



Small but heading for the big time

Nanobiotix establishes promising preclinical proof-of-concept in Immuno Oncology

Paris, France, Cambridge, MA, USA May 31, 2016 – NANOBOTIX (Euronext: NANO – ISIN: FR0011341205), a late clinical-stage nanomedicine company pioneering novel approaches for the local treatment of cancer, announces today that the Company has established preliminary preclinical proof-of-concept (POC) with the lead product NBTXR3 for its new program in Immuno Oncology (IO).

- Delivering first promising data with its Immuno Oncology preclinical program, showing the potential to turn the tumor itself into a vaccine using NBTXR3
- Creating a potential new usage and new market for NBTXR3 in parallel to its mainstream clinical development
- Providing new opportunities by combining NBTXR3 with other Immuno Oncology drugs with a unique competitive advantage

Immuno-oncology works by boosting patients' immune systems to recognise and attack tumours and therefore, kill the cancer. The approach is very efficient for a limited number of patients whose tumors have the ability to provoke an immune response i.e. they have a natural and sufficient immunogenicity, and are referred to as 'hot' tumors. However, in many patients, the tumours are 'cold' and the therapeutic approach has little response.

To be able to expand the number of patients that can respond to IO, thereby exploiting its full potential, immunogenicity needs to be increased at the tumor level. Nanobiotix's approach to achieve this is to trigger Immunogenic Cell Death (ICD) at the tumor level, transforming "cold tumors" into "hot tumors".

Preliminary *in vitro* and *in vivo* preclinical data suggest that Nanobiotix's radioenhancer NBTXR3 might be used, not only to destroy tumors (as it is currently being clinically developed), but also to enhance the power of radiotherapy to create intratumoral vaccines for IO, and convert 'cold' tumours to 'hot'.

NBTXR3 current clinical development to destroy tumors and provide better local control of cancer

NBTXR3 is a radio-enhancer, using a physical mode of action to destroy cancer cells in any solid tumors, in combination with radiotherapy.

Nanobiotix is running a global clinical development program with its lead product NBTXR3, in six indications across Europe, the US and the Asia-Pacific Region: a registration trial in soft tissue sarcoma, and Phase I/II trials in liver cancers (HCC and liver metastases), prostate cancer, head and neck cancer and rectal cancer (in Asia by Nanobiotix's partner PharmaEngine).

New usage of NBTXR3 for *in situ* (intratumoral) vaccination opening new potential prospects in Immuno Oncology: preliminary preclinical proof of concept

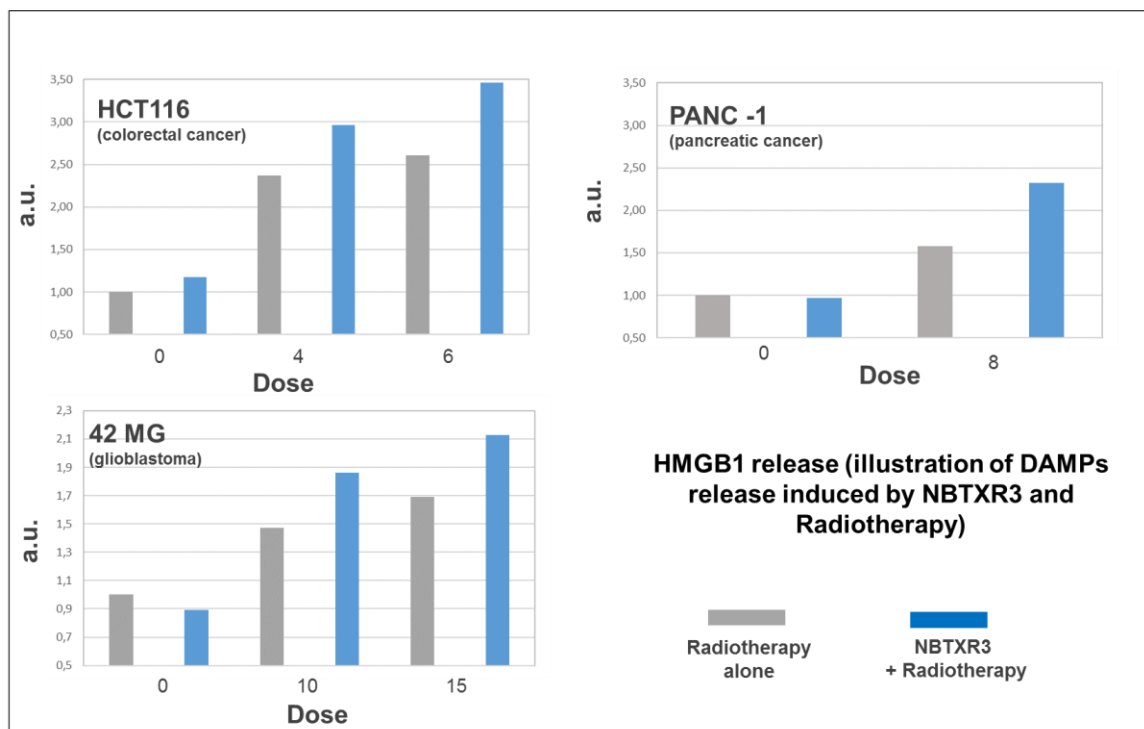
NBTXR3 nanoparticles' activation by radiation enhances the energy deposited where they are injected, improving cancer cell death and the efficacy of radiotherapy. This technology is based on physics and can potentially be applied across all radiotherapy indications. All preclinical model (in vitro and in vivo) have shown a systematic superiority of cell killing, when using NBTXR3 with radiotherapy, compared to radiotherapy alone.

