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Our vision is to change the face of treatment for millions of patients by bringing nanophysics to the heart of the cell
NANOBOTIX AT A GLANCE

FIRST-IN-CLASS PRODUCT
- NBTXR3 is a radioenhancer with the potential to improve outcomes for millions of oncology patients
- Disruptive technology with universal, physical MoA
- 15 clinical trials (H&N, lung, liver, pancreas, prostate, etc.)

DE-RISKED APPROACH
- Clinical proof of concept established in a randomized PIII trial in STS (featured in The Lancet Oncology)
- First European market approval (CE Marking) obtained
- IP (300+ patents issued or in process of issuance)
- Positive PI in H&N & Liver showing strong potential for improving survival and quality of life, excellent safety with 0 DLTs

UPCOMING VALUE DRIVERs
- Phase III in locally advanced H&N registration in US to begin
- IO combination trial results in PD-1 resistant patients in recurrent H&N
- European expansion phase I end of recruitment in locally advanced H&N

FINANCIAL POSITION
- Publicly-traded, Euronext: NANO – ISIN: FR0011341205
- EUR 54.9M as of June 30, 2019, visibility until end of 2020
Millions of patients receive radiotherapy each year but still have significant unmet medical needs
18M new patients per year

Radiotherapy is the most common treatment...

Receiving RTx

- 83% Breast cancer: 2,088,849
- 76% Lung cancer: 2,093,876
- 78% H&N: 705,781
- 60% Prostate: 1,276,106
- 61% Rectum: 704,376
- 57% Pancreas: 458,918
- 92% CNS: 296,851

Source: *World Health Organization (2014); **Radiation Therapy Equipment – A global strategic business report 01/06; Delaney et al. 2005; Globocan 2018
Inadequate local control
(Local invasion or systemic expansion)

Inadequate systemic control
(metastatic patients)

Unfavorable safety profile
(dose de-escalation/re-irradiation)

18M new patients per year

60% RTx

...BUT STILL PRESENTS SIGNIFICANT
UNMET MEDICAL NEEDS

THE UNMET NEED

Source: * World Health Organization (2014); **RADIATION THERAPY EQUIPMENT – A global strategic business report 08/06;
NBTXR3 is a first-in-class, universal solution to transform radiotherapy into nanoradiotherapy
FIRST-IN-CLASS RADIOENHANCER NBTXR3

- First-in-class radioenhancer
- Aqueous suspension of inorganic crystalline hafnium oxide (HfO2) nanoparticles
- Nanosized to enter the cell and designed to strongly absorb ionizing radiation
- Universal mode of action targeting all solid tumors
- Demonstrated clinical benefit in a Phase III trial
- First European market approval obtained
- One-time Intra tumoral administration
- Compatible with existing equipment
- Patient flow stays identical
- Patients receive standard radiation therapy
- Approach validated in several indications
**FIRST-IN-CLASS RADIOENHANCER NBTXR3**

**NBTXR3** creates hyper-focused dose delivery in the heart of the cell.

*Note: Dose enhancement determined by monte carlo simulation (CEA Saclay, France)*

- Usual dose delivered in the cell
- Clusters of Nanoparticles
- Local absorption of energy

Dose* around nanoparticles

![Diagram showing dose enhancement](image-url)
NBTXR3’s PHYSICAL, UNIVERSAL MOA triggers cellular destruction along with adaptative immune response.

**Physical damage inducing**
- Structural Damage
- DNA damage
- Stress
- Immunogenic Cell Death
- Sting pathway activation

**Direct Cell Death**
(Apoptosis, Necrosis, ...)

**Cell Killing by CD8/CD4 activation**
Nanobiotix will develop NBTXR3 across tumor indications with radiation alone and in combination with other therapies.
### Global Development Strategy

#### Product with Physical and Universal Mode of Action
- Transferability across solid tumors
- Front line treatment & metastatic treatment

#### Clinical PoC demonstrated in Soft Tissue Sarcoma Phase II/III
- CE Marking obtained
- New mode of action validated in randomized trial
- Primary endpoint: Pathological Complete Response Rate doubled vs radiation alone
  - Target: Start diffusing the product in EU

#### H&N first indication to be registered in US
- Positive Phase I data on advanced patients
- Showing potential impact on OS, ORR, QoL and well tolerated
  - Target: Demonstrate the medical value in a high unmet medical needs population

#### Clinical development in PD-1 resistant patients
- Phase I: Actively recruiting
  - Target: Demonstrate the value of NBTXR3 in metastatic disease, transforming cold tumors into hot tumors

