)	(6,482)	(9,435)
Payroll costs (including share-based payments)	(9,379)	(7,789)	(9,205)
Depreciation, amortization and provision expenses	(417)	(340)	(270)
Total SG&A expenses	**(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 changes of 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 facility leases in Paris (Oberkampf road and Faubourg Saint Antoine road).

Operating Income (Loss)

Our operating loss increased by €16.2 million, or 44.3%, from €36.5 million for the year ended December 31, 2020 to €52.6 million for the year ended December 31, 2021. This increase is mainly due to our efforts on our clinical trial development priorities (312 study), along with the expense of €5.4m pursuant to the termination and release agreement with PharmaEngine.

At December 31, 2021, our workforce totaled 100 employees, which is 10 positions more than the 90 employees for the same period in 2020.

Our operating loss decreased by €10.4 million, or 22.1%, from €46.8 million for the year ended December 31, 2019 to €36.4 million for the year ended December 31, 2020. This decrease is mainly due to our efforts to reduce SGA expenses during the COVID-19 pandemic, along with the changes to other income and research and development expenses.

At December 31, 2020, our workforce totaled 90 employees, which is 20 positions less than the 110 employees for the same period in 2019.

Net Financial Income (Loss)

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 as a result of gross proceeds of our global offering, which included our U.S. initial public offering 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.

B. Liquidity and Capital Resources

Introduction

Since our inception, we have consistently generated negative operating cash flows. Historically, we have financed our operations and growth through:

- the issuance and sale of ordinary shares, primarily including €12.1 million in net proceeds from our initial public offering on the Euronext market in Paris in October 2012, €28.1 million in net proceeds from a private placement capital increase in April 2019, €18.8 million in net proceeds from a private placement capital increase in July 2020, and $113.3 million (€93.5 million as of December 10, 2020) in net proceeds from our global offering, including our U.S. initial public offering, in December 2020.

- loans, conditional advances and grants awarded by governmental entities, including:
    - our EIB finance contract and royalties agreement granted by the EIB in July 2018, from which we drew (i) the initial tranche of €16.0 million (repayable in a single installment at maturity) upon satisfying the requisite documentary criteria in October 2018 and (ii) the second tranche of €14.0 million (repayable in semi-annual installments of principal and interest after a two year grace period) 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 our locally advanced head and neck cancers clinical trial).
    - a €2.1 million repayable advance received from Bpifrance in 2013 through France's Strategic Industrial Innovation program, an interest-free innovation loan of €2.0 million from Bpifrance received in September 2016 and a non-dilutive €1.0 million financing agreement granted in June 2020 as part of Bpifrance's Deep Tech program in order to support Curadigm's Nanoprimer technology.
    - an aggregate of €10 million in state guaranteed loans ("Prêt garanti par l'Etat" or "PGE") pursuant to a €5 million PGE agreement with HSBC France (the "HSBC PGE Loan") in June 2020 and a €5 million PGE agreement with Bpifrance in July 2020 (the "Bpifrance PGE Loan").

Terms of Our Primary Financing Agreements

EIB Finance Contract and Royalty Agreement

In July 2018, we and EIB entered into a finance contract and a royalty agreement. The EIB loan is comprised of three potential disbursement tranches, each drawable in the absence of an event of default or prepayment event, subject to our achieving specified documentary and/or performance criteria and making customary representations and warranties.

As noted above, we drew the initial tranche in October 2018 and the second tranche in March 2019. The terms of the EIB loan provide for a final €10.0 million third tranche if we satisfy 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) our raising of new equity financing, which was achieved with our 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 the conditions were not met by July 31, 2021, the Company will not request the final tranche of the EIB loan.

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%.

We 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 us to prepay all outstanding amounts under the EIB loan in connection with certain events, including a substantial reduction in the anticipated cost of our NBTXR3 development program, a prepayment of certain non-EIB financing, certain change of control events, Dr. Laurent Levy ceasing to be our principal executive officer or ceasing hold a specified number of shares, or certain dispositions of assets related to our 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 us or our 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 us and our subsidiaries that may impact the operation of our business, including, among others, restrictions on (i) the disposition of any part of our business or assets outside of arm's length ordinary-course transactions, (ii) restructuring or making any substantial change to the nature of our business, (iii) entering into certain merger or consolidation transactions, (iv) the disposition of our shareholdings in our 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 our assets, (x) paying dividends or repurchasing our shares, or (xi) impairing our intellectual property rights. Pursuant to these restrictions, we obtained EIB's consent to the HSBC PGE Loan (as defined below) and the Bpifrance PGE Loan, which represented an aggregate indebtedness of €10 million.

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

Pursuant to the royalty agreement, we also committed to pay royalties to EIB calculated 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 low single-digit royalty rates, which vary according to the number of tranches that have been drawn and indexed on our annual sales turnover.

In the event that we elect 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%.

PGE Loans

The HSBC PGE Loan is 90% guaranteed by the French State and had an initial 12-month term during which it bore no interest. At the end of this initial term, we (1) paid a guarantee fee equal to 0.25% of the €5 million principal amount and (2) 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 rate 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. The HSBC PGE Loan must be repaid upon the occurrence of customary events of default.

The Bpifrance PGE Loan has a six-year term and is 90% guaranteed by the French State. The Bpifrance PGE Loan bears no interest for the first 12-month period but, following such 12-month period and for the subsequent five years, bore 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 Bpifrance PGE Loan must be repaid upon the occurrence of customary events of default.

Bpifrance Advances and Loans

Except in the event we are unable to commercialize NBTXR3, we have undertaken to repay the total amount of our €2.1 million advance under the Strategic Industrial Innovation program according to the following schedule: €0.3 million no later than December 31, 2022, €0.5 million no later than December 31, 2023, €0.8 million no later than December 31, 2024 and the remaining balance no later than December 31, 2025.

We have undertaken to repay the €2.0 million interest-free innovation loan from 2016 in 16 quarterly installments of €125 thousand each, beginning in September 2018. Accordingly, we repaid €0.3 million in 2018 and €0.5 million in 2019. Due to COVID-19, Bpifrance allowed us to defer two quarterly payments otherwise due in 2020, which will be due, without fees or penalties, at the end of the initial reimbursement period.

Curadigm's €1.0 million financing agreement under Bpifrance's Deep Tech program (the "Deep Tech Grant"), which supports Curadigm's development of Nanoprimer technology, comprises (i) a €500 thousand conditional advance, the first €350 thousand of which was funded at signing and the remainder of which will be funded upon completion of a project related to a nanomedicine therapy, at our request, and (ii) a €500 thousand grant, the first €350 thousand of which was funded at signing and the remainder of which will be funded upon completion of a project related to a nanomedicine therapy, at our request. Curadigm received (i) €350 thousand of the €500 thousand conditional advance in June 2020, and (ii) €350 thousand of the €500 thousand grant, €187 thousand of which was recognized as revenue in during the year ended December 31, 2020. The conditional advance component of the financing is repayable each quarter, commencing March 31, 2023 and continuing through December 31, 2027.

Historical Changes in Cash Flows

The table below summarizes our cash inflows and outflows for the years ended December 31, 2021, 2020 and 2019:

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Net cash flows from (used in) operating activities	(29,872)	(27,538)	(41,169)
Net cash flows from (used in) investing activities	(242)	(112)	(1,459)
Net cash flows from financing activities	(5,180)	111,769	41,489
Effect of exchange rates changes on cash	64	(63)	29
Net increase (decrease) in cash and cash equivalents	**(35,230)**	**84,056**	**(1,109)**

Cash Flows from / used in operating activities

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:

- €11.5 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 Flows from / used in investing activities

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 due to the fixed asset acquisitions.

Cash Flows from / used in financing activities

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 €82.9 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.

The carrying value and activity of our repayable advances and loans is as follows:

(in thousands of euros)	**Bpifrance advance**	**Interest-free Bpifrance loan**	**EIB Loan**	**Curadigm Bpifrance advance**	**HSBC "PGE"**	**Bpifrance "PGE"**	**Total**
As of January 1, 2020	**2,165**	**1,210**	**34,746**	**—**	**—**	**—**	**38,121**
Principal received	—	—	—	350	5,000	5,000	10,350
Impact of discounting and accretion	19	14	(1,736)	(65)	14	34	(1,720)
Accumulated fixed interest expense accrual	32	—	1,731	—	7	10	1,780
Accumulated variable interest expense accrual	—	—	(4,789)	—	—	—	(4,789)
Repayment	—	(250)	(700)	—	—	—	(950)
As of December 31, 2020	**2,216**	**974**	**29,251**	**285**	**5,020**	**5,044**	**42,790**
Principal received	—	—	—	—	17	(14)	3
Impact of discounting and accretion	17	19	(5,817)	16	26	120	(5,619)
Accumulated fixed interest expense accrual	32	—	1,758	—	(33)	(112)	1,645
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**	**5,030**	**5,038**	**39,501**

Leases liabilities

We adopted IFRS 16 - Leases using the ‘‘modified retrospective method’’ starting on January 1, 2019 and recorded rights of use assets and lease liabilities for the amounts of the discounted lease payments outstanding for the remainder of our leases. The amount of the lease liabilities on initial recognition was €5.6 million, without impact on future cash payments in connection with the outstanding leases as of January 1, 2019. During the year ended December 31, 2021, net lease liabilities increased by €0.1 million to €6.5 million since December 31, 2019. See Note 12.2 of our consolidated financial statements for details regarding the lease liabilities.

Liquidity agreement

Consistent with customary practices in the French securities market, in 2012 we entered into a liquidity agreement with Gilbert Dupont, an investment company in France, which agreement authorizes Gilbert Dupont to carry out market purchases and sales of our shares on the regulated market of Euronext in Paris in order to provide liquidity for the trading market, such agreement has been amended on November 30, 2018. During the year ended December 31, 2020 and the year ended December 31, 2021, we did not contribute any cash or additional ordinary shares to the liquidity account. The cash and the value of the ordinary shares held in the liquidity account are classified in other non-current financial assets in our statement of consolidated financial position. As of December 31, 2021, a total of 15,456 ordinary shares and €97 thousand were allocated to the liquidity account with Gilbert Dupont. As of December 31, 2020, a total of 12,970 ordinary shares and €47 thousand, compared to 15,723 ordinary shares and €147 thousand as of December 31, 2019, were allocated to the liquidity account with Gilbert Dupont. The liquidity agreement has an automatically renewable term of one year unless otherwise terminated by either party.

Operating Capital Requirements

Although it is difficult to predict future liquidity requirements, we expect that our existing cash and cash equivalents will be sufficient to fund our current operations through the second quarter of 2023. However, this estimate is based on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. In any event, we will need additional capital to pursue preclinical and clinical activities, obtain regulatory approval for, and to commercialize our product candidates.

Until we can generate a sufficient amount of revenue from our product candidates, if ever, we expect to finance our operating activities through a combination of equity offerings, debt financings, research tax credits and other government subsidies, and potential milestone payments under third-party collaborations. Additional capital may not be available on reasonable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing shareholders, increased fixed payment obligations and these securities may have rights senior to those of our ordinary shares. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Any of these events could significantly harm our business, financial condition and prospects.

Our present and future funding requirements will depend on many factors, including, among other things:

- the size, progress, timing and completion of our clinical trials;
- the number of potential new product candidates we identify and decide to develop;
- the costs involved in filing patent applications and maintaining and enforcing patents or defending against claims or infringements raised by third parties;
- the time and costs involved in obtaining regulatory approval for our product candidates and any delays we may encounter as a result of evolving regulatory requirements or adverse results with respect to any of these product candidates;
- selling and marketing activities undertaken in connection with the anticipated commercialization of NBTXR3 and any other current or future product candidates and costs involved in the creation of an effective sales and marketing organization;
- the amount of revenue, if any, we may derive either directly or in the form of milestones or royalty payments from our existing or future partnership or collaboration agreements; and
- the severity, duration and impact of the COVID-19 pandemic, which may continue to adversely impact our business and clinical trials.

Capital Expenditures

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Increases in software and other intangible assets	5	11	353
Increases in property, plant, and equipment	228	96	1,091
Total increases in capital expenditures	**233**	**107**	**1,444**

For the year ended December 2021, our capital expenditures were comprised primarily of €73 thousand related to acquisitions of technical equipment and €53 thousand of new office and IT equipment.

For the year ended December 2020, our capital expenditures were comprised primarily of €42 thousand related to acquisitions of technical equipment and €37 thousand of new office and IT equipment.

For the year ended December 2019, our capital expenditures were comprised primarily of €292 thousand related to the implementation of a new human resources software and of €815 thousand related to improvements to our new office facilities.

C. Research and development, patents and licenses

Our research and development teams utilize our deep expertise to contribute to the growth of our business. In the years ended December 31, 2021, 2020 and 2019, we incurred expenses €30.4 million, €24.3 million and €30.4 million, respectively, on research and development. For a discussion of our research and development activities, see “Item 4B - Business Overview” and “Item 5A -Operating Results.”

D. Trend information

For a discussion of trends, see “Item 4B. Business Overview,” “Item 5A - Operating Results” and “Item 5B - Liquidity and Capital Resources.” Other than as disclosed in these sections, we are not aware of any trends, uncertainties, demands, commitments or events since December 31, 2021 that are reasonably likely to have a material adverse effect on our revenues, income, profitability, liquidity or capital resources, or that would cause the disclosed financial information to be not necessarily indicative of future operating results or financial condition.

E. Critical Accounting Estimates

Not applicable.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and Senior Management

Corporate Governance

We have a two-tier corporate governance system consisting of an executive board (*directoire*), which is responsible for managing the Company and a supervisory board (*Conseil de Surveillance*), which oversees the executive board.

Executive Board and Supervisory Board Members

The following table sets forth information regarding our executive board members and supervisory board members. The address for our supervisory board members and executive board members is 60, rue de Wattignies, 75012 Paris, France.

Name	Age	Position(s)
Executive Board Members:		
Dr. Laurent Levy, Ph.D.	50	Chairman of the Executive Board and Co-founder (*Principal Executive Officer*)
Mr. Bart Van Rhijn	49	Chief Financial Officer (*Principal Financial Officer*)
Ms. Anne-Juliette Hermant	47	Chief People Officer
Supervisory Board Members:		
Dr. Gary Phillips	56	Chairman
Ms. Anne-Marie Graffin	60	Vice Chairwoman
Dr. Alain Herrera, M.D.	71	Member
Mr. Enno Spillner	52	Member
Mr. Christophe Douat	57	Observer

The following is a brief summary of the business experience of the members of our executive board.

Dr. Laurent Levy, Ph.D. is the co-founder of Nanobiotix and has served as our Chairman of the 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, a field in which he has worked for more than 10 years. His research at the frontier of biotechnology and nanotechnologies has resulted in the development of a number of concrete applications such as NanoXray, 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 on the development of applications 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 from December 2012 to June 2019. He is the author of more than 35 international scientific publications and communications, has applied for several patents and regularly speaks on the topic of using nanoparticles to fight cancer, including at a recent 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 City of Paris Industrial Physics and Chemistry Higher Educational Institution (*École supérieure de physique et de chimie industrielles de la Ville de Paris*) (UPVI-ESPCI), followed by a post-doctoral fellowship at the Institute for Lasers, Photonics and Biophotonics, SUNY (State University of New York), Buffalo, USA.

Mr. Bart Van Rhijn has served as our Chief Financial Officer and as an executive board member since June 2021. Mr. Van Rhijn joins Nanobiotix after nearly 3 years as chief financial officer at Servier Pharmaceuticals, LLC ("Servier US"), from September 2018 through May 2021. Prior to Servier US, he served as Head of Finance of the US Prescription Business of Galderma from May 2015 through August 2018. Mr. Van Rhijn has also held leadership roles in other prominent organizations in Europe and North America, including Philips, where he has served in Head of Tax, Senior Director of Mergers and Acquisitions, and Head of Finance positions. Prior to that, Mr. Van Rhijn was a tax consultant at PricewaterhouseCoopers from 1997 to 1999. Mr. Van Rhijn brings 23 years of experience in consultancy, technology, and life sciences industries, including extensive experience in global financial management, business development and pharmaceutical commercialization. Mr. 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. In addition, Mr. Van Rhijn serves 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 podcasting hosting and production start-up.

Ms. Anne-Juliette Hermant has served as our Chief People Officer since April 2019 and as an executive board member since July 2019. Ms. Hermant brings over 14 years in talent management and development acquired in different entities at AXA, a multinational firm engaged in global insurance, investment management and other financial services. She worked at AXA Partners from September 2016 to April 2019 as Global Head of Talent, Development, Culture and Corporate Responsibility. Before AXA Partners, Ms. Hermant served as Chief Learning Officer of the AXA Group and was the Founder and Head of the AXA Research Fund, a fund created by the AXA Group to support frontier science in all fields related to an understanding of the risks faced by human society, from 2007 to 2011. Ms. Hermant holds a Ph. D in French literature from the Ecole Normale Supérieure and studied Politics at Sciences Po Paris.

On June 1, 2021, Mr. Bart Van Rhijn succeeded Mr. Philippe Mauberna as the Company's Chief Financial Officer and as a member of the executive board. Mr. Mauberna stepped down from those roles on May 31, 2021.

The following is a brief summary of the business experience of the members and observer of our supervisory board.

Dr. Gary Phillips has served as Chairman of our supervisory board since May 2021. Dr. Phillips has over 20 years of experience in the pharmaceutical and healthcare industries, leading commercial operations, clinical medicine, business strategy and development functions. Dr. Phillips serves as the president and chief executive officer of OrphoMed, Inc. in the United States. Before joining OrphoMed in 2018, Dr. Phillips worked with Mallinckrodt Pharmaceuticals, where he had served as Executive Vice President and Chief Strategy Officer since 2013. Prior to that role, he was Head of Global Health & Healthcare Industries at the World Economic Forum, served as President of Reckitt Benckiser Pharmaceuticals North America (now Indivior), and held dual roles as President, U.S. Surgical and Pharmaceuticals and Global Head of Pharmaceuticals at Bausch & Lomb. In addition, Dr. Phillips has served in executive roles at Merck Serono, Novartis, and Wyeth. Dr. Phillips earned a B.A. in Biochemistry with Summa Cum Laude and Phi Beta Kappa distinctions from the College of Arts and Sciences at the University of Pennsylvania, an MBA from the Wharton School at the University of Pennsylvania, and an M.D. with Alpha Omega Alpha distinction from the School of Medicine at the University of Pennsylvania. Dr. Phillips 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.

Ms. Anne-Marie Graffin has served as a supervisory board member since 2013, as chairwoman 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. Ms. 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. Ms. Graffin graduated from ESSEC Business School Paris.

Dr. Alain Herrera, M.D. has served as a supervisory board member since 2013. 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.

Mr. 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. Mr. 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. Mr. Spillner earned his Dipl.-Kaufmann degree (Masters in Business) at the University of Bamberg, Germany.

Mr. 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. Mr. 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. Mr. 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. Mr. 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).

Family Relationships

There are no family relationships among any of our executive board members or supervisory board members.

Diversity

The table below provides certain information regarding the Supervisory Board as of the date of this Annual Report.

Supervisory Board Diversity Matrix

Country of Principal Executive Offices:	France
Foreign Private Issuer	Yes
Disclosure Prohibited under Home Country Law	No
Total Number of Directors and Board Observers	5

	Female	Male	Non-Binary	Did Not Disclose Gender
Part I: Gender Identity				
Directors	1	4	0	0
Part II: Demographic Background				
Underrepresented Individual in Home Country Jurisdiction	0	0	0	0
LGBTQ+	0	0	0	0
Did Not Disclose Demographic Background	0	0	0	0

We continue to pursue a policy that reflects our commitment to diversity and equality at all levels of the Company. As of the date of this Annual Report, women are represented on both the Supervisory Board and the Executive Board and represent 67% of our total employees.

B. Compensation

Compensation of Supervisory Board and Executive Board Members

The aggregate compensation paid and benefits in kind granted by us to our current executive board members and supervisory board members, including share-based compensation, for the year ended December 31, 2021 was €6,846,376. The total amount set aside or accrued to provide pension, retirement or similar benefits was € 18,025 for the year ended December 31, 2021.

Pursuant to the "say on pay" regime applicable to companies listed on the regulated market of Euronext in Paris, the payment of compensation (whether fixed, variable or exceptional) attributed for a financial year to any member of the supervisory or executive board is subject to approval at the next ordinary general meeting. All payments of variable or exceptional compensation for the year ended December 31, 2021 detailed below are subject to approval at the annual combined shareholders' meeting to be held to approve the financial statements for the year ended December, 2021.

Executive Board Compensation

The following table sets forth information regarding the compensation earned by our executive board members for service on our executive board during the year ended December 31, 2021.

Name	Fixed Compensation (€)	Bonus (€)	Free Shares (€)	Stock Options (€)	All Other Compensation (€)	Total (€)
Dr. Laurent Levy, Ph.D.	380,000[(1)]	155,040[(3)]	2,417,400[(4)]	763,920[(5)]	18,025[(6)]	3,734,385
Ms. Anne-Juliette Hermant	210,000[(2)]	77,543[(3)]	1,208,700[(7)]	254,640[(8)]	—	1,750,883
Mr. Philippe Mauberna[(9)]	101,641[(10)]	25,874[(3)]	0[(11)]	—	255,000[(12)]	382,515
Mr. Bart Van Rhijn	195,715[(13)]	73,170[(3)]	—	458,400[(14)]	—	727,285

[(1)] Compensation earned for his corporate office (Chairman of the executive board) that was set by the supervisory board.

[(2)] Compensation earned under an employment agreement.

[(3)] Reflects compensation earned for the achievement of specified individual criteria (representing 30% of said bonus), as well as company-wide, performance criteria (representing 50% of said bonus) and the assessment of individual leadership qualities by the supervisory board (representing the remaining 20%) (together, the "strategic goals"). The executive board proposes the strategic goals annually, which are reviewed by the appointments and compensation committee and ultimately approved by the supervisory board. The payment of variable compensation is subject to approval at the annual combined shareholders' meeting to be held to approve the financial statements for the year ended December 31, 2021.

[(4)] Reflects the valuation of 180,000 free shares granted during the year ended December 31, 2021.

(5) Reflects the valuation of 180,000 stock options granted during the year ended December 31, 2021.

(6) Reflects the value of premiums paid for an unemployment insurance policy with the Garantie Sociale des Chefs et Dirigeants d'Entreprise.

(7) Reflects the valuation of 90,000 free shares granted during the year ended December 31, 2021.

(8) Reflects the valuation of 60,000 stock options granted during the year ended December 31, 2021.

(9) Mr. Mauberna stepped down as our Chief Financial Officer and executive board member on May 31, 2021, at which time Mr. Van Rhijn was appointed to those roles. See "—Employment Agreement with Bart Van Rhijn" below for additional information regarding Mr. Van Rhijn's compensation.

