PRESS RELEASE

NANOBIOTIX ANNOUNCES POSITIVE NEW PRE-CLINICAL DATA SUGGESTING RADIOENHANCER NBTXR3 COULD HAVE A SIGNIFICANT IMPACT IN IMMUNOTHERAPY

- **Positive new data from two (2) pre-clinical presentations delivered at The Society for the Immunotherapy of Cancer (SITC) 35th Anniversary Annual Meeting:**
  - ***Modulation of TCR Repertoire by Radiotherapy-activated NBTXR3 nanoparticles***
    - **NBTXR3 activated by radiation therapy produced a strong abscopal effect without a checkpoint inhibitor combination**
    - **NBTXR3 activated by radiation therapy stimulated adaptive antitumor immunity**
    - **NBTXR3 activated by radiation therapy increased TCR repertoire diversity in treated tumors compared to radiation therapy alone**
  - ***NBTXR3 Nanoparticle with Immunoradiation Improves Survival and Generates Long-term Anti-tumor Memory in an anti-PD-1 resistant Murine Lung Cancer Model***
    - **The combination of NBTXR3 plus high dose and low dose radiation (RadScopal™) with anti-PD-1 and anti-CTLA-4 significantly improved the control of both the primary and secondary tumors, extended survival, and reduced lung metastases in an anti-PD-1 resistant lung cancer model**
    - **NBTXR3 plus RadScopal™ plus checkpoint inhibition promoted anti-tumor response at both molecular and cellular levels**
    - **NBTXR3 plus RadScopal™ plus checkpoint inhibition produced long-term anti-tumor memory**
- **In addition to early efficacy data from the Nanobiotix phase I study evaluating NBTXR3 activated by radiation therapy in combination with anti-PD-1, these results further support the continued acceleration of development for NBTXR3 in immunotherapy**

Paris, France ; Cambridge, Massachusetts (USA) ; November 12, 2020 - NANOBOTIX (Euronext: NANO - ISIN: FR0011341205 – the **"Company"**), a clinical-stage nanomedicine company pioneering new approaches to the treatment of cancer, today announced positive new *in vivo* pre-clinical data from two (2) studies at The Society for Immunotherapy of Cancer (SITC) 35th Anniversary Annual Meeting. One ePoster presentation was delivered by Nanobiotix and one oral presentation was delivered by The University of Texas MD Anderson Cancer Center (MD Anderson).

Historically, data has shown that radiation therapy can modulate the immune system; however, clinical evidence of distant tumor control and sustained antitumor immunity is rare. As such, there is an opportunity for new treatment solutions with the potential to prime a strong anti-tumor response. If validated, this benefit could improve treatment outcomes for patients receiving radiation therapy alone and could also be combined with immune checkpoint inhibitors (ICIs) such as anti-PD-1 and anti-CTLA to improve response rates and survival outcomes.

NBTXR3 is a potentially first-in-class radioenhancer that is administered one time, directly into the tumor. When activated by radiation therapy, the product candidate is designed to increase the energy deposit within the tumor without increasing the deposit in surrounding healthy tissues. This physical, universal mode of action leads to an increased tumor-killing effect along with adaptive immune response.

Modulation of TCR Repertoire by Radiotherapy-activated NBTXR3 Nanoparticles
Audrey Darmon, Ping Zhang, Sébastien Paris

Abstract ID: 582

In this study, immunocompetent mice were injected in both flanks with colon carcinoma cells. Intratumoral injection of NBTXR3 or of a 5% glucose solution was administered to the right flank tumors at 25% of baseline tumor volume. The right flank tumors were then irradiated, and the left flank tumors remained untreated. To evaluate the role of CD8+ T cell infiltrates in tumor control and abscopal effect, the CD8+ T cells were depleted in some mice treated with NBTXR3.

Results show similar control of the treated tumor in both the NBTXR3 activated by radiation therapy and glucose plus radiation therapy groups, but only NBTXR3 activated by radiation therapy produced an abscopal effect. Depletion of CD8+ T cells completely abolished the abscopal effect, suggesting that CD8+ T cells drive the abscopal effect induced by NBTXR3 activated by radiation therapy.

TCR diversity analysis of NBTXR3 activated by only a 3x4Gy dose of radiation therapy indicated that that more TCR diversity can be found in tumors treated with NBTXR3 than with radiation therapy alone. Additionally, a significant different in TCR diversity was observed between treated and untreated tumors in the NBTXR3 group, while no significant difference was observed in the group that received radiation therapy alone.

NBTXR3 Nanoparticle with Immunoradiation Improves Survival and Generates Long-term Anti-tumor Memory in an anti-PD1 Resistant Murine Lung Cancer Model
Yun Hu, Sébastien Paris, Hampartsoum Barsoumian, Chike Osita Abana, Saumil Gandhi, Quynh-Nhu Nguyen, Maria Angelica Cortez, James W. Welsh

Abstract ID: 200

Although a previous study showed that treatment with high dose radiation and NBTXR3 on primary tumors in combination with systemic anti-PD-1 was able to significantly improve abscopal effect in a murine metastatic lung cancer model, most of the mice eventually died due to the growth of secondary tumors. This new study intended to evaluate the use of NBTXR3 in the primary tumor, high dose radiation therapy in the primary tumor and low dose radiation therapy in the secondary tumor (RadScopal™), and checkpoint inhibition in the form of anti-PD-1 and anti-CTLA-4 to achieve complete control of both primary and second tumors in mice.

All mice in all groups except the group receiving NBTXR3, RadScopal™, and checkpoint inhibition in combination died due to the growth of either the primary tumor or the secondary tumor. In the NBTXR3 plus RadScopal™ plus checkpoint inhibition group, both primary and secondary tumors were eliminated in 50% of mice. No tumor growth was observed in these mice after metastatic lung cancer cells were re-introduced to the body.

These data show that the combination of NBTXR3, RadScopal™, and immunotherapy was observed to significantly improve the control of both the primary and secondary tumors, extend survival, and reduce lung metastases in an anti-PD-1 resistant lung cancer model. Furthermore, this treatment combination was observed to promote anti-tumor response at both molecular and cellular levels, and to produce long-term anti-tumor immune memory.

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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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