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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
**NANObiotix 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
- 8 ongoing clinical trials (H&N, lung, liver, pancreas, prostate, etc.) and an additional 7 contemplated

**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, well tolerated

**Upcoming Milestones**
- Phase III in locally advanced H&N registration in US to begin
- IO combination trial results in anti-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
- Cash: EUR 28M as of March 31, 2020 and EUR 10 of State Guaranteed Loan, visibility until Q3 2021
Millions of patients receive radiotherapy each year but still have significant unmet medical needs.
Radiotherapy is the most common treatment...

- **RECEIVING RTx**
  - 60% RTx
  - **18M** new patients per year

- **NUMBER OF PATIENTS W/ RTX**
  - 87% Breast cancer: 1,800,000
  - 77% Lung cancer: 1,600,000
  - 74% H&N: 700,000
  - 58% Prostate: 740,000
  - 60% Rectum: 420,000
  - 49% Pancreas: 225,000
  - 80% CNS: 237,000
  - ... CNS: ...

Source: *World Health Organization (2014); **RADIATION THERAPY EQUIPMENT – A global strategic business report 08/06; Delaney et al. 2015; Globocan 2018*
THE UNMET NEED

...But still presents significant unmet medical needs

- Inadequate local control (Local invasion or systemic expansion)
- Inadequate systemic control (metastatic patients)
- Unfavorable safety profile (dose de-escalation/re-irradiation)

18M 60% RTx
new patients per year

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

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 in STS

First European market approval obtained

One-time Intra tumoral administration

Compatible with existing equipment

Patient flow stays identical

Patients receive standard radiation therapy

Administration route validated in several indications
NBTXR3 Creates Hyper-focused dose Delivery in the heart of the cell

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

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FIRST-IN-CLASS RADIOENHANCER NBTXR3

Dose* around nanoparticles
Usual dose delivered in the cell

Clusters of Nanoparticles

Local absorption of energy

DoseUsual dose delivered in the cell

Usual dose delivered in the cell

XRay

XRay

2 µm

*Note: Dose enhancement determined by monte carlo simulation (CEA Saclay, France)
NBTXR3’s PHYSICAL, UNIVERSAL MOA triggers cellular destruction along with potential adaptive 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 is developing NBTXR3 across tumor indications with radiation alone and in combination with other therapies.
1. Clinical Proof of Concept established in a randomized Phase III & marketing approval received in EU
2. A defined pathway to market in US & EU with an aim for high medical & economical value creation
3. Expansion through multiple ongoing or planned Phase I/II trials

Expansion path
to increase patients reach and number of indications
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

- 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 a independent central Pathological Review Board

\(^\*\) IT injection of a dose, 10% of baseline tumor volume
\(^\**\) 50 Gy, 25 fractions x 2 Gy, over 5 weeks
\(^\$\) Pathological Response evaluated by an independent central Pathological Review Board

\(^{(1)}\) Wardelmann E et al, Eur J Cancer, 2016
Primary endpoint met

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 a threshold of 0.04575
pCRR x4 in grade 2 & 3 subpopulation

Pathological Complete Response
<5% residual viable cancer cells

NBTXR3 activated by radiotherapy
Radiotherapy alone

June 20
The study also met its secondary endpoints

Significant increase in R0 rate in the NBTXR3 arm

- **Resection margin (RO rate)**
  - NBTXR3 activated by radiotherapy (N=87)
  - Radiotherapy alone (N=89)

- **p-value 0.0424***

Significant increase in tumor necrosis/infarction in the NBTXR3 arm

- **Tumor necrosis/infarction**
  - NBTXR3 activated by radiotherapy (N=87)
  - Radiotherapy alone (N=89)

- **p-value 0.0140***

*Statistically significant at an α of 5%
*)ITT FAS (Full Analysis Set)
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 TEAE</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 AE</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>

* Relative radiation therapy Dose intensity = (Actual Dose Intensity / Planned Dose Intensity)

---

* Treatment Emergent AEs are AE observed during the on-treatment period.
* Serious AEs are adverse events reported during the whole study period (i.e. on-treatment and follow-up periods).
NA, not applicable

