Heralding the Era of nanoXray™

CONTACTS & KEY INFORMATION

Hdqtrs	Nanobiotix SA 60, avenue Wattignies 75012 PARIS France
Tel **Fax**	+ 33 (0) 1 40 26 04 90 + 33 (0) 1 40 26 04 44
Website	www.nanobiotix.com
Sector	Nanomedicine/cancer
Financing	€12 million: Amorçage Rhône-Alpes, Cap Decisif, Matignon Technologies, OTC Asset Management
Investor Contact:	Dr. Laurent Levy, CEO + 33 (0) 1 40 26 04 90
Media Contact:	Ronald Trahan, President Ronald Trahan Asso. Inc. + 1 508 359 4005, x108

LEADERSHIP TEAM

Laurent Levy, PhD
Co-Founder and
Chief Executive Officer

Elsa Borghi, MD
Medical Director

Kader Boussaha
Co-Founder and COO

NON-EXECUTIVE BOARD

Patrick Langlois, Chairman
General Partner, PJL CONSEILS;
Sr. Adviser, JP Morgan Healthcare

Thierry Chopin, PhD, MBA
Head of R&D, Loist;
Fmr. Head of Inorganic Chemistry, Rhodia, Chemicals Division of Rhône-Poulenc before '98 spin-off

Jérôme Snollaerts
President, CapDecisif

Christophe Douat, MBA
Partner, Matignon Technologies;
Fmr. Strategy Consultant, Boston Consulting Group, Paris

Paul Henry Schmelck, MD, MBA
Partner, OTC Asset Management

● **Pioneering nanomedicine.** **Nanobiotix** is an emerging nanomedicine company combining dramatic advances in nanotechnology and molecular biology to develop **nanoXray™**— a technology platform that is expected to be turned **'on'** and **'off'** *outside the body* to *selectively treat* a variety of cancers safely *and* noninvasively. Nano*Xray* consists of non-drug *nanoparticles,* designed to be introduced by injection, which then attach themselves only to specifically targeted cancer cells. Nano*Xray* nanoparticles are comprised of two parts: (1) an inorganic core which, through outside-the-body activation, is designed to cause destruction of the targeted cancer cells via a physical reaction, and (2) a coating layer on the surface that prevents interaction with biology and increases the targeting of cancer cells. After accumulation in targeted cancer cells, the core of the nanoparticles is activated by applying an external energy source—an X-ray—triggering the nanoparticles to attack *only* the cells they are attached to—cancer cells. In short, **the goal is to treat cancer with an injection and Xray**. The targeted mechanism of action explains the accuracy of nano*Xray*'s medicinal activity and expected excellent tolerance by the body. Because therapeutic activity is triggered externally, this implies **total control** of the nano*Xray* cancer therapy.

● **NanoXray™, designed to resolve cancer therapy's biggest limitation.** Use of **NanoXray** is intended to resolve radiation therapy's biggest drawback: destruction of healthy tissue and its subsequent deleterious side effects when a high dose of Xray is necessary. The core of a nano*Xray* nanoparticle is an inactive and inert substance—not a drug—that can subsequently be activated in order to locally (intratumor) increase the dose of Xray, which is then expected to lead to higher efficiency. After nano*Xray* nanoparticles accumulate in the target tissues, a standard X-ray is applied that is intended to generate a *local* therapeutic effect, designed to destroy *only the targeted tumor cells*. This mechanism suggests **total control** of the intended therapeutic effect.

● **Big problem, elegant solution.** One in four deaths in the U.S. is from cancer, making it the second-leading cause of death after heart attack. Nano*Xray* offers a dramatic innovation in cancer therapy, based on a technology that is designed to allow **destruction of cancer cells only**. Nano*Xray* thus offers a new treatment weapon that could be used alone, or in concert with existing anticancer protocols: chemotherapy, surgery, and immunotherapy. Because nano*Xray* does not interact with healthy cells, it is expected to **prevent the toxic side effects** associated with chemotherapy. Additionally, nano*Xray* offers the potential of an **"on/off" therapy**, because the **nanoparticles by themselves are not active**; there is a need for physical stimulation of these compounds, with an Xray, after injection. Efficacy is expected to be proportional to the duration of activation and the number of nano*Xray* sessions. Taking into account the mechanism of action of nano*Xray*, it is expected that administration of nano*Xray* will not have to be chronic, thus preventing the risk of an immune response and toxicity by accumulation. Indeed, use of **nontoxic** nano*Xray* compounds should **decrease the risk of adverse events**, allowing the use of **higher doses**, leading to **superior anticancer activity**.

nanoXray™ Platform...