#### Expansion of NBTXR3 usage
- Five ongoing Phase I/II in multiple solid tumors
- Nine additional clinical development trials planned with MD Anderson global collaboration
### Global Development Strategy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Soft Tissue Sarcoma</strong>&lt;br&gt;Soft Tissue Sarcoma of the Extremity and Trunk Wall</td>
<td></td>
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</tr>
<tr>
<td><strong>Head and Neck</strong>&lt;br&gt;Locally advanced Head &amp; Neck cancers&lt;br&gt;Head &amp; Neck cancers&lt;br&gt;Ind, locally advanced H&amp;N cancers (re-irradiation)&lt;br&gt;Rec/met H&amp;N cancers w/ limited PD-L1 expression&lt;br&gt;Recurrent Head &amp; Neck cancers / Lung Liver metastases&lt;br&gt;Advanced solid tumors and lung or liver mets</td>
<td></td>
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<tr>
<td><strong>NSCLC</strong>&lt;br&gt;Stage IV lung cancer&lt;br&gt;Lung cancer in need of re-irradiation</td>
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<tr>
<td><strong>Esophagus</strong>&lt;br&gt;Esophageal cancer</td>
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<tr>
<td><strong>Pancreas</strong>&lt;br&gt;Pancreatic cancer</td>
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<tr>
<td><strong>Liver</strong>&lt;br&gt;Hepatocellular carcinoma / Liver metastasis</td>
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<tr>
<td><strong>Rectum</strong>&lt;br&gt;Rectum cancers</td>
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<tr>
<td><strong>Prostate</strong>&lt;br&gt;Prostate cancer</td>
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</tbody>
</table>
POSITIVE PHASE II/III RESULTS VALIDATE THE MODE OF ACTION OF NBTXR3 IN SOFT TISSUE SARCOMA (THE LANCET ONCOLOGY, AUGUST 2019)
LOCALLY-ADVANCED SOFT TISSUE SARCOMA
OF THE EXTREMITIES AND TRUNK WALL

- High risk tumor
- Borderline unresectable tumor or
  unfeasible carcinological surgical resection
- Preoperative radiotherapy alone
  is Standard of Care

PATIENTS IN NEED OF
BETTER LOCAL CONTROL
TO PREVENT RELAPSE
Phase II/III randomized, multi-center, open-label and active controlled two arms study

**Soft Tissue sarcoma (STS) of the extremity and trunk wall**

- Age ≥ 18 years-old
- Locally advanced soft tissue sarcoma, newly diagnosed or relapsed tumor
- High-risk tumor
- Unresectable tumor or unfeasible carcinological surgical resection
- WHO score of 0 to 2

**Primary endpoint:**
- Pathological complete response rate* (pCRR) following EORTC Guidelines(1)

**Secondary endpoints:**
- Safety
- Carcinologic resection (surgical margin, R0, ...)
- Pathological Response (pR)
- Amputation rate

**Stratification:**
- Myxoid liposarcoma / other

**Arm A**
NBTXR3* activated by EBRT**

**Arm B**
EBRT** alone

N=180 randomized

32 sites in 11 countries in Europe and Asia

---

* IT injection of a dose, 10% of baseline tumor volume
** 50 Gy, 25 fractions x 2 Gy, over 5 weeks

# 4 patients excluded from the ITT Full analysis set: 3 did not have STS (2 in Arm A, 1 in Arm B), 1 (in Arm A) was not eligible for preoperative RT

# Pathological Response evaluated by an independent central Pathological Review Board

Primary endpoint met

NBTXR3 activated by radiotherapy (N=87)
Radiotherapy alone (N=89)

Pathological Complete Response

p-value 0.0448*

16.1

X2

7.9

% of patients with pCR

Complete Pathological Response

180 patients / RTx vs RTx+NBTXR3
Primary Endpoint pCRR* x2 in ITT FAS* population

*pCRR = Pathological Complete Response Rate
**ITT FAS = Intention To Treat Full Analysis Set; statistically significant at α = 0.05 threshold of 0.04575
pCRR x4 in grade 2 & 3 subpopulation

Pathological Complete Response
<5% residual viable cancer cells

- Grade 1
  - n=15
  - 1.3%
  - NBTXR3 activated by radiotherapy

- Grade 2/3
  - n=61
  - 3.9%
  - Radiotherapy alone
  - 17.1%
  - x4

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The study also met its secondary endpoints

Significant increase in R0 rate in the NBTXR3 arm

Significant increase in tumor necrosis/infarction in the NBTXR3 arm

- p-value 0.0424*
- p-value 0.0140*
**NBTXR3 impact on the standard of care (planned radiation and surgery)**

- No change in Median Relative Radiation therapy dose intensity*
- No change in Median Duration of radiotherapy schedule (days)
- No change in % of surgery performed

**THE STUDY CONFIRMED:**
- Feasibility of injection
- No change in dosage and schedule of current radiotherapy standard of care
- Good local tolerance (similar radiation safety in both arms)
- Manageable acute immunological reaction occurring at the time of injection

*No impact on planned radiation and surgery*

---

**Safety – Phase II/III in STS**

<table>
<thead>
<tr>
<th></th>
<th>Arm A NBTXR3 activated by RT (N=89)</th>
<th>Arm B RT alone (N=90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with any TEAEa</td>
<td>87 (97.8%)</td>
<td>87 (96.7%)</td>
</tr>
<tr>
<td>Patients with any NBTXR3 related TEAE</td>
<td>31 (34.8%)</td>
<td>NA</td>
</tr>
<tr>
<td>Patients with any TEAE leading to death (death regardless the causality assessment)</td>
<td>0</td>
<td>2 (2.2%)</td>
</tr>
<tr>
<td>Patients with any serious TEAE</td>
<td>28 (31.5%)</td>
<td>14 (15.6%)</td>
</tr>
<tr>
<td>Patients with any serious NBTXR3 related TEAE</td>
<td>9 (10.1%)</td>
<td>NA</td>
</tr>
<tr>
<td>Patients with any serious TEAE related to radiation therapy</td>
<td>5 (5.6%)</td>
<td>5 (5.6%)</td>
</tr>
<tr>
<td>Patients with any serious AEb</td>
<td>35 (39.3%)</td>
<td>27 (30.0%)</td>
</tr>
<tr>
<td>Patients withdrawn from study treatment due to TEAE</td>
<td>1 (1.1%)</td>
<td>0</td>
</tr>
</tbody>
</table>