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ACT.IN.SARC

June 20
Focusing on Head & Neck Cancer to show improvement in Overall Survival and Quality of Life (ASCO 2020)
Locally-advanced Head and Neck cancer in elderly and frail patients

- Stage III and IV
- ≥65 years old, frail
- Oral cavity, Oropharynx
- HPV all status (positive & negative)
- Ineligible for chemotherapy and intolerant to cetuximab in combination with RT

Radiotherapy is often the only option to treat this fragile H&N cancer population and benefits are limited (i.e., Low ORR, Short PFS, Poor QoL)
Study design – dose escalation and Dose Expansion

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

*According to AJCC 7th edition for the dose escalation and 8th edition for the dose expansion

**Dose escalation:** 3 + 3 design to assess 4 dose levels*

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

**Dose expansion:** 44 additional patients at the RP2D

**PRIMARY ENDPOINTS**

**Dose escalation**
- Assess DLTs, Recommended dose (RP2D), MTD if possible
- Safety and tolerability

**Dose expansion**
- Objective Response Rate (ORR) and Complete Response Rate (CRR) of the primary tumor, by imaging according to RECIST 1.1

*Injected volume calculated as a % of tumor volume determined on an MRI performed <14 days prior to injection
Head & NECK CANCER

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

Medial OS at 12-13 months

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
### Safety – Phase I escalation in H&N

#### Dose Level

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>N</th>
<th>DLT</th>
<th>AE (n)</th>
<th>SAE (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
<td>3</td>
<td>No</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10%</td>
<td>3</td>
<td>No</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15%</td>
<td>5</td>
<td>No</td>
<td>Grade 1 tumor hemorrhage (N=1)</td>
<td>0</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>
<td>0</td>
</tr>
</tbody>
</table>

**Recommended dose defined by DSMB as 22%**
best observed primary lesion response on Evaluable patient population

- Progression: -100% change
- Stable Disease: 0% change
- Partial Response: -20% to -40% change
- Complete Response: -60% to -80% change

Dose Levels:
- Dose Level 1-5%
- Dose Level 2-10%
- Dose Level 3-15%
- Dose Level 4-22%
Target lesion response by recist 1.1/MRI – All patients

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HEAD AND NECK PHASE I ESCALATION

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Target lesion response by recist 1.1/MRI – All patients
Real World Evidence vs 102 study

**Real World Evidence Data**

- Head and Neck Newly Diagnosed and Treated (oral cavity, oropharynx)
- Elderly (65+)
- Stage 3 & 4
- No cisplatin use during all treatment lines

**102 data**

- Head and Neck Newly Diagnosed and Treated (oral cavity or oropharynx)
- Elderly (65+)
- Stage 3 & 4
- Ineligible for cisplatin
- Intolerant to cetuximab

---

102 patient population has a worse prognosis than RWE population
### Claims Eligible Patients

<table>
<thead>
<tr>
<th>Data Requirement</th>
<th>Patient Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and Neck Newly Diagnosed and Treated Jan’14 to Aug’17</td>
<td>35753.0</td>
</tr>
<tr>
<td>65+</td>
<td>14612.0</td>
</tr>
<tr>
<td>Tx,N1+,M0</td>
<td>3291.0</td>
</tr>
<tr>
<td>No Cisplatin use during all treatment lines captured</td>
<td></td>
</tr>
<tr>
<td>Additional longitudinal visibility for linked patients</td>
<td>259</td>
</tr>
<tr>
<td>Death data available</td>
<td>41</td>
</tr>
</tbody>
</table>

*The counts will be provided with initial readout post SOW approval*
RWE: PFS of patients treated by RT or RT + cetuximab vs other treatment

Data in months

Median PFS in literature: ~10 months*

RT alone median PFS: 7 months

Cetux only median PFS: 6 months

Systemic therapy (not cetux) median PFS: 4 months

On 135 systemic treatments, 89 are cetux (66%)

