Small but heading for the big time

Nanobiotix starts Phase I/II clinical trial in liver Metastasis and Hepatocellular Cancer with its lead product NBTXR3

Paris, France, 1 July, 2015 – NANOBIOTIX (Euronext: NANO), a late clinical-stage nanomedicine company pioneering novel approaches for the local treatment of cancer, has been authorized to begin a new clinical trial in liver cancers for its lead NanoXray product, NBTXR3.

- Clinical trial authorization given by French regulatory body in two cancer patient populations with high global incidence (more than 1.5M patients per year)
- Significant enlargement of potential use of NBTXR3 targeting the fourth and fifth indications after Soft Tissue Sarcoma, Head and Neck cancer and Rectum cancer
- Development strategy built to demonstrate "golden" endpoints in oncology such as Overall Survival and Quality of life

The French National Agency for Medicines and Health Products (ANSM) gave Nanobiotix the green light to start a Phase I/II trial in two new cancer populations - hepatocellular cancer (HCC) and liver metastases - for its lead product, NBTXR3. The multinational, non-randomized, open phase I/II study will evaluate the use of NBTXR3 with high precision radiation therapy, delivered as high dose fractions (SBRT - Stereotatic Body Radiation Therapy). This type of therapy is the safest and most modern radiotherapy currently available for the treatment of malignant liver tumors. Nanobiotix's liver cancer trial has been supported by a broad NBTXR3 preclinical program specific to these cancers showing that the use of the product is feasible and well tolerated in animals. The new clinical trial is part of the nanomedicine NICE consortium financed by Bpifrance.

Liver cancers are challenging diseases to address. Most patients, either with HCC or liver metastases cannot benefit from surgery and have few or no therapeutic options available to them.

Radiation therapy has been shown to improve clinical outcomes, including survival with clinical trials showing a direct correlation between higher doses of radiation therapy and better outcomes. However, high doses of radiation in the liver (vital organ) are not usually feasible. SBRT has been shown to be efficient only in specific subsets of population with small tumors. Complete response is a rare event and local control is often compromised in big tumors, metastases and HCC with portal vein tumor thrombosis and short progression Free Survival and Overall survival.

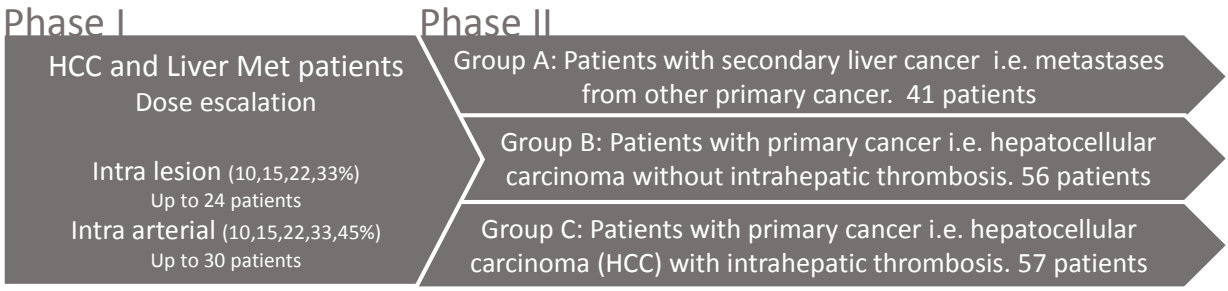
NBTXR3 is activated by radiotherapy and works by the deposit of increased energy doses (radio-enhancement) within the tumor. NBTXR3 may significantly increase the intratumor energy dose with

higher destruction and improve the patient outcome in terms of higher tumor shrinkage, local control and overall survival.

Elsa Borghi, CMO of Nanobiotix said: "*This clinical trial has been designed to test the safety and preliminary efficacy in patients representing three indications (two in HCC and one in liver metastases). Structure and number of patients per group have been chosen based on statistical hypothesis in comparison with literature for an efficient early de-risking. This approach could allow rapid efficacy results to be gathered, opening a faster pathway to market*".

The purpose of this clinical investigation (Phase I and II) is to introduce the use of NBTXR3 with SBRT in patients with liver cancers who need an alternative treatment when the standard of care (SOC) cannot be used or does not exist, such as:

- Patients with liver cancers or underlying liver disease which renders unfeasible some treatments with chemotherapy, biologicals;
- When available local treatments have not been effective e.g. in large tumors;
- HCC with Portal Vein Tumor Thrombosis;
- Inoperable liver metastases.



