



Combination of first-in-class NBTXR3, radiotherapy, and anti-PD-1 immunotherapy demonstrate efficacy in treating resistant pre-clinical *in vivo* models of lung cancer

Data presented at AACR Annual Meeting 2019

- *In vivo* study conducted alone or in collaboration with The University of Texas MD Anderson Cancer Center demonstrated:
 - NBTXR3 in combination with a PD-1 inhibitor enhanced an abscopal effect in both sensitive and PD-1-inhibitor-resistant lung cancer models
 - NBTXR3 in combination with a PD-1 inhibitor showed significant reduction of metastatic load in PD-1-inhibitor-sensitive lung cancer models
 - NBTXR3 in combination with a CTLA-4 inhibitor enhanced an abscopal effect in colorectal cancer models
- Data presented by the Weill Cornell Medical College showed that NBTXR3 mode of action induced interferon (IFN- β) expression in breast cancer cell line
- Altogether, the data presented support the ongoing clinical development plan for combinations of NBTXR3 with radiotherapy and immuno-oncology (IO) agents in multiple indications including lung- and head and neck cancers

Paris, France; Cambridge, Massachusetts (USA); April 2, 2019 – [NANOBIOTIX](#) (Euronext: NANO – ISIN: FR0011341205 – the “Company”) a clinical-stage nanomedicine company pioneering new approaches to the treatment of cancer, today announced preclinical data from studies currently being conducted under its collaborations with The University of Texas MD Anderson Cancer Center and the Weill Cornell Medical College. These results were presented during two poster sessions at the American Association for Cancer Research (AACR) Annual Meeting 2019, currently taking place in Atlanta, Georgia, USA from March 29 to April 3, 2019.

This initial pre-clinical set of NBTXR3/radiotherapy/IO combination data provides further insights into the immune-activation caused by NBTXR3 and strengthens the understanding of the potential systemic effects provided by NBTXR3. Thus, the Company believes it formulates sound rationale to support its clinical development program investigating the combination of NBTXR3, radiotherapy and IO agents.

Enhancement of anti-PD-1 and anti-CTLA4 efficacy by NBTXR3 nanoparticles exposed to radiotherapy Poster #3225

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In both **344SQ_P** (sensitive to anti-PD-1 treatment) and **344SQ_R** (resistant to anti-PD-1 treatment) lung cancer models, the combination of anti-PD-1 + radiotherapy + NBTXR3 demonstrated both better control of the treated tumor and the distant untreated tumor as well as increased survival when compared to monotherapy. Importantly, it was observed that this combination decreased spontaneous lung metastasis formation in the anti-PD-1 sensitive 344SQ_P model.

For the **CT26.WT** colon carcinoma model, as previously reported, NBTXR3 activated by radiotherapy generated an

abscopal effect. It was observed that administration of anti-CTLA4 monotherapy demonstrated control of both treated and distant untreated tumors, potentially indicating that the **CT26.WT** was sensitive to a checkpoint inhibitor. The addition of radiotherapy to anti-CTLA4 only improved the tumor control modestly compared to anti-CTLA4 alone. In contrast, the combination of anti-CTLA4 + radiotherapy + NBTXR3 in this trial showed the best control of the treated and distant untreated tumors, then any single agent or doublet combination.

NBTXR3 Potentiates Cancer-Cell Intrinsic Interferon beta Response to Radiotherapy Poster #3366

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Data suggests that NBTXR3 enhances the effectiveness of radiation and improves tumor immunogenicity in murine breast cancer cell lines, via the induction of type-I interferon (IFN-I). In the study, NBTXR3 activated by radiotherapy amplified cancer cell intrinsic IFN-I response and showed a significant improvement in tumor control compared to radiotherapy alone with complete durable regression of tumors.

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About NBTXR3

NBTXR3 is a first-in-class product candidate designed to destroy tumors and metastasis when activated by radiotherapy.

NBTXR3 has a high degree of biocompatibility and requires one single administration before the whole radiotherapy treatment. Nanobiotix believes NBTXR3 has the ability to fit into current worldwide standards of radiation care.

Nanobiotix's broad clinical program includes seven clinical trials. In June 2018, Nanobiotix established human proof of concept for this first-in-class product candidate in its soft tissue sarcoma (STS) Phase III clinical trial.

NBTXR3 is actively being studied in head and neck cancer with locally advanced squamous cell carcinoma of the oral cavity or oropharynx in elderly and frail patients who are unable to receive chemotherapy or cetuximab and have very limited therapeutic options. Promising results from these clinical studies have been observed from the ongoing Phase I/II trial regarding the local control of tumors.

Nanobiotix is also running an immuno-oncology development program. In the United States, Nanobiotix has received approval from the U.S. Food and Drug Administration to launch a clinical study of NBTXR3 activated by radiotherapy in combination with anti-PD1 antibodies in lung, and head and neck cancer patients (head and neck squamous cell carcinoma and non-small cell lung cancer).

The other ongoing NBTXR3 trials are treating patients with liver cancers (hepatocellular carcinoma and liver metastasis), locally advanced or unresectable rectal cancer in combination with chemotherapy, head and neck cancer in combination with concurrent chemotherapy, and prostate adenocarcinoma.

The first market authorization process (CE Marking) for the STS indication is ongoing in Europe.

About NANOBIOTIX:

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

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

Nanobiotix's first-in-class, proprietary lead technology, NBTXR3, aims to expand radiotherapy benefits for millions of cancer patients. 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 U.S. affiliate in Cambridge, MA, and European affiliates in Spain and Germany.

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