NANOBIOTIX: New Data Featuring NBTXR3 Plus Chemoradiation and in the Preoperative Setting Support Broad Applicability for Head and Neck Cancer and Other Solid Tumor Indications

June 5, 2022

Data reported at the 2022 Annual Meeting of the American Society for Clinical Oncology

- NBTXR3 is being developed as a product candidate with potential to integrate across the standards of care in oncology, and these data from collaborator-sponsored phase 1b/2 studies add support for the radioenhancer in combination with chemoradiation and in the preoperative setting
- Data from the phase 1b/2 head and neck cancer study in 12 evaluable patients with stage 4 disease showed that combining NBTXR3 with concurrent chemoradiation was feasible, had a favorable safety profile, produced a 100% disease control rate, and an overall response rate of 58.3%
- Data from the phase 1b/2 rectal cancer study in 31 evaluable patients with unresectable disease showed that combining NBTXR3 with concurrent chemoradiation in the preoperative setting was feasible, had a favorable safety profile, enabled 96% of evaluable patients to undergo R0 surgery, produced a 100% disease-control rate, a 35.5% overall response rate, and a 20% pathological complete response rate in 25 patients who underwent surgery

PARIS & CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 5, 2022-- Regulatory News:

NANOBIOTIX (Euronext : NANO — Nasdaq: NBTX – the " **Company**"), a late-clinical stage biotechnology company pioneering physics-based approaches to expand treatment possibilities for patients with cancer, today announced the reporting of new data at the 2022 Annual Meeting of the American Society for Clinical Oncology (ASCO) featuring potential first-in-class radioenhancer NBTXR3 in combination with concurrent chemoradiation for the treatment of head and neck cancer and rectal cancer. Nanobiotix also presented a trial-in-progress poster on the study design of the Company's ongoing pivotal phase 3 study, NANORAY-312, evaluating NBTXR3 as a single agent activated by radiotherapy for the treatment of elderly and frail patients with locally advanced head and neck squamous cell carcinoma (LA-HNSCC) who are ineligible for platinum-based chemotherapy (cisplatin).

In view of the Company's strategy for development of NBTXR3 as a product candidate that can integrate across solid tumor indications along with major treatment modalities within each indication, starting with head and neck cancer, the company believes these new data add support for the radioenhancer in combination with chemoradiation and as a neoadjuvant (preoperative) therapy with the potential to improve surgical outcomes. "Revolutionizing treatment outcomes for millions of patients with cancer will require integration of NBTXR3 across solid tumor indications, treatment modalities, and lines of therapy where radiation is a part of the treatment regimen—starting with head and neck cancer," said Laurent Levy, co-founder and chairman of the executive board at Nanobiotix. "Taken together with the clinical data we have already produced for NBTXR3 as a single agent activated by radiotherapy and as a combination agent with anti-PD-1, we view the new chemoradiation data presented at ASCO as critical validation of NBTXR3's feasibility across the standard of care. As we continue to prioritize our ongoing pivotal phase 3 study for elderly and frail patients with locally advanced head and neck squamous cell carcinoma, our aim is to build a comprehensive approach to the treatment of patients with locally advanced head and neck cancer that will serve as a model for our radioenhancer in other indications."

A Comprehensive Approach to Locally Advanced Head and Neck Cancer Inclusive of Chemoradiation

Most cisplatin-eligible patients with LA-HNSCC receive multimodal therapy including high dose concurrent chemoradiation (CCRT) as the standard of care. While CCRT has shown to improve local control and extend survival, the toxicity of high dose cisplatin creates challenges. These challenges appear both in terms of compliance with the treatment regimen for patients undergoing therapy that can impair efficacy, and in terms of the patients' quality of life after treatment. Although changes to the treatment protocol have been explored in randomized studies to reduce toxicity and improve compliance, reduction in toxicity has also led to reduction in efficacy.

These patients need innovative new therapeutic options that do not create additional burden in their administration, do not add combined toxicity to radiotherapy and chemotherapy, and have the potential to improve survival.

A Phase 1b/2 Study Evaluating NBTXR3 in Combination with Concurrent Chemoradiation for Patients with Locally Advanced or Recurrent Head and Neck Squamous Cell Carcinoma

This study, sponsored, executed, and reported by former Nanobiotix collaborator in Asia, PharmaEngine, Inc. (PEI), sought to evaluate the safety and feasibility of NBTXR3 intratumoral injection when added to low-dose weekly cisplatin-containing CCRT for patients with locally advanced or recurrent head and neck squamous cell carcinoma. The study also aimed to establish the recommended phase 2 dose (RP2D), however the RP2D was not determined due to stoppage of the phase 1b part of the trial resulting from the conclusion of the collaboration between PEI and Nanobiotix in 2021.

Adult patients with T3-4 LA-HNSCC suitable for cisplatin were eligible for the study and 12 such patients were enrolled. These patients received a single intratumoral injection of NBTXR3, followed by a low-dose weekly regimen of CCRT. All 12 patients were deemed evaluable and all had stage 4 locally advanced disease.

Of these evaluable patients, 3, 6, and 3 patients received NBTXR3 at the 5%, 10%, and 15% dose levels, respectively. No serious adverse events

(SAEs) inconsistent with what would normally be expected from a low-dose CCRT regimen were observed. Dose-limiting toxicities of grade 3 increased ALT and grade 3 increased AST were observed in one patient at the 10% dose level. Common Grade 3 adverse events (AEs) observed across dose levels were stomatitis, decreased WBC, decreased appetite, decreased neutrophil count, and leukopenia. One patient experienced grade 4 hyponatremia.

