



NANOBIOTIX

EXPANDING
LIFE

CORPORATE PRESENTATION

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**Developing disruptive, physics-based
treatment solutions to revolutionize
treatment for millions of patients**

Going small for big impact

What Sets Us Apart

01

Applying universal laws of physics to the complex biology of disease

A Scalable Therapeutic:

- By creating a mechanism of action that is physical, rather than biological or chemical, in theory the effect should be scalable across tumor types

02

Leveraging nanophysics expertise to develop potential first-in-class radioenhancer

De-risked Approach:

- **MoA validated** in randomized PIII study
- **Marketing authorization** in Europe for STS
- **8/8 clinical studies** with positive data

03

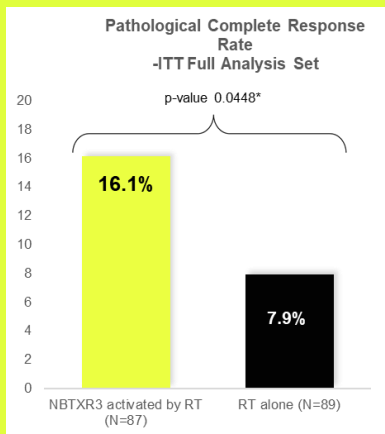
Breaking through barriers of patient and tumor heterogeneity

Creating Opportunities:

- Enhancing benefit for responders
- Expanding benefit to non-responders

Pipeline in a Product: proprietary nanotechnology platform creates opportunity to scale lead product into comprehensive oncology franchise

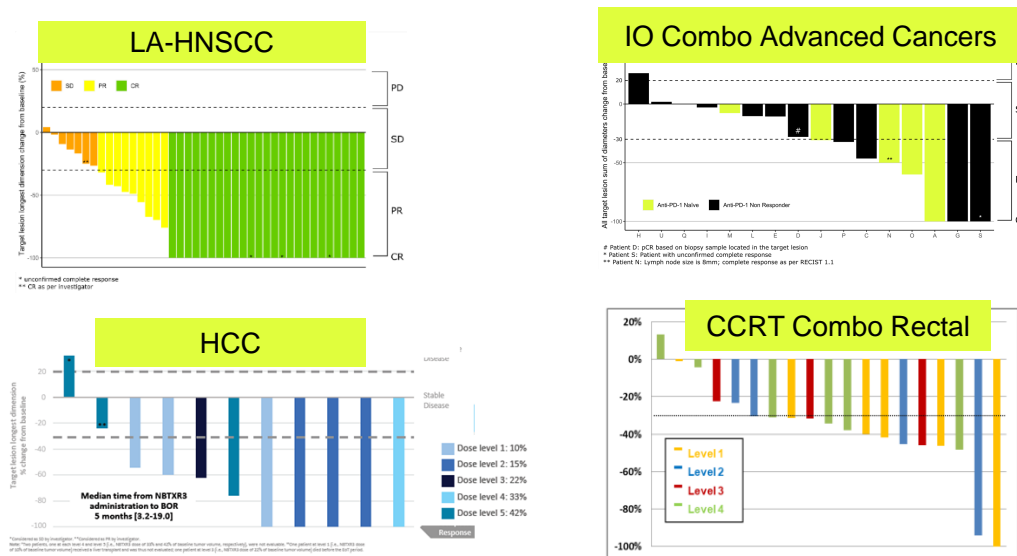
Established Proof-of-Concept & CE Mark



€70.6 million in cash and cash equivalents
As of March 31, 2022
+ Access to **untapped equity line**



Consistent Response Across Indications and Combinations



Feasible and Well-Tolerated Across Trials

AE profile has not differed in type or grade from what is expected with radiotherapy or anti-PD-1 agents

World-Class Partners to Advance & Expand Development

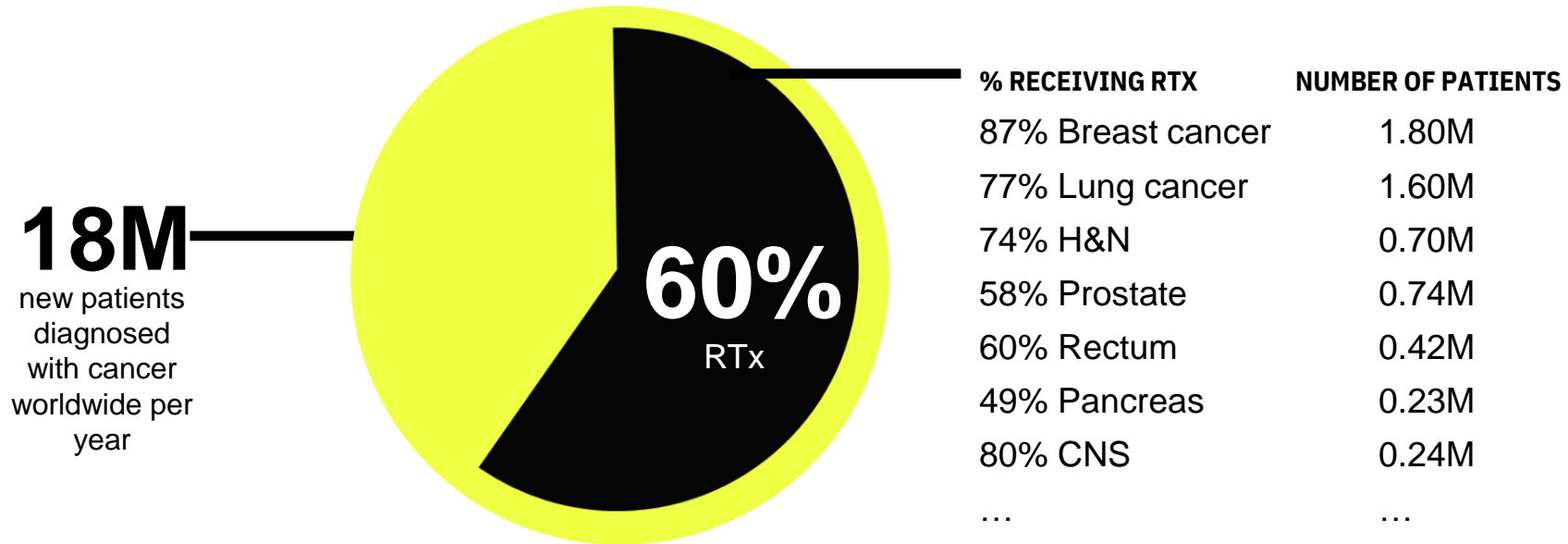


Extensive Experience & Significant Expansion Opportunities

- > 75 clinical sites worldwide
- ~300 patients treated
- Numerous indications targeted
- >13 trials completed or ongoing