<u>Phase I:</u> Dose escalation, safety assessment and determination of the Recommended Dose (volume) for the Phase II part

Based on a traditional algorithm design, three different types of tumors will be treated with increasing volumes of NBTXR3. This study step aims to determine the Recommended dose, which will then be evaluated further in the Phase II step with a more specific strategy.

<u>Phase II:</u> Efficacy evaluation and safety of the Recommended Dose (volume)

The Phase II part includes the evaluation of NBTXR3 in three patient groups, which will be investigated simultaneously. The groups are based on the prognosis of patient's disease, they are:

Group A*:* Patients with secondary liver cancer i.e. metastases from other primary cancer

Group B*:* Patients with primary cancer i.e. hepatocellular carcinoma (HCC) without intrahepatic thrombosis of the Portal Vein trunk

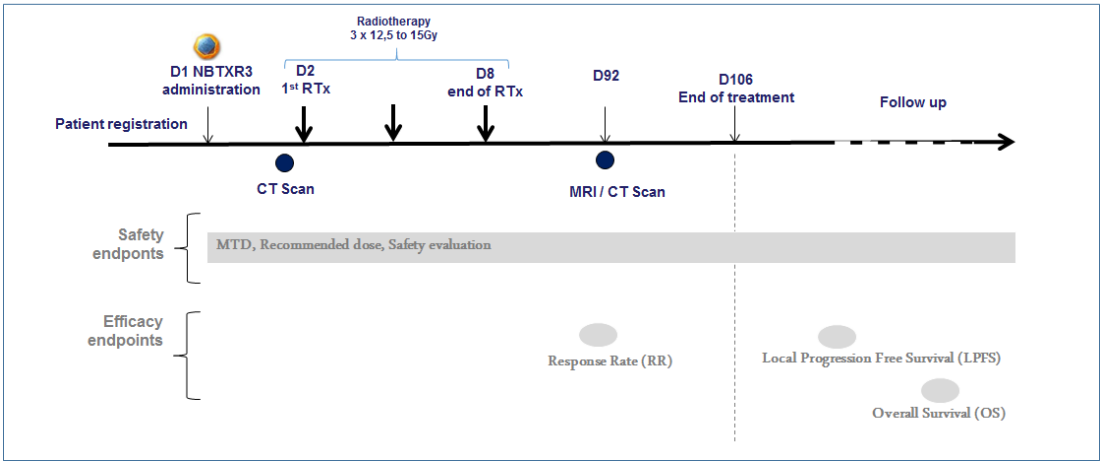
Group C*:* Patients with primary cancer i.e. hepatocellular carcinoma (HCC) with intrahepatic thrombosis of the Portal Vein trunk

Recruitment of patients in every group will be triggered once the Recommended Dose is determined from the previous Phase I part.

Safety and tolerability will be assessed by monitoring adverse events throughout study treatment and follow-up in all patients.

Primary efficacy will be assessed in terms of Complete Response Rate (CRR) as per mRECIST and other specific biomarkers. Local Progression Free Survival (LPFS) and Overall Survival (OS) will be evaluated as main secondary endpoints.

Patient's treatment schedule is described in the figure here below.



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About NBTXR3 clinical development plan

Cancer is a leading cause of death worldwide, which accounted for 8.2 million deaths in 2012. It is expected that annual cancer cases will rise from 14 million in 2012 to 22 within the next two decades (WHO).

Radiotherapy is the second most used treatment for cancer, ahead of pharmaceuticals. An estimated 60% of all newly diagnosed cancer patients receive radiotherapy at some point in the course of their disease. Current radiation therapy has however some limitations due to irradiation of healthy tissues surrounding the tumor.

The NanoXray technology is based on the physical properties of hafnium-oxide nanoparticles and is used to enhance the efficacy of radiotherapy treatment for a variety of cancer indications.