(10) Compensation earned under an employment agreement covering the six months during which Mr. Mauberna served as an employee of the Company.

(11) Reflects the valuation of 1 free share granted during the year ended December 31, 2021.

(12) The Company and Mr. 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 which he was entitled to an exceptional indemnity of €255,000.

(13) Amount converted into euros. Compensation earned under an employment agreement covering the seven months during which Mr. Van Rhijn served as a member of the Executive Board.

(14) Reflects the valuation of 120,000 stock options granted during the year ended December 31, 2021, which lapsed upon Mr. Mauberna's departure from the Company.

Supervisory Board Compensation

The aggregate amount of fees of the supervisory board is determined at the shareholders' annual ordinary general meeting. The supervisory board then divides all or part (at the supervisory board's discretion) of this aggregate amount among some or all of its members by a simple majority vote. In addition, the supervisory board may grant exceptional compensation (rémunérations exceptionnelles) to individual members on a case-by-case basis for special and temporary assignments. The supervisory board may also authorize the reimbursement of reasonable travel and accommodation expenses, as well as other expenses incurred by its members in the corporate interest. Furthermore supervisory board members 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. Supervisory board members who are employed by us receive separate compensation as officers or employees.

The members and observers, if any, of the supervisory board are entitled to compensation within the limits of the global annual amount set at the shareholders' general meeting. The shareholders' general meeting held on 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 set in 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 share subscription 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.

The following table sets forth information regarding the compensation earned by our supervisory board members and our supervisory board observer for service on our supervisory board during the year ended December 31, 2021.

Name	Fees earned (€)	Equity Incentives (€)	Total (€)
Mr. Laurent Condomine[1]	26,250	44,303[2]	70,553
Dr. Gary Phillips[3]	36,750	—	36,750
Ms. Anne-Marie Graffin	42,000	—	42,000
Dr. Alain Herrera, M.D.	35,000	—	35,000
Mr. Enno Spillner	50,000	—	50,000
Mr. Christophe Douat	35,000	—	35,000

[1] Mr. Laurent Condomine retired from the supervisory board, effective May 25, 2021, at which time Dr. Gary Phillips was appointed as a member of the supervisory board and elected as its chairman. The fees earned cover the period during which Mr. Laurent Condomine was a member of the supervisory board.

[2] Reflects the valuation of 14,431 warrants (BSA) granted during the year ended December 31, 2021, it being specified that Mr. Laurent Condomine paid the Company a total amount of €42,571.45 for these warrants.

[3] The fees earned cover the period during which Dr. Gary Phillips was a member of the supervisory board

Unemployment Insurance

We purchased officer unemployment insurance (*assurance perte d'emploi des dirigeants – GSC*) for our Chairman of the executive board, Dr. Laurent Levy, for each of the 2019, 2020 and 2021 fiscal years, at an annual cost of €17,757, €18,025 and €18,025, respectively.

Severance Pay

On May 27, 2004 and July 2, 2013, our supervisory board approved terms for severance pay to be awarded to our Chairman of the executive board, Dr. Laurent 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 the year when his departure occurs.

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.

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 Agreement with Bart Van Rhijn

We have entered into an employment agreement with our Chief Financial Officer and member of our executive board, Mr. Bart Van Rhijn, effective June 1, 2021. Under the employment agreement, Mr. 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. Mr. Van Rhijn is entitled to compensation during the non-compete period at a rate equal to 80% of his annual base salary and variable compensation. 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 Mr. Van Rhijn subject to a two-week notice period and by us with or without prior notice.

Employment Agreement with Anne-Juliette Hermant

On April 1, 2019, we entered into a permanent employment agreement (*contrat à durée indéterminée*) with our Chief People Officer and member of our executive board, Ms. Anne-Juliette Hermant. Ms. Hermant was entitled to an annual base salary of €180,000 in 2019, €200,000 in 2020, and €210,000 in 2021,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. Ms. Hermant is entitled to monthly compensation during the non-compete period of two-thirds of her gross monthly compensation for her last month of service with us. 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 10 years thereafter. This employment agreement may be terminated by both Ms. Hermant and us under the conditions provided for by regulation and the collective labor agreement applicable to the employee, and subject to a three-month prior notice.

Employment Agreement and Termination Agreement with Philippe Mauberna

On May 23, 2013, we entered into a permanent employment agreement (*contrat à durée indéterminée*), which was amended on April 25, 2019, with our former Chief Financial Officer and member of our executive board, Mr. Philippe Mauberna. Under the employment agreement, Mr. Mauberna was entitled to an annual base salary of €220,000 in 2018 and variable compensation in an amount up to 50% of the annual base salary, depending on the achievement of specified performance objectives. In 2021, Mr. Mauberna was entitled to an annual base salary of €242,000 and variable compensation in an amount up to 50% of the annual base salary, depending on the achievement of specified performance objectives.

Mr. Mauberna stepped down from his role as chief financial officer and executive board member, effective June 1, 2021. In connection with his departure, Mr. Mauberna and the Company 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 pro rata 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.

Limitations on Liability

Under French law, provisions of our By-laws that limit the liability of directors and officers are ineffective. However, French law allows *sociétés anonymes* to contract for and maintain liability insurance against civil liabilities incurred by any of their directors and officers involved in a third-party action, provided that they acted in good faith and within their capacities as directors or officers of the company. Criminal liability cannot be indemnified under French law, whether directly by the company or through liability insurance. Such rules apply to executive and supervisory board members.

We expect to maintain customary liability insurance coverage for our supervisory board members and executive board members, including insurance against liability under the Securities Act. We believe that this insurance coverage is necessary to attract qualified supervisory board members and executive board members.

Equity Incentives

We believe that our ability to grant incentive awards is a valuable and necessary compensation tool that allows us to attract and retain the best available personnel for positions of substantial responsibility, provide additional incentives to employees and promote the success of our business. Due to French corporate law and tax considerations, we have historically granted (and may continue to grant in the future) the following equity incentive instruments to our supervisory board members, executive board members, executive officers, employees and other service providers:

- founders' warrants (*bons de souscription de parts de créateur d'entreprise* or BSPCE), granted only to employees and members of our executive board. We can no longer issue these instruments;
- warrants (*bons de souscription d'actions* or BSA), granted only to non-employee supervisory board members and service providers not eligible for either founders' warrants or stock options;
- restricted stock units (*actions gratuites* or free shares or AGA), generally granted to our employees and corporate officers (including members of the executive board) and the employees and corporate officers of our subsidiaries; and
- stock options (*options de souscription et/ou d'achat d'actions* or OSA), generally granted to the employees of our subsidiaries.

Our executive board's authority to grant these equity incentive instruments and the aggregate amount authorized to be granted under these instruments must be approved by a two-thirds majority of the votes held by our shareholders present, represented or voting by authorized means, at the relevant extraordinary shareholders' meeting. Once approved by our shareholders, our executive board can, with the prior approval of the supervisory board, grant warrants (BSA) for up to 18 months, and free shares (the French equivalent of restricted stock units) and stock options for up to 38 months, in each case from the date of the applicable shareholders' approval. The authority of our executive board to grant equity incentives may be extended or increased only at extraordinary shareholders' meetings. As a result, we typically request that our shareholders authorize new pools of equity incentive instruments at every annual shareholders' meeting. However, notwithstanding any shareholder authorization, under applicable law we are no longer eligible to issue founders' warrants (BSPCE).

As of December 31, 2021, founders' warrants, warrants, employee stock options and free shares were outstanding allowing for the issuance or purchase of an aggregate of 3,006,532 ordinary shares (assuming that such instruments' vesting conditions are met) at a weighted average exercise price, if any, of €11.47 per ordinary share.

Founders' Warrants (BSPCE)

Historically, we have issued founders' warrants to certain of our employees. However, notwithstanding any shareholder authorization, under applicable law, we can no longer issue founders' warrants as a result of no longer meeting the criteria to do so.

Founders' warrants were granted only to our employees who were French tax residents, as they provided favorable tax and social security treatment for French tax residents. Founders' warrants could have also been granted to our corporate officers having an employee tax status at the time the founders' warrants were granted. Similar to stock options, founders' warrants entitle a holder to exercise the warrant for the underlying vested shares at an exercise price per share determined by our executive board and at least equal to the fair market value of an ordinary share on the date of grant.

Administration

Our shareholders, or pursuant to delegations granted by our shareholders, our executive board, determine, with prior approval of the supervisory board, the recipients of the founders' warrants, the grant dates, the number and exercise price of the founders' warrants to be granted, the number of shares issuable upon exercise of the founders' warrants and certain other terms and conditions of the founders' warrants, including the period of their exercisability and their vesting schedule. As stated above, we are no longer eligible to issue any further founders' warrants.

There is no legal limitation to the size of the founders' warrant pool. Founders' warrants are not transferable and may not be sold, pledged, assigned, hypothecated, transferred or disposed of in any manner other than by will or by laws of descent or distribution and may be exercised, during the lifetime of the founders' warrant holder, only by the employee warrant holder.

Term

The term of each founders' warrant is 10 years from the date of grant by the executive board. Any founders' warrants not exercised by this date will be automatically lapse. In addition, unless otherwise decided by the executive board and the supervisory board, founders' warrants 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 founder's warrant will lapse.

By way of exception, the executive board decided to lift, the continued service condition to which the exercise of certain founders' warrants was subject for Mr. Bernd Muehlenweg and Mr. Philippe Mauberna, former members of the executive board, and three of our other employees, notwithstanding the termination of their employment agreements or corporate offices. The executive board also decided to lift for Mr. Muehlenweg, where applicable, the performance conditions to which the exercise of certain founders' warrants was subject.

Change in Control

The terms of the founders' warrants usually provide that, unless otherwise decided by our supervisory and executive boards, in the event of a merger into another corporation or of the sale by one or several shareholders, acting alone or in concert, of our Company to one or several third parties of a number of shares resulting in a change of control (a "Liquidity Event"), the right of holders to exercise outstanding founders' warrants will be accelerated so that all of such shares may be exercised with effect immediately prior to the completion of the relevant Liquidity Event. Any founders' warrant not exercised for any reason on or prior to the date of completion of the relevant Liquidity Event will automatically lapse.

As of December 31, 2021, the following types of founders' warrants that we have issued are outstanding:

Grant	BSPCE 2012-2 [1]	BSPCE 08-2013 [1]	BSPCE 09-2014 [1]	BSPCE 2015-01 [1]	BSPCE 2015-03 [1]	BSPCE 2016 [1]	BSPCE 2016 Performance [2]	BSPCE 2017 Ordinary [1]	BSPCE 2017 [1]
Date of the shareholders' meeting	May 4, 2012	June 28, 2013	June 18, 2014	June 18, 2014	June 18, 2014	June 25, 2015	June 25, 2015	June 23, 2016	June 23, 2016
Grant date	December 18, 2012	August 28, 2013	September 16, 2014	February 10, 2015	June 10, 2015	February 2, 2016	February 2, 2016	January 7, 2017	January 7, 2017
Total number of BSPCE authorized	500,000	500,000	450,000	450,000	450,000	450,000	450,000	450,000	450,000
Total number of BSPCE granted	100,000	50,000	97,200	71,650	53,050	126,400	129,250	117,650	80,000
Starting date of the exercise of the BSPCE	December 18, 2012	August 28, 2013	September 16, 2015	February 10, 2016	June 10, 2016	February 2, 2017	February 2, 2016	January 8, 2018	January 7, 2017
BSPCE expiry date [3]	December 18, 2022	August 28, 2023	September 16, 2024	February 10, 2025	June 10, 2025	February 2, 2026	February 2, 2026	January 7, 2027	January 7, 2027
Exercise price per BSPCE	€6.63	€5.92	€18.68	€18.57	€20.28	€14.46	€14.46	€15.93	€15.93
Number of shares subscribed as of December 31, 2021	—	—	—	—	—	333	—	—	—
Total number of BSPCEs lapsed or cancelled as of December 31, 2021	—	—	11,050	3,200	22,700	25,500	28,976	18,150	—
Total number of BSPCEs outstanding as of December 31, 2021	100,000	50,000	86,150	68,450	30,350	100,567	100,274	99,500	80,000
Total number of shares available for subscription as of December 31, 2021	100,000	50,000	86,150	68,450	30,350	100,567	38,170	99,500	80,000
Maximum total number of shares that can be issued	100,000	50,000	86,150	68,450	30,350	100,567	100,274	99,500	80,000

[1] All such BSPCE can be exercised.

[2] The BSPCE 2016-Performance may be exercised as from their date of grant, subject to the achievement of the following targets:

- *up to 15% of the BSPCE may be exercised if the number of patients under treatment is at least equal to 200,*

- *additional 15% of the BSPCE may be exercised if the number of patients under treatment is at least equal to 300,*
- *additional 30% of the BSPCE 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, may be exercised if the number of patients under treatment is at least equal to 500. As of December 31, 2021, 30% of the BSPCE 2016-Performance can be exercised, it being specified that, on July 23, 2019, the executive board decided to lift the performance conditions to which the exercise of Mr. Bernd Muehlenweg's 11,500 BSPCE 2016-Performance was subject. Accordingly, all of Mr. Bernd Muehlenweg's BSPCE 2016-Performance may be exercised.*

[(3)] *See also "—Founders' Warrants (BSPCE)—Term" and "—Founders' Warrants (BSPCE)—Change in Control."*

Warrants (BSA)

Warrants are typically granted by our executive board to third-party service providers and members of the supervisory board not eligible for either founders' warrants or stock options. Similar to stock options, warrants entitle a holder to exercise the warrants for the underlying vested shares at an exercise price per share determined by our executive board that is meant to reflect the fair market value of an ordinary share on the date of grant. In addition to such exercise price, warrants are subscribed for at a price determined by the executive board that is meant to reflect the fair market value of the applicable warrants on the grant date.

Administration

Our shareholders, or pursuant to delegations granted by our shareholders, our executive board, with the prior approval of the supervisory board, determine the recipients of the warrants, the grant dates, the number and exercise price of the warrants to be granted, the number of shares issuable upon exercise of the warrants and certain other terms and conditions of the warrants, including the period of their exercisability and their vesting schedule.

There is no legal limitation to the size of the warrant pool.

Term

The term of warrants granted until June 25, 2015 (inclusive), and those granted from July 27, 2018 onwards is 10 years from the date of grant by the Executive Board.

The term of warrants granted on January 7, 2017 (which lapsed January 7, 2022) and March 6, 2018 is five years from the date of grant.

In addition, unless otherwise decided by our supervisory and executive boards, the warrants granted on January 7, 2017 (which lapsed January 7, 2022) must be exercised within six months from (i) the death or disability of the holder or (i) the termination of the holder from employment with us or any of our affiliates during such 10-year period, failing which the BSAs will lapse.

Change in Control

The terms of the warrants granted on February 10, 2015 and those granted from January 7, 2017 onwards provide that, unless otherwise decided by our supervisory and executive boards, in the event of a Liquidity Event, the right of any holder to exercise outstanding warrants will be accelerated so that all such warrants may be exercised with effect immediately prior to the completion of the relevant Liquidity Event, subject, if applicable, to continued service by the warrant holder. Any warrant not exercised for any reason on or prior to the date of completion of the relevant Liquidity Event will automatically lapse after this date.

The terms of the warrants granted on June 25, 2015 provide their holder with the right to exercise all of his or her warrants in the event of a change of control (i.e., through a merger, a transfer of shares or assets, an operation on share capital or liquidation).

As of December 31, 2021, the following types of warrants that we have issued are outstanding:

Grant	BSA 04-2012 (1)	BSA 2013 (1)	BSA 2014 (1)	BSA 2015-1 (2)	BSA 2015-2(a) (3)	BSA 2015-2(b) (3)	BSA 2016-Ordinary()	BSA 2016-Performance ()	BSA 2016-02 ()
Date of the shareholders' meeting	May 4, 2012	May 4, 2012	June 18, 2014	June 18, 2014	June 18, 2014	June 25, 2015	June 25, 2015	June 25, 2015	June 23, 2016
Grant date	May 4, 2012	April 10, 2013	September 16, 2014	February 10, 2015	June 25, 2015	June 25, 2015	February 2, 2016	February 2, 2016	November 3, 2016
Total number of BSA authorized	200,000	200,000	100,000	100,000	100,000	100,000	100,000	100,000	100,000
Total number of BSA granted	52,500	10,000	14,000	26,000	64,000	6,000	18,103	18,105	8,000
Starting date of the exercise of the BSA	October 23, 2013	April 30, 2014	September 16, 2014	February 10, 2015	June 25, 2015	June 25, 2015	February 2, 2016	February 2, 2016	November 3, 2016
BSA expiry date(15)	May 4, 2022	April 10, 2023	September 16, 2024	February 10, 2025	June 25, 2025	June 25, 2020	February 2, 2021	February 2, 2021	November 3, 2021
Exercise price per BSA	€6.00	€6.37	€17.67	€17.67	€19.54	€19.54	€13.74	€13.74	€15.01
Number of shares subscribed as of December 31, 2021	22,500	—	—	—	—	—	—	—	—
Total number of forfeited or cancelled BSAs as of December 31, 2021	—	4,000	4,000	5,000	—	6,000	18,103	18,105	8,000
Total number of BSAs outstanding as of December 31, 2021	30,000	6,000	10,000	21,000	64,000	—	—	—	—
Total number of shares available for subscription as of December 31, 2021	30,000	6,000	—	—	—	—	—	—	—
Maximum total number of shares that can be issued	30,000	6,000	10,000	21,000	64,000	—	—	—	—

Grant	BSA 2017 (2)	BSA 2018 (4)	BSA 2018-01 (4)	BSA 2018-02 (4)	BSA 2019-1 (2)	BSA 2020 (2)	BSA 2021(a) (5)	BSA 2021(b) (6)
Date of the shareholders' meeting	June 23, 2016	June 14, 2017	June 14, 2017	May 23, 2018	May 23, 2018	April 11, 2019	November 30, 2020	November 30, 2020
Grant date	January 7, 2017	March 6, 2018	March 6, 2018	July 27, 2018	March 29, 2019	March 17, 2020	April 20, 2021	April 20, 2021
Total number of BSA authorized	100,000	116,000	116,000	140,000	140,000	500,000	650,000	650,000
Total number of BSA granted	18,000	18,000	10,000	5,820	18,000	18,000	48,103	30,000
Starting date of the exercise of the BSA	January 7, 2017	March 6, 2018	March 6, 2018	July 27, 2018	March 29, 2019	March 17, 2020	April 20, 2021	April 20, 2021
BSA expiry date(15)	January 7, 2022	March 6, 2023	March 6, 2023	July 27, 2028	March 29, 2029	March 17, 2030	April 20, 2031	April 20, 2031
Exercise price per BSA	€15.76	€13.55	€13.55	€16.10	€11.66	€6.59	€13.47	€13.64
Number of shares subscribed as of December 31, 2021	—	—	—	—	—	—	—	—
Total number of forfeited or cancelled BSAs as of December 31, 2021	—	—	—	—	—	—	33,672	—
Total number of BSAs outstanding as of December 31, 2021	18,000	18,000	10,000	5,820	18,000	18,000	14,431	30,000
Total number of shares available for subscription as of December 31, 2021	—	—	—	—	—	—	—	—
Maximum total number of shares that can be issued	18,000	18,000	10,000	5,820	18,000	18,000	14,431	30,000

(1) 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] 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] 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] 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] 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] 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 "—Warrants (BSA)—Term" and "—Warrants (BSA)—Change in Control."

Stock Options (OSA)

We have granted stock options to our employees and the employees of our subsidiaries pursuant to our stock option plans. We currently have two plans, the 2020 Stock Option Plan ("2020 Plan"), which was adopted by our executive board on February 9, 2021 and approved by our shareholders during the annual combined shareholders' meeting held on April 28, 2021 and the 2021 Stock Option Plan ("2021 Plan"), which was adopted by our executive board on June 21, 2021 and shall be submitted to our shareholders for approval during the next annual combined shareholders' meeting. Our executive board has also previously adopted the 2019 Stock Option Plan, the LLY 2019 Plan, the 2018 Stock Option Plan, the 2017 Stock Option Plan and the 2016 Stock Option Plan (collectively, the "Former Plans" and together with the 2020 Plan and the 2021 Plan, the "Stock Option Plans").

Stock options may be granted to any individual employed by us or our subsidiaries. Stock options may also be granted to the members of our executive board. Incentive stock options may not be granted to holders of 10% or more of our share capital.

Under French law, the maximum number of shares issuable upon the exercise of outstanding stock options may not exceed one-third of the outstanding share capital on a non-diluted basis as of the grant date. Stock options may be granted under the 2020 Plan and the 2021 Plan until 2024.

Administration

Our executive board has the authority to administer and interpret the Stock Option Plans. Subject to the terms and conditions of the Stock Option Plans, our executive board, with the prior approval of the supervisory board, determines the recipients, grant dates, exercise prices, number of ordinary shares underlying and the terms and conditions of the stock options, including their periods of exercisability and their vesting schedules. Our executive board is not required to grant stock options with vesting and exercise terms that are the same for every participant. The term of each stock option granted under the Stock Option Plans is generally 10 years from the grant date.

Our executive board has the authority to amend and modify stock options outstanding under our Stock Option Plans, including the authority to extend the post-termination exercise period of the options, subject to the written consent of the optionees holding such options, if such amendments or modifications impair the rights of the optionees.

Employee Stock Options

The Stock Option Plans provide for the grant of incentive stock options within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended (the "Code"), and non-statutory Stock options.

These employee stock options are granted pursuant to employee stock option agreements adopted by the executive board. The executive board determines the exercise price for an employee stock option, within the terms and conditions of the applicable Stock Option Plan, provided that the exercise price of an employee stock option generally cannot be less than the per share fair market value of our ordinary shares on the grant date. Employee stock options granted under the Stock Option Plans vest at the rate specified by the executive board.

In accordance with French Law, our supervisory board decided that the members of our executive board must continue to hold at least 10% of the shares acquired by them upon exercise of the stock options until the termination of their respective term of office.

Stock options are not transferable (except by succession) and may not be sold, pledged, assigned, hypothecated, transferred or disposed of in any manner, other than by will or by laws of descent or distribution and may be exercised, during the lifetime of the optionee, only by the optionee.

Term

The term of each employee stock option is 10 years from the date of grant or, in the event of death or disability of the optionee during such 10-year period, six months from the date of such death or disability.

Unless a longer period is specified in the notice of grant or otherwise resolved by our executive board, an employee stock option shall remain exercisable by the optionee or his or her assigns, to the extent vested, for six months following an optionee's death, disability or termination from continuous employment with us. In the case of an "Incentive Stock Option" (as such term is defined in the Stock Option Plan), such period cannot exceed three months following an optionee's termination from continuous employment.