RT + cetux median PFS: 9 months

*Moye et al., The Oncologist, 2015
RWE: PFS OF patients treated by RT or RT+cetuximab

Note: PFS in RWE data is defined as «change in N or M staging», «change of treatment» or «death». Change of treatment is usually correlated to relapse. A second line is therefore most often used in patients in this dataset.
Real World Evidence vs 102 study

102 study patients
N=19

Claim data
PFS*
RT or RT + cetuximab
N=246

*PFS in RWE data is defined as «change in N or M staging », « change of treatment » or « death ». Change of treatment is usually correlated to relapse. A second line is therefore most often used in patients in this dataset.
### H&N Dose Expansion: Baseline Characteristics / All treated Population

#### Baseline Characteristics

<table>
<thead>
<tr>
<th>Gender</th>
<th>All Treated Patients N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>11 (27.5%)</td>
</tr>
<tr>
<td>Male</td>
<td>29 (72.5%)</td>
</tr>
<tr>
<td><strong>Age, years</strong></td>
<td>Median 70.7</td>
</tr>
<tr>
<td></td>
<td>Min, Max 50.7, 89.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Volume, mL**</th>
<th>All Treated Patients N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>43.1</td>
</tr>
<tr>
<td>Min, Max</td>
<td>1.3, 222.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Location</th>
<th>All Treated Patients N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity</td>
<td>22 (55.0%)</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>18 (45.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HPV status</th>
<th>All Treated Patients N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missing</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>HPV 16 +</td>
<td>11 (27.5%)</td>
</tr>
<tr>
<td>HPV 16 -</td>
<td>23 (57.5%)</td>
</tr>
<tr>
<td>Not done</td>
<td>5 (12.5%)</td>
</tr>
</tbody>
</table>

#### Baseline Characteristics

<table>
<thead>
<tr>
<th>Primary Tumor Stage*</th>
<th>All Treated Patients N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>I#</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>II#</td>
<td>5 (12.5%)</td>
</tr>
<tr>
<td>III</td>
<td>18 (45.0%)</td>
</tr>
<tr>
<td>IV/IVA</td>
<td>16 (40.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Karnofsky Score</th>
<th>All Treated Patients N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>9 (22.5%)</td>
</tr>
<tr>
<td>90%</td>
<td>10 (25.0%)</td>
</tr>
<tr>
<td>80%</td>
<td>15 (37.5%)</td>
</tr>
<tr>
<td>70%</td>
<td>5 (12.5%)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (2.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hyper-polypharmacy</th>
<th>All Treated Patients N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8 ongoing medication</td>
<td>7 (17.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comorbidities***</th>
<th>All Treated Patients N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac disorder risk</td>
<td>28 (70.0%)</td>
</tr>
<tr>
<td>Gastrointestinal disorder risk</td>
<td>21 (52.5%)</td>
</tr>
<tr>
<td>Weight loss risk</td>
<td>8 (20.0%)</td>
</tr>
</tbody>
</table>

*According to AJCC 8th edition. # Stage III/IV according to AJCC 7th edition.** As per local imaging data. Abbreviations: HPV, human papilloma virus, OPC, oropharyngeal cancer. *** Most frequent
## Summary of AE/SAE

### All Treated Patients N=40

<table>
<thead>
<tr>
<th></th>
<th>AEs</th>
<th>SAEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>404 (100%)</td>
<td>41 (10.1%)</td>
</tr>
<tr>
<td>Related to Injection procedure</td>
<td>13 (3.2%)</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>Related to NBTXR3</td>
<td>18 (4.4%)</td>
<td>3 (0.7%)</td>
</tr>
<tr>
<td>Related to Radiotherapy</td>
<td>204 (50.5%)</td>
<td>19 (4.7%)</td>
</tr>
</tbody>
</table>

Note: AE/SAE incidence is calculated based on total number or AEs

No fatal Adverse Event related to NBTXR3 or the Injection Procedure
Primary endpoint - Best observed % change from baseline in target response – Evaluable Population

83 % Objective Response (incl. 60% complete response)

As of 30 APR 2020
Evaluable Population for Objective Tumor Response has included all patients who have had at least 80% of the intended intratumoral dose of NBTXR3 AND 60 Gy of IMRT AND the required imaging for tumor burden evaluation (target lesions assessments), at baseline and at least once post treatment.

