



## AACR ANNUAL MEETING 2018: NANBIOTIX PRESENTED PRECLINICAL DATA SHOWING NBTXR3 NANOPARTICLES CAN ACTIVATE THE cGAS-STING PATHWAY

Paris, France and Cambridge, Massachusetts, April 17, 2018 – [NANBIOTIX](#) (Euronext: NANO – ISIN: FR0011341205), a late clinical-stage nanomedicine company pioneering new approaches to the local treatment of cancer, today announced that preclinical data evaluating the activation of the cGAS-STING pathway by NBTXR3 has been presented at the American Association for Cancer Research (AACR) Annual Meeting 2018 in Chicago, Illinois (April 14-18, 2018).

NBTXR3 is a first-in-class product designed to destroy, when activated by radiotherapy, tumors and metastasis through physical cell death and to induce immunogenic cell death leading to specific activation of the immune system.

Establishing how NBTXR3, activated by radiotherapy, impacts and primes the immune response against tumor cells is central to Nanobiotix's immuno-oncology program. Recently, the cGAS-STING pathway has emerged as the key component of the anti-tumor immune response, along with immunogenic cell death. Therefore, evaluation of the impact of NBTXR3 on this conserved signaling cascade is essential.

Dr Elsa Borghi, CMO, commented, "*cGAS-STING activation is of fundamental importance in establishing an adaptive anti-tumor immune response. These encouraging preliminary results suggest that NBTXR3 activated by radiotherapy could increase the activation of this pathway, compared to radiotherapy alone.*"

### ***"Activation of the cGAS-STING pathway by NBTXR3 nanoparticles exposed to radiotherapy"***

J. Marill, N. Mohamed Anesary, A. Darmon, P. Zhang and S. Paris.

Poster number #4571

In this poster, Nanobiotix presents data showing a dose-dependent increase in cGAS-STING pathway activation with NBTXR3 activated by radiotherapy through both *in vitro* and *in vivo* analyses.

*In vitro* analyses show a significant increase in luciferase activity (reflecting the transcriptional activity of IRF) was observed in HCT116-DUAL™ cells treated with NBTXR3 plus RT, compared to radiotherapy alone. Further, NBTXR3 activated by radiotherapy triggers an increased generation of micronuclei (involved cGAS-STING response) compared to radiotherapy alone.

*In vivo*, NBTXR3 activated by radiotherapy leads to a greater production of IFN- $\beta$  and overexpression of its gene, compared to radiotherapy alone.

Previous work has demonstrated that NBTXR3 activated by radiotherapy increased cancer cell killing efficiency along with Immunogenic Cell Death (ICD), compared to radiotherapy alone. Here, *in vitro* data generated from HCT116-DUAL™ and *in vivo* data from CT26 tumors further demonstrate that NBTXR3 activated by radiotherapy is able to trigger a stronger activation of the cGAS-STING pathway, compared to radiotherapy alone, even in combination with the STING agonist 2',3'-cGAMP. Moreover, NBTXR3 can maximize the effect of 2',3'-cGAMP, the natural agonist of STING, when activated by the radiotherapy.

These observations support the rationale for using NBTXR3 with radiation therapy in combination with immunotherapeutic agents and/or STING agonist to transform tumors into an *in-situ* cancer vaccine.

These results, obtained in human and mouse colorectal cancer cells models, could have a very positive impact on the anti-tumoral immune response, potentially transforming non-responding tumors into responding, *i.e.* turning them from “cold” to “hot”.

### **NBTXR3 positioning in IO**

Many IO combination strategies focus on ‘priming’ the tumor, which is now becoming a prerequisite of turning a “cold” tumor into a “hot” tumor.

Compared to other modalities that could be used for priming the tumor, NBTXR3 could have a number of advantages: the physical and universal mode of action that could be used widely across oncology, a one-time local injection and good fit within existing medical practice already used as a basis for cancer treatment, as well as a very good chronic safety profile and well-established manufacturing process.

Published preclinical and clinical data indicate that NBTXR3 could play a key role in oncology and could become a backbone in immuno-oncology.

Nanobiotix’s immuno-oncology combination program opens the door to new developments, potential new indications, and important value creation opportunities.

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### **About American Association for Cancer Research (AACR) [www.aacr.org](http://www.aacr.org)**

The AACR Annual Meeting is one of the main international oncology events highlighting the best cancer science and medicine from institutions all over the world. The American Association for Cancer Research (AACR) Annual Meeting 2018 in Chicago, Illinois (April 14-18, 2018).

### **About NBTXR3**

NBTXR3 is a first-in-class product designed to destroy, when activated by radiotherapy, tumors and metastasis through physical cell death and to immunogenic cell death leading to specific 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 being evaluated in head and neck cancer (locally advanced squamous cell carcinoma of the oral cavity or oropharynx), and the trial targets frail and elderly patients who have advanced cancer with very limited therapeutic options. The Phase I/II trial has already delivered very promising results regarding the local control of the tumors and a potential metastatic control through *in situ* vaccination.

Nanobiotix is running an Immuno-Oncology program with NBTXR3 that includes several studies. 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). This trial aims to expand the potential of NBTXR3, including using it to treat recurrent or metastatic disease.

The first market authorization process (CE Marking) is ongoing in Europe in the soft tissue sarcoma indication.

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.

### **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.

## Contact

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### Nanobiotix

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**Sarah Gaubert**

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

**Noël Kurdi**

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



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### Media relations

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**France - Springbok Consultants**

**Marina Rosoff**  
+33 (0)6 71 58 00 34  
[marina@springbok.fr](mailto:marina@springbok.fr)

**United States – RooneyPartners**

**Marion Janic**  
+1 (212) 223-4017  
[mjanic@rooneyco.com](mailto:mjanic@rooneyco.com)

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*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.*