By way of exception, the stock options granted under the LLY 2019 Plan are not subject to any continuous employment condition nor will they lapse in the event of death or disability of the optionee during the exercise period and six months after the death or disability of the optionee. In addition, the executive board decided to lift, for two of our employees and Mr. Philippe Mauberna, former member of the executive board, the continued service condition to which the exercise of their stock options is subject, notwithstanding the termination of their 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 Mr. Philippe Mauberna holds, enabling him to exercise all of them, in the context of his departure from the Company.

Change in Control

Pursuant to the Stock Option Plans, in the event of a Liquidity Event, an optionee's right to exercise his or her employee stock options governed by any such plans will be accelerated (subject, if applicable, to a certain stock price being reached) so that the optionee may exercise all vested and unvested employee stock options immediately prior to the completion of the Liquidity Event. Any employee stock option that is not exercised for any reason on or prior to the completion of the Liquidity Event will automatically lapse.

U.S. Tax Limitations on Incentive Stock Options

The aggregate fair market value, determined at the time of grant, of our ordinary shares issuable under incentive stock options that are exercisable for the first time by an optionee during any calendar year under all of our Stock Option Plans may not exceed $100,000. Employee stock options, or portions thereof, that exceed such limit will generally be treated as non-statutory stock options. No incentive stock option may be granted to any person who, at the time of grant, owns or is deemed to own shares representing more than 10% of our total combined voting power or that of any of our affiliates unless (1) the exercise price is at least 110% of the fair market value of the shares subject to the employee stock option on the date of grant and (2) the term of the incentive stock option does not exceed five years from the date of grant.

As of December 31, 2021, the following types of stock options that we have issued are outstanding:

Grant	OSA 2016-1 Performance [1]	OSA 2016-2 [2]	OSA 2017 Ordinary [3]	OSA 2018 [4]	OSA 2019-1 [5]	OSA LLY 2019 [6]
Date of the shareholders' meeting	June 25, 2015	June 23, 2016	June 23, 2016	June 14, 2017	May 23, 2018	April 11, 2019
Grant date	February 2, 2016	November 3, 2016	January 7, 2017	March 6, 2018	March 29, 2019	October 24, 2019
Total number of stock options authorized	450,000	450,000	450,000	526,800	648,000	500,000
Total number of stock options granted	6,400	4,000	3,500	62,000	37,500	500,000
Starting date of the exercise of the stock options	February 2, 2017	November 3, 2017	January 8, 2018	March 7, 2019	March 30, 2021	October 24, 2019
Stock options expiry date[8]	February 2, 2026	November 3, 2026	January 7, 2027	March 6, 2028	March 29, 2029	October 24, 2029
Exercise price per stock option	€13.05	€14.26	€14.97	€12.87	€11.08	€6.41
Number of shares subscribed as of December 31, 2021	—	—	—	—	—	—
Total number of stock options lapsed or cancelled as of December 31, 2021	6,000	—	3,000	10,000	9,250	—
Total number of stock options outstanding as of December 31, 2021	400	4,000	500	52,000	28,250	500,000
Maximum number of shares available for subscription as of December 31, 2021	120	4,000	500	52,000	19,165	—
Maximum total number of shares that can be issued	400	4,000	500	52,000	28,250	500,000

Grant	OSA 2020 [7]	OSA 2021-04 Ordinary [8]	OSA 2021-04 Performance [9]	OSA 2021-06 Performance [10]	OSA 2021-06 Ordinary [11]
Date of the shareholders' meeting	April 11, 2019	November 30, 2020	November 30, 2020	November 30, 2020	April 28, 2021
Grant date	March 11, 2020	April 20, 2021	April 20, 2021	June 21, 2021	June 21, 2021
Total number of stock options authorized	500,000	850,000	1,000,000	1,000,000	850,000
Total number of stock options granted	407,972	143,200	428,000	60,000	60,000
Starting date of the exercise of the stock options	March 11, 2021	April 20, 2022	April 20, 2022	June 21, 2022	June 21, 2022
Stock options expiry date[12]	March 11, 2030	April 20, 2031	April 20, 2031	June 21, 2031	June 21, 2031
Exercise price per stock option	€6.25	€13.74	€13.74	€12.99	€12.99
Number of shares subscribed as of December 31, 2021	—	—	—	—	—
Total number of stock options lapsed or cancelled as of December 31, 2021	20,516	50,000	30,000	—	—
Total number of stock options outstanding as of December 31, 2021	387,456	93,200	398,000	60,000	60,000
Maximum number of shares available for subscription as of December 31, 2021	122,738	—	—	—	—
Maximum total number of shares that can be issued	387,456	93,200	398,000	60,000	60,000

[1] The OSA 2016-1 Performance may be exercised as from their date of grant, subject to the achievement of the following targets:

- *up to 15% of the OSA may be exercised if the number of patients under treatment is at least equal to 200,*
- *an additional 15% of the OSA may be exercised if the number of patients under treatment is at least equal to 300,*
- *an additional 30% of the OSA 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, may be exercised if the number of patients under treatment is at least equal to 500. As of December 31, 2021, 30% of the OSA 2016-1-Performance, i.e., 120 OSA 2016-1 Performance, can be exercised.*

[2] All of the OSA 2016-2 may be exercised.

[3] All of the OSA 2017 Ordinary may be exercised.

[4] All of the OSA 2018 may be exercised.

[5] The OSA 2019-1 may be exercised as follows:

- *up to two-thirds of the OSA 2019-1 as from March 30, 2021; and*
- *the balance, i.e., one-third of the OSA 2019-1 as from March 30, 2022, subject to, for each increment, a continued service condition.*

(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 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 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 share on the regulated market of Euronext in Paris reaches €40;*
- *the balance, i.e. 40% of the OSA LLY 2019 may be exercised when the market value of a share on the regulated market of Euronext in Paris reaches €60; and*
- *it being specified that, in the event of a Liquidity Event, the performance conditions regarding the price of the Company's share price on the regulated market of Euronext in Paris will be automatically waived.*

(7) 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.*

The exercise of the OSA 2020 granted to members of the executive board and one of our employees was 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) 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 Study 1100, 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 Study 1100, 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 Study 1100, 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) 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 Study 1100, 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.*

(12) See also " Stock Options (OSA) Term" and "—Stock Options (OSA)—Change in Control."

Free Shares (AGA)

We have granted free shares to our employees, employees of our subsidiaries and members of our executive board pursuant to our free share plans (the "AGA Plans").

Free shares may be granted to any individual employed by us or by any affiliated company under the terms and conditions of an employment contract. Free shares may also be granted to members of our executive board. However, no free shares may be granted to a beneficiary holding more than 10% of our share capital or to a beneficiary who would hold more than 10% of our share capital as a result of such grant.

Administration

Our executive board has the authority to administer and interpret the AGA Plans. Subject to the terms and conditions of the AGA Plans, our executive board, with the prior approval of the supervisory board, determines recipients, dates of grant, the number of free shares to be granted and the terms and conditions of the free shares, including the length of their acquisition period (period starting on the date of grant during which the beneficiary holds a right to acquire shares for free, but does not currently hold any shares) and, as the case may be, holding period (period starting at the end of the acquisition period when the shares are issued and definitively acquired and issued, but may not be transferred) within the limit determined by the shareholders.

Our executive board has the authority to modify awards outstanding under our AGA Plans, subject to the consent of the beneficiary if such modification is detrimental to him/her, including the authority to release a beneficiary from the continued service condition during the acquisition period after the termination of the employment, on the continued service condition, see also the paragraph "—Vesting").

Vesting

The free shares granted under the AGA Plans will be definitively acquired at the end of the acquisition period as set by our executive board. At the end of the acquisition period, the beneficiary will be the owner of the shares. However, during the holding period (as set by our executive board), if any, the shares may not be sold, transferred or pledged. The sum of the duration of the acquisition and holding periods must be at least two years, in accordance with the provisions of Article L. 225-197-1 of the French Commercial Code.

Unless otherwise decided by our supervisory and executive boards, the AGA 2019-1 granted on March 23, 2019, the AGA 2020 granted on March 11, 2020 and the AGA 2021 granted on April 20, 2021 are subject to continued service during the acquisition period (i.e., for the AGA 2019-1, until March 29, 2021 for French tax residents and March 29, 2022 for foreign tax residents, 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 2019-1 or AGA 2020 or AGA 2021.

In accordance with the AGA Plans, the executive board decided to lift, for three of our employees and Mr. Philippe Mauberna, a former member of the executive board, the continued service condition to which the definitive acquisition of their AGA 2019-1, as applicable, is subject, notwithstanding the termination of their employment agreement.

Unless otherwise decided by our supervisory and executive boards, 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 In Control

In the event of a Liquidity Event, unless otherwise decided by the executive and supervisory board, all of the free shares shall be completely and definitely acquired:

1. For French tax residents, (i) if the Liquidity Event occurs before or on the first anniversary date of the grant, on such anniversary date, and (ii) if the change of control occurs after the first anniversary of grant, on the date of completion of the Liquidity Event, 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 Liquidity Event 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.

As of December 31, 2021, the following types of free shares that we have issued are outstanding:

Grant	AGA 2018-1	AGA 2018-2	AGA 2019-1	AGA 2020	AGA 2021
Date of the shareholders' meeting	June 14, 2017	May 23, 2018	May 23, 2018	April 11, 2019	November 30, 2020
Grant date	March 6, 2018	July 27, 2018	March 29, 2019	March 11, 2020	April 20, 2021
Total number of free shares authorized	526,800	648,000	648,000	650,000	850,000
Total number of free shares granted	396,250	6,000	438,250	50,000	362,515
Date of acquisition (end of the acquisition period)[6]	[1][2]	July 27, 2020	[3]	March 11, 2022[6]	April 20, 2023
Duration of the holding period[6]	[1]	1 year	[3]	1 year	1 year
Number of shares acquired as of December 31, 2021	340,583	6,000	369,250	—	—
Total number of free shares lapsed or cancelled as of December 31, 2021	55,667	—	69,000	—	2,003
Total number of free shares outstanding as of December 31, 2021	—	—	—	50,000	360,512
Maximum total number of shares that may be created	—	—	—	50,000	360,512

[1] The AGA 2018-1 granted to French tax residents were definitely acquired on March 6, 2020 and were now subject to a one-year holding period that ended on March 6, 2021. The AGA 2018-1 granted to foreign tax residents were definitely acquired on March 6, 2021 and are not subject to any holding period. Hence, as of the date of the Annual Report, all AGA 2018-1 are definitively acquired and freely transferable.

[2] The definitive acquisition of the AGA 2018-1 granted to the members 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 recorded by the executive board and the supervisory board on March 15, 2019. On July 23, 2019, the executive board decided that the two-thirds of the AGA 2018-1 granted to Mr. Bernd Muehlenweg, i.e. 28,333 AGA 2018-1 would be definitively acquired on March 6, 2020. The balance, i.e. 14,167 AGA 2018-1, was subject to the conclusion of a clinical trial supply contract before March 6, 2020. As this performance condition was not met, these 14,167 AGA 2018-1 lapsed on March 6, 2020.

[3] The AGA 2019-1 granted to French tax residents were definitely acquired on March 29, 2021 and were then subject to a one-year holding period which ended on March 29, 2022. The AGA 2019-1 granted to foreign tax residents would have be definitely acquired on March 29, 2022 and would not have been subject to any holding period. However, the AGA 2019-1 held by foreign tax residents have lapsed as the beneficiaries left the Company before the end of their acquisition period. The acquisition of the AGA 2019-1 granted to members of our executive board was subject to NBTXR3 receiving the CE mark before June 30, 2019. The satisfaction of this performance condition was acknowledged by the executive board on April 27, 2020, with the prior approval of the supervisory board, on April 6, 2020.

[4] The acquisition of the AGA 2020 granted to Ms. Hermant was 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 prior approval of the supervisory board, on March 17, 2021. The AGA 2020 were definitively acquired on March 11, 2022 and are now subject to a one-year holding period, ending on March 11, 2023.

[5] 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 Study 1100 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.

[6] See also "—Free Shares (AGA)—Vesting" and "—Free Shares (AGA)—Change In Control."

C. Board Practices

Board Structure

Our two-tier board structure consists of an executive board and a supervisory board. The roles and functions of each board and the interactions between them are described below.

Executive Board

We are managed by an executive board under the control of a supervisory board. The members of the executive board determine the broad lines of our business activities and ensure their implementation. Without prejudice to the powers expressly vested in the shareholders' meetings, and insofar as our By-laws allow, the executive board deals with all matters relating to the conduct of our business. The executive board is vested with the broadest powers to act in all circumstances on our behalf, within the limits of our corporate purpose and subject to the powers granted to the shareholders' meeting and supervisory board.

Our executive board must be composed of between two and seven members. Pursuant to our By-laws, the executive board, in its entirety, is appointed by the supervisory board for a four-year term renewable by the supervisory board. Executive board members may be dismissed at the ordinary general meeting and by the supervisory board. In the case of a vacancy between annual meetings, the supervisory board must within a two-month period appoint a temporary member to fill the vacancy or must change the number of executive board members.

We currently have three members of the executive board. The following table sets forth the names of the members of the executive board, the year of their initial appointment as members of the executive board and the expiration date of their current term.

Name	Current Position	Year of Initial Appointment	Current Term Expiration Year
Dr. Laurent Levy, Ph.D.	Chairman	2004	2024
Mr. Bart Van Rhijn	Member	2021	2024
Ms. Anne-Juliette Hermant	Member	2019	2024

Supervisory Board

The members of the supervisory board exercise control over the management of the executive board. The supervisory board operates pursuant to a separate charter adopted by its members on March 18, 2019.

On an annual basis, the Supervisory Board intends to review the voting results from our annual shareholders' meeting.

Under French law, our supervisory board must be composed of between three and eighteen members. Within this range, the number of members is determined by our shareholders. Further, Euronext Paris gender equality rules require that the number of members of each gender not be less than 40%. However, if the board is composed of eight or less members, the number of members of one gender cannot exceed the number of members of the other by more than two.

Any appointments made in violation of these limitations are null and void. In addition, payment of fees to any member of the board will be suspended until any such violation is remedied.

Members of our supervisory board are elected, re-elected and may be removed, with or without cause, at a shareholders general meeting with a simple majority vote of our shareholders. Pursuant to our By-laws, the members of our supervisory board are elected for six-year terms. In accordance with French law, our By-laws also provide that any vacancy on our supervisory board resulting from the death or resignation of a member, provided there are at least three members remaining, may be filled by a majority vote of our members then in office provided that there has been no shareholders meeting since such death or resignation. Members chosen or appointed to fill a vacancy are elected by the supervisory board for the remaining duration of the current term of the replaced member. The appointment must then be ratified at the next shareholders general meeting. In the event the supervisory board would be composed of less than three members as a result of a vacancy, the remaining members shall immediately convene a shareholders general meeting to elect one or several new members so there are at least three members serving on the supervisory board, in accordance with French law. In addition, any appointment made in violation of the gender equality rule described above that is not remedied within six months of such appointment, will be null and void.

We currently have four members of the supervisory board and one observer. The following table sets forth the names of the members and observer of the supervisory board, the year of their initial appointment as members or observer of the supervisory board and the expiration dates of their current term.

Name	Current Position	Year of Initial Appointment	Current Term Expiration Year
Dr. Gary Phillips	Chairman	2021	2023
Ms. Anne-Marie Graffin	Vice Chairwoman	2013	2024
Dr. Alain Herrera, M.D.	Member	2013	2024
Mr. Enno Spillner	Member	2014	2026
Mr. Christophe Douat[(1)]	Observer	2017	2023

(1) Mr. Christophe Douat previously served as member of the supervisory board from 2011 until 2017. Since 2017, Mr. Christophe Douat has served as an observer and is entitled to attend all meetings of the supervisory board in a non-voting capacity.

Supervisory Board Member Independence

As a foreign private issuer, under the listing requirements and rules of Nasdaq, we are not required to have independent members on our supervisory board, except with respect to our audit committee. Our supervisory board has undertaken a review of the independence of its members and considered whether any member has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based upon information requested from, and provided by, each supervisory board member concerning such member's background, employment and affiliations, including family relationships, our supervisory board 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 Exchange Act. In making these determinations, our supervisory board considered the current and prior relationships that each member has and has had with our company and all other facts and circumstances that our supervisory board deemed relevant in determining their independence, including the beneficial ownership of our ordinary shares by each member and his or her affiliate entities, if any.

Furthermore, the MiddleNext Corporate Governance Code is a reference governance code, as amended in September 2021, published by MiddleNext that is specifically tailored for small and mid-cap companies. Listed companies in France must comply with the corporate governance provisions of general corporate law and may also refer to the recommendations of a reference governance code, such as the MiddleNext Corporate Governance Code. French companies referring to a reference governance code must disclose whether their governance practices deviate from the recommendations set out in such reference code. The MiddleNext Corporate Governance 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, or banker) 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.

Our supervisory board believes that all of its members are independent under the independence criteria of the MiddleNext Corporate Governance Code.

Role of the Supervisory Board in Risk Oversight

Our supervisory board is responsible for the oversight of our risk management activities and has delegated to the audit committee the responsibility to assist our supervisory board in this task. The audit committee also monitors our system of disclosure controls and procedures and internal control over financial reporting and reviews contingent financial liabilities. Additionally, the audit committee reviews and discusses with management all reports regarding our enterprise risk management activities, including management's assessment of our major risk exposures and the steps taken to monitor and manage those exposures.

While our supervisory board oversees our risk management, our executive board is responsible for our day-to-day risk management processes. Our supervisory board expects our executive board to consider risk and risk management in each business decision and to proactively develop and monitor risk management strategies and

processes for day-to-day activities. We believe this division of responsibility is the most effective approach for addressing the risks we face.

Corporate Governance Practices

As a French *société anonyme* listed on the regulated market of Euronext in Paris, we are subject to various corporate governance requirements under French law. In addition, as a foreign private issuer listed on the Nasdaq Global Select Market, we are subject to the Nasdaq corporate governance listing standards. However, the Nasdaq listing standards permit foreign private issuers to follow home country corporate governance practices in lieu of the Nasdaq rules, with certain exceptions. Certain corporate governance practices in France may differ significantly from the Nasdaq corporate governance listing standards. For example, neither the corporate laws of France nor our By-laws require that (i) a majority of our directors be independent, (ii) our compensation committee include only independent directors, or (iii) our independent directors hold regularly scheduled meetings at which only independent directors are present. Other than as set forth below, we currently intend to comply with the corporate governance listing standards of Nasdaq to the extent possible under French law. However, we may choose to change such practices to follow home country practices in the future.

Even as a foreign private issuer, we are required to comply with Rule 10A-3 of the Exchange Act, relating to audit committee composition and responsibilities. Rule 10A-3 provides that the audit committee must have direct responsibility for the nomination, compensation and choice of our auditors, as well as control over the performance of the auditor's duties, management of complaints made, and selection of consultants. Under Rule 10A-3, if the laws of a foreign private issuer's home country require that any such matter be approved by board members or the shareholders of the company, the audit committee's responsibilities or powers with respect to such matter may instead be advisory.

Under French law, the audit committee may only have an advisory role and the appointment of our statutory auditors, in particular, must be approved by our shareholders at our annual meeting. Therefore, in accordance with Rule 10A-3, our audit committee only has an advisory role with respect to the aforementioned responsibilities. Under French law, an audit committee may have only two members, whereas Nasdaq listing standards require a three-member audit committee. We currently have only two members on our audit committee in accordance with French law. One observer currently attends the audit committee in a non-voting capacity.

French law does not require our independent directors to hold regularly scheduled meetings at which only independent directors are present. We currently follow home country practice in this regard, although, if the independent directors decide to meet in such executive sessions, they may do so.

In addition, Nasdaq rules require that a listed company specify that the quorum for any meeting of the holders of share capital be at least 33 1/3% of the outstanding shares of the company's common voting stock. We follow our French home country practice, rather than complying with this Nasdaq rule. Consistent with French law, our By-laws provide that when first convened, general meetings of shareholders may validly deliberate only if the shareholders present or represented hold at least (1) 20% of the shares entitled to vote in the case of an ordinary general meeting or of an extraordinary general meeting where shareholders are voting on a capital increase by capitalization of reserves, profits or share premium, or (2) 25% of the shares entitled to vote in the case of any other extraordinary general meeting. If such quorum required by French law is not met, the meeting is adjourned. There is no quorum requirement under French law when an ordinary general meeting or an extraordinary general meeting where shareholders are voting on a capital increase by capitalization of reserves, profits or share premium is reconvened, but the reconvened meeting may consider only questions that were on the agenda of the adjourned meeting. When any other extraordinary general meeting is reconvened, the required quorum under French law is 20% of the shares entitled to vote. If a quorum is not met at a reconvened meeting requiring a quorum, then the meeting may be adjourned for a maximum of two months. See the section of this Annual Report titled "Item 10B. Memorandum and Articles of Association."

Further, Nasdaq rules require that listed companies have a compensation committee comprised solely of independent directors and that director nominees be selected solely by independent directors. We currently comply with this Nasdaq rule, but may in the future elect to follow French home country practice.

Finally, Nasdaq rules require shareholder approval when a plan or other equity compensation arrangement is established or materially amended. Under French law our shareholders must decide any issuance of equity, as a general matter.

However, we follow our French home country practice and ask our shareholders to delegate their authority to issue incentive equity and define the final terms of any equity compensation plan or arrangements to our executive board. We may, from time to time, ask for our shareholders' subsequent approval on an equity compensation arrangement in order to obtain advantageous tax treatment or otherwise. In addition, under French law, our executive board must obtain the prior approval of our shareholders before establishing or amending a plan or arrangement that would exceed the limits of the granted delegation.

Supervisory Board Committees

Our supervisory board has established an audit committee and an appointments and compensation committee, each of which operates pursuant to a separate charter.

In accordance with French law, committees of our supervisory board will only have an advisory role and can only make recommendations to our supervisory board. As a result, decisions are made by our supervisory board, taking into account non-binding recommendations of the relevant board committee.

The Supervisory Board is carefully monitoring trends and developments with respect to corporate social and environmental responsibility issues, and intends to evaluate the Supervisory Board's oversight of the Company with respect to such issues.

Audit Committee

Our audit committee monitors the questions relating to the processing and control of accounting and financial information. To this end, it ensures the quality of our internal controls and the reliability of information provided to shareholders and financial markets.

The duties specifically assigned to the audit committee by our 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 our statutory auditors to be appointed by our shareholders, determining their compensation and ensuring their independence;
- making recommendations regarding the selection of any accounting firm, other than our statutory auditors, to be appointed for non-audit services;
- examining our procedures for the receipt, retention and treatment of complaints received by us regarding accounting, internal accounting controls or auditing matters, as well as for the confidential, anonymous submissions by our 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 our 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 our supervisory board and the chairman of our executive board are informed in advance. In particular, our audit committee has the right to interview the persons involved in the preparation or control of our financial statements, including our Chief Financial Officer and those persons responsible for significant areas within our financial department.

