



## NANOBIOTIX ANNOUNCES POSITIVE PHASE II/III TOPLINE DATA IN SOFT TISSUE SARCOMA WITH NBTXR3

- Trial achieved its primary endpoint of pathological Complete Response Rate
- Trial achieved its secondary endpoint in operability (R0 rate)
- NBTXR3 demonstrated significant superiority and clinical benefits for patients versus standard of care
- Safety profile confirmed
- Randomized trial validated the first-in-class mode of action of NBTXR3

Paris, France and Cambridge, Massachusetts, June 21, 2018 – [NANOBIOTIX](#) (Euronext: NANO – ISIN: FR0011341205), a late clinical-stage nanomedicine company pioneering new approaches in the treatment of cancer, announced today positive topline results of the Phase II/III act.in.sarc trial evaluating NBTXR3 in Soft Tissue Sarcoma (STS).

*“Data are exceptional and show without any doubt an improvement of radiation therapy impact with a significant number of complete response. NBTXR3 can bring real benefit to patients and it can change the standard of care. This innovation will play a role in many other indications and particularly where radiotherapy is used alone.”*

Pr. Sylvie Bonvalot, MD, Head of Sarcoma and Complex Tumor Surgery Unit at Institut Curie, Paris, France and Global Principal Investigator of the PII/III study

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

The Phase II/III study was a prospective, randomized (1:1), multinational, open label and active controlled two-armed study of 180 patients with locally advanced STS. The objective of the Phase II/III trial was to evaluate the efficacy and the safety of NBTXR3 activated by radiotherapy compared to the standard of care (radiotherapy alone). Patients have been treated with the standard dose of radiation (25x2 Gy) and efficacy endpoints have been measured on surgically resected tumors.

### **Primary endpoint achieved in the intend-to-treat population (ITT)**

The primary endpoint is the pathological Complete Response Rate (pCRR) defined as the rate of patients showing less than 5% of residual viable cancer cells in the tumor post treatment. This primary endpoint is related to NBTXR3's mode of action and product efficacy. Twice as many patients (16.1% vs 7.9%) achieved a pathological Complete Response (pCR) with NBTXR3 compared to the control arm ( $p = 0.0448$ ). The significant difference observed between both arms validates the superiority of the treatment with NBTXR3 versus radiation alone.

### **Secondary Endpoint achieved in the ITT - Resection margins status and operability**

The main secondary endpoint is the resection margin status evaluating the quality of surgery. The main objective is to achieve compartmental clean margins (negative margin defined as R0) *i.e.* no more cancer cells found within the surgical margins. NBTXR3 demonstrated a statistically significant increase in R0 surgical margin rate compared to radiotherapy alone (relative increase of 20%,  $p = 0.042$ ). The resection with negative margins is a validated surrogate endpoint for systemic and long-term benefit for patients such as local progression free survival (PFS) and distant PFS.

Pr Jean-Yves Blay, MD, Director of the Centre Léon Bérard, Lyon, France, commented, *“I am amazed by the difference of Response Rate, it is extremely uncommon to double the Rate of Complete histological Response and I do not see any other strategy able to accomplish that. Even more impressive is the RO rate, which is increased by more than 20% compared to an average rate of 64%. This difference is really impressive, considering that RO impacts patients relapses and survival.”*

#### **Safety and feasibility**

NBTXR3 demonstrated a good local tolerance among this patient’s population. Findings showed a very similar radiation-related safety in both arms. The patients in both the control and tested arms of the study received the planned radiotherapy (dose and schedule).

Notably, feasibility and follow-up of surgery were also equivalent. Acute immune adverse events of short duration observed in 7.9% of patients.

The Injection site caused pain in 13.5% of patients. In addition, 6.7% of patients experienced grade 1 injection site hematoma / ecchymosis.

Regarding long-term toxicity, less serious adverse events were reported for NBTXR3 arm.