Leveraging the most widely used cancer treatment to enhance multiple treatment modalities

Radiotherapy is well-established, fully-integrated part of cancer treatment both alone and in combination with surgery, chemotherapy and systemic treatments



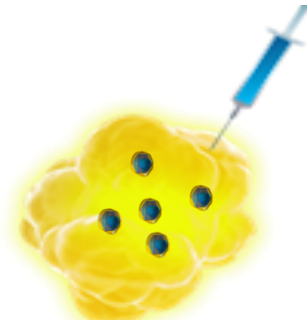
Disrupting patient outcomes without disrupting clinical practice

Suspension of hafnium oxide nanoparticles



» Nanosized (~50nm) to enter the cell

One-time intratumoral administration



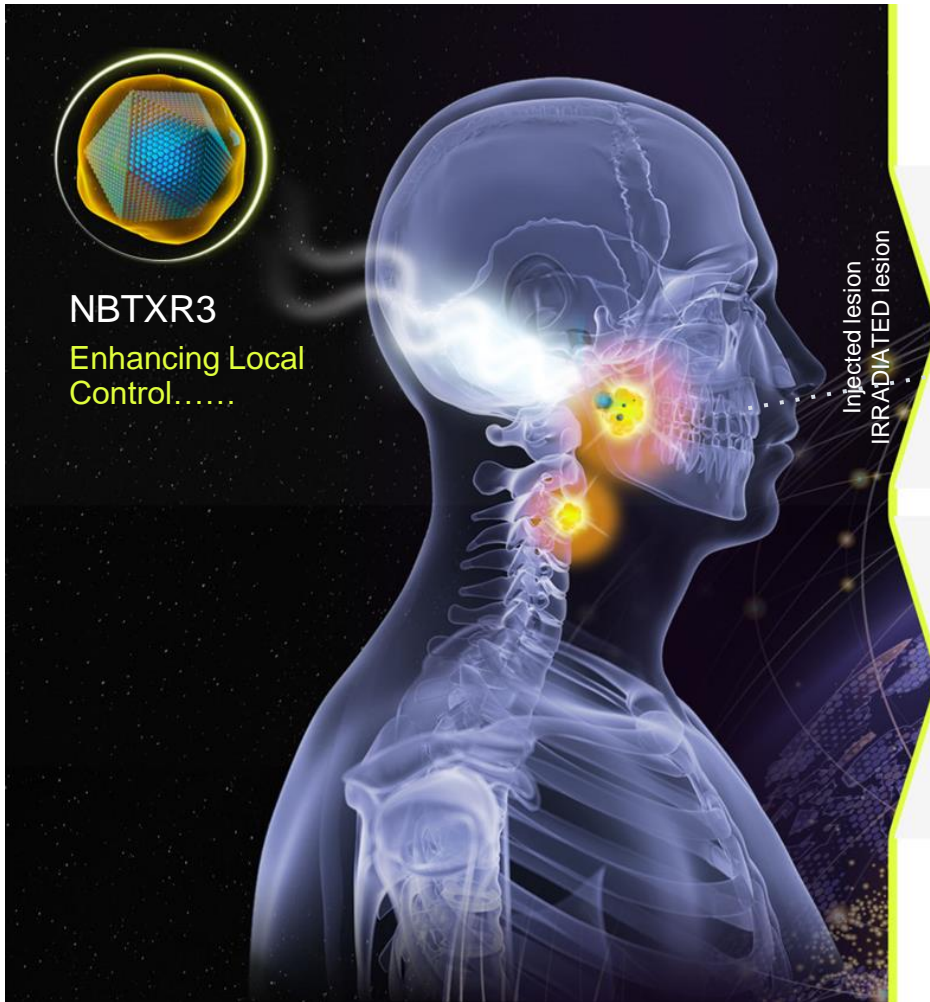
» Add **+1** visit to **~50** visits in typical patient flow