***In vitro* POC: Immunogenic Cell Death (ICD)**

The ability to generate ICD can be seen through the generation of Damage-Associated Molecular Pattern (DAMPs) such as HMGB1, ATP, Calreticulin. HMGB1 among other DAMPs have also been shown to be relevant as biomarkers that can be translated into the clinical setting.

Release of such DAMPs have been tested in different human resistant or sensitive cancer cell lines (including glioblastoma, colorectal and pancreatic cancers).

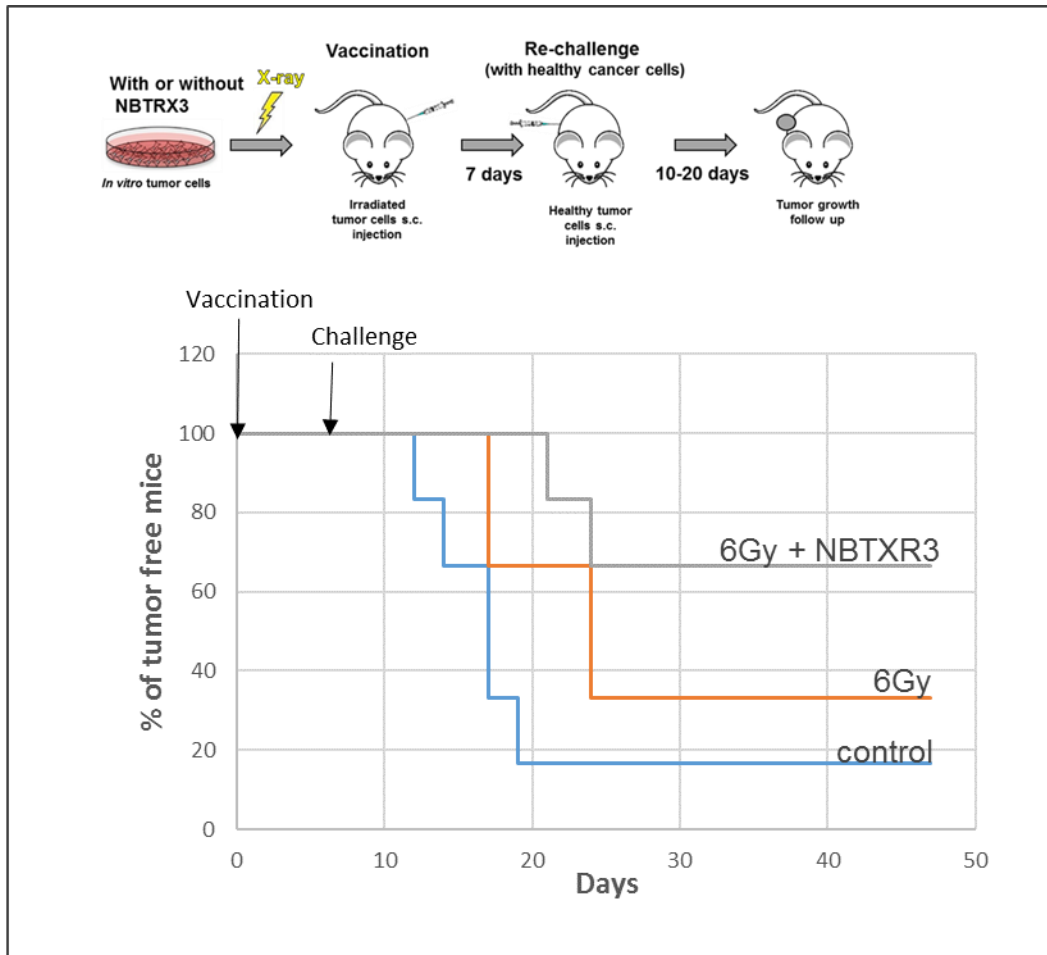
NBTXR3 in combination with radiotherapy has shown superiority versus radiation alone in the generation of DAMPs: HMGB1 (from 25% up to 47% increase) and ATP (around 30%).