*a Treatment Emergent AEs are AEs observed during the on-treatment period.*

*b Serious AEs are adverse events reported during the whole study period (i.e. on-treatment and follow-up periods), NA, not applicable.
FOCUSING ON HEAD & NECK CANCER TO SHOW IMPROVEMENT IN OVERALL SURVIVAL AND QUALITY OF LIFE (ASCO/ASTRO 2019)
Locally-advanced Head and Neck cancer in elderly and frail patients

- Stage III and IV
- >70 years old, frail
- Oral cavity, Oropharynx
- HPV all status (positive & negative)
- Ineligible for chemotherapy and intolerant to cetuximab in combination with RT

**RADIOTHERAPY IS THE ONLY OPTION TO TREAT THIS FRAGILE H&N CANCER POPULATION AND BENEFITS ARE LIMITED (I.E., LOW ORR, SHORT PFS, POOR QOL)**
**PATIENT POPULATION**

- ≥ 65 years-old
- KPS > 70
- Stage III or IV HNSCC* of the oral cavity or oropharynx
- Eligible for radiotherapy
- Not eligible for cisplatin or cetuximab
- No metastases
- Adequate organ functions

**3 + 3 Design to assess 4 dose levels**

- 5%
- 10%
- 15%
- 22%

Injected volume calculated as a % of tumor volume determined on an MRI performed <14 days prior to injection

**ENDPOINTS**

- Assess DLTs, RP2D, MTD if possible
- Safety and tolerability
- Early signs of anti-tumor activity: ORR

**Single intratumoral injection of NBTXR3 activated by Radiotherapy**
Literature data:
NBTXR3
Phase I/II
Study Population has a poor
Overall Survival prognostic
Stage III and IV

NBTXR3 PI/II patients should have equal or poorer prognosis
- Tumor location (Oropharynx & Oral cavity)
- Stage III-IV only
- >70 years

Amini et al., Cancer May 15, 2016
Bourhis et al., Journal of Clinical Oncology, June 2006
Moye et al., The Oncologist 2015;20:159–165
Depth of best response*
(update ICHNO 2019)

9 CR, ~90% ORR at highest doses
CR linked to QoL

*Disease Progression
*Disease Stabilization
*Partial Response
*Complete response

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Depth Follow up of patients*, PFS, Survival

(update SIOG 2019)

Potential impact on OS
NBTXR3 expected value in Head and Neck cancer
(ICHNO/ASCO 2019)

No SAEs related to NBTXR3/Good safety profile

100% of disease control at all doses*
9/11 CR at higher doses*
(10%, 15%, 22%)

Potential impact on QoL for patients

Median follow up of >20 months*

Potential impact on Survival

* Excluding non-evaluable patients & those recently added in the trial
## Safety – Phase I/II in H&N

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>N</th>
<th>DLT</th>
<th>AEs related to NBTXR3 injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
<td>3</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>3</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>15%</td>
<td>5</td>
<td>No</td>
<td>Grade 1 tumor hemorrhage (N=1)</td>
</tr>
<tr>
<td>22%</td>
<td>8</td>
<td>No</td>
<td>Grade 2 oral pain (N=1) Grade 1 asthenia (N+1) Grade 1 injection site pain (N+1)</td>
</tr>
</tbody>
</table>

**Recommended dose** defined by DSMB as **22%**
ACCELERATING LIVER DEVELOPMENT DUE TO STRONG PHASE I RESULTS (ASTRO/ESMO 2019)
Hepatocellular Carcinoma (HCC) & Liver Mets

Hard to treat patient population:
- Previous resection/local treatment is permitted
- Hepatocellular carcinoma or Liver Mets
- Unrespectable/Medically Inoperable tumors
- ECOG 0 or 1

HIGH UNMET NEEDS FOR PATIENTS AS THEY HAVE UNDERLYING LIVER DYSFUNCTION AND CONCOMITANT MALIGNANCIES THAT LIMIT TREATMENT OPTIONS
Material/Methods: Study design: Phase 1 dose escalation

**PATIENT POPULATION**

- ≥ 18 years-old
- ECOG 0 or 1
- Hepatocellular Carcinoma (HCC) patients
  - Unsuitable for surgery or local treatment
  - Child Pugh A–57
  - With or without portal vein thrombosis
  - Life expectancy > 3 months
- Liver metastases (Mets) patients
  - Unrespectable tumor(s)
  - Life expectancy > 6 months

3 + 3 Design to assess 5 dose levels

10%  15%  22%  33%  42%

Injected volume calculated as a % of tumor volume determined on an MRI performed <14 days prior to injection

Single intratumoral injection of NBTXR3 activated by Radiotherapy

**ENDPOINTS**

- Assess DLTs, RP2D, MTD
- Safety and tolerability
- Liver function: Child-Pugh score (ALBI also explored)
- Early signs of anti-tumor activity per mRECIST (HCC) / RECIST 1.1 (Mets)
HCC: Follow up of patients, PFS, Survival

Oral presentation at ASTRO 2019

Cut-off date: 10 JUN 2019

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Evaluable Patients n</th>
<th>Complete Response n, (%)</th>
<th>Partial Response n, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>8</td>
<td>5 (62.5)</td>
<td>3 (37.5)</td>
</tr>
</tbody>
</table>

† Cause of death unknown
* Patient response evaluation is performed by CT-scan only due to pacemaker
†† patient with secondary cancer (myeloma)
$ patient on liver transplant list
††† Non cancer-related death

* Average median survival in HCC
† patients treated by RTx
Liver cancer & Radiotherapy: Sayan et al. 2019 Front Oncol

TABLE 4 | Studies of 3D CRT and IMRT for hepatocellular carcinoma.