Metabolically inert until activated by radiotherapy



» Standard equipment/ radiation therapy

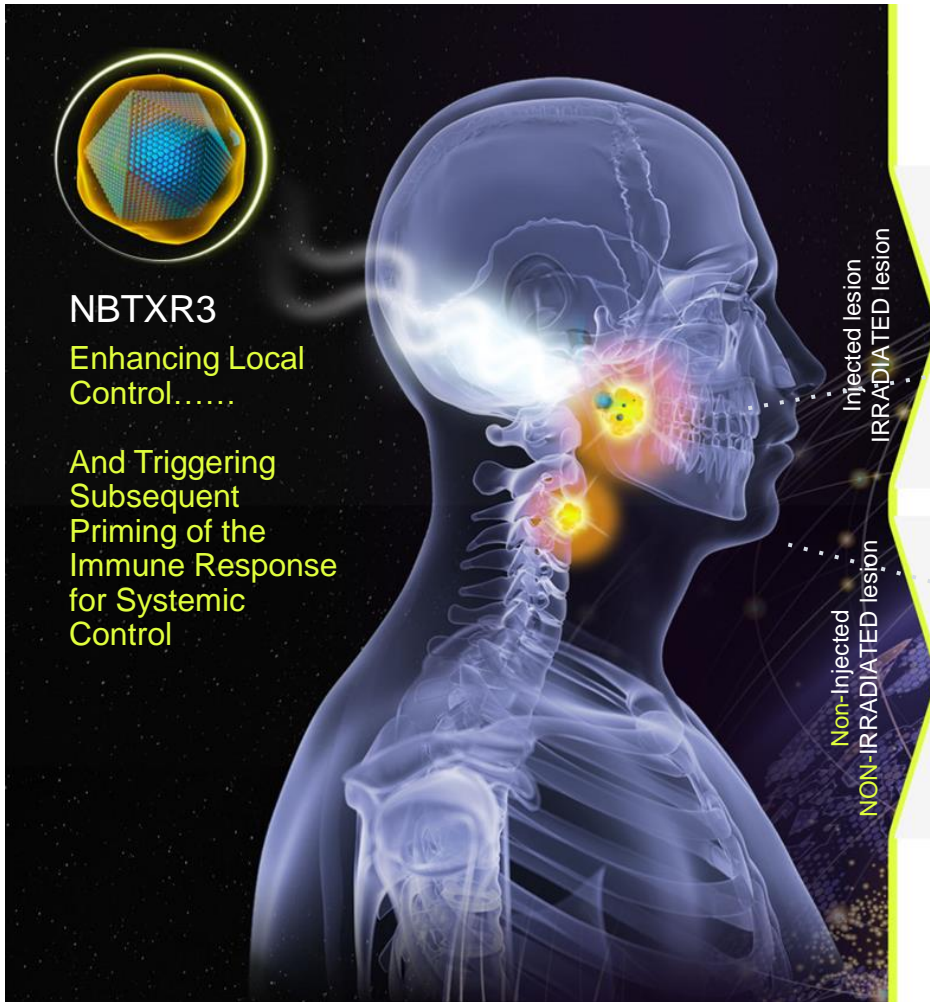
Primary physical MOA creates novel local treatment effect



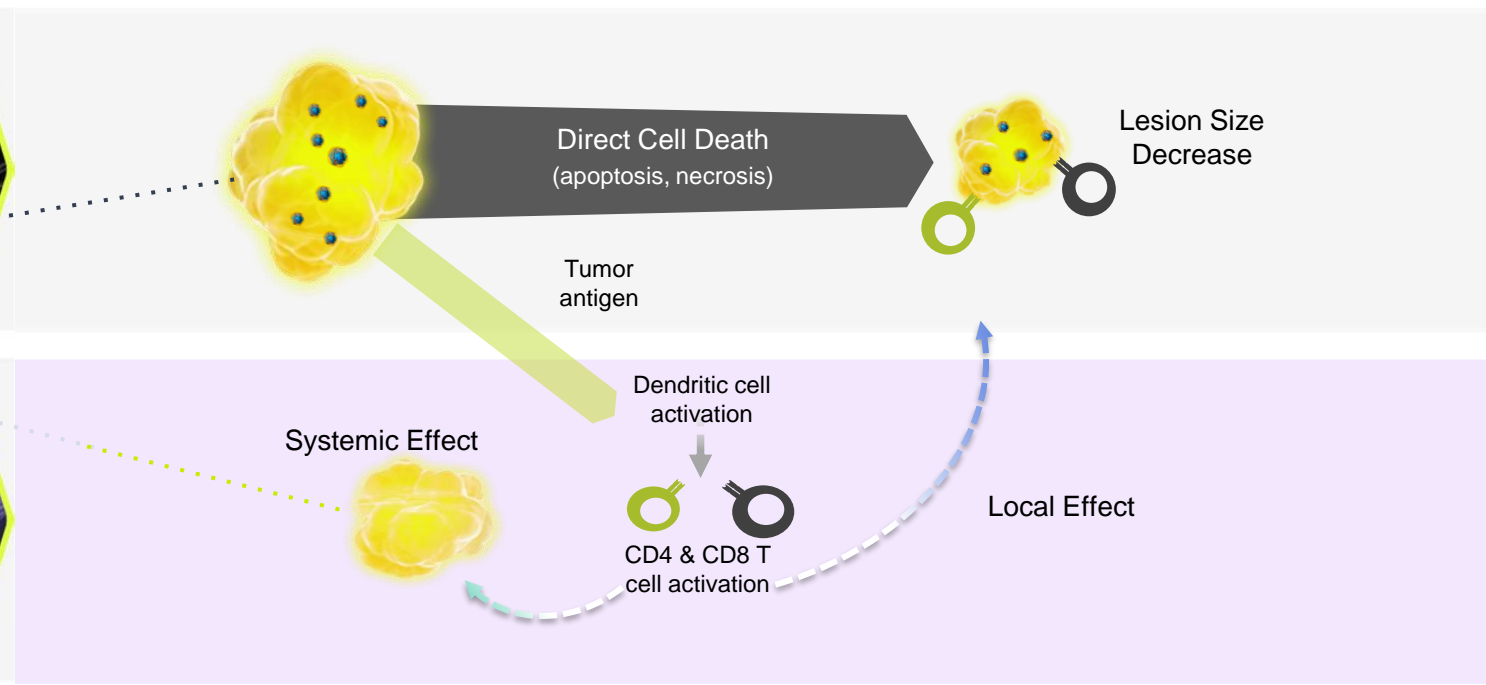
1- physical destruction of cancer cell for local control