Our audit committee shall be comprised of at least two members from, and appointed by, the supervisory board, after consultation with our appointments and compensation committee. Members shall be independent in accordance with Nasdaq's listing rules and Rule 10A-3 of the Exchange Act as well as the criteria established by the MiddleNext Corporate Governance Code. At least one member shall have specific financial and accounting skills. Further, under French law an audit committee may only have two members, whereas Nasdaq requires a three-member audit committee. We currently have two members on our audit committee in accordance with French law.

Currently, our audit committee is comprised of two members: Mr. Enno Spillner (chairman and independent member) and Dr. Gary Phillips (independent member), and one observer, Mr. Christophe Douat, who attends in a non-voting capacity. Our supervisory board has determined that Mr. 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.

Our audit committee met five times in 2021. Mr. Laurent Condomine served on the audit committee for the year 2020 and until his retirement on May 25, 2021.

Appointments and Compensation Committee

Our appointments and compensation committee provides recommendations and proposals to our executive and supervisory board members on the composition and compensation policies of our executive and supervisory boards, and also prepares any related reports to be provided by us.

The principal duties and responsibilities of our 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 our 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 Exchange Act as well as the criteria set forth in the MiddleNext Corporate Governance Code;
- establishing a succession plan for our executive officers and assisting our 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 our 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 our 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 charter (règlement intérieur);
- making any other recommendation that might be requested by our supervisory board regarding compensation; and
- generally advising the supervisory board and making recommendations with respect to all of the areas above.

Our appointments and compensation committee shall be comprised of at least two members from and appointed by the supervisory board. Currently, our appointments and compensation committee is comprised of three members: Ms. Anne-Marie Graffin (chairwoman), Dr. Alain Herrera and Dr. Gary Phillips.

Our appointments and compensation committee met four times in 2021. Mr. Laurent Condomine served on the appointments and compensation committee for the year 2020 and until his retirement on May 25, 2021.

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics ("Code of Conduct") that is applicable to all of our, and our subsidiaries', employees, executive board members and supervisory board members. The Code of Conduct is available on our website at *www.nanobiotix.com*. Our supervisory board is responsible for overseeing the Code of Conduct and is required to approve any waivers of the Code of Conduct for employees, executive board members and supervisory board members. We expect that any amendments to the Code of Conduct, or any waivers of its requirements, will be disclosed on our website.

D. Employees

As of December 31, 2021, we had 100 full-time employees. Of our full-time employees 74 are engaged in research and development and 37 hold a doctorate in medicine, pharmacy or science.

As of December 31, 2021, 84 of our employees were located in Europe and 16 of our employees were located in the United States. None of our employees is subject to a collective bargaining agreement.

We consider our relationship with our employees to be good.

E. Share Ownership

For information regarding the share ownership of our Supervisory and Executive Board members, see "Item 6B.Compensation" and "Item 7A. Major Shareholders."

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major Shareholders

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of April 8, 2022 for:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding ordinary shares;
- each of our supervisory board members and executive board members; and
- all of our supervisory board members and executive board members as a group.

Beneficial ownership is determined in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include ordinary shares that can be acquired within 60 days of April 8, 2022. The percentage ownership information shown in the table is based upon 34,875,872 ordinary shares outstanding as of April 8, 2022. In computing the number of ordinary shares beneficially owned by a person and the percentage ownership of that person, we deemed outstanding ordinary shares subject to founders' warrants, warrants and stock options held by that person that are immediately exercisable or exercisable within 60 days of April 8, 2022 (and we have assumed no vesting of outstanding free shares). We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

Except as otherwise indicated in the footnotes below the table, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all shares beneficially owned by them, subject to applicable community property laws where applicable. The information is not necessarily indicative of beneficial ownership for any other purpose, including for purposes of Sections 13(d) and 13(g) of the Securities Act.

The information in the table below is based on information furnished to us or ascertained by us from public filings made by the shareholders in France. Except as otherwise indicated in the table below, addresses of the supervisory board members, executive board members and named beneficial owners are in care of Nanobiotix S.A., 60, rue de Wattignies, 75012 Paris, France.

Name of Beneficial Owner	Ordinary Shares Beneficially Owned	
	Number	%
5% Shareholders		
Entities affiliated with Invus Public Equities, L.P.[(1)]	3,069,034	8.8
Caisse des Dépôts et consignation[(2)]	1,921,722	5.5
Baillie Gifford & Co[(3)]	1,809,326	5.2
Amiral Gestion[(4)]	1,750,624	5
Supervisory Board and Executive Board Members:		
Laurent Levy, Ph.D.[(5)]	1,142,260	3.28
Anne-Juliette Hermant[(6)]	81,000	[*]
Bart Van Rhijn	—	[*]
Alain Herrera, M.D.	—	[*]
Christophe Douat[(7)]	22,500	[*]
Anne-Marie Graffin	—	[*]
Gary Phillips	—	[*]
Enno Spillner	—	[*]
All Supervisory Board and Executive Board members as a group (8 persons)[(8)]	1,245,760	3.45

** Represents beneficial ownership of less than 1%.*

(1) Consists of 2,069,034 ordinary shares and 1,000,000 ADSs. Amounts beneficially owned by entities affiliated with Invus Public Equities, L.P. ("Invus"). Amounts beneficially owned by entities affiliated with Invus were reported pursuant to a Schedule 13G amendment filed with the SEC on February 11, 2022 by such entities. The registered office of the entities affiliated with Invus is 750 Lexington Ave., 30th Floor, New York, NY 10022.

(2) Consists of 1,921,722 ordinary shares

(3) Consists of 409,836 ordinary shares and 1,400,000 ADSs. Amounts beneficially owned by Baillie Gifford & Co were reported pursuant to a Schedule 13G amendment with the SEC on January 26, 2022 by Baillie Gifford & Co. The address of Baillie Gifford & Co. is Calton Square, 1 Greenside Row, Edinburgh EH1 3AN.

(4) Consists of 1,750,624 ordinary shares

(5) Consists of 936,310 ordinary shares and 205,950 ordinary shares issuable upon exercise of founders' warrants and stock options.

(6) Consists of 45,000 ordinary shares and 36,000 ordinary shares issuable upon exercise of founders' warrants and stock options.

(7) Consists of 22,500 ordinary shares issuable upon exercise of warrants.

(8) Consists of 981,010 ordinary shares and 264,450 ordinary shares issuable upon exercise of founders' warrants and stock options.

As of December 31, 2021, we estimate that approximately 19% respectively of our outstanding ordinary shares were held in the United States.

B. Related Party Transactions

It is the policy of the supervisory board that in order to mitigate the risk of any actual or perceived conflicts of interest, whenever a matter comes before the supervisory board for its consideration in which a related party supervisory board member has a potential interest, such member shall be recused from participating in any discussions and voting in any decisions on such matter.

Agreements with Our Directors and Executive Officers

Director and Executive Officer Compensation

See "Item 6B. Compensation of Directors and Executive Officers" for information regarding compensation of directors and executive officers.

Equity Awards

Since January 1, 2022, we have not granted equity awards to certain of our directors and executive officers. See "Item 7A. Major Shareholders" for information regarding equity awards to certain of our executive officers.

Related-Person Transactions Policy

We have adopted a related-party transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related-party transactions. For purposes of our policy only, a related-party transaction is defined as (1) a transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships), in which we and any related parties are, were or will be participants, or otherwise have a direct or indirect interest, in which the amount involved exceeds $120,000, or (2) any agreement or similar transaction under French law which falls within the scope of Article L. 225-86 of the French Commercial Code. For purposes of this policy, a related party is any executive board member, supervisory board member or beneficial owner of more than five percent (5%) of any class of our voting securities, including any of their respective immediate family members and any entity owned or controlled by such persons.

Under the policy, related-party transactions must be reported to us by the relevant related parties. If a transaction has been identified as a related-party transaction, including any transaction that was not a related-party transaction when originally consummated or any transaction that was not initially identified as a related-party transaction prior to consummation, our management must present information regarding the related-party transaction to our supervisory board for review, consideration and approval or ratification. Certain transactions may be presented to the audit committee, which may make recommendations to the supervisory board on whether the transaction is a related-party transaction; in any case, the related-party transaction will be submitted to our supervisory board for review, consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests in the transaction, direct and indirect, of the related parties, the benefits to us of the transaction and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third-party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each member of our executive board and supervisory board and, to the extent feasible, significant shareholder to enable us to identify any existing or potential related-party transactions and to effectuate the terms of the policy.

We comply with French law regarding approval of transactions with related parties. In particular, in accordance with articles L. 225-86 et seq. of the French Commercial Code, our executive board informs on an annual basis our supervisory board of any agreement or similar transaction under French law which falls within the scope of Article L. 225-86 of the French Commercial Code entered into during the past fiscal year. Our supervisory board shall review the purpose and financial conditions of these agreements and confirm or deny their classification as current agreements, meaning agreements relating to current operations and entered into under normal conditions. In

accordance with Article L. 225-88-2 of the French Commercial Code, we shall disclose on our website information related to any related-party transaction entered into by no later than the day of the relevant transaction's conclusion. In addition, we have adopted a Code of Business Conduct and Ethics policy. Under this policy, our employees and members of our supervisory and executive boards have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest.

In considering related-party transactions, our supervisory board will take into account the relevant available facts and circumstances including, but not limited to:

- the benefits and perceived benefits to us;
- the opportunity costs of alternative transactions;
- the materiality and character of the related party's interest;
- the actual or apparent conflict of interest of the related party; and
- the terms available to or from, as the case may be, unrelated third parties or to or from employees generally.

The policy requires that, in determining whether to approve, ratify or reject a related-party transaction, our supervisory board must consider, in light of known circumstances, whether the transaction is in, or is not inconsistent with, our best interests and those of our shareholders, as our supervisory board determines in the good faith exercise of its discretion.

All of the transactions referred to above were entered into prior to the adoption of the written related-party transaction policy but all were approved by our supervisory board to the extent required by, and in compliance with, French law.

C. Interests of Experts and Counsel

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. Consolidated Statements and Other Financial Information

Consolidated Financial statements

Our audited consolidated financial statements are appended at the end of this Annual Report starting at page F-1, and form a part hereof.

Legal Proceedings

From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. We are not currently a party to any legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Dividend Distribution

We have never declared or paid any cash dividends on our ordinary shares. We do not anticipate paying cash dividends on our equity securities in the foreseeable future and intend to retain all available funds and any future earnings for use in the operation and expansion of our business.

Subject to the requirements of French law and our By-laws, dividends may only be distributed from our distributable profits, plus any amounts held in our available reserves, which are our reserves other than the legal and statutory reserves and the revaluation surplus. The section of this Annual Report titled "Item 8A. Consolidated Statements and Other Financial Information—Dividend Distribution" provides further details on the limitations on our ability to declare and pay dividends. Dividend distributions, if any, will be made in euros and converted into U.S. dollars with respect to the ADSs, as provided in the deposit agreement.

Approval of Dividends. Pursuant to French law, our executive board may propose a dividend and/or reserve distribution for approval by the shareholders at the annual ordinary general meeting related to the statutory financial statements of Nanobiotix S.A.

Upon recommendation of our executive board, our shareholders may decide to allocate all or part of any distributable profits to special or general reserves, to carry them forward to the next fiscal year as retained earnings or to allocate them to the shareholders as dividends. However, dividends may not be distributed when as a result of such distribution our net assets are or would become lower than the amount of the share capital plus the amount of the legal reserves which, under French law, may not be distributed to shareholders. The amount of our share capital

plus the amount of our legal and other reserves which may not be distributed was equal to $1.1 million on December 31, 2021. Moreover, the statutory accumulated deficit is €284 million as of December 31, 2021.

Our executive board may distribute interim dividends after the end of the fiscal year but before the approval of the financial statements for the relevant fiscal year when the interim balance sheet, established during such year and examined by an auditor, reflects that we have earned distributable profits since the close of the last fiscal year, after recognizing the necessary depreciation and provisions and after deducting prior losses, if any, and the sums to be allocated to reserves, as required by law or the By-laws, and including any retained earnings. The amount of such interim dividends may not exceed the amount of the profit so defined.

Distribution of Dividends. Dividends are distributed to shareholders proportionally to their shareholding interests. In the case of interim dividends, distributions are made to shareholders on the date set by our executive board during the meeting in which the distribution of interim dividends is approved. The actual dividend payment date is decided by the shareholders at an ordinary general shareholders' meeting or by our executive board in the absence of such a decision by the shareholders. Shareholders that own shares on the actual payment date are entitled to the dividend. Dividends may be paid in cash or, if the shareholders' meeting so decides, in kind, provided that all the shareholders receive a whole number of assets of the same nature paid in lieu of cash. Our By-laws provide that, subject to a decision of the shareholders' meeting taken by ordinary resolution, each shareholder may be given the choice to receive his dividend in cash or in shares.

B. Significant Changes

None.

ITEM 9. THE OFFER AND LISTING

A. Offer and Listing Details

Our ADSs have been listed on Nasdaq Global Select Market under the symbol "NBTX" since December 11, 2020. Prior to that date, there was no public trading market for out ADSs. Our ordinary shares have been trading on the regulated market of Euronext in Paris under the symbol "NANO" since October 2012. Prior to that date, there was no public trading market for our ADSs or our ordinary shares. No significant trading suspensions have occurred in the prior three years.

B. Plan of Distribution

Not applicable.

C. Markets

For information regarding the stock exchanges and regulated markets on which our ADSs and ordinary share are listed, see "Item 9A. Offer and Listing Details."

D. Selling Shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the Issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share Capital

Not applicable.

B. Memorandum and Articles of Association

The information set forth in the prospectus dated February 4, 2022 as part of our Registration Statement on Form F-3 (File No. 333-262545), declared effective by the SEC on February 16, 2022, under the headings "Description of Share Capital—Key Provisions of Our Bylaws and French Law Affecting Our Ordinary Shares," "Description of Share Capital—Differences in Corporate Law" and "Limitations Affecting Shareholders of a French Company" is incorporated herein by reference.

Listing

Our ADSs are listed on the Nasdaq Global Select Market under the symbol “NBTX” and our ordinary shares are listed on the regulated market of Euronext in Paris under the symbol “NANO.”

Transfer Agent and Registrar

The transfer agent and registrar for our ADSs is Citibank, N.A. The transfer agent and registrar for our ordinary shares is CIC Securities.

C. Material Contracts

For additional information on our material contracts entered into during the two years immediately preceding the date of the filing of this Annual Report, please refer to “Item 4B. Business Overview” and “Item 7B Related Party Transactions” of this Annual Report.

D. Exchange Controls

Under current French foreign exchange control regulations there are no limitations on the amount of cash payments that we may remit to residents of foreign countries. Laws and regulations concerning foreign exchange controls do, however, require that all payments or transfers of funds made by a French resident to a non-resident such as dividend payments be handled by an accredited intermediary. All registered banks and substantially all credit institutions in France are accredited intermediaries.

E. Taxation

Material U.S. Federal Income Tax Considerations

The following is a discussion of the material U.S. federal income tax consequences of owning and disposing of ADSs. This summary does not address any aspect of U.S. federal non-income tax laws, such as U.S. federal estate and gift tax laws, or state, local or non-U.S. tax laws, and does not purport to be a comprehensive description of all of the U.S. tax considerations that may be relevant to particular holders.

The discussion applies to you only if you hold the ADSs as capital assets for U.S. federal income tax purposes (generally, for investment). This section does not apply to you if you are a member of a special class of holders subject to special tax rules, including:

- a broker;
- a dealer in securities, commodities or foreign currencies;
- a trader in securities that elects to use a mark-to-market method of accounting for its securities holdings;
- a bank or other financial institution;
- a tax-exempt organization or governmental organization;
- an insurance company;
- a regulated investment company or real estate investment trust;
- a U.S. expatriate, former U.S. citizen or former long term resident of the United States;
- a mutual fund;
- an individual retirement or other tax-deferred account;
- a holder liable for alternative minimum tax;
- a holder that actually or constructively owns 10% or more, by voting power or value, of our stock (including stock represented by ADSs);
- a partnership or other pass-through entity for U.S. federal income tax purposes;
- a holder that holds ADSs as part of a straddle, hedging, constructive sale, conversion or other integrated transaction for U.S. federal income tax purposes; or

- a U.S. holder (as defined below) whose functional currency is not the U.S. dollar.

This section is based on the Internal Revenue Code of 1986, as amended, or (the Code), existing and proposed income tax regulations issued under the Code, legislative history, and judicial and administrative interpretations thereof, all as of the date of this Annual Report. All of the foregoing are subject to change at any time, and any change could be retroactive and could affect the accuracy of this discussion. In addition, the application and interpretation of certain aspects of the passive foreign investment company, or PFIC, rules, referred to below, require the issuance of regulations which in many instances have not been promulgated and which may have retroactive effect. There can be no assurance that any of these regulations will be enacted or promulgated, and if so, the form they will take or the effect that they may have on this discussion. This discussion is not binding on the U.S. Internal Revenue Service, or IRS, or the courts. No ruling has been or will be sought from the IRS with respect to the positions and issues discussed herein, and there can be no assurance that the IRS or a court will not take a different position concerning the U.S. federal income tax consequences of an investment in the ADSs or that any such position would not be sustained.
YOU SHOULD CONSULT YOUR OWN TAX ADVISORS CONCERNING THE U.S. FEDERAL, STATE, LOCAL AND NON-U.S. TAX CONSEQUENCES OF OWNING AND DISPOSING OF THE ADSs IN YOUR PARTICULAR SITUATIONS.

You are a “U.S. holder” if you are a beneficial owner of ADSs or are treated for U.S. federal income tax purpose as:

- a citizen or resident of the United States;
- a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate whose income is subject to U.S. federal income tax regardless of its source; or
- a trust if (1) a U.S. court can exercise primary supervision over the trust’s administration and one or more U.S. persons are authorized to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person for U.S. federal income tax purposes.

In addition, this discussion is limited to holders who are not resident in France for purposes of the income tax treaty between the United States and France.

If a partnership (including for this purpose any entity treated as a partnership for U.S. federal income tax purposes) is a beneficial owner of the ADSs, the U.S. tax treatment of a partner in the partnership generally will depend on the status of the partner and the activities of the partnership. A holder of the ADSs that is a partnership and partners in such a partnership should consult their own tax advisors concerning the U.S. federal income tax consequences of purchasing, owning and disposing of ADSs.

A “non-U.S. holder” is a beneficial owner of ADSs that is neither a U.S. holder nor a partnership for U.S. federal income tax purposes.

Generally, holders of ADSs should be treated for U.S. federal income tax purposes as holding the ordinary shares represented by the ADSs. Accordingly, no gain or loss will be recognized upon an exchange of ordinary shares for ADSs or an exchange of ADSs for ordinary shares. The U.S. Treasury has expressed concerns that intermediaries in the chain of ownership between the holder of an ADS and the issuer of the security underlying the ADS may be taking actions that are inconsistent with the claiming of foreign tax credits for U.S. holders of ADSs. Accordingly, the credibility of foreign taxes, if any, as described below, could be affected by actions taken by intermediaries in the chain of ownership between the holder of an ADS and the company.

PFIC Considerations

The Code provides special rules regarding certain distributions received by U.S. persons with respect to, and sales, exchanges and other dispositions, including pledges, of, shares of stock (including ordinary shares represented by ADSs) in, a PFIC. A non-U.S. corporation will be treated as a PFIC for any taxable year in which either: (1) at least 75% of its gross income is “passive income” or (2) at least 50% of its gross assets during the taxable year (based on the average of the fair market values of the assets determined at the end of each quarterly period) are “passive assets,” which generally means that they produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, dividends, interest, rents, royalties, gains from commodities and securities transactions, and gains from assets that produce passive income. In determining whether a foreign corporation is a PFIC, a pro rata portion of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account.

Although not free from doubt, we do not believe that we were a PFIC for the taxable year ended December 31, 2021. No assurances may be given at this time as to our PFIC status for the taxable year ending December 31, 2022 or subsequent taxable years. Our PFIC status must be determined annually and therefore is subject to change. Because this determination is made annually at the end of each taxable year and is dependent upon a number of factors, some of which are beyond our control, including the amount and nature of our income (including whether

reimbursements of certain refundable research tax credits will constitute gross income for purpose of the PFIC income test), as well as on the market valuation of our assets and our spending schedule for our cash balances, and because certain aspects of the PFIC rules are not entirely certain, there can be no assurance that we were not a PFIC, that we are not or will not become a PFIC or that the IRS will agree with our conclusion regarding our PFIC status. If we are not a PFIC during any taxable year in which you hold ADSs, then the remainder of the discussion under "Taxation—Material U.S. Federal Income Tax Considerations," outside of this "—PFIC Considerations" portion may be relevant to you. U.S. holders should consult their tax advisors as to the applicability of the PFIC rules.

A U.S. holder that holds ADSs during any taxable year in which we qualify as a PFIC is subject to special tax rules with respect to (a) any gain realized on the sale, exchange or other disposition of the ADSs and (b) any "excess distribution" by the corporation to the holder, unless the holder elects to treat the PFIC as a "qualified electing fund" (QEF) or makes a "mark-to-market" election, each as discussed below. An "excess distribution" is that portion of a distribution with respect to ADSs that exceeds 125% of the annual average of such distributions over the preceding three-year period or, if shorter, the U.S. holder's holding period for its ADSs. Excess distributions and gains on the sale, exchange or other disposition of ADSs of a corporation which was a PFIC at any time during the U.S. holder's holding period are allocated ratably to each day of the U.S. holder's holding period. Amounts allocated to the taxable year in which the disposition occurs and amounts allocated to any period in the shareholder's holding period before the first day of the first taxable year that the corporation was a PFIC will be taxed as ordinary income (rather than capital gain) earned in the taxable year of the disposition. Amounts allocated to each of the other taxable years in the U.S. holder's holding period are not included in gross income for the year of the disposition, but are subject to the highest ordinary income tax rates in effect for individuals or corporations, as applicable, for each such year and the interest charge generally applicable to income tax deficiencies will be imposed on the resulting tax attributable to each year. The tax liability for amounts allocated to years before the year of disposition or "excess distribution" cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the ADSs cannot be treated as capital, even if a U.S. holder held such ADSs as capital assets.

If we are a PFIC for any taxable year during which a U.S. holder holds ADSs, then we generally will continue to be treated as a PFIC with respect to the holder for all succeeding years during which such holder holds ADSs, even if we no longer satisfy either the passive income or passive asset tests described above, unless the U.S. holder terminates this deemed PFIC status by making a "deemed sale" election. If such election is made, a U.S. holder will be deemed to have sold the ADSs at their fair market value on the last day of the last taxable year for which we were a PFIC, and any gain from such deemed sale would be subject to the excess distribution rules as described above. After the deemed sale election, the ADSs with respect to which the deemed sale election was made will not be treated as shares in a PFIC unless we subsequently become a PFIC.