<table>
<thead>
<tr>
<th>References</th>
<th>Study design</th>
<th>Modality</th>
<th>N</th>
<th>Tumor size</th>
<th>CPS A/C/ (%)</th>
<th>Radiation therapy dose</th>
<th>Follow-up</th>
<th>Response (C/F)</th>
<th>Overall survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chong et al. (72)</td>
<td>Prospective</td>
<td>3D CRT</td>
<td>13</td>
<td>15 cm (6-25)</td>
<td>60/31/0</td>
<td>40-60 Gy @ 1.8-2 Gy/fx</td>
<td>40 mo</td>
<td>60%</td>
<td>1 yr 100%</td>
</tr>
<tr>
<td>Liu et al. (73)</td>
<td>Prospective</td>
<td>3D CRT</td>
<td>44</td>
<td>N/A</td>
<td>73/27/0</td>
<td>40-60 Gy @ 1.5 Gy/fx</td>
<td>8 mo</td>
<td>61%</td>
<td>1 yr 61%</td>
</tr>
<tr>
<td>Momox et al. (74)</td>
<td>Prospective</td>
<td>3D CRT</td>
<td>27</td>
<td>3.2 cm (1-6)</td>
<td>56/41/0</td>
<td>66 Gy @ 2 Gy/fx</td>
<td>29 mo</td>
<td>92%</td>
<td>2 yr 40%</td>
</tr>
<tr>
<td>Kim et al. (75)</td>
<td>Retrospective</td>
<td>3D CRT</td>
<td>70</td>
<td>7.5 cm (2-17)</td>
<td>80/20/0</td>
<td>44-54 Gy @ 2.3 Gy/fx</td>
<td>9 mo</td>
<td>54%</td>
<td>1 yr 43%</td>
</tr>
<tr>
<td>Kim et al. (76)</td>
<td>Prospective</td>
<td>IMRT</td>
<td>35</td>
<td>N/A</td>
<td>80/20/0</td>
<td>45-60 Gy @ 1.6 Gy/fx</td>
<td>13 mo</td>
<td>52%</td>
<td>2 yr 22%</td>
</tr>
<tr>
<td>Chi et al. (77)</td>
<td>Prospective</td>
<td>IMRT</td>
<td>23</td>
<td>N/A</td>
<td>65/35/0</td>
<td>52.5 Gy @ 2.5 Gy/fx</td>
<td>16 mo</td>
<td>74%</td>
<td>1 yr 70%</td>
</tr>
<tr>
<td>McNichol et al. (78)</td>
<td>Retrospective</td>
<td>IMRT</td>
<td>20</td>
<td>9 cm (1.3-1.7)</td>
<td>55/45/0</td>
<td>30-60 Gy @ 2 Gy/fx</td>
<td>60%</td>
<td>1 yr 76%</td>
<td></td>
</tr>
<tr>
<td>Kang et al. (79)</td>
<td>Retrospective</td>
<td>IMRT</td>
<td>27</td>
<td>11 cm (8-13)</td>
<td>70/30/0</td>
<td>45-64 Gy @ 2.5 Gy/fx</td>
<td>5 mo</td>
<td>44%</td>
<td>2 yr 50%</td>
</tr>
<tr>
<td>Dong et al. (80)</td>
<td>Retrospective</td>
<td>IMRT</td>
<td>22</td>
<td>4.4 cm (0.9-1.9)</td>
<td>68/32/0</td>
<td>30-60 Gy @ 1.8 Gy/fx</td>
<td>14 mo</td>
<td>73%</td>
<td>1 yr 86%</td>
</tr>
<tr>
<td>Huang et al. (81)</td>
<td>Retrospective</td>
<td>IMRT</td>
<td>38</td>
<td>4.6 cm (2.5-17)</td>
<td>71/20/0</td>
<td>45-72 Gy @ 1.8-2.4 Gy/fx</td>
<td>17 mo</td>
<td>53%</td>
<td>1 yr 56%</td>
</tr>
</tbody>
</table>

CPS, Child-Pugh score; 3D CRT, 3-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy; N/A, not reported; C/F, complete/partial.