And triggers systemic effect



1- physical destruction of cancer cell for local control

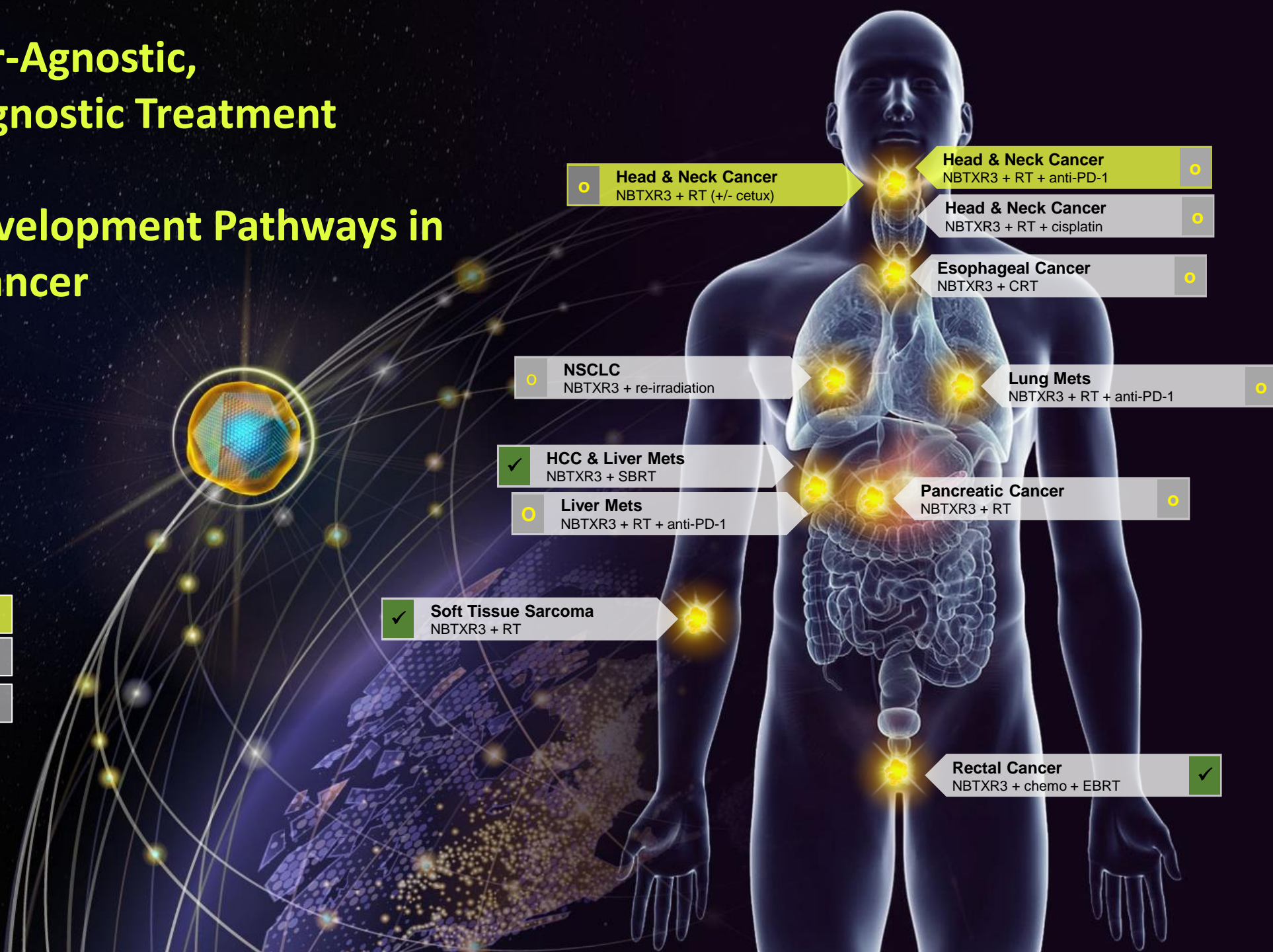


2- subsequent effect intended to prime the immune response for systemic control

Potential Tumor-Agnostic, Combination-Agnostic Treatment

Two Priority Development Pathways in Head & Neck Cancer

- Priority Pathway
- Trial Ongoing
- Trial Completed



NSCLC = non-small cell lung cancer.

Focused Development Strategy

Leverage Proof of Concept in Soft Tissue Sarcoma

01

Secure Initial US Approval as a **Single Agent** in **Locally Advanced HNSCC**



02

Establish NBTXR3 as a **Foundation to Immunotherapy in Combination** with Anti-PD-1 Agents in **Advanced Cancers**



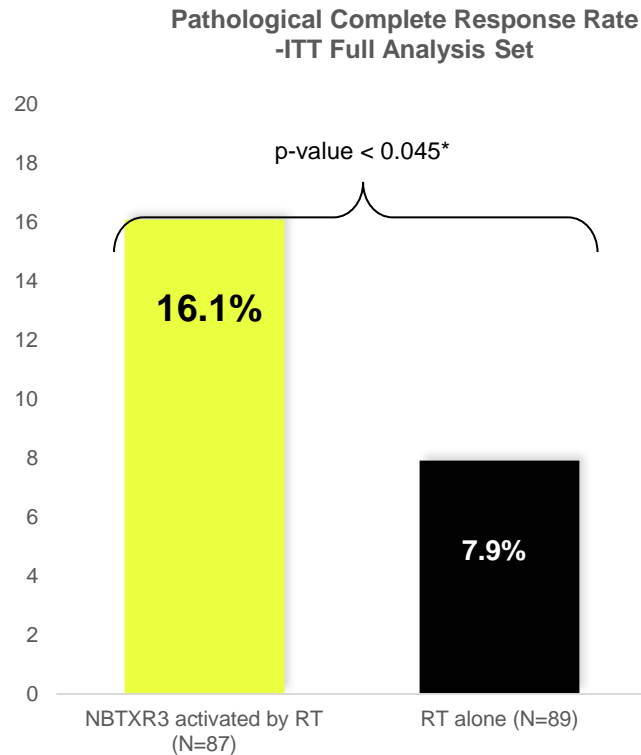
03

Advance and Expand **Tumor-Agnostic** and **Combination-Agnostic** Approaches Through **Key Strategic Alliances**



Proof-of-concept established in randomized PII/III, and European marketing authorization (CE mark) secured in tough to treat soft tissue sarcoma population

Doubling of Pathological Complete Response in Phase II/III



Results

- Achieved its primary endpoint of pathological CRR
- Achieved its secondary endpoint in quality of margins (R0)
- Demonstrated long-term persistent bioavailability
- No impact on patient ability to receive planned dose of RT

Published in Lancet Oncol. 2019

NBTXR3, a potential first-in-class radioenhancer hafnium oxide nanoparticle, plus radiotherapy versus radiotherapy alone in patients with locally advanced soft-tissue sarcoma (Act.In.Sarc): a multicentre, phase 2-3, randomised, controlled trial.