If we are or become a PFIC, the excess distribution rules may be avoided if a U.S. holder makes a QEF election effective beginning with the first taxable year in the holder's holding period in which we are treated as a PFIC with respect to such holder. A U.S. holder that makes a QEF election with respect to a PFIC is required to include in income its pro rata share of the PFIC's ordinary earnings and net capital gain as ordinary income and capital gain, respectively, subject to a separate election to defer payment of taxes, which deferral is subject to an interest charge. In general, a U.S. holder makes a QEF election by attaching a completed IRS Form 8621 to a timely filed (taking into account any extensions) U.S. federal income tax return for the year beginning with which the QEF election is to be effective. In certain circumstances, a U.S. holder may be able to make a retroactive QEF election. A QEF election can be revoked only with the consent of the IRS. In order for a U.S. holder to make a valid QEF election, the non-U.S. corporation must annually provide or make available to the holder certain information. At this time, we have not determined whether we will provide to U.S. holders the information required to make a valid QEF election and we currently make no undertaking to provide such information.

As an alternative to making a QEF election, a U.S. holder may make a "mark-to-market" election with respect to its ADSs if the ADSs meet certain minimum trading requirements, as described below. If a U.S. holder makes a valid mark-to-market election for the first taxable year in which such holder holds (or is deemed to hold) ADSs in a corporation and for which such corporation is determined to be a PFIC, such holder generally will not be subject to the PFIC rules described above in respect of its ADSs. Instead, a U.S. holder that makes a mark-to-market election will be required to include in income each year an amount equal to the excess, if any, of the fair market value of the ADSs that the holder owns as of the close of the taxable year over the holder's adjusted tax basis in the ADSs. The U.S. holder will be entitled to a deduction for the excess, if any, of the holder's adjusted tax basis in the ADSs over the fair market value of the ADSs as of the close of the taxable year; provided, however, that the deduction will be limited to the extent of any net mark-to-market gains with respect to the ADSs included by the U.S. holder under the election for prior taxable years. The U.S. holder's basis in the ADSs will be adjusted to reflect the amounts included or deducted pursuant to the election. Amounts included in income pursuant to a mark-to-market election, as well as gain on the sale, exchange or other disposition of the ADSs, will be treated as ordinary income. The deductible portion of any mark-to-market loss, as well as loss on a sale, exchange or other disposition of ADSs to the extent that the amount of such loss does not exceed net mark-to-market gains previously included in income, will be treated as ordinary loss. If a U.S. holder makes a valid mark-to-market election, any distributions made by us in a year in which we are a PFIC would generally be subject to the rules discussed below under "—Taxation of Dividends," except the lower rate applicable to qualified dividend income would not apply. If we are not a PFIC when a U.S. holder has a mark-to-market election in effect, gain or loss realized by a U.S. holder on the sale of our ADSs will be a

capital gain or loss and taxed in the manner described below under "—Taxation of Sale, Exchange or other Disposition of ADSs."

The mark-to-market election applies to the taxable year for which the election is made and all subsequent taxable years, unless the ADSs cease to meet applicable trading requirements (described below) or the IRS consents to its revocation. The excess distribution rules generally do not apply to a U.S. holder for taxable years for which a mark-to-market election is in effect. If we are a PFIC for any year in which the U.S. holder owns ADSs but before a mark-to-market election is made, the interest charge rules described above will apply to any mark-to-market gain recognized in the year the election is made.

A mark-to-mark election is available only if the ADSs are considered "marketable" for these purposes. ADSs will be marketable if they are regularly traded on a national securities exchange that is registered with the SEC (such as the Nasdaq Global Select Market) or on a non-U.S. exchange or market that the IRS determines has rules sufficient to ensure that the market price represents a legitimate and sound fair market value. For these purposes, ADSs will be considered regularly traded during any calendar year during which more than a de minimis quantity of the ADSs is traded on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. Each U.S. holder should ask its own tax advisor whether a mark-to-market election is available or desirable.

If we are a PFIC for any year in which a U.S. holder holds ADSs, such U.S. holder must generally file an IRS Form 8621 annually. A U.S. holder must also provide such other information as may be required by the U.S. Treasury Department if the U.S. holder (1) receives certain direct or indirect distributions from a PFIC, (2) recognizes gain on a direct or indirect disposition of ADSs, or (3) makes certain elections (including a QEF election or a mark-to-market election) reportable on IRS Form 8621.

If we are a PFIC, then under attribution rules, U.S. holders of our ADSs will be deemed to own their proportionate shares of our subsidiaries that are PFICs, if any. It is possible that one or more of our subsidiaries is or will become a PFIC. This determination is made annually at the end of each taxable year and depends upon a number of factors, some of which are beyond our control, including the amount and nature of a subsidiary's income, as well as the valuation and nature of a subsidiary's assets. In the event that we are a PFIC and we have a subsidiary that is a PFIC, assuming a U.S. holder does not receive from such subsidiary the information that the U.S. holder needs to make a QEF election with respect to such a subsidiary, a U.S. holder generally will be deemed to own a portion of the shares of such lower-tier PFIC and may incur liability for a deferred tax and interest charge if we receive a distribution from, or dispose of all or part of our interest in, or the U.S. holder otherwise is deemed to have disposed of an interest in, the lower-tier PFIC, even though the U.S. holder has not received the proceeds of those distributions or dispositions directly. There is no assurance that we will have timely knowledge of the status of any such lower-tier PFIC, or that we will cause the lower-tier PFIC to provide the required information for a U.S. holder to make and maintain a QEF election with respect to the lower-tier PFIC. In addition, a mark-to-market election generally would not be available with respect to such a lower-tier PFIC and, consequently, if you make a mark-to-market election with respect to our ADSs, you could be subject to the PFIC rules with respect to income of lower-tier PFICs the value of which already had been taken into account indirectly via mark-to-market adjustments. U.S. holders are advised to consult with their tax advisors regarding the tax issues raised by lower-tier PFICs.

U.S. holders are urged to consult their tax advisors as to our status as a PFIC, and, if we are treated as a PFIC, as to the effect on them of, and the reporting requirements with respect to, the PFIC rules and the desirability of making, and the availability of, either a QEF election or a mark-to-market election with respect to our ADSs.

Taxation of Dividends

U.S. Holders. Subject to the PFIC rules described above under "—PFIC Considerations," if you are a U.S. holder, you must include in your gross income the gross amount of any distributions of cash or property (other than certain pro rata distributions of ADSs) with respect to ADSs, to the extent the distribution is paid out of our current or accumulated earnings and profits, as determined for U.S. federal income tax purposes. A U.S. holder must include the dividend as ordinary income at the time of actual or constructive receipt. Distributions in excess of current and accumulated earnings and profits, as determined for U.S. federal income tax purposes, will be treated as a non-taxable return of capital to the extent of your basis in the ADSs and thereafter as capital gain from the sale or exchange of such ADSs. Notwithstanding the foregoing, we do not intend to maintain calculations of our earnings and profits as determined for U.S. federal income tax purposes. Consequently, distributions generally will be reported as dividend income for U.S. information reporting purposes. The dividend will not be eligible for the dividends-received deduction generally allowed to U.S. corporations in respect of dividends received from other U.S. corporations.

Subject to the PFIC rules described above under "—PFIC Considerations," dividends paid by a non-U.S. corporation generally will be taxed at the preferential tax rates applicable to long-term capital gain of non-corporate taxpayers if (a) such non-U.S. corporation is eligible for the benefits of certain U.S. treaties or the dividend is paid by such non-U.S. corporation with respect to stock that is readily tradable on an established securities market in the United

States, (b) the U.S. holder receiving such dividend is an individual, estate, or trust, (c) such dividend is paid on shares that have been held by such U.S. holder for at least 61 days during the 121-day period beginning 60 days before the "ex-dividend date," and (d) we are not a PFIC in the year of the dividend or the immediately preceding year. If the requirements of the immediately preceding paragraph are not satisfied, a dividend paid by a non-U.S. corporation to a U.S. holder, including a U.S. holder that is an individual, estate, or trust, generally will be taxed at ordinary income tax rates (and not at the preferential tax rates applicable to long-term capital gains). As discussed above under "—PFIC Considerations," it is not yet known whether we will be a PFIC for taxable years ending after December 31, 2021. The dividend rules are complex, and each U.S. holder should consult its own tax advisor regarding the dividend rules.

The amount of dividend will include any amounts withheld by the Company in respect of French taxes. Subject to applicable limitations, some of which vary depending upon the U.S. holder's circumstances and subject to the discussion above regarding concerns expressed by the U.S. Treasury, French income taxes withheld from dividends on ADSs at a rate not exceeding the rate provided by the Treaty will be creditable against the U.S. holder's U.S. federal income tax liability.

Dividends received generally will be income from non-U.S. sources, which may be relevant in calculating your U.S. foreign tax credit limitation. Such non-U.S. source income generally will be "passive category income," or in certain cases "general category income" or "foreign branch" income, which is treated separately from other types of income for purposes of computing the foreign tax credit allowable to you. The rules with respect to the foreign tax credit are complex and involve the application of rules that depend upon a U.S. holder's particular circumstances. You should consult your own tax advisor to determine the foreign tax credit implications of owning the ADSs.

Non-U.S. Holders. If you are a non-U.S. holder, dividends paid to you generally will not be subject to U.S. income tax unless the dividends are "effectively connected" with your conduct of a trade or business within the United States, and the dividends are attributable to a permanent establishment (or in the case of an individual, a fixed place of business) that you maintain in the United States if that is required by an applicable income tax treaty as a condition for subjecting you to U.S. taxation on a net income basis. In such cases you generally will be taxed in the same manner as a U.S. holder (other than with respect to the Medicare Tax described below). If you are a corporate non-U.S. holder, "effectively connected" dividends may, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or a lower rate if you are eligible for the benefits of an income tax treaty that provides for a lower rate.

Taxation of Sale, Exchange or other Disposition of ADSs

U.S. Holders. Subject to the PFIC rules described above under "—PFIC Considerations," if you are a U.S. holder and you sell, exchange or otherwise dispose of your ADSs, you generally will recognize capital gain or loss for U.S. federal income tax purposes equal to the difference between the value of the amount realized and your tax basis in those ADSs. Gain or loss recognized on such a sale, exchange or other disposition of ADSs generally will be long-term capital gain if you have held the ADSs for more than one year. Long-term capital gains of U.S. holders who are individuals (as well as certain trusts and estates) are generally taxed at preferential rates. The gain or loss will generally be income or loss from sources within the United States for foreign tax credit limitation purposes, unless it is attributable to an office or other fixed place of business outside the United States and certain other conditions are met. Your ability to deduct capital losses is subject to limitations. As discussed above under "—PFIC Considerations," it is not yet known whether we will be a PFIC for taxable years ending after December 31, 2021.

Non-U.S. Holders. If you are a non-U.S. holder, you will not be subject to U.S. federal income tax on gain recognized on the sale, exchange or other disposition of your ADSs unless:

- the gain is "effectively connected" with your conduct of a trade or business in the United States, and the gain is attributable to a permanent establishment (or in the case of an individual, a fixed place of business) that you maintain in the United States if that is required by an applicable income tax treaty as a condition for subjecting you to U.S. taxation on a net income basis; or
- you are an individual, you are present in the United States for 183 or more days in the taxable year of such sale, exchange or other disposition and certain other conditions are met.

In the first case, the non-U.S. holder will be taxed in the same manner as a U.S. holder (other than with respect to the Medicare Tax described below). In the second case, the non-U.S. holder will be subject to U.S. federal income tax at a rate of 30% on the amount by which such non-U.S. holder's U.S.-source capital gains exceed such non-U.S. holder's U.S.-source capital losses.

If you are a corporate non-U.S. holder, "effectively connected" gains that you recognize may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or at a lower rate if you are eligible for the benefits of an income tax treaty that provides for a lower rate.

Medicare Tax

Certain U.S. holders who are individuals, estates or trusts are required to pay a 3.8% Medicare surtax on all or part of that holder's "net investment income," which includes, among other items, dividends on, and capital gains from the sale or other taxable disposition of, the ADSs, subject to certain limitations and exceptions. Prospective investors should consult their own tax advisors regarding the effect, if any, of this surtax on their ownership and disposition of the ADSs.

Information with Respect to Foreign Financial Assets

U.S. holders that are individuals (and, to the extent provided in regulations, certain entities) that own "specified foreign financial assets," including possibly the ADSs, with an aggregate value in excess of $50,000 are generally required to file IRS Form 8938 with information regarding such assets. Depending on the circumstances, higher threshold amounts may apply. Specified foreign financial assets include any financial accounts maintained by foreign financial institutions, as well as any of the following, but only if they are not held in accounts maintained by financial institutions: (i) stocks and securities issued by non-U.S. persons, (ii) financial instruments and contracts held for investment that have non-U.S. issuers or counterparties and (iii) interests in non-U.S. entities. If a U.S. holder is subject to this information reporting regime, the failure to timely file IRS Form 8938 may subject the U.S. holder to penalties. In addition to these requirements, U.S. holders may be required to annually file FinCEN Report 114 (Report of Foreign Bank and Financial Accounts) with the U.S. Department of Treasury. Prospective investors are encouraged to consult their own tax advisors with respect to these and other reporting requirements that may apply to their acquisition of the ADSs.

Backup Withholding and Information Reporting

In general, information reporting requirements will apply to distributions made on our ADSs within the United States to a non-corporate U.S. holder and to the proceeds from the sale, exchange, redemption or other disposition of ADSs by a non-corporate U.S. holder to or through a U.S. office of a broker. Payments made (and sales or other dispositions effected at an office) outside the U.S. will be subject to information reporting in limited circumstances.

In addition, U.S. holders may be subject to backup withholding with respect to dividends on and proceeds from the sale, exchange or other disposition of the ADSs. A paying agent within the United States will be required to withhold at the applicable statutory rate, currently 24%, in respect of any payments of dividends on, and the proceeds from the disposition of, ADSs within the United States to a U.S. holder (other than U.S. holders that are exempt from backup withholding and properly certify their exemption) if the holder fails to furnish its correct taxpayer identification number or otherwise fails to comply with applicable backup withholding requirements. U.S. holders who are required to establish their exempt status generally must provide a properly completed IRS Form W-9.

Backup withholding is not an additional tax. Amounts withheld as backup withholding may be credited against a U.S. holder's U.S. federal income tax liability. A U.S. holder generally may obtain a refund of any amounts withheld under the backup withholding rules by filing the appropriate claim for refund with the IRS in a timely manner and furnishing any required information. U.S. holders are advised to consult with their own tax advisors regarding the application of the United States information reporting rules to their particular circumstances.

A non-U.S. holder generally may eliminate the requirement for information reporting and backup withholding by providing certification of its non-U.S. status to the payor, under penalties of perjury, on IRS Form W-8BEN or W-8BEN-E, as applicable. You should consult your own tax advisor as to the qualifications for exemption from backup withholding and the procedures for obtaining the exemption.

The foregoing does not purport to be a complete analysis of the potential tax considerations relating to the ownership and disposition of the ADSs. Prospective investors should consult their own tax advisors as to the particular tax considerations applicable to them relating to the ownership and disposition of the ADSs, including the applicability of U.S. federal, state and local income tax laws or non-income tax laws, non-U.S. tax laws, and any changes in applicable tax laws and any pending or proposed legislation or regulations.

Material French Income Tax Considerations

The following describes the material French income tax consequences to U.S. Holders (as defined below for the purposes of this section) of purchasing, owning and disposing of the ADSs and, unless otherwise noted, this discussion is the opinion of Jones Day, our French tax counsel, insofar as it relates to matters of French tax law and legal conclusions with respect to those matters.

This discussion does not purport to be a complete analysis or listing of all potential tax effects of the acquisition, ownership or disposition of our ADSs to any particular investor, and does not discuss tax considerations that arise from rules of general application or that are generally assumed to be known by investors. All of the following is subject to change. Such changes could apply retroactively and could affect the consequences described below.
In 2011, France introduced a comprehensive set of new tax rules applicable to French assets that are held by or in foreign trusts. These rules, among other things, provide for the inclusion of trust assets in the settlor's net assets for purpose of applying the French real estate wealth tax, for the application of French gift and death duties to French assets held in trust, for a specific tax on capital on the French assets of foreign trusts not already subject to the French real estate wealth tax and for a number of French tax reporting and disclosure obligations. The following discussion does not address the French tax consequences applicable to securities (including ADSs) held in trusts. If securities are held in trust, the grantor, trustee and beneficiary are urged to consult their own tax advisors regarding the specific tax consequences of acquiring, owning and disposing of securities.

The description of the French income tax and wealth tax consequences set forth below is based on the Convention between the Government of the United States of America and the Government of the French Republic for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income and Capital of August 31, 1994 which came into force on December 30, 1995 (as amended by any subsequent protocols, including the protocol of January 13, 2009), and the tax guidelines issued by the French tax authorities in force as of the date hereof, or the Treaty.

For the purposes of this discussion of French income tax consequences, the term "U.S. Holder" means a beneficial owner of ADSs that is (1) an individual who is a U.S. citizen or resident for U.S. federal income tax purposes, (2) a U.S. domestic corporation or certain other entities created or organized in or under the laws of the United States, any state thereof, or the District of Columbia, or (3) otherwise subject to U.S. federal income taxation on a net income basis in respect of ADSs.

If a partnership (or any other entity treated as partnership for U.S. federal income tax purposes) holds ADSs, the tax treatment of a partner generally will depend upon the status of the partner and the activities of the partnership. If a U.S. Holder is a partner in a partnership that holds ADSs, such holder is urged to consult its own tax adviser regarding the specific tax consequences of acquiring, owning and disposing of ADSs.

This discussion applies only to investors that hold our ADSs as capital assets that have the U.S. dollar as their functional currency, that are entitled to Treaty benefits under the "Limitation on Benefits" provision contained in the Treaty, and whose ownership of the ADSs is not effectively connected to a permanent establishment or a fixed base in France. Certain U.S. Holders (including, but not limited to, U.S. expatriates, partnerships or other entities classified as partnerships for U.S. federal income tax purposes, banks, insurance companies, regulated investment companies, tax-exempt organizations, financial institutions, persons subject to the alternative minimum tax, persons who acquired the ADSs pursuant to the exercise of employee share options or otherwise as compensation, persons that own (directly, indirectly or by attribution) 5% or more of our voting stock or 5% or more of our outstanding share capital, dealers in securities or currencies, persons that elect to mark their securities to market for U.S. federal income tax purposes and persons holding ADSs as a position in a synthetic security, straddle or conversion transaction) may be subject to special rules not discussed below.

U.S. Holders are urged to consult their own tax advisors regarding the tax consequences of the purchase, ownership and disposition of ADSs in light of their particular circumstances, especially with regard to the "Limitations on Benefits" provision.

Estate and Gift Taxes

In general, a transfer of ADSs by gift or by reason of death of a U.S. Holder that would otherwise be subject to French gift or inheritance tax, respectively, will not be subject to such French tax by reason of the Convention between the Government of the United States of America and the Government of the French Republic for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Estates, Inheritances and Gifts, dated November 24, 1978 (as amended by the protocol dated from December 8, 2004), unless the donor or the transferor is domiciled in France at the time of making the gift or at the time of his or her death, or the ADSs were used in, or held for use in, the conduct of a business through a permanent establishment or a fixed base in France.

Financial Transactions Tax

Pursuant to Article 235 ter ZD of the French Tax Code (*Code général des impôts*), or the FTC, purchases of certain securities issued by a French company, including ADSs, which are listed on a regulated market of the EU or a foreign regulated market formally acknowledged by the AMF (in each case within the meaning of the French Monetary and Financial Code, or the FMFC) are subject in France to a 0.3% tax on financial transactions, or the FTT, provided inter alia that the issuer's market capitalization exceeds €1.0 billion as of December 1 of the year preceding the taxation year.

A list of French relevant companies whose market capitalization exceeds €1.0 billion as of December 1 of the year preceding the taxation year within the meaning of Article 235 ter ZD of the French Tax Code is published annually by the French tax authorities. As of December 1, 2021, our market capitalization did not exceed €1 billion.

As a result, the ADSs are not currently within the scope of the FTT. Purchases of our ADSs may however become subject to the FTT if our market capitalization exceeds €1.0 billion

Registration Duties

In the case where the FTT is not applicable, (1) transfers of shares issued by a French company which are listed on a regulated or organized market within the meaning of the FMFC are subject to uncapped registration duties at the rate of 0.1% if the transfer is evidenced by a written statement (*acte*) executed either in France or outside France, whereas (2) transfers of shares issued by a French company which are not listed on a regulated or organized market within the meaning of the FMFC are subject to uncapped registration duties at the rate of 0.1% notwithstanding the existence of a written statement (*acte*).

As ordinary shares of Nanobiotix are listed on the regulated market of Euronext in Paris, which is an organized market within the meaning of the FMFC, their transfer should be subject to uncapped registration duties at the rate of 0.1% subject to the existence of a written agreement (*acte*).

Although there is neither case law nor official guidelines published by the French tax authorities on this point, transfers of ADSs should not be subject to the aforementioned 0.1% registration duties.

Wealth Tax

The French wealth tax (*impôt de solidarité sur la fortune*) has been repealed by the finance bill for 2018 (*loi de finances pour 2018*) dated December 30, 2017. It used to apply only to individuals and did not generally apply to ADSs held by a U.S. resident, as defined pursuant to the provisions of the Treaty, provided that such U.S. Holder did not own directly or indirectly more than 25% of the issuer's financial rights and that the ADSs did not form part of the business property of a permanent establishment or fixed base in France.

Since January 1, 2018, it has been replaced by a new real estate wealth tax (*impôt sur la fortune immobilière*), which applies only to individuals owning French real estate assets or rights, directly or indirectly through one or more legal entities and whose net taxable assets amount to at least €1,300,000.

French real estate wealth tax may only apply to U.S. Holders to the extent the company holds real estate assets that are not allocated to its operational activity, for the fraction of the value of the financial rights representing such assets, and should not generally apply to securities held by an eligible U.S. Holder who is a U.S. resident, as defined pursuant to the provisions of the Treaty, provided that such U.S. Holder does not own directly or indirectly more than 25% of the issuer's financial rights.

Taxation of Dividends

Dividends paid by a French corporation to non-residents of France are generally subject to French withholding tax at a rate of 25% for corporate bodies or other legal entities or 12.8% for individuals. Dividends paid by a French corporation in a non-cooperative State or territory, as set out in the list referred to in Article 238-0 A of the FTC, other than those mentioned in 2° of 2 bis of the same Article 238-0 A of the FTC, will generally be subject to French withholding tax at a rate of 75%.

However, eligible U.S. Holders, other than individuals subject to the French withholding tax at a rate of 12.8%, entitled to Treaty benefits under the "Limitation on Benefits" provision contained in the Treaty who are U.S. residents, as defined pursuant to the provisions of the Treaty, will not be subject to this 25% or 75% withholding tax rate, but may be subject to the withholding tax at a reduced rate (as described below).

