



NANOBIOTIX: NEW TRANSLATIONAL DATA PRESENTED AT ASTRO, NCI AND SITC'S IMMUNOTHERAPY WORKSHOP

- **Translational data showing tumor immune activity and positive Tumor Infiltrating Lymphocytes (TILs) in human and mouse model**
- **Confirmation of the ability to transform “cold” tumors into “hot” tumors and that NBTXR3 treatment may have an impact on the tumor microenvironment**
- **Opening up of the potential for NBTXR3 to treat metastases**

Paris, France and Cambridge, Massachusetts (USA), June 15, 2017 – [NANOBIOTIX](#) (Euronext: NANO – ISIN: FR0011341205), a late clinical-stage nanomedicine company pioneering new approaches to the treatment of cancer, today presented new translational data at the “Immunotherapy workshop - Incorporating Radiation Oncology into Immunotherapy” co-sponsored by the American Society of Radiation Oncology (ASTRO), the National Cancer Institute (NCI) and the Society for Immunotherapy of Cancer (SITC), that takes place from June 15 to 16, 2017 in Bethesda, Maryland, USA.

Nanobiotix's lead product, NBTXR3, has a universal physical mode of action which is designed for the local destruction of tumors. In addition to the physical destruction of cancer cells, recently published data suggests that NBTXR3 generates immunogenic cell death which could trigger a specific immune response to attack the tumor.

Many tumors exhibit little or no response to therapies targeting the immune system and are considered “cold”. The explanation for the lack of response in its simplest form, is a lack of immunogenicity. The ability of NBTXR3 to generate intratumoral immunogenic cell death (ICD) could be a key to significantly increasing the number of patients who can benefit from the help of their immune system to fight their cancer.

Today, Nanobiotix presented new translational data from its immuno-oncology program.

“Hafnium oxide nanoparticle, a potent radiation enhancer for *in situ* cancer vaccine” (June 15, 2017)

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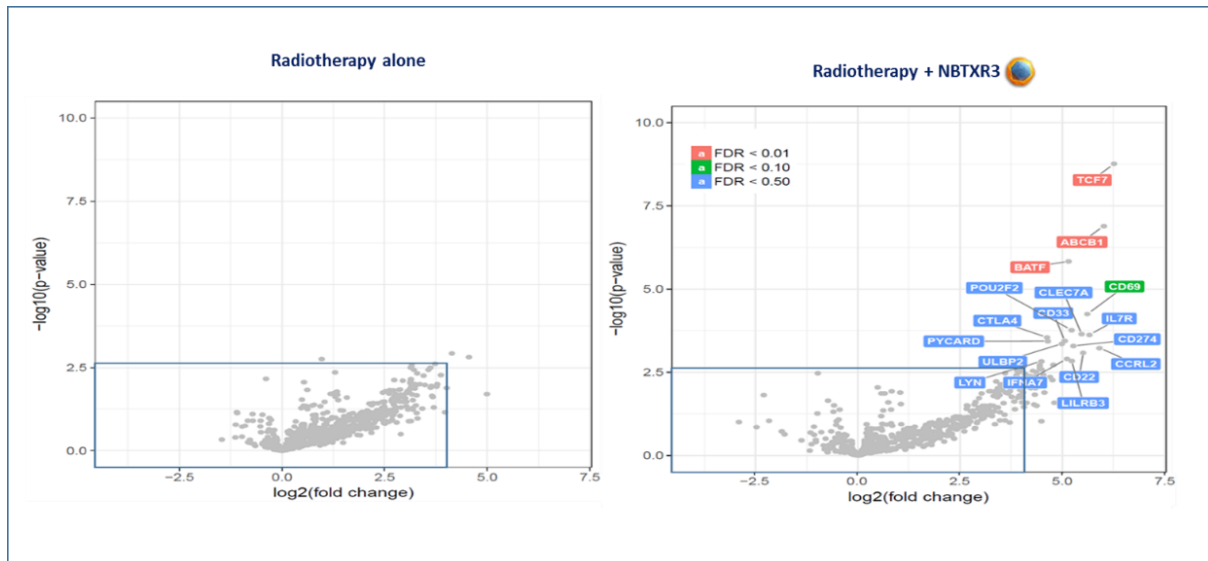
1. Human Soft Tissue Sarcoma (STS) patients data

In tumors of STS patients, a significant increase of T cells (CD3+, CD8+) and a marked increase of dendritic cell (CD103+) infiltrates in post- versus pre-treatment were observed for NBTXR3 plus radiotherapy arm, while no differences were seen in the use of radiotherapy alone. These findings demonstrate the ability of NBTXR3 to transform cold tumors (as Soft Tissue Sarcoma) in hot tumors.

Large hemorrhagic zones have been found in tumor tissues treated with NBTXR3, whereas tumors treated with radiotherapy alone did not show such patterns. This finding shows that NBTXR3 could affect the tumor microenvironment and potentially allow better infiltration of activated T Cells.

The upregulation of adaptive immunity gene expression between pre- and post-treatment was pronounced for NBTXR3 plus radiotherapy - 72 genes only up-regulated with the NBTXR3 treatment, showing enrichment of cytokine activity and of the T cell receptor signaling pathway.