Sylvie Bonvalot, Piotr L Rutkowski, Juliette Thariat, Sébastien Carrière, Anne Ducassou, Marie-Pierre Sunyach, Peter Agoston, Angèle Hong, Augustin Meneyer, Marco Rastrelli, Victor Moreno, Rubi Kili, Béatrice Tiarago, Antonio Casado Hierrez, Alessandro Gronchi, László Mangal, Teresa Sy-Otien, Peter Hohenberger, Thierry de Baere, Axel Le Cesne, Sylvie Hoffre, Emma Scaudo-Bouard, Aneta Bokowska, Rodica Anghel, Ann-Cu, Michael Gebert, Guy Karnez, Angel Montan, Herbert H Long, Ramona Viegas, Lore Legrand, Soth-Deme, Gabriel Krasa, Lyn Aurdan, Laurence Maurice-Zabotto, Vincent Servais, Eva Wardelmann, Philippe Terrier, Alexander J Lazar, Judith VM G Bovic, Cécile Le Pichoux, Zsuzsanna Papai

Summary

Background Pathological complete response to preoperative treatment in adults with soft-tissue sarcoma can be achieved in only a few patients receiving radiotherapy. This phase 2-3 trial evaluated the safety and efficacy of the hafnium oxide (HfO₂) nanoparticle NBTXR3 activated by radiotherapy versus radiotherapy alone as a pre-operative treatment in patients with locally advanced soft-tissue sarcoma.



Lancet Oncol 2019
July 8, 2019
http://dx.doi.org/10.1016/S1473-3099(19)3026-2

Secure Global Approval (US, EU, Asia) as a Single Agent in Locally Advanced HNSCC

Targeting high-risk, tough-to-treat elderly head & neck cancer population

Radiation therapy is the primary treatment modality for unresectable head and neck cancer, administered alone or concurrent with chemotherapy

Elderly patients who cannot tolerate standard-of-care cisplatin are especially vulnerable

- Limited treatment options
- Low response rate
- Short progression free survival
- Short overall survival

Opportunity to demonstrate high medical value in patients with significant need

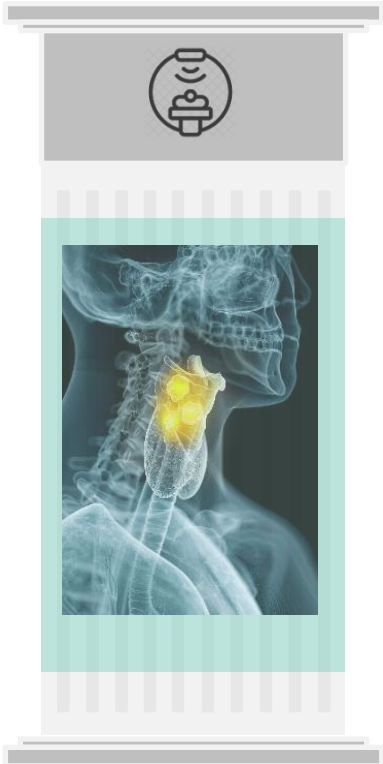
Incidence of Oral Cavity, Oropharynx, Hypopharynx, and Larynx Cancer **212,305**¹

Locally Advanced²
127,383 **60%**

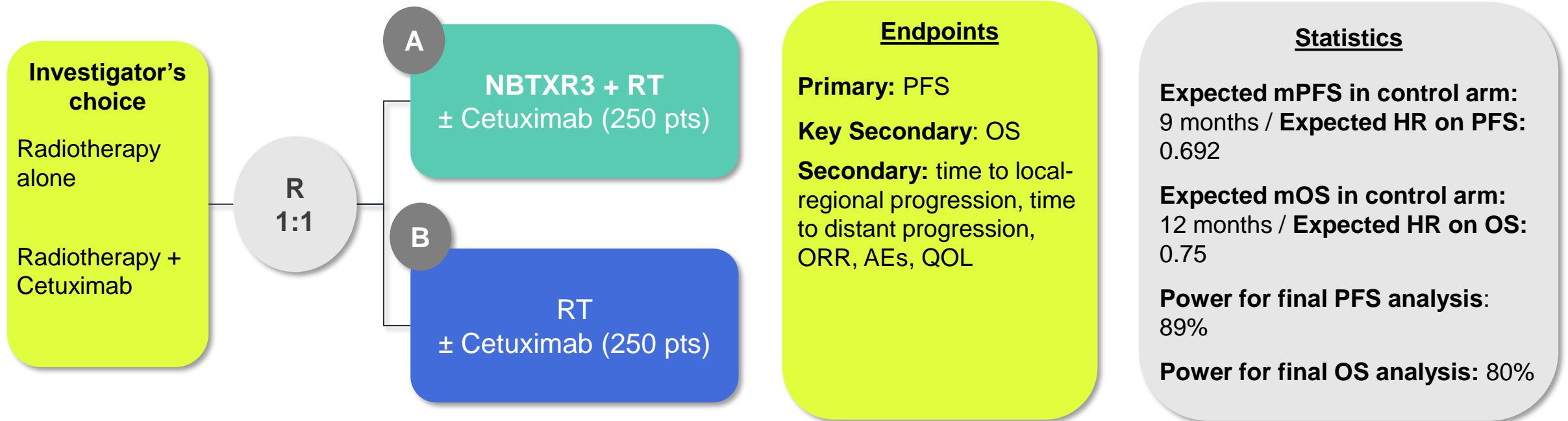
Squamous Cell Carcinomas³
114,645 **90%**