Under the Treaty, the rate of French withholding tax on dividends paid to an eligible U.S. Holder who is a U.S. resident as defined pursuant to the provisions of the Treaty and whose ownership of the ADSs is not effectively connected with a permanent establishment or fixed base that such U.S. Holder has in France, is generally reduced to 15%, or to 5% if such U.S. Holder is a corporation and owns directly or indirectly at least 10% of the share capital

of the issuer; such U.S. Holder may claim a refund from the French tax authorities of the amount withheld in excess of the Treaty rates of 15% or 5%, if any.

For U.S. Holders that are not individuals but are U.S. residents, as defined pursuant to the provisions of the Treaty, the requirements for eligibility for Treaty benefits, including the reduced 5% or 15% withholding tax rates contained in the "Limitation on Benefits" provision of the Treaty, are complex, and certain technical changes were made to these requirements by the protocol of January 13, 2009. U.S. Holders are advised to consult their own tax advisors regarding their eligibility for Treaty benefits in light of their own particular circumstances.

In the event that dividends are paid by us, dividends paid to an eligible U.S. Holder may immediately be subject to the reduced rates of 5% or 15% provided that:

- such holder establishes before the date of payment that it is a U.S. resident under the Treaty by completing and providing the depositary with treaty forms (Forms 5000 and 5001); or
- the depositary or other financial institution managing the U.S. Holder's securities account in the U.S. provides the French paying agent, which will complete Forms 5000 and 5001 (as described above), with a document listing certain information about the U.S. Holder and its ADSs and a certificate whereby the financial institution managing the U.S. Holder's securities account in the U.S. takes full responsibility for the accuracy of the information provided in the document.

Otherwise, dividends paid to a U.S. Holder that is a legal person or another legal entity and has not filed Forms 5000 and 5001 before the dividend payment date will be subject to French withholding tax at the rate of 25%, or 75% for any U.S. Holder if paid in a non-cooperative State or territory (as set out in the list referred to in Article 238-0 A of the FTC other than those mentioned in 2° of 2 bis of the same Article 238-0 A of the FTC) (unless the company proves that neither the purpose nor the effect of paying the dividend in that State or territory is that of allowing, with the intent of tax evasion or avoidance, the U.S. Holder to be located in such a State or territory), and then reduced at a later date to 5% or 15%, provided that such holder duly completes and provides the French tax authorities with Forms 5000 and 5001 before December 31 of the second calendar year following the year during which the dividend is paid.

Certain qualifying pension funds and certain other tax-exempt entities are subject to the same general filing requirements as other U.S. Holders except that they may have to supply additional documentation evidencing their entitlement to these benefits.

Forms 5000 and 5001, together with appropriate instructions, will be provided by the depositary to all U.S. Holders registered with the depositary. The depositary will arrange for the filing with the French tax authorities of all such forms properly completed and executed by U.S. Holders of ADSs and returned to the depositary in sufficient time so that they may be filed with the French tax authorities before the distribution in order to obtain immediately a reduced withholding tax rate. Otherwise, the depositary must withhold tax at the full rate of 25% or 75%, as applicable. In that case, the U.S. Holders may claim a refund from the French tax authorities of the excess withholding tax. Since the withholding tax rate applicable under French domestic law to U.S. Holders who are individuals does not exceed the cap provided in the Treaty (i.e., 15%), the 12.8% rate shall apply, without any reduction provided under the Treaty.

Subject to certain specific conditions, a corporate U.S. Holder which is in a tax loss position for the fiscal year during which the dividend is received may be entitled to a deferral regime and to obtain a withholding tax refund. Furthermore subject to certain conditions, a corporate U.S. Holder may compute the withholding tax on a net basis (i.e., after deduction of expenses) and obtain a partial withholding tax refund.

Tax on Sale or Other Disposition

As a matter of principle, under French tax law, a U.S. Holder should not be subject to any French tax on any capital gain from the sale, exchange, repurchase or redemption by us of ADSs, provided such U.S. Holder is not a French tax resident for French tax purposes and has not held more than 25% of our dividend rights, known as "*droits aux bénéfices sociaux*" at any time during the preceding five years, either directly or indirectly, and, as relates to individuals, alone or with relatives (as an exception, a U.S. Holder resident, established or incorporated in a non-cooperative State or territory as set out in the list referred to in Article 238-0 A of the FTC other than those mentioned in 2° of 2 bis of the same Article 238-0 A of the FTC should be subject to a 75% withholding tax in France on any such capital gain, regardless of the fraction of the dividend rights it holds).

Under the Treaty, a U.S. Holder who is a U.S. resident for purposes of the Treaty and entitled to Treaty benefit will not be subject to French tax on any such capital gain from the sale, exchange, repurchase or redemption by us (other than redemption proceeds which may, under certain circumstances, be partially or fully characterized as dividends under French domestic tax law or administrative guidelines) of ADSs unless such ADSs form part of the business property of a permanent establishment or fixed base that the U.S. Holder has in France. U.S. Holders who own ADSs through U.S. partnerships that are not resident for Treaty purposes are advised to consult their own tax advisors regarding their French tax treatment and their eligibility for Treaty benefits in light of their own particular circumstances. A U.S. Holder that is not a U.S. resident for Treaty purposes or is not entitled to Treaty benefit (and in

both cases is not resident, established or incorporated in a non-cooperative State or territory as set out in the list referred to in Article 238-0 A of the FTC other than those mentioned in 2° of 2 bis of the same Article 238-0 A of the FTC) and has held more than 25% of our dividend rights, known as "*droits aux bénéfices sociaux*" at any time during the preceding five years, either directly or indirectly, and, as relates to individuals, alone or with relatives, will be subject to a levy in France at the rate of the standard corporate income tax (at a rate of 25%), if such U.S. Holder is a legal person, or 12.8%, if such U.S. Holder is an individual.

For a non-French resident entity that holds more than 25% of our dividend rights and may be subject to French tax on capital gains, the Amended Finance Bill for 2021 dated July 19, 2021 (published July 20, 2021) amended the provisions of Article 244 bis B of the FTC in order to comply with European Union (EU) law as French courts have recently ruled that such provisions previously did not comply with European principles and therefore could not be applied by the French tax authorities as the basis for French taxation of foreign shareholders (CE, 14 October 2020, n°421524, AVM International and CAA Versailles, 20 October 2020, n°18VE03012, Sté Runa Capital Fund I LP). The Amended Finance Bill for 2021 provides for a refund mechanism allowing an eligible non-French resident corporate investors to claim a refund of the non-resident French capital gains tax to the extent such tax exceeds the amount of the French corporate income tax it would have borne if it had been a French resident. This refund mechanism is available to entities established in (i) an EU Member State or a Member State of the European Economic Area (EEA), other than a non-cooperative State or Territory within the meaning of Article 238-0 A of the FTC that has concluded a tax treaty with France that includes an administrative assistance provision to combat tax fraud and tax evasion (an "EU/EEA State") or (ii) a State, other than a non-cooperative State or Territory that has concluded a tax treaty with France that includes an administrative assistance clause regarding the exchange of information aimed at combating tax fraud and tax evasion (a "Treaty State"), provided that the transferor is not effectively involved in the management or control of the entity whose shares are disposed of or redeemed. In addition, the Amended Finance Bill provides that specific collective investment funds established in EU/EEA States or Treaty States are excluded from the scope of the nonresident capital gain tax mentioned above under certain conditions. The recent amendments described above will apply to dispositions and redemptions of shares, and distributions, subject to Section 244 bis B of the FTC, realized as from June 30, 2021.

Special rules apply to U.S. Holders who are residents of more than one country.

The discussion above is a summary of the material French tax consequences of an investment in our ADSs and is based upon laws and relevant interpretations thereof in effect as of the date hereof, all of which are subject to change, possibly with retroactive effect. It does not cover all tax matters that may be of importance to a prospective investor. Each prospective investor is urged to consult its own tax advisor about the tax consequences to it of an investment in ADSs in light of the investor's own circumstances.

F. Dividends and Paying Agents

Not applicable.

G. Statement by Experts

Not applicable.

H. Documents on Display

We are subject to the information reporting requirements of the Exchange Act applicable to foreign private issuers and under those requirements file reports with the SEC. Those reports may be inspected without charge at the locations described below. As a foreign private issuer, we are exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our supervisory and executive board members and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as United States companies whose securities are registered under the Exchange Act. Nevertheless, we file with the SEC an Annual Report containing financial statements that have been examined and reported on, with and opinion expressed by an independent registered public accounting firm, and we submit quarterly interim consolidated financial data to the SEC under cover of the SEC's Form 6-K.

We maintain a corporate website at *www.nanobiotix.com*. We intend to post our Annual Report on our website promptly following it being filed with the SEC. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference.

The SEC maintains a website (http://www.sec.gov) that contains reports, proxy and information statements and other information regarding registrants, such as Nanobiotix, that file electronically with the SEC.

With respect to references made in this Annual Report to any contract or other document of Nanobiotix, such references are not necessarily complete and you should refer to the exhibits attached or incorporated by reference to this Annual Report for copies of the actual contract or document.

I. Subsidiary Information

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Foreign Currency Exchange Risk

We use the euro as our functional currency and the substantial majority of our operations are denominated in euros. At this stage in our development, we are exposed to minimal foreign exchange risk due to our low exposure to transactions outside the eurozone in the normal course of business.

As of the date of this Annual Report, we have not used hedging to protect our business against exchange rate fluctuations. However, a significant increase in business activity in jurisdictions in which currencies other than the euro are used could lead to greater exposure to currency risk. As of December 31, 2021, we recorded foreign exchange gains for an amount of €6.3 million as a result of USD proceeds from IPO held (see Notes 14 and 18 of our consolidated financial statements). As of December 31, 2020, we recorded foreign exchange losses for an amount of €1.7 million (see Notes 14 and 18 of our consolidated financial statements). This impact was first arising from retaining $113.3 million of gross proceeds from the IPO on the Nasdaq in a US dollar bank account. After deduction of the transaction costs, this amount was a total of €84.0 million, net of related transaction expenses. As of December 31, 2020, the proceeds from our initial public offering are still held in US dollars on our current account for a total amount of €72.0 million and will be used to pay services invoiced in USD. The remaining factors for this increase in foreign exchange risk is the one-off Neuflize account's closing. While part the reasons for these foreign exchange losses were related to one-off events, we are currently updating our assessment of this risk for the year 2021 (see Note 14 of our consolidated financial statements).

Interest Rate Risk

Our exposure to interest rate risk is primarily related to our cash equivalents and investment securities, which consist of money market mutual funds (SICAVs). We had cash and cash equivalents of €83.9 million as of December 31, 2021, as compared with €119.15 million as of December 31, 2020, which amounts at each date consisted of bank accounts and short-term deposits. Changes in interest rates have a direct impact on the interest earned from these investments and the cash flows generated; however, historical fluctuations in interest income have not been significant.

In July 2018, we entered into an agreement for the EIB loan under which we may borrow a total of up to €40 million, divided into three disbursement tranches, two of which were received as of December 31, 2019. The interest rate payable under the loan agreement is a fixed rate based on the applicable disbursement tranche: 6% (payable on maturity), 5% (payable semi-annually) and 4% (payable semi-annually) for the first, second and third tranches, respectively. We also committed, under a royalty agreement entered into in connection with the EIB loan, for a period of six years beginning on January 1, 2021, to pay additional interest in the form of royalties, calculated according to the number of tranches that have been withdrawn and indexed on our annual sales turnover. Any such royalties would be due by June 30 of the year following such sales. In the event the loan is repaid early, or in the event of a change of control after repayment of the loan, the EIB is entitled to request payment of an amount 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. As the variable rate of any such royalties due will depend not on the performance of the financial markets, but on our performance, our exposure to interest rate and market risk is deemed low.

On June 18, 2020, Curadigm executed the Deep Tech Funding. The Deep Tech Funding did not have a material impact on our interest rate risk.

On June 22, 2020, the Company entered into a €5 million PGE with HSBC France (the ‘‘HSBC PGE Loan’’). The HSBC PGE Loan did not have a material impact on our interest rate risk.

On July 20, 2020, the Company entered into a €5 million PGE with BpiFrance (the ‘‘BpiFrance PGE Loan’’). The BpiFrance PGE Loan did not have a material impact on our interest rate risk.

In the ordinary course of business, we may enter into contractual arrangements to reduce our exposure to interest rate risks. However, we do not believe that a 10% change in current interest rates would have a significant impact on our consolidated financial statements.

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.
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 its customers' high credit rating for other receivables.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt Securities

Not applicable.

B. Warrants and Rights

Not applicable.

C. Other Securities

Not applicable.

D. American Depositary Shares

Citibank, N.A., as depositary for our ADSs, registers and delivers ADSs. Each ADS represents one ordinary share deposited with Citibank Europe PLC, located at 388 Greenwich Street, New York, NY 10013 or any successor, as custodian for the depositary. Each ADS will also represent any other securities, cash or other property which may be held by the depositary in respect of the depositary facility. The depositary's corporate trust office at which the ADSs will be administered is located at 388 Greenwich Street, New York, New York 10013.

A deposit agreement among us, the depositary and the ADS holders sets out the ADS holder rights as well as the rights and obligations of the depositary. New York law governs the deposit agreement and the ADSs. A copy of the Agreement is incorporated by reference as an exhibit to this Annual Report.

For additional information on our ADSs, please refer to Exhibit 2.3 "Description of Securities" of this Annual Report.

Fees and Charges

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

Service	Fees
Issuance of ADSs (e.g., an issuance of ADS(s) upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares pursuant to stock dividends or other free stock distributions or to the exercise of rights to purchase additional ADSs	Up to U.S. 5¢ per ADS issued
Issuance of ADSs (e.g., an issuance of ADS(s) upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares pursuant to stock dividends or other free stock distributions or to the exercise of rights to purchase additional ADSs	Up to U.S. 5¢ per ADS cancelled
Issuance of ADSs (e.g., an issuance of ADS(s) upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares pursuant to stock dividends or other free stock distributions or to the exercise of rights to purchase additional ADSs	Up to U.S. 5¢ per ADS held
Issuance of ADSs (e.g., an issuance of ADS(s) upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares pursuant to stock dividends or other free stock distributions or to the exercise of rights to purchase additional ADSs	Up to U.S. 5¢ per ADS held
Issuance of ADSs (e.g., an issuance of ADS(s) upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares pursuant to stock dividends or other free stock distributions or to the exercise of rights to purchase additional ADSs to purchase additional ADSs	Up to U.S. 5¢ per ADS held
Issuance of ADSs (e.g., an issuance of ADS(s) upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares pursuant to stock dividends or other free stock distributions or to the exercise of rights to purchase additional ADSs	Up to U.S. 5¢ per ADS held on the applicable record date(s) established by the depositary bank
Issuance of ADSs (e.g., an issuance of ADS(s) upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares pursuant to stock dividends or other free stock distributions or to the exercise of rights to purchase additional ADSs to purchase additional ADSs	Up to U.S. 5¢ per ADS transferred
Issuance of ADSs (e.g., an issuance of ADS(s) upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares pursuant to stock dividends or other free stock distributions or to the exercise of rights to purchase additional ADSs	Up to U.S. 5¢ per ADS converted

As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;
- the fees, expenses, spreads, taxes and other charges of the depositary and/or conversion service providers in connection with the conversion of foreign currency, such fees, expenses, spreads, taxes, and other charges to be deducted from the foreign currency;
- any reasonable and customary out-of-pocket expenses incurred in such conversion and/or on behalf of holders and beneficial owners of ADSs in complying with currency exchange control or other governmental requirements; and

- the fees, costs and expenses incurred by the depositary, the custodian, or any nominee in connection with the servicing or delivery of deposited property.

ADS fees and charges payable upon (1) deposit of ordinary shares against issuance of ADSs and (2) surrender of ADSs for cancellation and withdrawal of ordinary shares are charged to the person to whom the ADSs are delivered (in the case of ADS issuances) and to the person who delivers the ADS, for cancellation (in the case of ADS cancellations). In the case of ADSs issued by the depositary into DTC or presented to the depositary via DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs or the DTC participant(s) surrendering the ADSs for cancellation, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account(s) of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participant(s) as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (1) distributions other than cash and (2) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs.

In the event of refusal to pay the depositary fees, the depositary may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees from any distribution to be made to the ADS holder.

The fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary. You will receive prior notice of such changes. The depositary may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary agree from time to time.

PART II

ITEM 13. DEFAULTS, DIVIDENDS ARREARAGES AND DELINQUENCIES

Not applicable.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

Initial Public Offering

On December 15, 2020, we sold 7,300,000 new ordinary shares, including 5,445,000 ADSs, each representing one ordinary share, nominal value €0.03, in our initial public offering in the United States (the "U.S. Offering") at a price of $13.50 per ADS and 1,855,000 ordinary shares in a concurrent offering of ordinary shares in certain jurisdictions outside of the United States to certain investors (the "European Offering" and, together with the U.S. Offering, the "Global Offering") at a corresponding offering price of €11.14 per ordinary share, for aggregate gross proceeds of $98.6 million. On December 18, 2020, in connection with the exercise by the underwriters of their option to purchase additional shares, we sold an additional 1,095,000 ADSs at the public offering price of $13.50 per ADS resulting in additional gross proceeds of $14.8 million. We incurred aggregate underwriting discounts of $7.9 million and expenses of $5.0 million, resulting in net proceeds to us of $100.4 million. The net proceeds from the Global Offering have been used and are expected to continue to be used as described in the final prospectus filed with the U.S. Securities and Exchange Commission on December 11, 2020. No payments were made directly or indirectly to any executive or supervisory board member of ours or to their associates, persons owning ten percent or more of any class of our equity securities, or to any of our affiliates. The offering commenced on December 10, 2020 and did not terminate before all of the securities registered in the registration statement were sold. Jefferies LLC acted as global coordinator and joint book-running manager for the Global Offering, and Evercore Group, L.L.C. and UBS Securities LLC acted as joint book-running managers for the U.S. Offering. Gilbert Dupont acted as manager for the European Offering.

ITEM 15. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

Our management, with the participation of our Chairman of the Executive Board (principal executive officer) and our chief financial officer (principal financial officer), has evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of the end of the period covered by this Annual Report on Form 20-F.

Based on the foregoing, our Chairman of the Executive Board (principal executive officer) and chief financial officer (principal financial officer) have concluded that, as of December 31, 2021, our disclosure controls and procedures were effective and ensure that information required to be disclosed by us in reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chairman of the Executive Board (principal executive officer) and chief financial officer (principal financial officer), to allow timely decisions regarding required disclosure and is recorded, processed, summarized and reported within the time periods specified by the SEC's rules and forms.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Our management, with the participation of our Chairman of the Executive Board (principal executive officer) and our chief financial officer (principal financial officer), has assessed the effectiveness of internal control over financial reporting as of December 31, 2021. Our management's assessment was based on the framework in "Internal Control Integrated Framework", or 2013 framework, issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO.

Based on that assessment, our management concluded that, as of December 31, 2021, our internal control over financial reporting was effective to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes, in accordance with generally accepted accounting principles.

Due to its inherent limitations, internal control over financial reporting may not prevent or detect misstatements, and can only provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Changes in Control over Financial Reporting

We have made certain changes in internal controls over financial reporting in preparation for the inclusion of our first Section 404 report in this Annual Report.

In addition, prior to the issuance of our interim financial statements as of and for the six months ended June 30, 2021, a deficiency, which constituted a material weakness in our internal control over financial reporting, was identified. The material weakness related to the timing of the recognition of expenses associated with new contracts signed with certain contract research organizations for one of our clinical trials.

During the year ended December 31, 2021, we remediated the identified material weakness in internal control over financial reporting identified above, under the supervision of management and the oversight of our Audit Committee, as described below:

- The Company expanded its internal control staffing, with the hiring of an employee with significant expertise in the deployment, maintenance and ongoing monitoring of Sarbanes-Oxley Section 404 controls, and strengthened the applicable skills for employees involved in internal control over financial reporting.
- The Company implemented a more robust data collection system, including circularizing the purchase-to-pay process such that a sample of customers are asked to confirm receivables and reinforcing data completeness controls through reliance on management-identified key reports.
- At the time contracts are executed, the Company implements a process in which a more detailed accounting analysis is undertaken and the Company's accounting personnel create an exhaustive list of all contractual obligations that will have an impact on financial accounts over the life of the agreement.
- The Company engaged an independent third-party specialist firm to perform and modernize certain internal audit functions. Based on this firm's specialized expertise and industry knowledge, it provides ongoing process improvements across the Company's internal control cycle.

We have tested and evaluated the implementation of these new and revised processes and internal controls to ascertain whether they are designed and operating effectively to provide reasonable assurance that they will prevent or detect a material error in our financial statements and have concluded that our internal control over financial reporting was effective as of December 31, 2021.

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Except as noted above, there were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the three months ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16. RESERVED

Not applicable.

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERT

Currently, our audit committee is comprised of two members: Mr. Enno Spillner (chairman) and Mr. Gary Phillips, and one observer, Mr. Christophe Douat, who attends in a non-voting capacity. Our supervisory board has determined that Mr. 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. Messrs. Spillner, Phillips and Douat are independent as such term is defined in Rule 10A-3 under the Exchange Act and under the listing standards of the Nasdaq Stock Market.

ITEM 16B. CODE OF ETHICS

We have adopted a Code of Conduct that is applicable to all of our, and our subsidiaries', employees, executive board members and supervisory board members. The Code of Conduct is available on our website at *www.nanobiotix.com*. Our supervisory board is responsible for overseeing the Code of Conduct and is required to approve any waivers of the Code of Conduct for employees, executive board members and supervisory board members. We expect that any amendments to the Code of Conduct, or any waivers of its requirements, will be disclosed on our website.

ITEM 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Ernst & Young et Autres, or Ernst & Young, has served as our independent registered public accounting firm for 2020 and 2021. Our accountants billed the following fees to us for professional services in each of those fiscal years:

	Year ended December 31,	
(in thousands of euros)	**2021**	**2020**
Audit Fees	655	1,264
Audit-Related Fees	100	—
Tax Fees	—	—
All Other Fees	—	—
Total	**755**	**1,264**

"Audit Fees" are the aggregate fees billed for the audit of our annual financial statements. This category also includes services that generally the independent accountant provides, such as consents and assistance with and review of documents filed with the SEC. In 2020 and in 2021, "Audit Fees" also includes fees billed for professional services regarding our initial public offering.

"Audit-Related Fees" are the aggregate fees billed for assurance and related services that are reasonably related to the performance of the audit and are not reported under Audit Fees.

"Tax Fees" are the aggregate fees billed for professional services rendered by the principal accountant for tax compliance, tax advice and tax planning related services.

"All Other Fees" relate to services provided with respect to our registration statement for our Global Offering.