N=30

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H&N PHASE I EXPANSION

June 20
### Best observed response – Target lesions – investigator assessment – evaluable population

<table>
<thead>
<tr>
<th>Escalation (n=16)</th>
<th>All dose levels (5%, 10%, 15%, 22%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=16)</td>
</tr>
<tr>
<td><strong>Best Observed Target Lesion Response</strong></td>
<td>CR</td>
</tr>
<tr>
<td></td>
<td>PR</td>
</tr>
<tr>
<td></td>
<td>SD</td>
</tr>
</tbody>
</table>

| **Objective Response (Target Lesions)** | CR + PR | 11 (68.75%) |
|                                        | Other Response | 5 (31.25%) |

<table>
<thead>
<tr>
<th>Expansion (n=30)</th>
<th>22% of Tumor Volume (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Best Observed Target Lesion Response</strong></td>
<td>CR</td>
</tr>
<tr>
<td></td>
<td>PR</td>
</tr>
<tr>
<td></td>
<td>SD</td>
</tr>
</tbody>
</table>

| **Objective Response (Target Lesions)** | CR + PR | 25 (83.3%) |
|                                        | Other Response | 5 (16.7%) |
Anti-tumor activity: 3-D reconstruction

CT-scan 24h post IT injection

CT-scan post radiotherapy

CT-scan 7 months after RT
Randomized Phase III trial in an advanced population:
Elderly head and neck cancer patients ineligible for cisplatin

**Investigator’s choice**
- Radiotherapy alone
- Radiotherapy + Cetuximab

**R 1:1**

**A**
- NBTXR3 + RT ± Cetuximab (250 pts)

**B**
- RT ± Cetuximab (250 pts)

**Endpoints**
- Primary: PFS
- Secondary: OS, ORR, AEs, QoL
  (trial powered to demonstrate a significant difference on OS)
Liver Cancer
phase I results
(ASCO GI 2020)
HCC & LIVER METS

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
  - Unresectable 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 ASCO-GI 2020*

<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>

Patients are recruited at different time points during the trial, those receiving the highest doses are thus the ones with the lowest follow-up.
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/B/C (%)</th>
<th>Radiation therapy dose</th>
<th>Follow-up</th>
<th>Response (C/F/P)</th>
<th>Overall survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chong et al. (72)</td>
<td>Prospective</td>
<td>3D-CRT</td>
<td>15</td>
<td>16 cm (6-28)</td>
<td>60/31/0</td>
<td>40-60 Gy @ 1.8 GY/fx</td>
<td>40 mo</td>
<td>68%</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>NR</td>
<td>73/27/0</td>
<td>40-60 Gy @ 1.8 GY/fx</td>
<td>8 mo</td>
<td>61%</td>
<td>1 yr 61% 2 yr 40%</td>
</tr>
<tr>
<td>Marini et al. (74)</td>
<td>Prospective</td>
<td>3D-CRT</td>
<td>27</td>
<td>3.2 cm (1-9)</td>
<td>59/41/0</td>
<td>68 Gy @ 2 Gy/fx</td>
<td>20 mo</td>
<td>92%</td>
<td>NR</td>
</tr>
<tr>
<td>Kim et al. (75)</td>
<td>Retrospective</td>
<td>2D-CRT</td>
<td>70</td>
<td>7.5 cm (3-17)</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% 2 yr 18%</td>
</tr>
<tr>
<td>Kim et al. (75)</td>
<td>Prospective</td>
<td>IMRT</td>
<td>35</td>
<td>NR</td>
<td>80/20/0</td>
<td>45-60 Gy @ 4.6 Gy/fx</td>
<td>13 mo</td>
<td>52%</td>
<td>1 yr 51% 2 yr 22%</td>
</tr>
<tr>
<td>Chi et al. (77)</td>
<td>Prospective</td>
<td>IMRT</td>
<td>23</td>
<td>NR</td>
<td>65/55/0</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>McNicol et al. (73)</td>
<td>Retrospective</td>
<td>IMRT</td>
<td>20</td>
<td>9 cm (1-3-17)</td>
<td>55/45/0</td>
<td>30-60 Gy @ 2.5 Gy/fx</td>
<td>NR</td>
<td>60%</td>
<td>1 yr 76% 2 yr 50%</td>
</tr>
<tr>
<td>Kang et al. (79)</td>
<td>Retrospective</td>
<td>IMRT</td>
<td>27</td>
<td>11 cm (3-18)</td>
<td>70/30/0</td>
<td>45-04.8 Gy @ 1.8 Gy/fx</td>
<td>5 mo</td>
<td>44%</td>
<td>5 mo (median)</td>
</tr>
<tr>
<td>Kong et al. (80)</td>
<td>Retrospective</td>
<td>IMRT</td>
<td>22</td>
<td>4.4 cm (1.9-16)</td>
<td>68/32/0</td>
<td>30-60 Gy @ 1.8-4.5 Gy/fx</td>
<td>14 mo</td>
<td>73%</td>
<td>1 yr 86% 2 yr 69%</td>
</tr>
<tr>
<td>Huang et al. (81)</td>
<td>Retrospective</td>
<td>IMRT</td>
<td>36</td>
<td>4.5 cm (2.5-17)</td>
<td>71/20/0</td>
<td>46-72 Gy @ 1.8-2.4 Gy/fx</td>
<td>17 mo</td>
<td>53%</td>
<td>1 yr 56% 2 yr 32%</td>
</tr>
</tbody>
</table>

