

PRESS RELEASE

NANOBIOTIX ANNOUNCES POSITIVE FIRST CLINICAL DATA SHOWING CONVERSION OF ANTI-PD-1 NON-RESPONDERS TO RESPONDERS WITH RADIOENHANCER NBTXR3

Data presented at The Society for the Immunotherapy of Cancer 35th Anniversary Annual Meeting

- Eight of nine patients treated on the study to date showed tumor regression, including six of seven prior anti-PD-1 non-responders
- Four of the anti-PD-1 non-responders had multiple lesions, and three of the four experienced tumor regression in the non-injected local and/or distant lesions
- One patient with prior anti-PD-1 resistance experienced delayed tumor regression, suggesting an adaptive immune response aided by NBTXR3 activated by radiation therapy
- Data show that, to date, administration of NBTXR3 via intra-tumoral injection has been feasible and well tolerated in all patients (head and neck cancer, lung metastasis, and liver metastasis)
- One patient in the head and neck cancer cohort experienced 4 severe adverse events related to anti-PD-1, of which 2 events were also reported as possibly related to NBTXR3
- Early observation data supports continued clinical development of NBTXR3 activated by radiation therapy in combination with anti-PD-1 across multiple tumor types regardless of prior anti-PD-1 exposure

“There is a significant clinical need to develop treatment options for patients who are not responding to anti-PD-1 therapy,” said lead investigator Colette Shen, MD, PhD, an assistant professor of radiation oncology at the University of North Carolina Lineberger Comprehensive Cancer Center. “These early data suggest that stereotactic body radiotherapy when combined with the radioenhancer NBTXR3 may help prime the immune response and thus the efficacy of anti-PD-1 therapy.”

“It is very promising that tumor regression has been observed not only at injected and irradiated lesions but also at distant lesions, and certainly we will see if these responses continue to be observed in additional patients treated on this study,” added Jared Weiss, MD, co-investigator and an associate professor of medicine at the University of North Carolina Lineberger Comprehensive Cancer Center.

Paris, France ; Cambridge, Massachusetts (USA) ; November 10, 2020 - [NANOBIOTIX](#) (Euronext: NANO - ISIN: FR0011341205 – the “**Company**”), a clinical-stage nanomedicine company pioneering new approaches to the treatment of cancer, today announced positive first clinical results from a phase I study evaluating potentially first-in-class NBTXR3 activated by radiation therapy in combination with pembrolizumab or nivolumab (anti-PD-1 checkpoint inhibitors) for the treatment of patients with advanced cancers. The results were presented at The Society for the Immunotherapy of Cancer 35th Anniversary Annual Meeting.

Addressing Unmet Needs in Cancer Immunotherapy

Cancer immunotherapies such as immune checkpoint inhibitors (ICIs) have shown promising clinical outcomes over the past two decades; and they are often used for patients with advanced cancers once other therapies have reached the end of their effectiveness. Additionally, the vast majority of patients only receive a temporary benefit or no benefit from ICIs, as they either develop resistance to the treatment during the course of therapy or are non-responsive to the treatment altogether (only 15%-20% of patients respond, according to published data). Taken together, these barriers present a significant unmet need to improve the efficacy ICIs and expand their potentially curative benefits to more patients with advanced cancers.

Combining ICIs with radiation therapy is emerging as a valuable strategy to “prime” an immune response and thereby increase the response rate, however the efficacy of radiation therapy is limited by toxicities related to the exposure of healthy tissues.

NBTXR3 is injected one time, directly into solid tumors. The product candidate is designed to increase the energy deposit from radiation therapy within the target tumor and subsequently increase the tumor-killing effect without increasing toxicity in surrounding healthy tissue. Pre-clinical and clinical data also suggest that NBTXR3 activated by radiation therapy can prime the immune system, creating an anti-tumor immune response that

produces both local and systemic effects.

A Phase I Study of Intratumoral NBTXR3 in Combination with anti-PD-1 in Patients with Advanced Cancers

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Study 1100 is a multicenter, open-label, non-randomized, phase I dose escalation with dose expansion study evaluating NBTXR3 activated by radiation therapy in combination with anti-PD-1 (pembrolizumab or nivolumab) in three (3) cohorts of patients with advanced cancers: (i) inoperable locoregional recurrent or recurrent/metastatic head and neck cancer; (ii) lung metastasis; (iii) liver metastasis. The study is being administered [across ten \(10\) sites](#) in the United States.

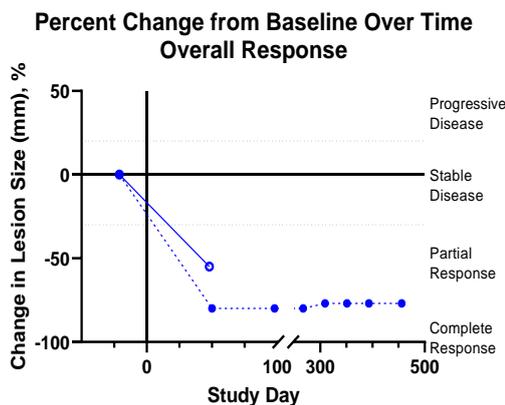
The primary endpoint of the trial is recommended phase II dose (RP2D); the secondary endpoints are objective response rate (ORR), safety and feasibility, and body-kinetics; and the exploratory endpoints are survival outcomes, duration of response, and biomarkers of response.