Audit and Non-Audit Services Pre-Approval Policy

The audit committee has responsibility for appointing, setting compensation of and overseeing the work of the independent registered public accounting firm. In recognition of this responsibility, the audit committee has adopted a policy governing the pre-approval of all audit and permitted non-audit services performed by our independent registered public accounting firm to ensure that the provision of such services does not impair the independent registered public accounting firm's independence from us and our management. Unless a type of service to be provided by our independent registered public accounting firm has received general pre-approval from the audit committee, it requires specific pre-approval by the audit committee. The payment for any proposed services in excess of pre-approved cost levels requires specific pre-approval by the audit committee. All audit and non-audit services rendered by our independent registered public accounting firm in 2021 were pre-approved by the audit committee.

Pursuant to its pre-approval policy, the audit committee may delegate its authority to pre-approve services to the chairperson of the audit committee. The decisions of the chairperson to grant pre-approvals must be presented to the full audit committee at its next scheduled meeting. The audit committee may not delegate its responsibilities to pre-approve services to the management.

The audit committee has considered the non-audit services provided by Ernst & Young as described above and believes that they are compatible with maintaining Ernst & Young's independence as our independent registered public accounting firm.

ITEM 16D. EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Not applicable.

ITEM 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

Not applicable.

ITEM 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

Not applicable.

ITEM 16G. CORPORATE GOVERNANCE

As a French *société anonyme* listed on the regulated market of Euronext in Paris, we are subject to various corporate governance requirements under French law. In addition, as a foreign private issuer listed on the Nasdaq Global Select Market, we will be subject to the Nasdaq corporate governance listing standards. However, the Nasdaq listing standards permit foreign private issuers to follow home country corporate governance practices in lieu of the Nasdaq rules, with certain exceptions. Certain corporate governance practices in France may differ significantly from the Nasdaq corporate governance listing standards. For example, neither the corporate laws of France nor our By-laws require that (i) a majority of our directors be independent, (ii) our compensation committee include only independent directors, or (iii) our independent directors hold regularly scheduled meetings at which only independent directors are present. Other than as set forth below, we currently intend to comply with the corporate governance listing standards of Nasdaq to the extent possible under French law. However, we may choose to change such practices to follow home country practices in the future.

Even as a foreign private issuer, we are required to comply with Rule 10A-3 of the Exchange Act, relating to audit committee composition and responsibilities. Rule 10A-3 provides that the audit committee must have direct responsibility for the nomination, compensation and choice of our auditors, as well as control over the performance of the auditor's duties, management of complaints made, and selection of consultants. Under Rule 10A-3, if the laws of a foreign private issuer's home country require that any such matter be approved by board members or the shareholders of the company, the audit committee's responsibilities or powers with respect to such matter may instead be advisory.

Under French law, the audit committee may only have an advisory role and the appointment of our statutory auditors, in particular, must be approved by our shareholders at our annual meeting. Therefore, in accordance with Rule 10A-3, our audit committee will only have an advisory role with respect to the aforementioned responsibilities. Under French law, an audit committee may have only two members, whereas Nasdaq listing standards require a three-member audit committee. We currently intend to have only two members on our audit committee in accordance with French law. French law does not require our independent directors to hold regularly scheduled meetings at which only independent directors are present. We intend to follow home country practice in this regard, although, if the independent directors decide to meet in such executive sessions, they may do so.

In addition, Nasdaq rules require that a listed company specify that the quorum for any meeting of the holders of share capital be at least 33 1/3% of the outstanding shares of the company's common voting stock. We follow our French home country practice, rather than complying with this Nasdaq rule. Consistent with French law, our By-laws provide that when first convened, general meetings of shareholders may validly deliberate only if the shareholders present or represented hold at least (1) 20% of the shares entitled to vote in the case of an ordinary general meeting or of an extraordinary general meeting where shareholders are voting on a capital increase by capitalization of reserves, profits or share premium, or (2) 25% of the shares entitled to vote in the case of any other extraordinary general meeting. If such quorum required by French law is not met, the meeting is adjourned. There is no quorum requirement under French law when an ordinary general meeting or an extraordinary general meeting where shareholders are voting on a capital increase by capitalization of reserves, profits or share premium is reconvened, but the reconvened meeting may consider only questions that were on the agenda of the adjourned meeting. When any other extraordinary general meeting is reconvened, the required quorum under French law is 20% of the shares entitled to vote. If a quorum is not met at a reconvened meeting requiring a quorum, then the meeting may be adjourned for a maximum of two months. Further, Nasdaq rules require that listed companies have a compensation committee comprised solely of independent directors and that director nominees be selected solely by independent directors. We currently comply with this Nasdaq rule, but may in the future elect to follow French home country practice.

Finally, Nasdaq rules require shareholder approval when a plan or other equity compensation arrangement is established or materially amended. Under French law our shareholders must decide any issuance of equity, as a general matter. However, we intend to follow our French home country practice and ask our shareholders to delegate their authority to issue incentive equity and define the final terms of any equity compensation plan or arrangements to our executive board. We may, from time to time, ask for our shareholders' subsequent approval on an equity compensation arrangement in order to obtain advantageous tax treatment or otherwise. In addition, under French law, our executive board must obtain the prior approval of our shareholders before establishing or amending a plan or arrangement that would exceed the limits of the granted delegation.

ITEM 16H. MINE SAFETY DISCLOSURE

Not applicable.

ITEM 16I. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 17. FINANCIAL STATEMENTS

See pages F-1 through F-64 of this Annual Report.

ITEM 18. FINANCIAL STATEMENTS

Not applicable.

ITEM 19. EXHIBITS

Exhibit Index

The following exhibits are filed as part of this Annual Report:

Exhibit	Number Description of Exhibit	Schedule/ Form	File Number	Exhibit	File Date
1.1*	By-laws (*statuts*) of the registrant (English translation)	6-K	001-39777	4.1	February 4, 2022
2.1*	Deposit Agreement, by and among Nanobiotix S.A. and Citibank, N.A., as Depositary, and the holders and beneficial owners of American Depositary Shares, dated as of December 15, 2020	F-3	333-262545	4.2	February 4, 2022
2.2*	Form of American Depositary Receipt (included in Exhibit 2.1)	F-1	333-250707	Included in 4.2	November 20, 2020
2.3	Description of Securities registered under Section 12 of the Exchange Act				Filed herewith
4.1†^*	Finance Contract, by and between the European Investment Bank and Nanobiotix S.A., dated as of July 26, 2018 (the "EIB Finance Contract")	F-1	333-250707	10.3	November 20, 2020
4.2*	Amendment to the EIB Finance Contract, by and between the European Investment Bank and Nanobiotix S.A., dated as of July 20, 2020	F-1	333-250707	10.4	November 20, 2020
4.3†^*	Royalty Agreement, by and between the European Investment Bank and Nanobiotix S.A., dated as of July 26, 2018	F-1	333-250707	10.5	November 20, 2020
4.4†^*	Amended and Restated Strategic Collaboration Agreement, by and between The University of Texas M.D. Anderson Cancer Center and Nanobiotix S.A., dated as of January 23, 2020	F-1	333-250707	10.6	November 20, 2020
4.4.1†^	Amendment No. 1 to Amended and Restated Strategic Collaboration Agreement, by and between The University of Texas M.D. Anderson Cancer Center and Nanobiotix S.A., dated as of June 4, 2021				Filed herewith
4.5†	License, Development and Commercialization Agreement, by and between Nanobiotix S.A. and LianBio Oncology Limited, dated as of May 11, 2021				Filed herewith
4.6	Summary of HSBC France Loan, by and between HSBC France and Nanobiotix S.A., dated as of June 22, 2020				Filed herewith
4.7	Summary of Bpifrance Loan, by and between Bpifrance Financement and Nanobiotix S.A., dated as of July 10, 2020				Filed herewith
4.8*	Summary of BSA Plans	F-1	333-250707	10.7	November 20, 2020
4.9*#	Summary of BSPCE Plans	F-1	333-250707	10.8	November 20, 2020
4.10*#	2016 Stock Option Plan	F-1	333-250707	10.9	November 20, 2020
4.11*#	2016-2 Stock Option Plan	F-1	333-250707	10.10	November 20, 2020
4.12*#	2017 Stock Option Plan	F-1	333-250707	10.11	November 20, 2020
4.13*#	2018 Stock Option Plan	F-1	333-250707	10.12	November 20, 2020
4.14*#	2019 Stock Option Plan	F-1	333-250707	10.13	November 20, 2020

4.15*#	LLY 2019 Stock Option Plan	F-1	333-250707	10.14	November 20, 2020
4.16*#	Summary of Free Share Plans	F-1	333-250707	10.15	November 20, 2020
4.17*#	2020 stock option plan	20-F/A	001-39777	4.16	April 8, 2021
4.18*#	Summary of BSA Plan	20-F/A	001-39777	4.17	April 8, 2021
4.19*#	Summary of Free share Plan	20-F/A	001-39777	4.18	April 8, 2021
4.20#	2021 stock option plan	S-8	333-257239	99.2	June 21, 2021
8.1*	List of Subsidiaries of the Registrant	F-1	333-250707	21.1	November 20, 2020
12.1	Certification by the Principal Executive Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				Filed herewith
12.2	Certification by the Principal Financial Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				Filed herewith
13.1	Certification by the Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				Filed herewith
13.2	Certification by the Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				Filed herewith
15.1	Consent of Ernst & Young et Autres				Filed herewith
101	The following materials from Nanobiotix S.A.'s Report on Form 20-F formatted in iXBRL (Inline eXtensible Business Reporting Language): (i) the Statements of Consolidated Financial Position, (ii) the Statements of Consolidated Operations, (iii) the Statements of Consolidated Comprehensive Loss, (iv) the Statements of Consolidated Changes in Shareholders' Equity, (v) the Statements of Consolidated Cash Flows and (vi)				Filed herewith
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)				Filed herewith

** Indicates a document previously filed with the SEC.*
† Portions of this exhibit have been redacted in compliance with Regulation S-K Item 601(b)(10). The omitted information is not material and would likely cause competitive harm to the registrant if publicly disclosed.
^ Certain exhibits and schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The registrant hereby undertakes to furnish supplementally a copy of any omitted exhibit or schedule upon request by the SEC.
 # Indicates a management contract or any compensatory plan, contract or arrangement.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Supervisory Board and Shareholders of Nanobiotix S.A.,

Opinion on the Financial Statements

We have audited the accompanying statements of consolidated financial position of Nanobiotix S.A. (“the Company”) as of December 31, 2021 and 2020, and the related statements of consolidated operations, comprehensive loss, changes in shareholders’ equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its consolidated operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board (“IFRS”) and in accordance with International Financial Reporting Standards as endorsed by the European Union.

Basis for Opinion

These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ ERNST & YOUNG et Autres

We have served as the Company’s auditor since 2012.

Paris-La Défense, France

April 8, 2022

STATEMENTS OF CONSOLIDATED FINANCIAL POSITION
(Amounts in thousands of euros)

	Notes	As of December 31, 2021	2020
ASSETS			
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**

	Notes	As of December 31, 2021	2020
LIABILITIES AND SHAREHOLDER'S EQUITY			
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**

The accompanying notes form an integral part of these audited consolidated financial statements.

STATEMENTS OF CONSOLIDATED OPERATIONS
(Amounts in thousands of euros, except per share numbers)

	Notes	For the year ended December 31, 2021	2020	2019
Revenues and other income				
Revenues	**15**	10	50	68
Other income	**15**	2,637	2,462	2,473
Total revenues and other income		**2,647**	**2,512**	**2,541**
Research and development expenses	**16.1**	(30,378)	(24,330)	(30,411)
Selling, general and administrative expenses	**16.2**	(19,434)	(14,611)	(18,909)
Other operating income and expenses	**16.5**	(5,414)	—	—
Total operating expenses		**(55,226)**	**(38,941)**	**(49,320)**
Operating income (loss)		**(52,579)**	**(36,428)**	**(46,779)**
Financial income	**18**	6,360	201	837
Financial expenses	**18**	(780)	2,646	(4,970)
Financial income (loss)		**5,580**	**2,847**	**(4,133)**
Income tax	**19**	(5)	(9)	(3)
Net loss for the period		**(47,003)**	**(33,590)**	**(50,915)**
Basic loss per share (euros/share)	**21**	**(1.35)**	**(1.38)**	**(2.35)**
Diluted loss per share (euros/share)	**21**	**(1.35)**	**(1.38)**	**(2.35)**

The accompanying notes form an integral part of these audited consolidated financial statements.

STATEMENTS OF CONSOLIDATED COMPREHENSIVE LOSS
(Amounts in thousands of euros)

	Notes	For the year ended December 31, 2021	2020	2019
Net loss for the period		**(47,003)**	**(33,590)**	**(50,915)**
Actuarial gains and losses on retirement benefit obligations (IAS 19)	**11.1**	182	(4)	88
Tax impact		—	—	—
Other comprehensive loss that will not be reclassified subsequently to income or loss		**182**	**(4)**	**88**
Currency translation adjustment		(94)	125	(36)
Tax impact		—	—	—
Other comprehensive income that may be reclassified subsequently to income or loss		**(94)**	**125**	**(36)**
Total comprehensive loss		**(46,915)**	**(33,469)**	**(50,863)**

The accompanying notes form an integral part of these audited consolidated financial statements.

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 January 1, 2019		**19,633,373**	**589**	**122,799**	**381**	**(124)**	**(79,057)**	**(30,345)**	**14,243**
Net loss for the period		—	—	—	—	—	—	(50,915)	(50,915)
Currency translation adjustments		—	—	—	(36)	—	—	—	(36)
Actuarial gains and losses (IAS 19)	**11.2**	—	—	—	88	—	—	—	88
Total comprehensive loss		**—**	**—**	**—**	**52**	**—**	**—**	**(50,915)**	**(50,863)**
Allocation of prior period loss		—	—	—	—	—	(30,345)	30,345	—
Capital increase, net		2,566,666	77	28,002	—	—	—	—	28,079
BSPCE exercise		215,000	6	1,300	—	—	—	—	1,306
Subscription of warrants	**10.3**	—	—	8	—	—	13	—	21
Share based payment	**17**	—	—	—	—	—	4,320	—	4,320
Treasury shares		—	—	—	—	(45)	—	—	(45)
U.S. Initial public offering costs offset	**10.1**	—	—	1,030	—	—	—	—	1,030
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, net		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, net		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**

The accompanying notes form an integral part of these audited consolidated financial statements.

STATEMENTS OF CONSOLIDATED CASH FLOWS
(Amounts in thousands of euros)

	Notes	For the year ended December 31, 2021	2020	2019
Cash flows used in operating activities				
Net loss for the period		(47,003)	(33,590)	(50,915)
Elimination of other non-cash, non-operating income and expenses				
Depreciation and amortization	**16.4**	1,560	1,754	1,767
Provisions		152	(48)	164
Expenses related to share-based payments	**17**	3,201	2,924	4,320
Cost of net debt		2,224	2,115	1,940
Loss on disposals		—	—	45
U.S. Initial public offering 2018 costs reversal		—	—	201
Impact of deferred income related to financial liabilities discounting effect		(1,554)	(6,463)	2,833
Other charges with no impact on cash		8	7	(5)
Cash flows used in operations, before tax and changes in working capital		**(41,412)**	**(33,300)**	**(39,647)**
(Increase) / Decrease in trade receivables	**8.1**	62	(51)	(85)
Decrease in Research tax credit receivable	**8.2**	1,927	5,688	—
Increase in other receivables	**8.2**	(5,034)	(721)	(4,640)
Increase / (Decrease) in trade and other payables	**13.1**	(281)	(995)	2,057
Increase / (Decrease) in other current liabilities	**13.2**	(1,652)	1,840	1,146
Increase in deferred income and contract liabilities	**13.3**	16,518	—	—
Changes in operating working capital		**11,540**	**5,762**	**(1,522)**
Net cash flows used in operating activities		**(29,872)**	**(27,538)**	**(41,169)**
Cash flows from (used in) investing activities				
Acquisitions of intangible assets	**5**	(5)	(11)	(353)
Acquisitions of property, plant and equipment	**6**	(228)	(96)	(1,091)
Addition in non-current financial assets	**7**	(9)	(4)	(16)
Net cash flows from (used in) investing activities		**(242)**	**(112)**	**(1,459)**
Cash flows from financing activities				
Capital increases	**10.1**	—	113,650	29,517
Warrants subscription	**10.1**	43	5	1,327
Transaction costs	**10.1**	(349)	(10,359)	(1,438)
Increase in loans and conditional advances	**12**	—	10,350	14,000
Loans repayments	**12**	(2,833)	(250)	(500)
Payment of lease liabilities	**12**	(909)	(928)	(1,067)
Interest paid	**12**	(1,132)	(700)	(350)
Net cash flows from financing activities		**(5,180)**	**111,769**	**41,489**
Effect of exchange rates changes on cash		64	(63)	29
Net increase (decrease) in cash and cash equivalents		**(35,230)**	**84,056**	**(1,109)**
Net cash and cash equivalents at beginning of period		**119,151**	**35,094**	**36,203**
Net cash and cash equivalents at end of period	**9**	**83,921**	**119,151**	**35,094**

The accompanying notes form an integral part of these audited consolidated financial statements.

NOTES TO THE AUDITED CONSOLIDATED FINANCIAL STATEMENTS AS OF DECEMBER 31, 2021 AND 2020, AND FOR THE YEARS ENDED DECEMBER 31, 2021, 2020 AND 2019

Note 1. Company information

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").

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 in March 2021 a $2.5 million payment following the announcement of Nanobiotix's collaboration with LianBio for the Asia-Pacific region. In May 2021, PharmaEngine received an additional $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**"). Mr. 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.

Note 2. General Information, Statement of Compliance and Basis of Presentation

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, 2020 and 2019 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.

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 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.

Note 3. Consolidation principles and methods

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 and $1.1234 and $1.1196 for 2019, 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.

The consolidated financial statements as of and for the year ended December 31, 2019 include the operations of each of these subsidiaries from the date of their incorporation, excluding Curadigm Corp which was created in 2020.

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).

Note 4. Significant transactions

4.1 LianBio

In May 2021, Nanobiotix announced a partnership with LianBio Oncology Limited 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.

4.2 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 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 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.

4.3 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, 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 Company has not yet met the criteria to request this tranche. 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.

4.4 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 product 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 were 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.

Note 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:

(in thousands of euros)	**As of As of January 1, 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*

(in thousands of euros)	**As of January 1, 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	(0)	(0)	(630)
Accumulated depreciation of intangible assets [(1)]	**(548)**	**(152)**	**5**	**—**	**—**	**(695)**
Net book value of intangible assets	**163**	**(141)**	**—**	(0)	(0)	**21**

[(1)] *Expenses for the period are detailed in Note 16.4 Depreciation, amortization and provisions expenses*

Note 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 1, 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**

In 2021, the €1,362 thousand increase in Right of use – Buildings mainly relates to the extension of Villejuif leases for 4 years for €1,390 thousand reduced by approximately €25 thousand related to rent indexation impact.

The €139 thousand decrease in Right of use – Buildings relates to the termination of a lease contract in Faubourg Saint-Antoine in Paris, France.

(in thousands of euros)	As of January 1, 2020	Increases	Decreases	Other movements & 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 Rue Oberkampf in Paris, France for €155 thousand, the other in Rue du 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 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.

Note 7. Non-current financial assets

Accounting policies

Non-current financial assets are recognized and measured in accordance with IFRS 9 – *Financial Instruments.*
No non-current financial assets are estimated at fair value through other comprehensive income (OCI).

Pursuant to IFRS 9 – *Financial Instruments*, financial assets are classified in three 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 Company 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:

(in thousands of euros)	**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)
Transfer	—	—	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 a €9 thousand deposit paid in connection with a new 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.

Note 8. Trade receivables and other current assets

Accounting policies for trade receivables and other current assets are described in Note 7.

8.1 Trade receivables

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 the related receivables have been settled.

	As of December 31,	
(in thousands of euros)	**2021**	**2020**
Trade receivables	—	62
Trade receivables	**—**	**62**

Trade receivables break down as follows:

	As of December 31,	
(in thousands of euros)	**2021**	**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**

8.2 Other current assets

Other current assets break down as follows:

	As of December 31,	
(in thousands of euros)	**2021**	**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 the 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.

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 research tax credit receivables breaks down as follows:

(in thousands of euros)	
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**

Note 9. Cash and cash equivalents

Accounting policy

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

Cash and cash equivalent break down as follows:

(in thousands of euros)	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 of €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 €0.5 million; and
- other cash flows used in operating activities.

Note 10. Share Capital

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 or 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	0	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	Private placement Capital increase	99	20,030	3,300,000
July 28, 2020	Private placement 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 definitive acquisition of free shares 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.

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.

10.3 Founders' warrants, warrants, stock options and free shares

Accounting policies

Accounting policies for share-based payments are described in Note 17.

Detail of change in founders' warrants, warrants, 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, 2021 and 2020.

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	December 18, 2012	6.63	100,000	—	—	—	100,000	100,000
BSPCE 08-2013	August 28, 2013	5.92	50,000	—	—	—	50,000	50,000
BSPCE 09-2014	September 16, 2014	18.68	86,150	—	—	—	86,150	86,150
BSPCE 2015-1	February 10, 2015	18.57	68,450	—	—	—	68,450	68,450
BSPCE 2015-3	June 10, 2015	20.28	30,700	—	—	(350)	30,350	30,350
BSPCE 2016	February 2, 2016	14.46	202,617	—	—	(1,776)	200,841	200,841
BSPCE 2017	January 7, 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	December 18, 2012	6.63	100,000	—	—	—	100,000	100,000
BSPCE 08-2013	August 28, 2013	5.92	50,000	—	—	—	50,000	50,000
BSPCE 09-2014	September 16, 2014	18.68	92,100	—	—	(5,950)	86,150	86,150
BSPCE 2015-1	February 10, 2015	18.57	70,950	—	—	(2,500)	68,450	68,450
BSPCE 2015-3	June 10, 2015	20.28	38,400	—	—	(7,700)	30,700	30,700
BSPCE 2016	February 2, 2016	14.46	212,969	—	—	(10,352)	202,617	202,617
BSPCE 2017	January 7, 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 office.

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.