Unresectable⁴
71,045 **63%**

Cisplatin ineligible⁵ Cisplatin ineligible and >65 years old⁵
25,655 – 29,128 **18,351 – 25,655**



NANORAY-312: Global Phase III Registration Trial in Elderly Locally Advanced Head and Neck Cancer Patients Ineligible for Cisplatin



Stratification: mCCI, HPV status, cetuximab usage, country

Building on consistently high response in frail head and neck cancer patients

Moving from successful Phase I dose escalation and expansion study in very frail, elderly patients to global Phase III registration trial in larger population with better expected prognosis

Study 102: Cetuximab Ineligible

Phase I escalation and expansion (75 patients):

- Feasible
- Well tolerated
- ~63% CRR*
- 18 mOS in all patients / 23 mOS in evaluable patients in expansion cohort

NANORAY-312: Cetuximab Eligible

Global randomized phase III (~500 patients, incl. 100 patients from LianBio):

- Fast Track designation
- Potential for accelerated approval based on interim analysis
- First patient randomized in January 2022
- US site activation expected mid-2022

Head & Neck Study 102

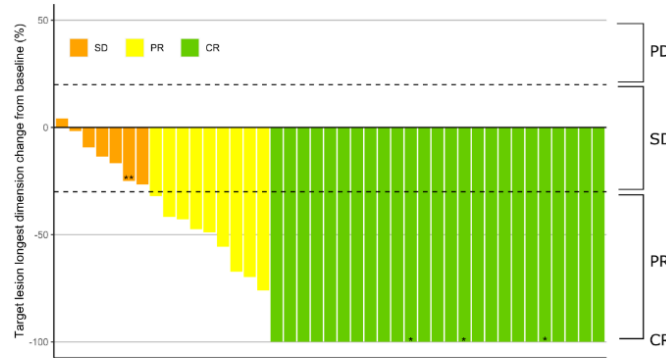
UPDATE @ ASTRO 2021

Dose expansion
N= 41 evaluable patients

Source: NBTXR3-102 - Cut-off date: 03Sep2021

High Response Rate Correlates to Improved PFS and OS

Overall Objective Response Rate of 85.4%
Complete Response Rate of 63.4%****

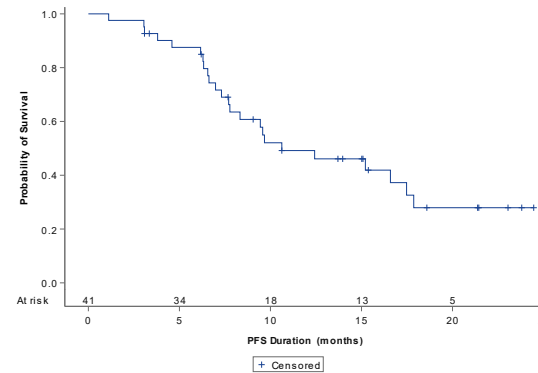


* unconfirmed complete response
** CR as per investigator

**Only 1 patient with CR died from disease progression
6 patients with CR died for non-oncologic reasons**

2-3 times prevalence of comorbidity compared to overall LA-HNSCC population¹

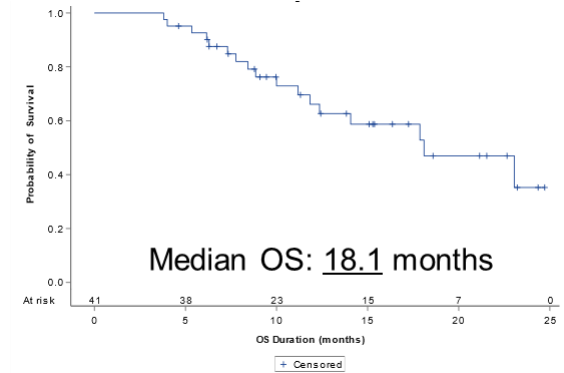
Median PFS: 10.6 months



**All patients treated population (n=54):
PFS: 9.4 months**

Real World Evidence Suggest overall LA-HNSCC: mPFS: 7.3 months⁵