A number of upregulated genes correspond to existing or promising IO targets, enabling a potential combination of NBTXR3 with therapeutic approaches, like products targeting PD1, PDL1, CTLA4, etc. This data requires confirmation in additional studies.



Asymmetrical volcano plot shows a trend toward the upregulation of panimmune genes in post-treated tumors of Soft Tissue Sarcoma patients.

The two charts compare the results of patients treated with radiotherapy alone (left), with patients treated with radiotherapy plus NBTXR3 (right).

2. Mice model (CT26) data

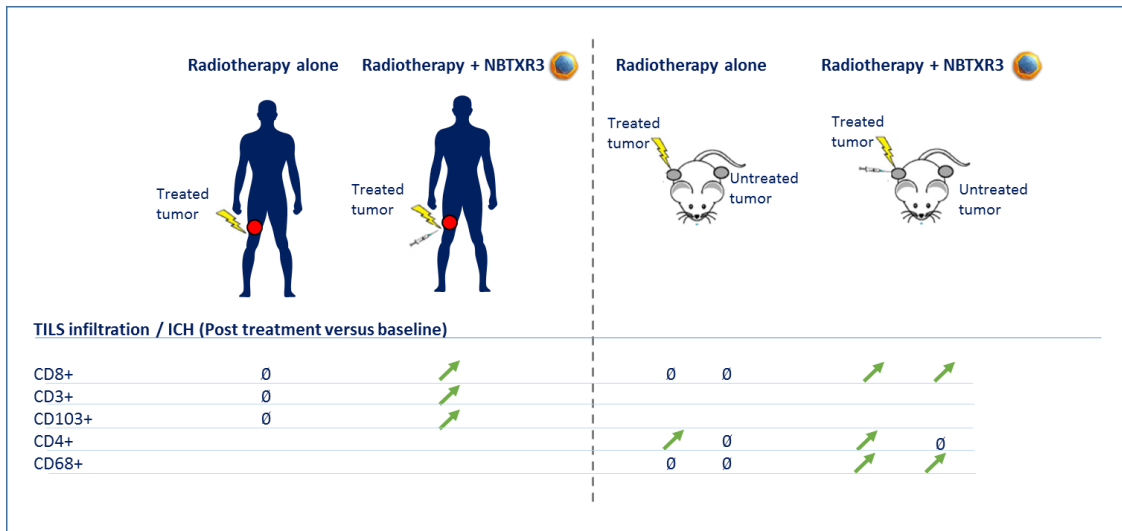
In mice, the abscopal effect (i.e. an effect outside the scope of the localized treatment) was evaluated. A tumor was implanted on each side of each mouse; one of the tumors was treated with either NBTXR3 and radiotherapy, or radiotherapy alone; while the other remained untreated. The treated tumors, both those that received NBTXR3 and radiotherapy and those that received radiotherapy alone, demonstrated volume shrinkage.

However, the study showed that only the use of NBTXR3 with radiotherapy resulted in a control on the untreated tumors (abscopal effect). No effect was observed in control groups and groups treated with radiation therapy alone.

In this model, NBTXR3 plus radiotherapy induces a noticeable increase of CD8+ and macrophages infiltrates in both tumors (treated and untreated). At the same time, no effect was observed in cases where radiotherapy was used alone, when compared to control groups (that received no irradiation). This demonstrates that NBTXR3 plus radiotherapy can induce a marked systemic antitumor immune response on distant and untreated tumors where radiotherapy alone couldn't.

3. Conclusion

Taken together, these non-clinical and preliminary clinical results confirm that NBTXR3 plus radiotherapy could efficiently prime the adaptive antitumor immune response, turning "cold" tumors in "hot" tumors. Additionally, these results suggest that the physically-induced response and subsequent immune activation triggered by the NBTXR3 treatment could be generic. NBTXR3 with radiotherapy could transform these tumors into an effective *in situ* vaccine, opening up very promising perspectives in the treatment of local cancer and metastases.



Tumor Immune Cell Infiltrates (TILs)

NBTXR3 competitive 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 widely applied across oncology; the 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.

The new clinical data and previous pre-clinical data indicate that NBTXR3 could play a key role in oncology and could become a backbone in immuno-oncology.

About NANOBOTIX: www.nanobiotix.com

Nanobiotix (Euronext: NANO / ISIN: FR0011341205) is a late clinical-stage nanomedicine company pioneering novel approaches for the 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.

NBTXR3 is being evaluated in: soft tissue sarcoma (STS), head and neck cancers, prostate cancer, and liver cancers (primary and metastases). Additionally, head and neck cancer and rectal cancer trials led by Nanobiotix’s Taiwanese partner, PharmaEngine, are underway in the Asia Pacific region. The Company has filed in August 2016 for market approval (CE Marking) in Europe for its lead product NBTXR3.

The Company started in 2016 a new preclinical research program in Immuno-oncology with its lead product NBTXR3, which could have the potential to bring a new dimension to cancer immunotherapies.

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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