NBTXR3

| NBTXR3 | Study design | Modality | N  | Tumor size | CPS A/C/ (%) | Radiation therapy dose | Follow-up | Response (C/F) | Overall survival |
| NBTXR3 | Prospective | SBRT | 11 | 4 cm (1.1-5.4) | 90/10/0 | 45-50 Gy @ 10-15 Gy/fx | - | 100% | 1 yr 100% |

*On evaluable patients

GLOBAL DEVELOPMENT STRATEGY

JANUARY 2020
Liver mets: Follow up of patients, PFS, Survival

Oral presentation at ASTRO 2019

[Diagram showing treatment periods and response rates]
## Safety – Phase I/II in Liver

<table>
<thead>
<tr>
<th>NBTXR3 dose</th>
<th>Preferred term</th>
<th>Worse grade</th>
<th>AE (n)</th>
<th>SAE (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>Malaise</td>
<td>Grade 2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>15%</td>
<td>Abdominal pain</td>
<td>Grade 3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>22%</td>
<td>Bilateral pleural effusion</td>
<td>Grade 1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Bile ductstenosis</td>
<td>Grade 3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>33%</td>
<td>Fatigue</td>
<td>Grade 1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*No NBTXR3 related DLT / No leakage in surrounding tissue*
EXPANDING NBTXR3 TO PRIME AN IMMUNE RESPONSE AND COMBINE WITH CHECKPOINT INHIBITORS
Patients have a significant unmet need as a vast majority tumors are unresponsive to checkpoint inhibitors & other I/O approaches.
Example:
Immunotherapy
Nivolumab
in recurrent
patients H&N

Nivolumab: Checkmate 141
*Recurrent Head and Neck*
Phase I/II in NSCLC & H&N to be initiated in combination with PD-1 Inhibitors

Checkpoint inhibitors refractory patients in NSCLC & H&N

Transform the non-responders into responders with NBTXR3 and RTx
Phase I Dose Escalation

**anti PD-1 non responders**
(pembrolizumab or nivolumab):
- SD for at least 12 weeks or confirmed PD at 12 weeks

**COHORT 1:**
Locoregionally recurrent AND metastatic HNSCC

**COHORT 2:**
Patients with lung metastasis
Any primary tumor

**COHORT 3:**
Patients with liver metastasis pre-treated
Any primary tumor
Combination of R3 + RTx + cPI is always the best (local control & systemic control)
**NBTXR3**

**increases**

**activated CD8**

**tumor infiltration**

Phase III Soft Tissue Sarcoma biomarker data
EXPANDING NBTXR3 ACROSS THE ONCOLOGY TREATMENT PARADIGM WITH MD ANDERSON
Expanding across oncology with MD Anderson: 9 clinical trials planned

- Clinical collaboration will initially support 9 phase I/II or phase II
- Multiple indications: head & neck, pancreatic, thoracic, lung, gastrointestinal and genitourinary cancers
- Involving approximately 340 patients
- Risk sharing funding scheme: backloaded payment & post FDA registration payment

<table>
<thead>
<tr>
<th>H&amp;N</th>
<th>Phase II Trial of reirradiation with NBTXR3 combined with anti-PD-1/L1 for inoperable, locally advanced HN cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUNG</td>
<td>Phase II Trial for NBTXR3 for recurrent/metastatic HNSCC patients with limited PD-L1 expression</td>
</tr>
<tr>
<td>LUNG</td>
<td>Phase II Trial for NBTXR3 combined with anti-PD-1 or anti-PD-L1 in Stage IV lung cancer</td>
</tr>
<tr>
<td>ADVANCED TUMORS/LUNG/LIVER</td>
<td>Phase I Trial for NBTXR3 combined with anti-CTLA4 and anti-PD-1 or PD-L1 in patients with advanced solid tumors and lung or liver mets</td>
</tr>
<tr>
<td>PANCREAS</td>
<td>Phase I Trial for NBTXR3 in pancreatic cancer</td>
</tr>
<tr>
<td>ESOPHAGUS</td>
<td>Phase I Trial for NBTXR3 in esophageal cancer patients</td>
</tr>
</tbody>
</table>

TWO ADDITIONAL TRIALS UNDER DISCUSSION
NBTXR3 has the opportunity to help millions of patients each year across the standard of care.
**SUMMARY**

**FIRST-IN-CLASS PRODUCT**
- NBTXR3 is a radioenhancer with the potential to improve outcomes for millions of oncology patients
- Disruptive technology with universal, physical MoA
- 15 clinical trials (H&N, lung, liver, pancreas, prostate, etc.)

**DE-RISKED APPROACH**
- Clinical proof of concept established in a randomized PIII trial in STS (featured in *The Lancet Oncology*)
- First European market approval (CE Marking) obtained
- IP (300+ patents issued or in process of issuance)
- Positive PI in H&N & Liver showing strong potential for improving survival and quality of life, 0 SAEs and 0 DLTs

**UPCOMING VALUE DRIVERS**
- Phase III in locally advanced H&N registration in US to begin
- IO combination trial results in PD-1 resistant patients in recurrent H&N
- European expansion phase I end of recruitment in locally advanced H&N

**FINANCIAL POSITION**
- Publicly-traded, Euronext : NANO – ISIN : FR0011341205
- EUR 54.9M as of June 30, 2019, visibility until end of 2020
<table>
<thead>
<tr>
<th>Soft Tissue Sarcoma</th>
<th>Preclinical</th>
<th>IND</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft Tissue Sarcoma of the Extremity and Trunk Wall</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Head and Neck</th>
<th>Preclinical</th>
<th>IND</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
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<tbody>
<tr>
<td>Locally advanced Head &amp; Neck cancers</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Head &amp; Neck cancers</td>
<td></td>
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<tr>
<td>Ind. locally advanced H&amp;N cancers (re-irradiation)</td>
<td></td>
<td></td>
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<tr>
<td>Rec. metastatic H&amp;N cancers w/ limited PD-L1 expression</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Recurrent Head &amp; Neck cancers / Lung/Liver metastases</td>
<td></td>
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<tr>
<td>Advanced solid tumors and lung or liver meta</td>
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</tbody>
</table>

