



NANOBIOTIX: POSITIVE PHASE II/III RESULTS FOR NBTXR3 IN SOFT TISSUE SARCOMA PRESENTED AT ESMO

- **Dr. Sylvie Bonvalot, Head of Sarcoma and Complex Tumor Surgery Unit at Institut Curie - Paris, presented first-in-class NBTXR3 positive Phase II/III results during the Sarcoma Proffered Paper Oral session at ESMO**
- **NBTXR3 is the first radiotherapy enhancer to demonstrate clinically meaningful benefit for patients with locally advanced Soft Tissue Sarcoma compared to radiotherapy alone**
- **The Primary and main Secondary Endpoints were met: pathological Complete Response Rate, R0 Resection Margin and percentage of Necrosis/Infarction**
- **In the subgroup of patients having an advanced disease, 4-times more patients achieved a pathological Complete Response in the NBTXR3 arm compared to the control arm**

Paris, France, and Cambridge, Massachusetts (USA) October 19 2018 – [NANOBIOTIX](#) (Euronext : NANO – ISIN : FR0011341205), a late clinical-stage nanomedicine company pioneering new approaches in the treatment of cancer, presented NBTXR3 positive Phase II/III Act.in.sarc results in patients with locally advanced Soft Tissue Sarcoma at the European Society for Medical Oncology (ESMO) 2018 Congress (*Munich, Germany*) during the Proffered Paper Oral presentation of the Sarcoma Section (LBA66).

NBTXR3 is a first-in-class product with a new mode of action designed to physically destroy cancer cells when activated by radiation therapy (RT). NBTXR3 is designed to directly destroy tumors and activate the immune system for both local control and systemic disease treatment.

Dr. Sylvie Bonvalot, Head of Sarcoma and Complex Tumor Surgery Unit at Institut Curie, Paris, France and Global Principal Investigator commented: *“The medical community was very enthusiastic about the results, presented at ESMO, one of the largest international multicentric studies carried out in Soft Tissue Sarcoma patients following guidelines from the EORTC- European Organization for Research and Treatment of Cancer. The results show unequivocally that NBTXR3 improves current radiation therapy. This should change the standard of care in the treatment of sarcoma but also potentially of other cancers.”*

In the Phase II/III Act.in.sarc study, a total of 180 adult patients with locally advanced Soft Tissue Sarcoma of the extremities or trunk wall were randomly allocated, in a 1:1 ratio, to either (i) Arm A, and received a single intratumoral injection of NBTXR3 at the recommended dose (10% of baseline tumor volume) followed by radiation therapy or (ii) Arm B, the control arm, and treated with radiation therapy alone. In both arms, radiotherapy was followed by surgery. The primary efficacy analysis was performed on the intent-to-treat population following the Full Analysis Set principle (ITT-FAS) population as per protocol.

Pathological Complete Response Rate (pCRR): the study met its primary endpoint

The study met its primary endpoint with a pathological complete response (<5% viable cancer cells) rate of 16.1% in the NBTXR3 arm vs 7.9% in the control arm (p=0.0448).

In addition, in the subgroup of patients with a more advanced disease (histologic grade 2 and 3) pathological complete response was achieved in 4 times more patients in the NBTXR3 arm than in the control arm (17.1% vs 3.9%).

An increase in the proportion of patients with a pathological response regardless of the pre-defined cut-off was observed in Arm A. The proportion of patients with pathological nearly complete response (<7% of viable cancer cells) and pathological response with 10% or less of viable cells were 24.7% and 34.6%, respectively, in the NBTXR3 arm vs 14.8% and 19.8% in the control arm.

R0 resection margin: the study met its main secondary endpoint

The main secondary endpoint of carcinologic resection was also met with R0 resection margin achieved in 77% of the patients who received NBTXR3 compared to 64% of patients in the control arm (p=0.0424).

Tumor necrosis/infarction: the study also met this secondary endpoint

Histologic analysis showed that the mean percentage of tumor necrosis/infarction was also increased in the NBTXR3 arm compared to the control arm (28.8% vs 19.2%; p=0.014).

Safety profile similarity across study arms

Similar safety profiles were observed in the NBTXR3 arm and the radiation therapy alone arm. NBTXR3 did not impact the patients' ability to receive the planned dose of radiotherapy and the radiotherapy safety profile was similar in both arms, including the rate of postsurgical wound complications. NBTXR3 was associated with grade 3-4 acute immune reactions in 7.9% of patients, which were manageable and of short duration.