#### **Regulatory strategy and CE mark**

The positive results from this study support and further validate the European regulatory strategy of the previously submitted CE marking application in STS. The company will submit the new data as a supplement to the European Notified Body in a timely manner.

#### **Next steps**

The Company will present the results at an upcoming international medical conference.

The clinical validation of NBTXR3’s physical mode of action in a very heterogeneous and hard-to-treat disease strengthens the universal profile of the product and confirms the development strategy in multiple indications.

Currently, the company is evaluating NBTXR3 in seven clinical trials with a focus on head and neck cancers and Immuno-Oncology programs.

David Raben MD, Professor of Radiation Oncology, University of Colorado Cancer Center, CO, USA, commented, *“These results from a Phase III study are impressive in a notoriously difficult disease like Soft Tissue Sarcoma. These cancers are generally less sensitive to radiation and previous attempts to improve local control with chemo-radiation regimens were considered too toxic. This study substantiates the medical benefit of safely enhancing the effect of radiation therapy with novel physics-based approaches delivered locally within the cancer. In addition, this product may potentiate a pro-inflammatory environment suitable for immune enabling or DNA damage inhibitor drugs. These findings set the foundation for additional studies in areas such as head and neck cancer and perhaps in areas such as high-risk prostate, bladder or pancreas cancer.”*

Webcast and dial-in (English) June 22 at 4pm Paris time: <https://origin.yuca.tv/en/nanobiotix/press-conference-2018>

For more information about the STS study: [www.clinicaltrial.gov](http://www.clinicaltrial.gov) (Identifier: NCT02379845)  
<http://www.actinsarc.com/>

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## About PII/III clinical trial (act.in.sarc study)

Nanobiotix and its partner, PharmaEngine recruited 180 patients in 43 sites across 13 countries in Europe and Asia. The Global Principal Investigator is Pr. Sylvie Bonvalot, MD, PhD (Institut Curie, Paris, France).

### Primary endpoint

**Pathological complete response rate (pCRR):** 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).

### Main secondary endpoint

**Resection margin status:** The resection margin status is evaluating 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 predict the risk of local and distant recurrence. In particular, negative surgical margins are significantly correlated to increased patients' survival.

## 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 has the ability to fit into current worldwide standards of radiation care.

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 unable to receive chemotherapy or cetuximab with very limited therapeutic options. The Phase I/II trial has already delivered very promising results regarding the local control of the tumors.

Nanobiotix is running an Immuno-Oncology development program . In the U.S., the Company received the FDA's approval 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 studies 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 soft tissue sarcoma indication.

## About NANObIOTIX: [www.nanobiotix.com](http://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.

The Company's first-in-class, proprietary lead technology, NanoXray, aims to expand radiotherapy benefits for millions of cancer patients. Furthermore, the Company'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.

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## Disclaimer

*This press release contains certain forward-looking statements concerning Nanobiotix and its business. Such forward-looking statements are based on assumptions that Nanobiotix considers to be reasonable. However, there can be no assurance that the estimates contained in such forward-looking statements will be verified, which estimates are subject to numerous risks including the risks set forth in the reference document of Nanobiotix filed with the French Financial Markets Authority (Autorité des Marchés Financiers) under number D.17-0470 on April 28, 2017 as well as in its 2017 annual financial report filed with the French Financial Markets Authority on March 29, 2018 (a copy of which is available on [www.nanobiotix.com](http://www.nanobiotix.com)) and to the development of economic conditions, financial markets and the markets in which Nanobiotix operates. The forward-looking statements contained in this press release are also subject to risks not yet known to Nanobiotix or not currently considered material by Nanobiotix. The occurrence of all or part of such risks could cause actual results, financial conditions, performance or achievements of Nanobiotix to be materially different from such forward-looking statements.*

*This press release and the information that it contains do not constitute an offer to sell or subscribe for, or a solicitation of an offer to purchase or subscribe for, Nanobiotix shares in any country. At the moment NBTXR3 does not bear a CE mark and is not permitted to be placed on the market or put into service until NBTXR3 has obtained a CE mark.*