First Results

To date, first results show that twenty AEs related to NBTXR3 or injection procedure (80% Grade 1-2) were reported in four patients (two each in the head and neck cancer and liver metastasis cohorts). One patient in the head and neck cancer cohort experienced 4 SAEs related to anti-PD-1 (nivolumab) of which two were also reported as possibly related to NBTXR3 (Grade 4 hyperglycemia and Grade 5 pneumonitis) and were considered dose-limiting toxicities. Pneumonitis is a known adverse event associated with nivolumab. There were no NBTXR3- or injection-related AEs, nor treatment-related SAEs in any of the patients treated in the lung metastasis cohort.

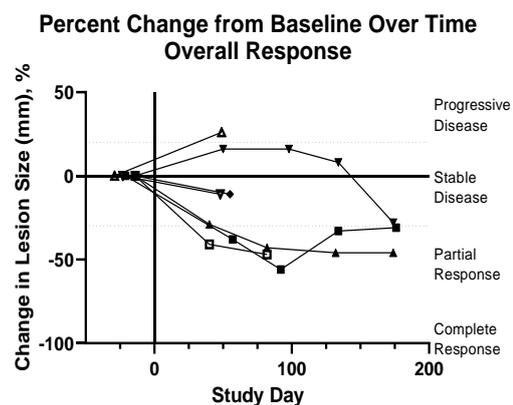
Regarding efficacy and generation of immune response linked to NBTXR3, tumor regression was observed in eight of nine patients including six of seven prior anti-PD-1 non-responders. Three out of seven patients who exhibited prior resistance to anti-PD-1 showed an overall partial response. Four of the anti-PD-1 non-responders also had multiple lesions, and three of those four experienced tumor regression in local and/or distant, non-injected lesions. One patient with prior resistance to anti-PD-1 experienced delayed tumor regression, which is an additional sign that an immune response may have been aided by NBTXR3 activated by radiation therapy.

anti-PD-1 Naïve Patients



Spider plot showing individual response of two (2) anti-PD-1 naïve patients over time

anti-PD-1 Prior Non-Responders



Spider plot showing individual response of seven (7) patients with prior anti-PD-1 resistance over time

Next Steps in Immunotherapy

Given the major opportunity to significantly improve treatment outcomes for patients by increasing the

proportion of patients that respond to ICIs and positive early signs that potentially first-in-class NBTXR3 activated by radiation therapy could provide this benefit, Nanobiotix is preparing to accelerate development in immunotherapy. Recruitment in Study 1100 remains ongoing and the next update from the study is expected in the second quarter of 2021.

Nanobiotix will conduct a web conference to discuss the results in detail at 8:00AM Eastern Standard Time, 2PM Central European Time, on Friday, November 13th 2020. The web conference will include presentations from Colette Shen, M.D., Ph.D., and Jared Weiss, M.D.
Access the webcast: [here](#)

About NBTXR3

NBTXR3 is a novel, potentially first-in-class radioenhancer composed of functionalized hafnium oxide nanoparticles that is administered via one-time intra-tumoral injection and activated by radiation therapy. The primary mode of action (MoA) of NBTXR3 is designed to generate increased cellular destruction when activated by radiation therapy without increasing damage to healthy tissues. Subsequently, this cellular destruction also triggers an adaptive immune response.

NBTXR3 is being evaluated in locally advanced head and neck squamous cell carcinoma (HNSCC) of the oral cavity or oropharynx in elderly patients unable to receive chemotherapy or cetuximab with limited therapeutic options. Promising results have been observed in the phase I trial regarding local control. In the United States, the Company has started the regulatory process to commence a phase III clinical trial in locally advanced head and neck cancers. In February 2020, the United States Food and Drug Administration granted the regulatory Fast Track designation for the investigation of NBTXR3 activated by radiation therapy, with or without cetuximab, for the treatment of patients with locally advanced head and neck squamous cell cancer who are not eligible for platinum-based chemotherapy.

Nanobiotix is also running an Immuno-Oncology development program. The Company has launched a Phase I clinical trial of NBTXR3 activated by radiotherapy in combination with anti-PD-1 checkpoint inhibitors in locoregional recurrent (LRR) or recurrent and metastatic (R/M) HNSCC amenable to re-irradiation of the HN and lung or liver metastases (mets) from any primary cancer eligible for anti-PD-1 therapy.

Other ongoing NBTXR3 trials are treating patients with hepatocellular carcinoma (HCC) or liver metastases, locally advanced or unresectable rectal cancer in combination with chemotherapy, head and neck cancer in combination with concurrent chemotherapy, and pancreatic cancer. The Company is also engaged in a broad, comprehensive clinical research collaboration with The University of Texas MD Anderson Cancer Center to further expand the NBTXR3 development program.

About NANOBIOTIX: www.nanobiotix.com

Incorporated in 2003, Nanobiotix is a leading, clinical-stage nanomedicine company pioneering new approaches to significantly change patient outcomes by bringing nanophysics to the heart of the cell.

The Nanobiotix philosophy is rooted in designing pioneering, physical-based approaches to bring highly effective and generalized solutions to address unmet medical needs and challenges.

Nanobiotix's novel, proprietary lead technology, NBTXR3, aims to expand radiotherapy benefits for millions of cancer patients. Nanobiotix's Immuno-Oncology program has the potential to bring a new dimension to cancer immunotherapies.

Nanobiotix is listed on the regulated market of Euronext in Paris (Euronext: NANO / ISIN: FR0011341205; Bloomberg: NANO: FP). The Company's headquarters are in Paris, France, with a US affiliate in Cambridge, MA, and European affiliates in France, Spain and Germany.

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