CPS: Child Pugh score; 3D-CRT: 3-dimensional conformal radiotherapy; IMRT: intensity-modulated radiotherapy; NR: not reported; C/F/P: complete/partial.

**NBXTR3**

<table>
<thead>
<tr>
<th>Study design</th>
<th>Modality</th>
<th>N</th>
<th>Tumor size</th>
<th>Radiation therapy dose</th>
<th>Follow-up</th>
<th>Response</th>
<th>Overall survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective</td>
<td>SBRT</td>
<td>11</td>
<td>4 cm (1.1-5.4)</td>
<td>45-50 Gy @ 10-15 Gy/fx</td>
<td>100%</td>
<td>1 yr 100%</td>
<td></td>
</tr>
</tbody>
</table>

*On evaluable patients

NANOBIO TX

CORPORATE PRESENTATION

GLOBAL DEVELOPMENT STRATEGY

June 20
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 duct stenosis</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
NBTXR3 + Checkpoint inhibitors

patients have a significant unmet need as a VAST majority of tumors are UNresponsive to checkpoint INHIBITORS & other I/O approaches.

Adapted from Alexandrov et al. (2013) and Gentles et al. (2015)
Example:
Immunotherapy
Nivolumab
in recurrent
patients H&N

Nivolumab: Checkmate 141
Recurrent Head and Neck

Overall Survival (%) vs Months

Non-responder
Responder
NBTXR3 + Checkpoint inhibitors

Phase I/II in NSCLC & H&N to be initiated in combination with PD-1 Inhibitors

Checkpoint inhibitors refractory patients in NSCLC & H&N

Goal: 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
NBTXR3 increases activated CD8 tumor infiltration
Phase III Soft Tissue Sarcoma biomarker data

<table>
<thead>
<tr>
<th></th>
<th>RTx Alone</th>
<th>RTx + NBTXR3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy Baseline Pre Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biopsy Baseline Pre Treatment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

log2 ≥1
6/26 (23%)
11/23 (48%)

log2 ≤1
8/26 (31%)
4/23 (17%)

log2 ≥1
9/26 (35%)
22 (41%)

log2 ≤1
9/26 (35%)
5/22 (23%)

CD8

RT alone
HfO₂-NP activated by RT

PD-1

RT alone
HfO₂-NP activated by RT

NANOBIOXTIX
CORPORATE PRESENTATION

GLOBAL DEVELOPMENT STRATEGY

June 20
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 clinical trials
- 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