Median OS: 18.1 months



**All patients treated population (n=54)
mOS: 14.1 months**

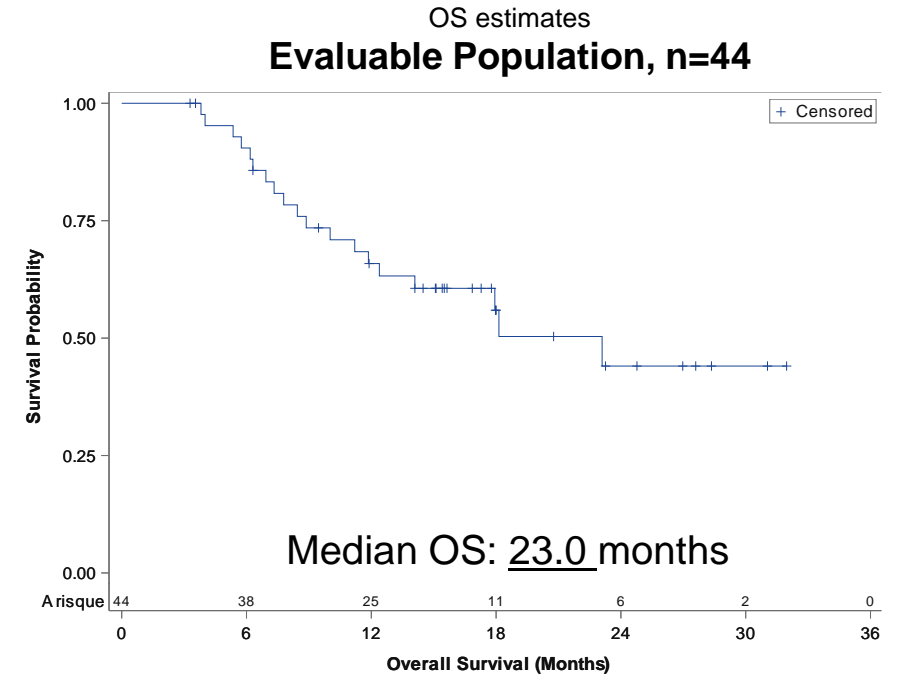
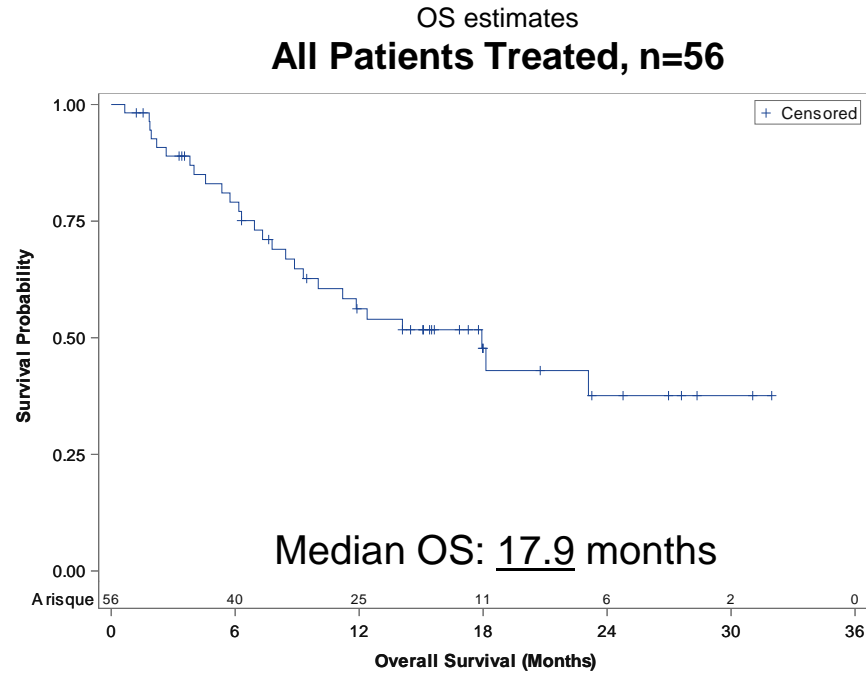
Literature Suggests overall LA-HNSCC: mos ~12 months^{2,3,4}

Median follow-up: 9.5 months

(1) expected to be 2-3 times higher than in literature * Zumsteg ZS, et al., Cancer 2017;123:1345-53. (2). Amini et al. (2016), (3). Bourhis et al. (2006) and (4). Moyo et al. (2015). This historical literature is presented solely to illustrate the current market opportunity arising from existing application of the standard treatment. Because of the unique design of such studies applied to specific patient populations, no comparison with any of our clinical trials is possible and none should be inferred from this background data.

Continued Improvement in mOS

Head & Neck Study 102



- Enrollment Complete
- Final data expected mid-2023

Dose expansion
N= 44 evaluable patients

Source: NBTXR3-102 - Cut-off date:22Feb2022

Advancing toward registration in head & neck cancer: NANORAY-312

500 patient global Phase III registration study in patients with locally advanced head and neck squamous cell carcinoma ineligible for cisplatin

- FDA granted Fast Track designation
- 100 patients, out of the planned 500, expected to be enrolled by LianBio in Asia

Anticipated Study Timelines:

- ✓ European site activations initiated Q4 21
- ✓ First Patient Randomized, January 2022
- ✓ US site activations Q3 22
- Futility analysis: ~18 months after first randomization
- Interim analysis event-driven: ~30 months
 - potential to file for accelerated approval in the US
- Final analysis on OS, PFS and quality of life

Establish NBTXR3 as a Pillar in Immunotherapy in Combination with Anti-PD-1 Agents in Advanced Cancers

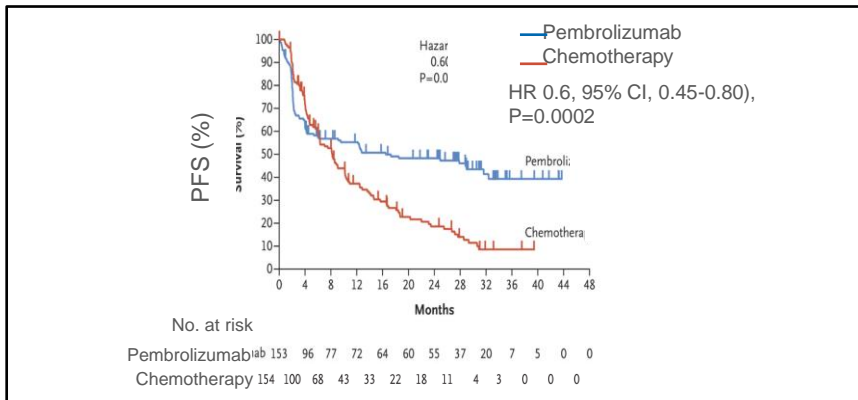
The promise and limitations of immuno-oncology agents