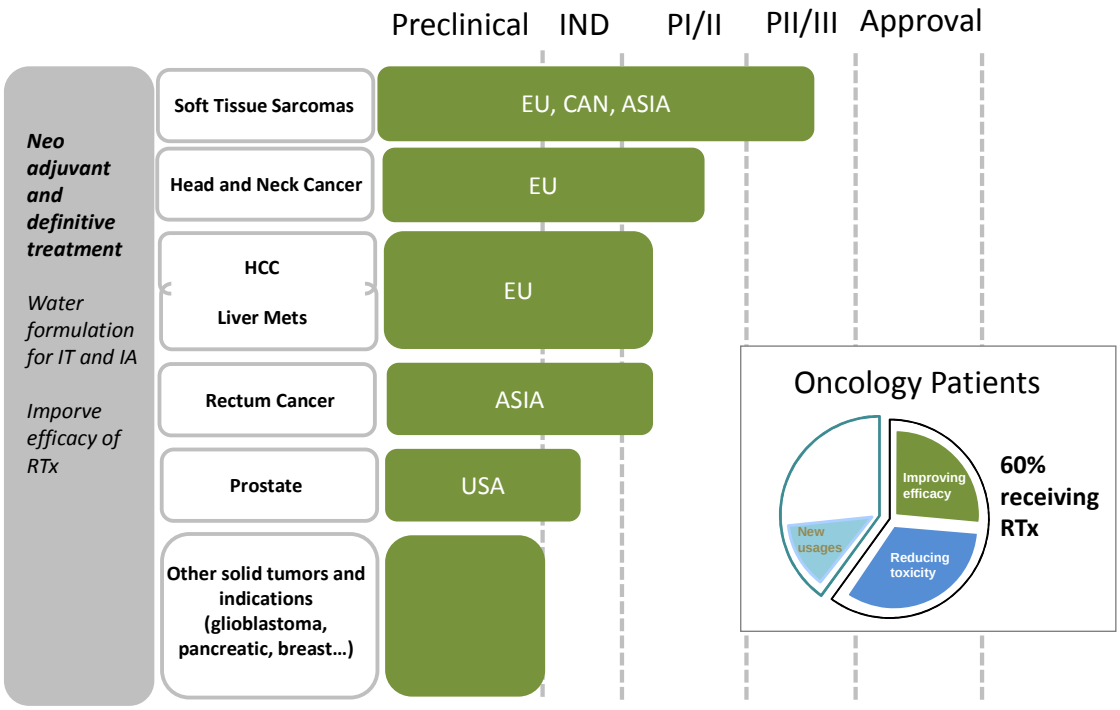
Nanoparticles are designed to enter tumor cells and, upon activation by a standard dose of radiation, they emit large amounts of electrons resulting in the generation of free radicals that destroy cancer cells (they use the same mode of action as radiotherapy). Nanoparticle-enhanced radiotherapy therefore amplifies the lethal dose of energy locally within the tumor without changing the effect of the dose passing through surrounding healthy tissues.

NanoXray Technology could be used to either increase the dose within the tumor (by increasing the curative power of RTx) keeping the usual total dose given to patient. Alternatively, it could reduce the potential toxicity of RTx by reducing the total dose given to patients but keeping the same or higher efficacy of the therapy.

By changing the coating of the nanoparticles, Nanobiotix is developing three different products that can be administered either by direct injection into the tumor (NBTXR3), intravenous injection (NBTX-IV) or topical application to fill tumor cavities after surgery (NBTX-TOPO). The product applied will depend on type of tumor and the patient's specific clinical needs. NanoXray products are compatible with current radiotherapy methods with respect to equipment and protocols, as well as with older radiotherapy equipment or any radiation based therapy (brachytherapy, proton therapy...).

Nanobiotix's focus is to develop NBTXR3 in indications where the standard radiotherapy dose can be given to patients with the intent to increase efficacy. The company pipeline currently includes STS registration trial, H&N PI/II trial, Liver Met PI/II trial, HCC PI/II trial and Rectum cancer PI/II trial (by PharmaEngine). Those trials are running across EU, Asia and Canada. A new prostate cancer trial is also planned to be launched later this year in the US.

Other indications, usage of NBTX3 (e.g. reduce toxicity of RTx) or other products (NBTX TOPO, NBTX IV) of the pipeline will be developed later.



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 cancers including Soft Tissue Sarcoma, Head and Neck Cancer, 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, locally advanced Head and Neck Cancer, Rectum cancer (PharmaEngine) and Liver cancers. 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 Head Quarter is based in Paris, France. Affiliate in Cambridge United States.

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