Preliminary efficacy results showed a disease control rate of 100%, with an overall response rate of 58.3% according to RECIST 1.1. The study concluded that adding a single intratumoral injection of NBTXR3 to weekly low dose cisplatin-containing CCRT was feasible and had a favorable safety profile for patients with LA-HNSCC.

Strengthening Support for NBTXR3 in Combination with Chemoradiation in the Preoperative Setting

Colorectal cancer (CRC) is the third most common cancer indication worldwide and the second leading cause of cancer-related death in the United States. One-third of CRCs appear in the rectum. For patients with locally advanced rectal cancer (LARC), combined modality therapy with neoadjuvant CCRT, followed by total mesorectal excision (TME; surgery), followed by adjuvant (post-operative) systemic chemotherapy is the current standard of care. The aim of the neoadjuvant portion of the treatment regimen is to control and downstage the disease to allow for R0 TME (surgical removal with a negative margin in which no gross or microscopic tumor remains in the primary tumor bed), as clinical studies have shown a positive correlation between improved cancer-specific survival and R0 TME. While outcomes have improved, patients are still faced with a highly toxic treatment regimen that can lead to a lack of compliance which may hamper efficacy, along with deteriorated quality of life after treatment.

Innovation with the potential to improve the rate of R0 resection without adding toxicity is an urgent need for this patient population.

A Phase 1b/2 Study Evaluating NBTXR3 in Combination with Concurrent Chemoradiation in the Neoadjuvant Setting for Patients with Locally Advanced or Unresectable Rectal Cancer

This study, sponsored, executed, and presented by PEI, sought to evaluate safety, feasibility, and early signs of efficacy for neoadjuvant NBTXR3 combined with CCRT followed by surgery for patients with locally advanced or unresectable rectal cancer. The study established the recommended phase 2 dose of NBTXR3 at 22% of gross tumor volume, however the phase 2 part of the trial was stopped as a result of the conclusion of the collaboration between PEI and Nanobiotix in 2021. Adult and older patients with T3-T4 locally advanced or unresectable rectal cancer suitable for chemoradiation were eligible for the study and 32 such patients were enrolled. These patients received a single intratumoral injection of NBTXR3, followed by a weekly regimen of CCRT. 31 of 32 patients were deemed evaluable and none of the evaluable patients had tumors eligible for surgery at the time of diagnosis.

Of the 31 evaluable patients, 6, 4, 3, and 18 patients received NBTXR3 at the 5%, 10%, 15%, and 22% dose levels, respectively. No NBTXR3-related SAEs or grade ≥ 3 AEs were observed. The most frequently reported AEs were grade 1 or 2 decreased WBC, diarrhea, increased CRP, UTI, and decreased lymphocyte count which were all consistent with what would normally be expected from CCRT.

Preliminary efficacy results showed a disease control rate of 100%, with an overall response rate of 35.5% according to RECIST 1.1. Pathological tumor downstaging was observed in 14 of 31 patients after therapy, 25 patients underwent surgery, and 96% of those patients achieved R0 surgical margins. Pathological complete response was observed in 20% of the patients who received surgery. The study concluded that a single intratumoral injection of NBTXR3 in combination with CCRT is feasible and has a favorable safety profile in the neoadjuvant setting for patients with locally advanced or unresectable rectal adenocarcinoma.

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About NBTXR3

NBTXR3 is a novel, potentially first-in-class oncology product composed of functionalized hafnium oxide nanoparticles administered via one-time intratumoral injection and activated by radiotherapy. The product candidate's physical mechanism of action (MoA) is designed to induce significant tumor cell death in the injected tumor when activated by radiotherapy, subsequently triggering adaptive immune response and long-term anti-cancer memory. Given the physical MoA, Nanobiotix believes that NBTXR3 could be scalable across any solid tumor that can be treated with radiotherapy and across any therapeutic combination, particularly immune checkpoint inhibitors.

About NANOBIOTIX

Nanobiotix is a late-stage clinical biotechnology company pioneering disruptive, physics-based therapeutic approaches to revolutionize treatment outcomes for millions of patients; supported by people committed to making a difference for humanity. The company is leveraging its proprietary nanoparticle platform, including its lead product candidate, radiotherapy activated NBTXR3, to develop a pipeline of therapeutic options designed to enhance local and systemic control of solid tumors with an initial focus on the treatment of head and neck cancers.

For more information about Nanobiotix, visit us at www.nanobiotix.com or follow us on LinkedIn and Twitter.

Disclaimer

This press release contains certain "forward-looking" statements within the meaning of applicable securities laws, including the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words such as "at this time," "anticipate," "believe," "expect," "intend," "on track," "plan," "scheduled," and "will," or the negative of these and similar expressions. These forward-looking statements, which are based on our management's current expectations and assumptions and on information currently available to management, include statements about the timing and progress of clinical trials, the timing of our presentation of data, the results of our preclinical and clinical studies and their potential implications. Such forward-looking statements are made in light of information currently available to us and based on assumptions that Nanobiotix considers to be reasonable. However, these forward-looking statements are subject to numerous risks and uncertainties, including with respect to the risk that subsequent studies and ongoing or future clinical trials may not generate favorable data notwithstanding positive early clinical results and the risks associated with the evolving nature of the duration and severity of the COVID-19 pandemic and governmental and regulatory measures implemented in response to it. Furthermore, many other important factors, including those described in our Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission (the SEC) on April 8, 2022 under "Item 3.D. Risk Factors" and those set forth in the universal registration document of Nanobiotix filed with the French Financial Markets Authority (Autorité des Marchés Financiers – the AMF) on April 8, 2022, each as updated in our Half-Year Financial Report filed with the AMF and the SEC on September 8, 2021 (a copy of which is available on

www.nanobiotix.com), as well as other known and unknown risks and uncertainties may adversely affect such forward-looking statements and cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

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