<table>
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<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
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<tbody>
<tr>
<td>Stage IV lung cancer</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Lung cancer in need of re-irradiation</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Esophagus</th>
<th>Preclinical</th>
<th>IND</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal cancer</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Pancreas</th>
<th>Preclinical</th>
<th>IND</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic cancer</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Liver</th>
<th>Preclinical</th>
<th>IND</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatocellular carcinoma / Liver metastasis</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Rectum</th>
<th>Preclinical</th>
<th>IND</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
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</thead>
<tbody>
<tr>
<td>Rectum cancers</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Prostate</th>
<th>Preclinical</th>
<th>IND</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate cancer</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>NETX3</th>
<th>R3 + chemotherapy</th>
<th>R3 + checkpoint inhibitors</th>
<th>Nanobiotix trials</th>
<th>Partner trials</th>
</tr>
</thead>
</table>

**Global Development Strategy**

**January 2020**
2020 MILESTONES

Jan 2020 – FLOW-312 trial: Submission of protocol to FDA
Q1 2020 – EU Phase I in H&N cancer: Update of dose escalation patient follow-up
Q1 2020 – Phase I in liver cancers: Update on results
Q2 2020 – Phase I in pancreatic cancer (MDA trial): First patient treated

Mid 2020 – EU Phase I expansion in H&N cancer: First data on efficacy and safety
Q2-Q3 2020 – MDA Anderson trials (in combo with ICI & HN with limited PD-L1 expression): Submission of protocols to FDA
Mid 2020 – Phase I IO Basket Trial: First data reported

Q3 2020 – Phase I in esophageal cancer (MDA trial): First patient treated
Q3 2020 – Phase I in lung cancer patients in need of reirradiation (MDA trial): First patient treated
Q4 2020 – Phase I in prostate cancer: Update on results
H2 2020 – Phase I/II in H&N cancer (PE trial): Last patient in
H2 2020 – Phase I/II in rectal cancer (PE trial): Report Phase I results
H2 2020 – Phase III in STS: Further follow up of patients
H2 2020 – Post approval trial in STS: trial authorization
### Financials

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total revenue and other income</td>
<td>3,479</td>
<td>3,722</td>
</tr>
<tr>
<td>Sales</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Services</td>
<td>116</td>
<td>252</td>
</tr>
<tr>
<td>Other sales</td>
<td>109</td>
<td>229</td>
</tr>
<tr>
<td>Licences</td>
<td>7</td>
<td>23</td>
</tr>
<tr>
<td>Other revenues</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research Tax Credit</td>
<td>3,363</td>
<td>3,470</td>
</tr>
<tr>
<td>Subsidies</td>
<td>3,251</td>
<td>3,259</td>
</tr>
<tr>
<td>Other</td>
<td>90</td>
<td>154</td>
</tr>
<tr>
<td>Research &amp; Development (R&amp;D) costs</td>
<td>(20,893)</td>
<td>(17,733)</td>
</tr>
<tr>
<td>Selling, General and Administrative (SG&amp;A) costs (incl. Share-based payments)</td>
<td>(12,653)</td>
<td>(11,255)</td>
</tr>
<tr>
<td>Operating loss</td>
<td>(30,067)</td>
<td>(25,267)</td>
</tr>
<tr>
<td>Financial loss</td>
<td>(277)</td>
<td>(876)</td>
</tr>
<tr>
<td>Income tax</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Net loss for the period</td>
<td>(30,345)</td>
<td>(26,143)</td>
</tr>
</tbody>
</table>

Consolidated cash available as of 30 Jun 2019: €54.9M

* €30.5m from ABB (April 2019) & exercising of founders’ warrants

### Shareholding Structure as of April 2019

- Institutional Investors
- Family offices
- Management & employees
- Retail

![Shareholding Structure Chart]

22,360,039 shares

46.87%
44.87%
4.55%
3.72%

### Analyst Coverage

- **Jefferies** – Peter Welford
- **Kempen** – Ingrid Gafanhao
- **Gilbert Dupont** – Jamila Elbougrini
- **Kepler Cheuvreux** – Arsene Guekam
- **Stifel** – Christian Glennie
- **H.C. Wainright** – Ramakanth Swayampakula
- **Portzamparc** – Christophe Dombu
- **Degroof Petercam** – Benoit Louage