NBTXR3 showed a good local tolerance and no impact on the severity or incidence of radiotherapy-related adverse events.

Long-term follow-up of the patients is ongoing to evaluate the Time-to-Local/Distant Recurrence and Local/Distant Recurrence Rate (LRR/DRR) at 12 and 24 months.

About Act.in.sarc study

The Phase II/III study was a prospective, randomized (1:1), multinational, open label and active controlled two arm study of the efficacy and safety of NBTXR3 activated by radiotherapy compared to radiotherapy alone in patients with locally advanced Soft Tissue Sarcoma (STS) of the extremity or trunk wall. Patients have been treated with the standard dose of radiation, a total dose of 50 Gy given in 25 fractions of 2 Gy over 5 weeks, followed by surgical resection of the tumor. The primary objective was to evaluate the pathological complete response rate (pCRR)* in both arms. The secondary endpoints included a safety profile and assessment of carcinologic resection rate** in terms of margin status. Efficacy endpoints have been measured on surgically resected tumors by a pathological central review board. The primary efficacy analysis was planned to be performed on the intent-to-treat (ITT) population***. The ITT-FAS population (176 patients) was used for the analysis, and 4 patients were excluded from the ITT-FAS: 3 did not have STS (2 in Arm A, 1 in Arm B) and 1 (in Arm A) was not eligible for preoperative RT.

**A pathological Complete Response is defined as the presence of less than 5% of residual malignant viable cells in the surgically removed tissue. The primary endpoint compared the proportion of patients presenting pathological Complete Response (pCR) between the two arms. This was determined by an independent pathological central review according to EORTC score (Wardelmann et al., 2016).*

*** The resection margin status is an evaluation of the quality of surgery. Surgery remains the mainstay of care for locally advanced soft tissue sarcoma. The primary surgical objective is the complete removal of the tumor with negative resection margins (R0). Several retrospective studies suggest that surgical margin status predicts the risk of local and distant recurrence. In particular, negative surgical margins are significantly correlated to increased patient survival.*

**** Intent-to-treat (ITT) population includes all patients with an informed consent given and a successful and confirmed randomization number allocation through the treatment allocation system (IWRS) with a non-missing date of randomization. All analysis using this population is based on the treatment assigned by randomization. ITT population following the Full Analysis Set principle (ITT-FAS) is considered with specific attention paid to the following cases: Patients randomized and having received no treatment / Patients without any data post-randomization / Patients randomized in spite of the non-satisfaction of a major entry criterion (eligibility violation).*

About NBTXR3

NBTXR3 is a first-in-class product designed to destroy, when activated by radiotherapy:

- tumors through physical cell death
- metastasis due to immunogenic cell death leading to activation of the immune system

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

Nanobiotix's broad clinical program includes 10 patient populations evaluated in 7 clinical trials.

In June 2018, Nanobiotix established human proof of concept for this first-in-class product in its Soft Tissue Sarcoma (STS) Phase III clinical trial.

NBTXR3 is actively being evaluated in head and neck cancer with locally advanced squamous cell carcinoma of the oral cavity or oropharynx in elderly and frail patients that are unable to receive chemotherapy or cetuximab and have very limited therapeutic

options. Promising results have been observed from the ongoing Phase I/II trial regarding the local control of tumors.

Nanobiotix is running an Immuno-Oncology development program. In the United States, Nanobiotix has received approval from the U.S. Food and Drug Administration (FDA) 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) is ongoing in Europe in the STS indication.

About NANOBOTIX: www.nanobiotix.com

Incorporated in 2003, Nanobiotix is a leading, late 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 one rooted in designing pioneer physical based approaches to bring highly effective and generalized solutions to address high unmet medical needs and challenges.

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

Contact

Nanobiotix

Sarah Gaubert

Director, Communication & Public Affairs
+33 (0)1 40 26 07 55
sarah.gaubert@nanobiotix.com /
contact@nanobiotix.com

Noël Kurdi

Director, Investor Relations
+1 (646) 241-4400
noel.kurdi@nanobiotix.com /
investors@nanobiotix.com

Ricky Bhajun

Investor Relations Europe
+33 (0)1 79 97 29 99
ricky.bhajun@nanobiotix.com /
investors@nanobiotix.com

Media relations

France - **Springbok Consultants**

Marina Rosoff
+33 (0)6 71 58 00 34
marina@springbok.fr

United States –

RooneyPartners
Marion Janic
+1 (212) 223-4017
mjanic@rooneyco.com



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