H&N
Phase II Trial of reirradiation with NBTXR3 combined with anti-PD-1/L1 for inoperable, locally advanced HN cancer

H&N
Phase II Trial for NBTXR3 for recurrent/metastatic HNSCC patients with limited PD-L1 expression

Lung
Phase II Trial for NBTXR3 combined with anti-PD-1 or anti-PD-L1 in Stage IV lung cancer

Lung
Phase I Trial for NBTXR3 in lung cancer patients in need of reirradiation

Advanced tumors/Lung/Liver
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

Pancreas
Phase I Trial for NBTXR3 in pancreatic cancer

Esophagus
Phase I Trial for NBTXR3 in esophageal cancer patients

Two additional trials under discussion
NBTXR3 has the potential 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
- 8 ongoing clinical trials (H&N, lung, liver, pancreas, prostate, etc.) and an additional 7 contemplated

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, well tolerated

Upcoming Milestones
- 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
- Cash: EUR 28M as of March 31, 2020 and EUR 10 of State Guaranteed Loan, visibility until Q3 2021
**NExT STEPS**

### H&N and Immuno-oncology
- Feedback from FDA for the phase III design in the coming weeks
- Completion of Phase I expansion
- First data in IO trial to be reported by Q3 2020
- Preclinical data in IO data by MDA expected at AACR to be presented later in 2020 at first possible conference

### Expansion across oncology with our partners
- Phase I/II in H&N cancer with PE (w/ chemo): recruitment completion
- Phase I/II in rectum cancer with PE (w/ chemo): recruitment completion
- MDA trials: Pancreas trial launched, first patient expected to be injected in by Q3 2020
- MDA trials: moving through regulatory process in several indications, FPI to be defined post-COVID-19

### Other
- Phase I in liver cancers: follow up to be presented by the end of the year
- Post-approval trial in STS: trials authorization postponed to Q2 2021 due to COVID-19
- Prostate cancer trial under management’s review

*Timelines are subject to changes depending on the COVID-19 situation*
## SUMMARY

### FINANCIALS

<table>
<thead>
<tr>
<th></th>
<th>2019 (€)</th>
<th>2018 (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total revenue and other income</td>
<td>2,541</td>
<td>3,479</td>
</tr>
<tr>
<td>Sales</td>
<td>68</td>
<td>116</td>
</tr>
<tr>
<td>Service</td>
<td>40</td>
<td>109</td>
</tr>
<tr>
<td>Other sales</td>
<td>28</td>
<td>7</td>
</tr>
<tr>
<td>Licences</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other revenues</td>
<td>2,473</td>
<td>3,363</td>
</tr>
<tr>
<td>Research Tax Credit</td>
<td>2,437</td>
<td>3,251</td>
</tr>
<tr>
<td>Subsidies</td>
<td>20</td>
<td>90</td>
</tr>
<tr>
<td>Other</td>
<td>17</td>
<td>22</td>
</tr>
<tr>
<td>Research &amp; Development (R&amp;D) costs (incl. Share-based payments)</td>
<td>(30,411)</td>
<td>(20,893)</td>
</tr>
<tr>
<td>Selling, General and Administrative (SG&amp;A) costs (incl. Share-based payments)</td>
<td>(18,909)</td>
<td>(12,653)</td>
</tr>
<tr>
<td>Operating loss</td>
<td>(46,770)</td>
<td>(30,066)</td>
</tr>
<tr>
<td>Financial loss</td>
<td>(4,133)</td>
<td>(277)</td>
</tr>
<tr>
<td>Income tax</td>
<td>(3)</td>
<td>-</td>
</tr>
<tr>
<td>Net loss for the period</td>
<td>(50,915)</td>
<td>(30,345)</td>
</tr>
</tbody>
</table>

Cash available as of March 31, 2020 amounted to €28M

Share capital breakdown (as of March 2020) based on 22,731,122 shares
CONTACT US
contact@nanobiotix.com