The nanoparticles that comprise the **nanoXray™** platform allow for an extensive combination of therapeutic modalities and malignant pathologies. **Nbtxr3**, the first product to be developed from the nano*Xray* pipeline, also is the first-in-class product to be activated by radiotherapy. Below are the intended initial indications for *Nbtxr3*.

Prostate Cancer	Breast Cancer	Colon Cancer	Lung Cancer	Pancreatic Cancer
The most common cancer, after skin cancer, in American men.	Worldwide, the second most common type of cancer after lung cancer.	Second leading cause of cancer related death in the Western world.	Most common cause of cancer related death in men annually worldwide.	Early diagnosis is difficult, because symptoms are non-specific and varied.

Tiny Science, Big Time Cure

Groundbreaking nano*Xray*™ cancer therapy may enable the precise 'on/off' *and* selective extermination of cancer cells practically anywhere in the body:

TREATING CANCER WITH ONE INJECTION AND AN X-RAY?

The Nanobiotix leadership team believes that the *nanoXray*™ platform has the potential to treat a variety of cancers with an injection of patented nanoparticles that are activated by an X-ray.

"NanoXray is not toxic in animals, so we expect very good patient tolerance and an increase in efficacy that will kill more tumor cells."
Kader Boussaha
Co-Founder and COO
Nanobiotix

"NanoXray offers a new modality of cancer care: a breakthrough allowing destruction of cancer cells by physical, *not* chemical, *mechanisms."*
Elsa Borghi, MD
Chief Medical Officer
Nanobiotix

"A new approach to treating cancer is needed. NanoXray is the first product in its class that, by itself, will play the pivotal therapeutic role."
Christophe Douat
Matignon Technologies
Nanobiotix investor

"The company has mastered the critical synthesis issues related to nanoXray—reproducibility, scalability, and stability."
Patrick Langlois
PJL CONSEILS
Nanobiotix Chairman

"NanoXray has demonstrated outstanding safety in preclinical tests, with even a single dose making possible significant tumor growth delay."
Paras N. Prasad, PhD
SUNY
Nanobiotix science adviser

Nanomedicine is the medical application of nanotechnology. Nanotechnology allows the manufacturing of matter at any scale, ranging from single atoms and molecules to micrometer-sized objects. Its application in biology is potentially very large: from new diagnostic tests *in vitro* or *in vivo* to novel delivery methods that improve the efficacy of pharmaceutical therapy; from reducing drug- and radiation-therapy side effects to making drug administration much more convenient. These applications exploit nanotechnology to improve the quality and sensitivity of a wide variety of different technologies in order to create new approaches for drug delivery and imaging, with novel targeted agents too. In fact, for the most part, nanotechnology in medicine has an *enabling* function in many different areas.

Nanobiotix has explored other fields, enabling the use of nanomaterials as the "active product" with therapeutic purposes. The Company has successfully integrated two worlds, the promising nanotechnology industry and medicine. It is developing **Nbtxr3** (its patented nanoparticle) as a non-drug agent able *on its own* to kill tumor cells. *Nbtxr3* nanoparticles can be injected into cancer patients at a tumor site and taken up by cancer cells—*but not normal cells and tissue*. Then patients would undergo a standard X-ray procedure that would "switch on" the destructive capability of the *nbtxr3* nanoparticles, causing the membranes of cancer cells to rupture. "NanoXray, in short, allows for the *controlled* generation of *physical* reactions in targeted cells triggered by the application of an *external* energy source—a standard X-ray. This may have significant ramifications for cancer therapy in the not-too-distant future," says **Paras N. Prasad, PhD**, executive director of the Institute for Lasers, Photonics and Biophotonics at SUNY (Buffalo) and one of the world's leading authorities on nanotechnology.

"Our platform technology, nanoXray, will allow the precise destruction of cancer cells via the controlled application of an outside-the-body energy source—an X-ray,"
says Laurent Levy, PhD, co-founder and CEO of Nanobiotix, and co-inventor of nano*Xray*™.