***In vivo* POC: vaccination assays on Immuno competent mice**

Classical vaccination assays have been performed to demonstrate that *in vitro* generation of ICD could stimulate the immune response and provide bases for long term vaccination. Vaccination experiment have shown superiority in combining NBTXR3 with radiotherapy versus radiotherapy alone.

CT26 cells (murine colorectal cancer cells) were irradiated in the presence of NBTXR3 and without, and injected subcutaneously (s.c.) into one flank of the mice (vaccination phase). One week later, living CT26 cells were injected s.c. in the opposite flank of the same animals (challenge phase). The host immune response against these cells was evaluated by the apparition of at least one tumor (vaccination and/or challenge site). The percentage of tumor free mice (see figure below) with 6Gy+NBTXR3 is 66%, compared to 33% for 6Gy alone and 17% for the control group. This suggests a better immune response against CT26 cells for animals vaccinated with cells treated with NBTXR3 and irradiation, compared to irradiation alone. These results strongly suggest that combination of NBTXR3 with radiation therapy could significantly increase the immune response against cancer cells compared to irradiation alone.



Laurent Levy, Chief Executive Officer of Nanobiotix commented: *“Radiotherapy is a standard of care in oncology. Today it is also being widely explored for its potential to transform ‘cold’ tumors into ‘hot’ tumors, which could lead to expand the number of patients eligible to Immuno Oncology across oncology.*

“These promising preliminary proof-of-concept results show that NBTRX3 may have the power to not only destroy cancer cells more effectively than by radiotherapy alone, but also to enhance the immunogenicity of the tumor. This new program could potentially broaden the use of our product NBTRX3 beyond its current development plan and, if successful, increase the effectiveness of IO in more patients.”

NBTRX3 could offer a unique competitive positioning in IO, and potentially increase the number of cancer patients eligible for treatment

More and more preclinical and clinical evidence are showing that radiotherapy could play a key role in Immuno oncology especially in combination. Compared to chemo or biologics, radiotherapy (RTx) could be used in many more clinical situations across oncology. Moreover, radiotherapy is the only approach that is well established as a standard of care and having limited or no systemic toxicity.

Increasing the ICD induced by radiotherapy at the tumor level across oncology with a patented NBTRX3 product, could provide a unique medical and competitive advantage to many IO drugs.

Nanobiotix core business remains focused on the development of NBTRX3 to be use as a single agent in combination with radiotherapy. This program is expected to deliver important clinical data in several indications for the coming months and years, with a first market approval in Europe anticipated for the end of the year 2016.

Given this additional potential on this new field, Nanobiotix will reinforce its R&D effort in Immuno Oncology. The company could also further explore the potential synergies with current advanced approaches in the field such as Immune checkpoint targeted mabs or drugs, Adoptive T-cell therapy, Oncolytic viruses, Vaccines, etc.

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About NANObIOTIX: www.nanobiotix.com

Nanobiotix (Euronext: NANO / ISIN: FR0011341205) is a late clinical-stage nanomedicine company pioneering novel approaches for the local treatment of cancer. The Company's first-in-class, proprietary technology, NanoXray, enhances radiotherapy energy with a view to provide a new, more efficient treatment for cancer patients.

NanoXray products are compatible with current radiotherapy treatments and are meant to treat potentially a wide variety of solid tumors including soft tissue sarcoma, head and neck cancers, liver cancers, prostate cancer, breast cancer, glioblastoma, etc., via multiple routes of administration.

Nanobiotix's lead product NBTXR3, based on NanoXray, is currently under clinical development for soft tissue sarcoma, head and neck Cancer, prostate cancer, rectal cancer (PharmaEngine) and liver cancers (HCC and liver metastases). The Company has partnered with PharmaEngine for clinical development and commercialization of NBTXR3 in Asia.

Nanobiotix is listed on the regulated market of Euronext in Paris (ISIN: FR0011341205, Euronext ticker: NANO, Bloomberg: NANO:FP). The Company Headquarter is based in Paris, France. Affiliate in Cambridge, United States.

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