Warrant Plans (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	May 4, 2012	6.00	30,000	—	—	—	30,000	30,000
BSA 2013	April 10, 2013	6.37	6,000	—	—	—	6,000	6,000
BSA 2014	September 16, 2014	17.67	10,000	—	—	—	10,000	10,000
BSA 2015-1	February 10, 2015	17.67	21,000	—	—	—	21,000	21,000
BSA 2015-2(a)	June 25, 2015	19.54	64,000	—	—	—	64,000	64,000
BSA 2015-2(b)	June 25, 2015	19.54	—	—	—	—	—	—
BSA 2016	February 2, 2016	13.74	36,208	—	—	(36,208)	—	—
BSA 2016-2	November 3, 2016	15.01	8,000	—	—	(8,000)	—	—
BSA 2017	January 7, 2017	15.76	18,000	—	—	—	18,000	18,000
BSA 2018-1	March 6, 2018	13.55	28,000	—	—	—	28,000	28,000
BSA 2018-2	July 27, 2018	16.102	5,820	—	—	—	5,820	5,820
BSA 2019-1	March 29, 2019	11.66	18,000	—	—	—	18,000	18,000
BSA 2020	March 17, 2020	6.59	18,000	—	—	—	18,000	18,000
BSA 2021 (a)	April 21, 2021	13.47	—	48,103	—	(33,672)	14,431	14,431
BSA 2021 (b)	April 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	May 4, 2012	6.00	30,000	—	—	—	30,000	30,000
BSA 2013	April 10, 2013	6.37	6,000	—	—	—	6,000	6,000
BSA 2014	September 16, 2014	17.67	10,000	—	—	—	10,000	10,000
BSA 2015-1	February 10, 2015	17.67	21,000	—	—	—	21,000	21,000
BSA 2015-2(a)	June 25, 2015	19.54	64,000	—	—	—	64,000	64,000
BSA 2015-2(b)	June 25, 2015	19.54	6,000	—	—	(6,000)	—	—
BSA 2016	February 2, 2016	13.74	36,208	—	—	—	36,208	36,208
BSA 2016-2	November 3, 2016	15.01	8,000	—	—	—	8,000	8,000
BSA 2017	January 7, 2017	15.76	18,000	—	—	—	18,000	18,000
BSA 2018-1	March 6, 2018	13.55	28,000	—	—	—	28,000	28,000
BSA 2018-2	July 27, 2018	16.102	5,820	—	—	—	5,820	5,820
BSA 2019-1	March 29, 2019	11.660	18,000	—	—	—	18,000	18,000
BSA 2020	March 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 was 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 10-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 Option Plans (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	February 2, 2016	13.05	400	—	—	—	400	400
OSA 2016-2	November 3, 2016	14.26	4,000	—	—	—	4,000	4,000
OSA 2017	January 7, 2017	14.97	500	—	—	—	500	500
OSA 2018	March 6, 2018	12.87	52,000	—	—	—	52,000	52,000
OSA 2019-1	March 29, 2019	11.08	28,750	—	—	(500)	28,250	28,250
OSA LLY 2019	October 24, 2019	6.41	500,000	—	—	—	500,000	500,000
OSA 2020	March 11, 2020	6.25	400,709	—	—	(13,253)	387,456	387,456
OSA 2021-04	April 20, 2021	13.74	—	571,200	—	(80,000)	491,200	491,200
OSA 2021-06	June 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	February 2, 2016	13.05	400	—	—	—	400	400
OSA 2016-2	November 3, 2016	14.26	4,000	—	—	—	4,000	4,000
OSA 2017	January 7, 2017	14.97	500	—	—	—	500	500
OSA 2018	March 6, 2018	12.87	54,000	—	—	(2,000)	52,000	52,000
OSA 2019-1	March 29, 2019	11.08	30,250	—	—	(1,500)	28,750	28,750
OSA LLY 2019	October 24, 2019	6.41	500,000	—	—	—	500,000	500,000
OSA 2020	March 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 10-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 Mr. 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 Mr. 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 Mr. 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 Mr. 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.

By way of exception, the Executive Board decided to lift the continued service condition of the OSA 2020 for two former Executive Board members as well as to accelerate, as from June 30, 2021, the vesting of the OSA 2020 one of these former executive board members holds, enabling him to exercise all of them, in the context of his departure from the Company.

Free share plans (AGA)

Type	Grant date	Exercise price (in euros)	Outstanding at January 1, 2021	Issued	Definitively acquired	Forfeited	Outstanding at December 31, 2021	Number of shares exercisable
AGA 2018-1	March 6, 2018	n.a.	24,500	—	(24,500)	—	—	—
AGA 2018-2	July 27, 2018	n.a.	—	—	—	—	—	—
AGA 2019-1	March 29, 2019	n.a.	372,000	—	(369,250)	(2,750)	—	—
AGA 2020	March 11, 2020	n.a.	50,000	—	—	—	50,000	50,000
AGA 2021	April 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	Definitively acquired	Forfeited	Outstanding at December 31, 2020	Number of shares exercisable
AGA 2018-1	March 6, 2018	n.a.	355,250	—	(316,083)	(14,667)	24,500	24,500
AGA 2018-2	July 27, 2018	n.a.	6,000	—	(6,000)	—	—	—
AGA 2019-1	March 29, 2019	n.a.	385,000	—	—	(13,000)	372,000	372,000
AGA 2020	March 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 Ms. 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 Ms. 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 March 17, 2021, the Executive Board acknowledged the definitive acquisition of 24,500 free shares granted on March 6, 2018 following a three-year acquisition period, thus acknowledging the related share capital increase of €735.

At a meeting on April 1, 2021, the Executive Board acknowledged the definitive acquisition of 369,250 free shares granted on March 29, 2019 following a two-year acquisition period, thus acknowledging the related share capital increase of €11,077.50.

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).

Note 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).

(in thousands of euros)	As of January 1, 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 thousands of euros)	As of January 1, 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*

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.

11.2 Non-current provisions

Commitments for retirement benefits

	As of December 31,	
(in thousands of euros)	2021	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.

Note 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

	As of December 31,	
(in thousands of euros)	**2021**	**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 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, is bearing 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.

12.1 Conditional advance, bank loan and loans from government and public authorities

The table below shows the detail of liabilities recognized on the statements of financial position by type of conditional advances and loans from government and public authorities.

Conditional advances and loans from government and public authorities

(in thousands of euros)	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

(in thousands of euros)	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.

12.2 Lease liabilities

The table below shows the detail of changes in lease liabilities recognized on the statements of financial position over the periods disclosed:

(in thousands of euros)	Lease liabilities
As of January 1st, 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**

12.3 Due dates of the financial liabilities

The due dates for repayment of the advances loans and lease liabilities at their nominal value and including fixed-rate interest are as follows:

	As of December 31, 2021			
(in thousands of euros)	**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.

Note 13. Trade payables and other current liabilities

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 of invoices received at the closing date.

Details of trade and other payables

	As of December 31,	
(in thousands of euros)	**2021**	**2020**
Accrued expenses - clinical trials	1,486	1,532
Trade payables & other accruals	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.

13.2 Other current liabilities

	As of December 31,	
(in thousands of euros)	**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.

13.3 Deferred revenues and contract liabilities

	As of December 31,	
(in thousands of euros)	**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.

Note 14. Financial instruments included in the statement of financial position and impact 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			
(in thousands of euros)	**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 thousands of euros)	**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 financial 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. subsidiaries, 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 outside the euro zone 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. subsidiaries as of December 31, 2021, and 2020.

	For the year ended December 31, 2021			
Impact	**Net income**		**Equity**	
(in thousands of euros)	**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**	
(in thousands of euros)	**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 its customers' 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.

Note 15. Revenues and other income

Accounting policies

Revenue

Revenue is recognized in accordance with IFRS 15.

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.

We identified the separate performance obligations of the contract under IFRS 15. The agreement 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 payments 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 per category for the years ended December 31, 2021, 2020, and 2019.

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Services	5	50	40
Other sales	5	—	28
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	**2,637**	**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.

100% of the revenues recognized in 2021, 2020 and 2019 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.

Note 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).

Accounting policies for research and development expenses are described in Note 5.

16.1 Research and development expenses

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Purchases, sub-contracting and other expenses	(19,562)	(12,734)	(16,804)
Payroll costs (including share-based payments)	(9,605)	(10,306)	(11,980)
Depreciation, amortization and provision expenses[(1)]	(1,211)	(1,290)	(1,627)
Total research and development expenses	**(30,378)**	**(24,330)**	**(30,411)**

(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 and 81 research and development staff, including 2 additional positions created during the year ended December 31, 2019.

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 and €902 thousand in 2019.

16.2 Selling, General and Administrative (SG&A) expenses

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Purchases, fees and other expenses	(9,638)	(6,482)	(9,435)
Payroll costs (including share-based payments)	(9,379)	(7,789)	(9,205)
Depreciation, amortization and provision expenses [(1)]	(417)	(340)	(270)
Total SG&A expenses	**(19,434)**	**(14,611)**	**(18,909)**

(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.

These increases in fees and other expenses were partially offset by the decrease in rental expenses following the application of IFRS 16 for the year ended December 31, 2019.

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 and a Company's workforce of 29 staff in SG&A functions, including 6 additional positions created during the year ended December 31, 2019.

The impact of share-based payments (excluding employer's contribution) on SG&A expenses amounted to €2.5 million in 2021, as compared with €2.3 million in 2020 and €3.4 million in 2019.

16.3 Payroll costs

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Wages and salaries	(11,391)	(11,141)	(11,876)
Payroll taxes	(4,308)	(3,953)	(4,913)
Share-based payments	(3,201)	(2,924)	(4,320)
Retirement benefit obligations	(84)	(76)	(76)
Total payroll costs	**(18,984)**	**(18,094)**	**(21,185)**
Average headcount	96	97	112
End-of-period headcount	100	90	110

As of December 31, 2021, the Company's workforce totaled 100 employees, compared with 90 December 31, 2020 and 110 as of December 31, 2019.

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 2019, wages and salaries and payroll taxes, together, reached €16.8 million due to the Company's growth and a related increase in the number of employees during the year ended December 31, 2019, together with the impact of its compensation policy.

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 and €4.3 million as of December 31, 2019 (see Note 17).

16.4 Depreciation, amortization and provision expenses

Depreciation, amortization and provision expenses by function are detailed as follows:

	For the year ended December 31, 2021		
(in thousands of euros)	**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)**

	For the year ended December 31, 2020		
(in thousands of euros)	**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)**

	For the year ended December 31, 2019		
(in thousands of euros)	**R&D**	**SG&A**	**Total**
Amortization expense of intangible assets	(289)	(3)	(292)
Depreciation expense of property, plant and equipment	(1,208)	(270)	(1,478)
Utilization of provision for charges	—	55	55
Provision for charges	(112)	(52)	(164)
Total depreciation, amortization and provision expenses	**(1,609)**	**(270)**	**(1,879)**

16.5 OTHER OPERATING INCOME AND EXPENSES

	For the year ended December 31, 2021	
(in thousands of euros)	**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.

Note 17. Share-based payments

Accounting policy

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 remuneration 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**
Type of underlying asset	New shares	New shares	New shares	New shares	New shares
Number of founder's warrants granted	100,000	50,000	97,200	71,650	53,050
Date of shareholders' resolution approving the plan	05/04/2012	06/28/2013	06/18/2014	06/18/2014	06/18/2014
Grant date	12/18/2012	08/28/2013	09/16/2014	02/10/2015	06/10/2015
Contractual expiration date	12/18/2022	08/28/2023	09/16/2024	02/10/2025	06/10/2025
Grant price	—	—	—	—	—
Exercise price	€6.63	€5.92	€18.68	€18.57	€20.28
Number of founders' warrants as of Number of founders' warrants as of December 31, 2021	**100,000**	**50,000**	**86,150**	**68,450**	**30,350**
Number of founders' warrants exercised	—	—	—	—	—
Including founders' warrants exercised during the period	—	—	—	—	—
Number of founders' warrants lapsed or cancelled	—	—	11,050	3,200	22,700
Including founders' warrants lapsed or cancelled during the period	—	—	—	—	*350*

	Pre-2021 founders' warrant plans			
	BSPCE 2016 Ordinary	**BSPCE 2016 Performance**	**BSPCE 2017 Ordinary**	**BSPCE 2017**
Type of underlying asset	New shares	New shares	New shares	New shares
Number of founder's warrants granted	126,400	129,250	117,650	80,000
Date of shareholders' resolution approving the plan	06/25/2015	06/25/2015	06/23/2016	06/23/2016
Grant date	02/02/2016	02/02/2016	01/07/2017	01/07/2017
Contractual expiration date	02/02/2026	02/02/2026	01/08/2027	01/07/2027
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	—	—	—
Including founders' warrants exercised during the period	—	—	—	—
Number of founders' warrants lapsed or cancelled	25,500	28,976	18,150	—
Including founders' warrants lapsed or cancelled during the period	*350*	*1,426*	*1,350*	—

Warrants

	Pre-2021 warrant plans						
	BSA 04-2012	**BSA 2013**	**BSA 2014**	**BSA 2015-1**	**BSA 2015-2 (a)**	**BSA 2015-2 (b)**	**BSA 2016 ordinary**
Type of warrants	New shares	New shares	New shares	New shares	New shares	New shares	New shares
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	05/04/2012	05/04/2012	06/18/2014	06/18/2014	06/18/2014	06/25/2015	06/25/2015
Grant date	05/04/2012	04/10/2013	09/16/2014	02/10/2015	06/25/2015	06/25/2015	02/02/2016
Contractual expiration date	05/04/2022	04/10/2023	09/16/2024	02/10/2025	06/25/2025	06/25/2020	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 warrants exercised	*22,500*	—	—	—	—	—	—
Including warrants exercised during the period	—	—	—	—	—	—	—
Number of warrants lapsed or cancelled	—	4,000	4,000	5,000	—	6,000	18,103
Including warrants lapsed or cancelled during the period	—	—	—	—	—	—	*18,103*

	Pre-2021 warrant plans						
	BSA 2016 performance	**BSA 2016-2**	**BSA 2017**	**BSA 2018-1**	**BSA 2018-2**	**BSA 2019-1**	**BSA 2020**
Type of warrants	New shares	New shares	New shares	New shares	New shares	New shares	New shares
Number of warrants granted	18,105	8,000	18,000	28,000	5,820	18,000	18,000
Date of shareholders' resolution approving the plan	06/25/2015	06/23/2016	06/23/2016	06/14/2017	05/23/2018	05/23/2018	04/11/2019
Grant date	02/02/2016	11/03/2016	01/07/2017	03/06/2018	07/27/2018	03/29/2019	03/17/2020
Contractual expiration date	02/02/2021	11/03/2021	01/07/2022	03/06/2023	07/27/2028	03/29/2029	03/17/2030
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	€16.102	€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	—	—	—	—	—	—	—
Including warrants exercised during the period	—	—	—	—	—	—	—
Number of warrants lapsed or cancelled	18,105	8,000	—	—	—	—	—
Including warrants lapsed or cancelled during the period	*18,105*	*8,000*	—	—	—	—	—

	2021 warrants	
	BSA 2021 (a)	**BSA 2021 (b)**
Type of warrants	New shares	New shares
Number of warrants granted	48,103	30,000
Date of shareholders' resolution approving the plan	11/30/2020	11/30/2020
Grant date	04/20/2021	04/20/2021
Contractual expiration date	04/20/2031	04/20/2031
Grant price	€2.95	€0.68
Number of warrants as of Exercise price	€13.47	€13.64
Number of warrants as of December 31, 2021	**14,431**	**30,000**
Number of warrants exercised	—	—
Including warrants exercised during the period	—	—
Number of warrants lapsed or cancelled	33,672	—
Including warrants lapsed or cancelled during the period	*33,672*	—

Stock options

	Pre-2021 stock option plans						
	OSA 2016-1 Performance	**OSA 2016-2**	**OSA 2017 Ordinary**	**OSA 2018**	**OSA 2019-1**	**OSA LLY 2019**	**OSA 2020**
Type of underlying asset	New shares	New shares	New shares	New shares	New shares	New shares	New shares
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	—	—	—	—	—	—	—
Number of options as of Including options exercised during the period	—	—	—	—	—	—	—
Number of options lapsed or cancelled	6,000	—	3,000	10,000	9,250	—	13,253
Including options lapsed or cancelled during the period	—	—	—	—	*500*	—	*13,253*

	2021 stock option plans	
	OSA 2021-04	**OSA 2021-06**
Type of underlying asset	New shares	New shares
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	—	—
Number of options as of Including options exercised during the period	—	—
Number of options lapsed or cancelled	80,000	—
Including options lapsed or cancelled during the period	*80,000*	—

Free shares

	Pre-2021 free shares plan not yet vested				2021 free shares plan
	AGA 2018-1	**AGA 2018-2**	**AGA 2019-1**	**AGA 2020**	**AGA 2021**
Type of underlying assets	New shares	New shares	New shares	New shares	New shares
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 cancelled	55,667	—	69,000	—	2,003
Including free shares lapsed or cancelled 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**

	BSPCE	BSA	OSA	AGA	Total
Total number of shares underlying grants outstanding as of December 31, 2019	**751,585**	**251,028**	**589,150**	**746,250**	**2,338,013**

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.

BSPCE	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 for the year ended 2021 *(in thousands of euros)*	Expense for the year ended 2020 *(in thousands of euros)*	Expense for the year ended 2019 *(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	—	—	10
BSPCE 2016 Performance	14.46	14.46	59%	5	0.19%	0.00 %	1,212	32	99	79
BSPCE 2017 Ordinary	15.93	15.93	58% - 61% - 59%	5.5/6/6.5	0.23%	0.00 %	1,000	0	8	86
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**	**175**

BSA	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 for the year ended 2021 *(in thousands of euros)*	Expense for the year ended 2020 *(in thousands of euros)*	Expense for the year ended 2019 *(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 %	0.00 %	37	—	—	—
BSA 2016p-1	13.74	13.74	57 %	2.4	0.00 %	0.00 %	143	—	—	(41)
BSA 2016-2	15.01	15.01	57 %	2.4	0.00 %	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% - 0.1%	0.00 %	2	—	—	—
BSA 2018-2	16.102	16.102	38 %	4.8	0.7% - 0.1%	0.00 %	1	—	—	—
BSA 2019-1	11.66	11.66	37 %	9.8/9.9	0.16% - 0.50%	0.00 %	24	—	—	24
BSA 2020	—	6.59	38 %	10	-0.13%/ -0.07%	0.00 %	19	—	19	—
BSA 2021 (a)	13.47	13.47	39.10 %	10	0.27 %	0.00 %	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**	**(16)**

OSA	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 for the year ended 2021 *(in thousands of euros)*	Expense for the year ended 2020 *(in thousands of euros)*	Expense for the year ended 2019 *(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	—	—	3
OSA 2017 Ordinary	15.93	14.97	58% - 61% - 59%	5.5 / 6 /6.5	0.23%	0.00%	31	—	—	1
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%	0.00%	252	—	7	66
OSA 2019-1	11.08	11.08	38.1% / 37.4%	6 /6.5	0.103% / 0.149%	0.00%	140	17	49	38
OSA 2019-2	6.41	6.41	37 %	10	0.40%	0.00%	252	—	—	436
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 %	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 %	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**	**543**

AGA	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 for the year ended 2021 *(in thousands of euros)*	Expense for the year ended 2020 *(in thousands of euros)*	Expense for the year ended 2019 *(in thousands of euros)*
AGA 2018-1	12.87	0.00	n.a.	n.a.	0.00%	0.00%	4,951	16	268	2,052
AGA 2018-2	12.87	0.00	n.a.	n.a.	0.00%	0.00%	75	—	21	37
AGA 2019-1	10.90	0.00	n.a.	n.a.	0.19% / 0.141%	0.00%	4,776	422	1,884	1,529
AGA 2020	5.90	0.00	n.a.	n.a.	-0.74%/-0.69%	0.00 %	287	144	116	—
AGA 2021	13.60	0.00	n.a.	n.a.	-0.63%/ -0.59%	0.00%	4,869	1,784	—	—
Total AGA	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**n.a.**	**2,366**	**2,289**	**3,618**

(in thousands of euros)	BSPCE	BSA	OSA	AGA	Total
Expense for the year ended December 31, 2021	32	44	760	2,366	**3,202**

(in thousands of euros)	BSPCE	BSA	OSA	AGA	Total
Expense for the year ended December 31, 2020	107	19	509	2,289	**2,924**

(in thousands of euros)	BSPCE	BSA	OSA	AGA	Total
Expense for the year ended December 31, 2019	175	(16)	543	3,618	**4,320**

Note 18. Net financial income (loss)

	For the years ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Income from cash and cash equivalents	—	—	105
Foreign exchange gains	6,347	104	599
Other financial income	13	97	133
Total financial income	**6,360**	**201**	**837**
Interest cost	(383)	4,676	(4,434)
IFRS 16 related interests	(288)	(333)	(359)
Foreign exchange losses	(109)	(1,697)	(176)
Total financial expenses	**(780)**	**2,646**	**(4,970)**
Net financial income (loss)	**5,580**	**2,847**	**(4,133)**

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.

Note 19. Income tax

Accounting policy

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.

Detail of 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:

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Net loss	(47,003)	(33,590)	(50,915)
Effective tax expense	5	9	3
Recurring loss before tax	**(47,058)**	**(33,581)**	**(50,912)**
Theoretical tax rate (statutory rate in France)	26.50 %	28.00 %	31.00 %
Theoretical tax (benefit) expense	**(12,470)**	**(9,403)**	**(15,782)**
Share-based payment	848	819	1,339
Other temporary differences	117	(6)	(1)
Other non-taxable items	(644)	(540)	(736)
Unrecognized tax losses	12,154	9,138	15,177
Effective tax expense	**5**	**9**	**3**
Effective tax rate	**0.00 %**	**0.00 %**	**0.00 %**

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.

Note 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, 2020 and 2019 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.

Note 21. Loss per share

Accounting policy

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.

	For the year ended December 31,		
	2021	**2020**	**2019**
Net loss for the period (in thousands of euros)	(47,063)	(33,590)	(50,915)
Weighted average number of shares	34,733,418	24,385,827	21,631,514
Basic loss per share (in euros)	**(1.35)**	**(1.38)**	**(2.35)**
Diluted loss per share (in euros)	**(1.35)**	**(1.38)**	**(2.35)**

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.

Note 22. Commitments

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.

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.

22.3 Obligations related to 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 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 6 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 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.

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.

Note 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:

	For the year ended December 31,		
(in thousands of euros)	**2021**	**2020**	**2019**
Salaries, wages and benefits	1,245	1,073	1,306
Share-based payments	2,018	1,723	2,066
Supervisory Board's fees	375	70	70
Total compensation to related parties	**3,638**	**2,866**	**3,442**

The methods used to measure share-based payments are presented in Note 17.

Note 24. Subsequent events

Accounting policy

The statements of consolidated financial position and statements of consolidated operations are adjusted for post-closing events prior to the approval of the financial statements for issuance as long as they have a significant impact of the amounts presented at the closing date of the statement of financial position. If they do not, they are disclosed.

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, it is currently impossible to exclude any delay in this clinical trial activity, even if no significant delay has been identified as of the date of issuance of this Annual 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.

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SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

NANOBIOTIX S.A.

/s/ LAURENT LEVY

By: Laurent Levy, Ph.D.

Title: Chairman of the Executive Board

Date: April 8, 2022