Early Data Impress Oncologists

"Preclinical data involving nano*Xray* are very impressive," says **Dr. Jean Bourhis**, MD, PhD, Head of the Radiation-Oncology Department at Institut Gustave-Roussy, one of the largest cancer centers in Europe. "To date, we have evaluated the pharmacodynamic of nano*Xray* in mice bearing colon tumors after intravenous injection of nano*Xray* nanoparticles. Their accumulation takes place principally in the tumor, between 8 and 16 hours after injection. This active overloading in the tumor compared to healthy organs demonstrates the specificity of nano*Xray* as a cancer treatment. The selective biodistribution and rapid clearance of the nanoparticles suggest that nano*Xray* could be very suitable for selectively fighting a wide variety of cancer.

"Between 50 and 60 percent of cancer patients are treated with radiotherapy, which is used to treat *localized* solid tumors, including breast, head and neck, bladder, lung and skin cancers," adds Dr. Bourhis. "Radiation therapy, of course, requires a stream of high-energy gammas rays, for example, to kill cancer cells, which, unfortunately, affects *both* cancer and normal cells. Wouldn't it be wonderful if we could selectively treat *only* cancer cells, while avoiding destruction of normal cells?" ■

'30-Something' Nanotech Mastermind Laurent Levy Wants To Play the Seminal Role In Making Cancer Treatments More Effective, Less Deadly To Healthy Tissues

A DECADE OF PIONEERING THE MARRIAGE OF MOLECULAR BIOLOGY AND PHYSICS... DR. LEVY WANTS TO BE ABLE TO TREAT CANCER ALMOST ANYWHERE INSIDE THE HUMAN BODY—WITH AN INJECTION AND XRAY... FOR STARTERS. "I was raised to be curious *and* pragmatic. I've always had an interest in learning how things work. And I have also been interested in exploring the unknown. When I was young, I said to my parents: 'Okay, people say that the universe is infinite, but what is *after* it?' Until I was 25, I was pretty bored by all my studies," admits Dr. Levy. "But after years of university studies, something just connected for me: I could understand enough of physics, chemistry and biology to do something with this combination, something perhaps that had not been done before. So I started my doctorate, and at the end I began to develop my *own* vision about using nanotechnology to treat cancer." At a nanotechnology-focused scientific meeting in France, Dr. Levy sought out **Dr. Paras Prasad**, Director of the renowned Institute for Lasers, Photonics and Biophotonics at SUNY in Buffalo, told him what he wanted to do, and Dr. Prasad said, 'Why not?' "I quickly enrolled at SUNY to complete my PhD," says Dr. Levy. "From the start, Paras and I were on the same wavelength. Fortunately for me, he is one of the giants working in the nanophotonic and nanobiotech field."

DR. LEVY'S BIG PLANS FOR HIS TINY SCIENCE: VALIDATING A NEW MODALITY OF CANCER TREATMENT

One *nanometer*, which is one-*billionth* of a meter, spans 10 atoms. Put another way... "How small do we mean by *nano*? Let's take a trip down the powers of ten: a dime is 1,000 microns thick, a human egg cell is a tenth of that, a red blood cell is a tenth of that, a nerve axon is a tenth thinner still, and you can fit ten viruses along that axon's diameter. Now we're down to 100 nanometers. A cell's membrane is a tenth as thick as that, a DNA strand is a fifth as thick as that, and an amino acid is a third of that. *Now* we're down to *one nanometer*." (Source: Stephan Herrera, "The Big Science of Nanomedicine", *Red Herring* Mag., Oct. 30, 2000)

NANOMEDICINE EVOLUTION: "NANOXRAY™" — THE NEXT BIG THING IN CANCER THERAPY??

Nano*Xray*™, co-invented by Dr. Levy and Dr. Prasad, is designed to circumvent radiation therapy's biggest drawback: destruction of healthy tissue and other subsequent deleterious side effects on the human body when a high dose of radiation is necessary to destroy the targeted tumor(s). The core of a nano*Xray* nanoparticle is an inactive and inert substance—*not a drug*—that can subsequently be activated in order to locally (intratumor) increase the dose of Xray, which is then expected to lead to higher cell death and efficiency. After nano*Xray* nanoparticles accumulate in the target tissues, a standard X-ray is applied that is intended to generate a *local* therapeutic effect, designed to destroy *only the targeted tumor cells* and not harm surrounding healthy tissue. "This **total control** of the intended therapeutic effect is the holy grail," insists Dr. Levy. ■