NANOBIOTIX
CORPORATE PRESENTATION

SUMMARY

JANUARY 2020
**Nanobiotix Publications**

- Mariagrazia Di Marco et al., International Journal of Nanomedicine, 2010, “Overview of the main methods used to combine proteins with nanosystems: absorption, bioconjugation, and encapsulation”
- Mike A.W. Eaton et al., Nanomedicine, Biology, and Medicine, 2015, Delivering nanomedicines to patients: A practical guide
- Agnes Pottier et al., Br J Radiol, 2015, The future of nanosized radiation enhancers
- Agnes Pottier et al., Biochem Biophys Research Comm, 2015, Metals as radio-enhancers in oncology: The industry perspective
- Sébastien Paris et al., SiteC Annual meeting, 2016, Hafnium oxide nanoparticle, a radiation enhancer for in situ cancer vaccine
- Marion Paolini et al., J Nanomedicine, 2017, Nano-sized cytochrome P450 3A4 inhibitors to block hepatic metabolism of diclofenac
- Le Tourneau et al., ASCO, 2017, A phase I trial of NBTXR3 nanoparticles activated by intensity-modulated radiation therapy (IMRT) in the treatment of locally advanced head and neck squamous cell carcinoma (HNSCC)
- Agnès Pottier et al., AACR Annual meeting, 2017, The radiophotons NBTXR3 brings anticancer efficacy to the cisplatin-based chemoradiation in vitro
- Peng Zhang et al., AACR Annual meeting, 2017, “Hafnium oxide nanoparticles (NBTXR3), a novel radiation enhancer achieves marked anti-tumor efficacy across five tumor types”
- J. Galon et al., Immunotherapy Workshop, 2017, Hafnium oxide nanoparticle, a potent radiation enhancer for in situ cancer vaccine
- S. Paris et al., SOCRATES SIRIC, 2017, Effective antitumor immunity with hafnium oxide at the nanoscale
- J. Marili et al., AACR-SORTC-NCI, 2017, Hafnium oxide nanoparticles with radiotherapy induce immunogenic cell death
- A. Pottier et al., AACR-EORTC-NCI, 2017, Radiation therapy with presence of nanoparticles at the tumor cell level: optimizing treatment efficacy through nanoparticle design
- Sébastien Paris et al., SiteC Annual meeting, 2017, Transforming immunologically “cold” tumor into “hot” tumor with hafnium oxide nanoparticles and radiotherapy
- J Galon et al., SiteC Annual meeting, 2017, Antitumor immunity in patients with locally advanced soft tissue sarcoma treated with Hafnium oxide nanoparticles and radiotherapy
- J. Galon et al., CTOS, 2017, NBTXR3 treatment induces antitumoral immune response in human soft tissue sarcoma
- L. Levy et al., CFS, 2017, Hafnium oxide nanoparticles: an emergent promising treatment for solid tumors
- Dimitri et al., Journées annuelles Cancérople Grand Sud Ouest, 2017, Hafnium oxide nanoparticles as an emergent promising treatment for solid tumors
- C. Le Tourneau et al., THNO, 2017, A phase I dose-escalation study of intratumoral injection of NBTXR3 in combination with IMRT in patients with locally advanced HNSCC
- Tetreau et al., Immuno-Oncology Summit, 2018, Hafnium Oxide Nanoparticles and Radiotherapy to Convert Immunologically “Cold” Tumor into “Hot” Tumor
- Enrique Chajon et al., ASCO GI, 2018, A phase III trial of NBTXR3 nanoparticles activated by SBRT in the treatment of liver cancers.
- C. Le Tourneau et al., Multidisciplinary head and neck symposium, 2018, Hafnium oxide nanoparticles as a promising emergent treatment for head and neck cancer
- Julie Marili et al., AACR, 2018, Activation of the cGAS-STING pathway by NBTXR3 nanoparticles exposed to radiotherapy
- C. Le Tourneau et al., EORTC 2018, 2018, Hafnium oxide nanoparticles and radiotherapy for solid tumors: a promising new treatment strategy
- C. Hoffmann et al., ECHNO, 2018, 2018, NBTXR3, an innovative treatment option for elderly, frail, head and neck squamous cell carcinoma patients: a phase I trial
- Enrique Chajon et al., ASCO 2018, 2018, NBTXR3, hafnium oxide nanoparticles in the treatment of liver cancer: a phase III trial
- E. Chajon et al., ESMO WGI 2018, 2018, A phase III trial of hafnium oxide nanoparticles activated by radiotherapy in head and neck squamous cell carcinoma and liver metastasis
- T. Seiwert et al., Oncorad, 2018, Phase III trial: NBTXR3 activated by SABR for patients with advanced HNSCC or NSCLC in combination with an anti-PD1 treatment
- Audrey Darmon et al., Oncorad, 2018, Hafnium oxide nanoparticles activated by radiotherapy triggers an abscopal effect dependent on CD8 T cells.
- S. Bonvalot et al., ESMO 2018, 2018, A phase III trial of hafnium oxide nanoparticles activated by radiotherapy in the treatment of locally advanced soft tissue sarcoma of the extremity and trunk wall
- C. Le Tourneau et al., ESMO 2018, 2018, Elderly patients with locally advanced head and neck squamous cell carcinoma treated with NBTXR3 nanoparticles activated by radiotherapy: a phase I trial
- E. Chajon et al., ESMO 2018, 2018, Hepatocellular carcinoma and liver metastasis treated by Hafnium Oxide Nanoparticles activated by stereotactic body radiation therapy in a phase III trial
- S. Bonvalot et al., ASTRO 2018, 2018, Act-In-Sarc: An international randomized phase III trial evaluating efficacy and safety of first-in-class NBTXR3 hafnium oxide nanoparticles activated by preoperative radiotherapy in locally advanced soft tissue sarcoma
- V. Calugaru et al., ASTRO 2018, 2018, Elderly patients: NBTXR3 as a novel treatment option in locally advanced HNSCC
- G. Graulé et al., ASTRO 2018, 2018, Explorative dosimetric study of the impact of the pre-radiotherapy intra-tumoral injection of hafnium oxide nanoparticles along the radiation treatment of extremity and trunk wall soft tissue sarcomas
- J. Galon et al., ASTRO 2018, 2018, Hafnium oxide nanoparticle activated by radiotherapy generates an anti-tumor immune response
- J. O. Thariat et al., ASTRO 2018, 2018, Hafnium oxide nanoparticles activated by radiotherapy for the treatment of solid tumors
Liver Data References


NBTXR3 – abscopal assay – local and distant control

2 independent experiments
12-14 mice per group

Treated tumor

Untreated tumor

5% Glc  NBTXR3  5% Glc +3x4Gy  NBT3+3x4Gy
NBTXR3 – abscopal assay-effect on T cells

A – Schematic representation of treatment schedule for the second abscopal assay. B – Mice were sacrificed 72h after the last fraction of irradiation and tumors (treated and untreated) excised for IHC analyses (4 mice/group, 3 slices/tumor). CD4+ and CD8+ T cell lymphocytes and macrophages (CD68) infiltrates in treated (left panel) and untreated (right panel) tumors were analyzed. Bars represent the median.
NBTXR3 triggers immune response
Phase III
Soft Tissue Sarcoma biomarker data

IHC analyses of CD3, CD8, CD103 (dendritic cells), PD-1, CD68 (macrophages) and FoxP3 (Treg) positive cell infiltrates in post-treated tumors compared to pre-treated tumors of patients with STS, for RT alone and NBTXR3 activated by RT arms. Ratio ‘post/pre’ are presented as log2 (fold change). Each dot represents a patient. The values represented on the figures indicate the number (and percentage) of patients with Log2 (fold change) ≥1 or ≤1 in each arm. Red bar represents median. n represents the number of patients analyzed.
NBTXR3 decreases tumor burden, increases anti-PD-1 efficacy and abscopal effect

Figure 3. Abscopal assay - 344SQ_P cells (sensitive to anti-PD1 treatment)

A

Irradiated

Tumor volume (mm$^3$)

Time (day)

Non irradiated

Tumor volume (mm$^3$)

Time (day)

- 5% Glic
- 5% Glic + anti-PD1
- 5% Glic + 3x120Gy
- NBTXR3 + 3x120Gy
- 5% Glic + anti-PD1 + 3x120Gy
- NBTXR3 + anti-PD1 + 3x120Gy

B

Percent survival

Time (day)

- 5% Glic
- 5% Glic + anti-PD1
- 5% Glic + 3x120Gy
- NBTXR3 + 3x120Gy
- 5% Glic + anti-PD1 + 3x120Gy
- NBTXR3 + anti-PD1 + 3x120Gy

C

Number of lung metastasis

NBTXR3
- - - - -
RT (3x120Gy)
- - - - -
Anti-PD1
- - - - -

Abscopal assay on 344SQ_P tumor bearing mice (8 mice per group). A – Mean tumor volume ± SEM. B – Survival percentage. C – Number of lung metastasis. 4 mice were sacrificed on D10. *, p<0.05

Presented at AACR Annual Meeting, March 29 – April 4, 2019, Atlanta - USA
NBTXR3 decreases tumor burden, increases anti-PD-1 efficacy and abscopal effect
# Radioenhancer Nanoparticles

## Efficacy

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>NBTXR3</th>
<th>Gold nanoparticle</th>
<th>Gadolinium-clusters</th>
<th>AguiX</th>
<th>Gold cluster Auranofin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density of electrons</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Maximum intratumoral dose</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Persistence in tumor (window of efficacy and utilization)</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Inter-patient and–tumor variability concentration</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

## Clinical efficacy

- IT vs. IV (ease of use): IT, IT, IV, IV, IV

## Administration

- All solid tumor: ++, ++, -, -, -
- Solid tumor and met. (with IO): ++, ++, -, -, -

## Potential application

- Product stability/degradation: ++, -, -, -, -
- Intrinsic toxicity (e.g. red/ox): ++, -, -, -, -
- Exposure of healthy tissues: ++, -, -, -, -
- Sensitization of irradiated healthy tissues: ++, ++, -, -, -

## Risk

- Validated PIII STS: Preclinical, Failed PIII Brain met, Ongoing PI Brain met, Preclinical

## Radio-enhancers represent the optimal option in terms of benefit risk ratio

Aviesan 2016; Candolaria et al., 2006; Coloman et al. 1999; Haunie et al. 2016; Kucic et al., 2018; Meyers et al., 2004; Pottier et al., 2015; Pottier et al., 2015; Runge, 2017; Sancey et al., 2015; Schulze et al., 2013; Vianier et al., 2009; Wang et al., 2017; Zhang et al., 2014;
Not a direct comparison

+45.9% in absolute ORR
(R3 vs average ORR)

+54.2% in absolute CRR
(R3 vs average CRR)

1. Qin, H., et. al
2. Price, et. al
3. Kang, M. K., et. al
4. Kim, J.-Y, et. al
5. Bujold, A., et. al
6. Huang, C.-M., et. al
7. Kim, T. H., et. al
8. Kong, M., et. al
9. Park, H. C., et. al
10. Liu, M.-T., et. al
11. Mornex, F., et. al

*Mornex et al. dismissed due to extreme dose of radiation, high frequency of grade 3 and more adverse events & small tumors only