DR. LAURENT LEVY

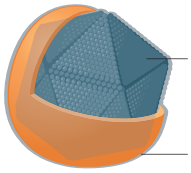
Co-Founder and Chief Executive Officer

LAURENT LEVY, PhD, *has a deep understanding of the technical, scientific, intellectual property and marketing issues associated with nanotechnologies, because he has been working—and achieving—in these areas for more than a decade. His* **pioneering research** *at the frontier of molecular biology and physics has empowered him to develop a number of* **practical applications**, *not the least of which is* **nanoXray™**, *the technology foundation of* **Nanobiotix**, *which is focused on making possible a whole* **new era in cancer medicine**. *Dr. Levy has worked for many years as a consultant in business development and in the implementation of nanotechnologies with major companies, including* **Sanofi Aventis** *(an international pharmaceutical giant),* **Guerbet** *(a multinational medical imaging company), and* **Rhodia** *(a global specialty chemicals company), as well as start-up biotechs. He is the president of the* **French Technology Platform of Nanomedicine** *and is involved with many international groups working in the field. The author of 35 international publications and communications, Dr. Levy holds several patents and completed post-doctoral work at the* **Institute for Laser Photonics and Biophotonics, State University of New York (SUNY), Buffalo**. *Dr. Levy holds a PhD in Physical Chemistry specializing in Nanomaterials from Pierre et Marie Curie University-CEA, and a DEA (first doctoral diploma) in Condensed Matter from UPVI-ESPCI (Paris).*

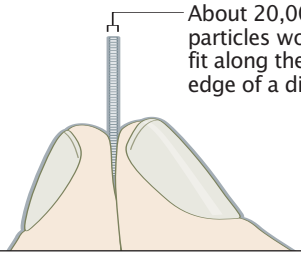
Small wonders

The nanoXray™ technology developed by Nanobiotix uses miniscule particles to dramatically improve the efficiency of radiation therapy in the treatment of cancer.

A tiny device



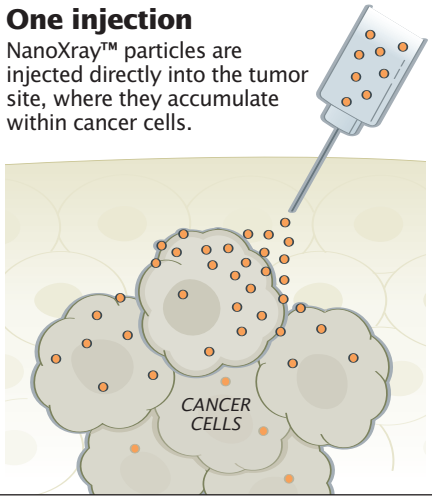
The nanoXray™ particle is made of a *nanocrystal* (dense, highly organized core) surrounded by a *thin amorphous coating*.



About 20,000 particles would fit along the edge of a dime.

One injection

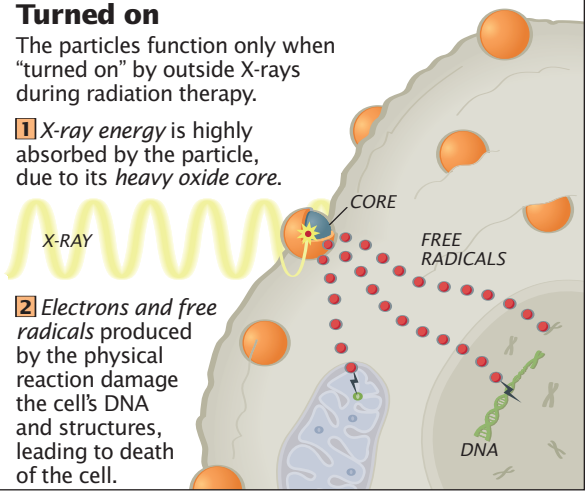
NanoXray™ particles are injected directly into the tumor site, where they accumulate within cancer cells.



Turned on

The particles function only when "turned on" by outside X-rays during radiation therapy.

1 *X-ray energy* is highly absorbed by the particle, due to its *heavy oxide core*.



2 *Electrons and free radicals* produced by the physical reaction damage the cell's DNA and structures, leading to death of the cell.