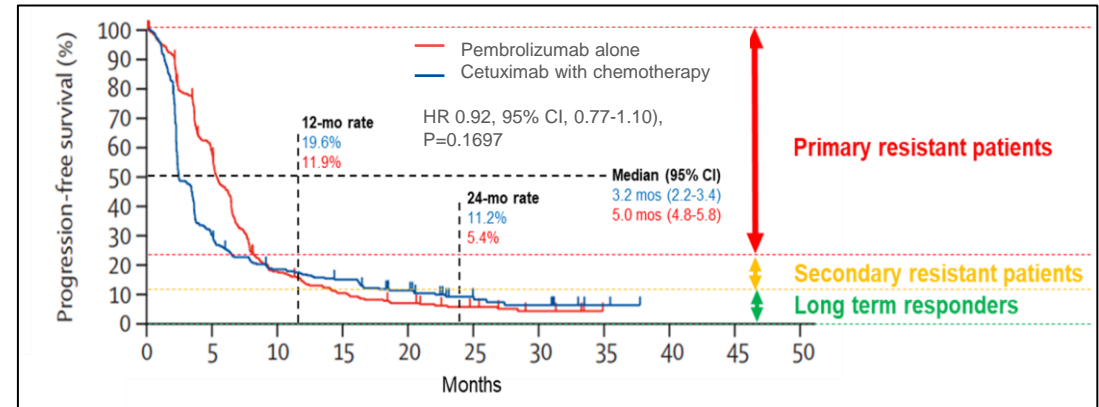
IO has been practice changing and life changing for many patients with cancer

.....but continues to leave many patients out in the “cold”

KEYNOTE-177 in mMSI-H/dMMR CRC¹



KEYNOTE-048 in R/M HNSCC²



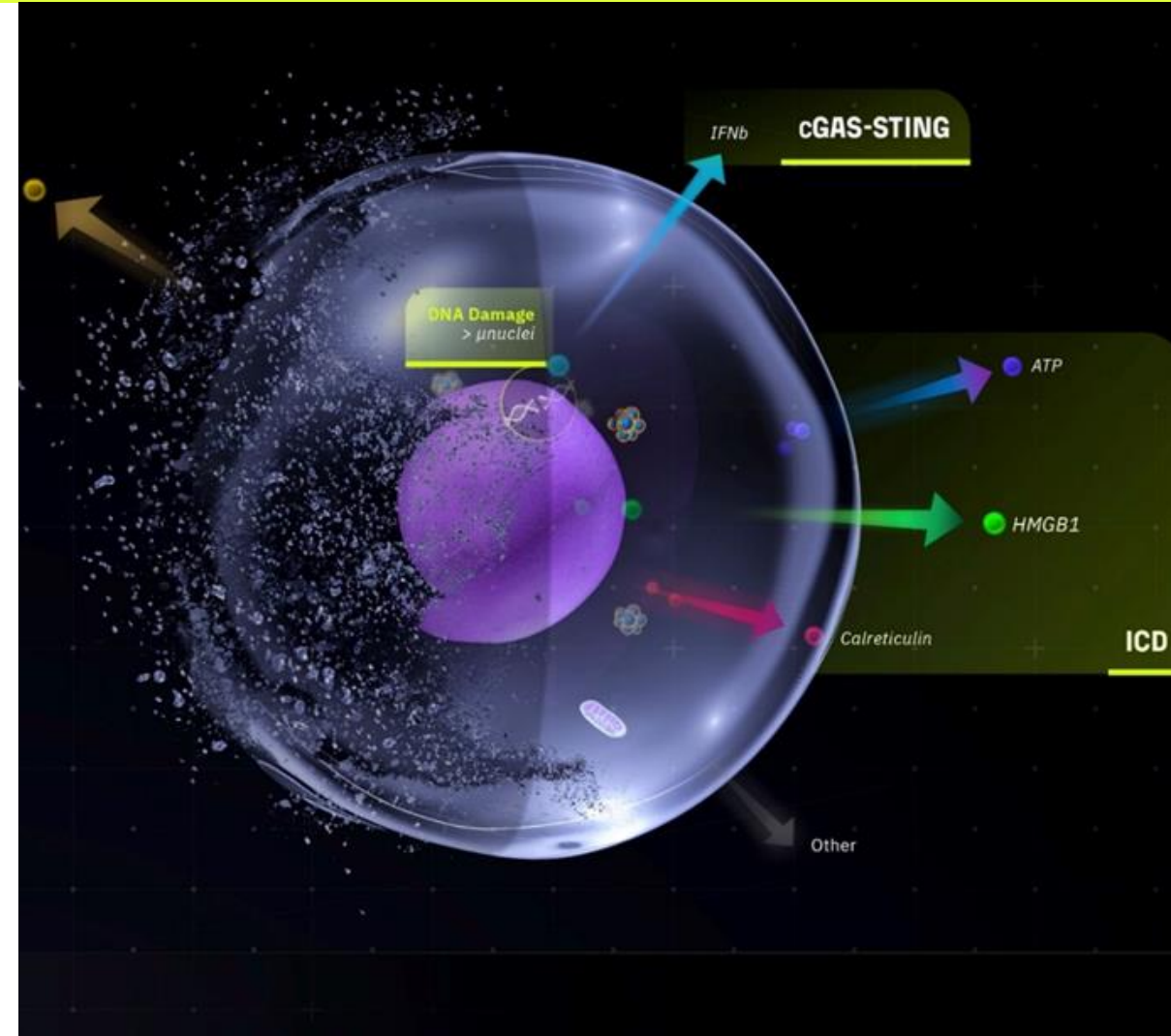
NBTXR3 offers a powerful orthogonal approach to modulate the tumor microenvironment & augment checkpoint inhibitors & other I/O agents

A primary physical MOA triggering multiple subsequent biological pathways for priming adaptive immune response

Physical priming: potential checkpoint inhibitor-agnostic agent

NBTXR3 may:

- Enhance the therapeutic index of radiotherapy, maximizing local effect
- Increase the local efficacy of immunotherapy and improve distant tumor control via a systemic effect
- Potential long-term effect with memory t-cells



Exploring Adaptive Immune Response Triggered by NBTXR3 to the Benefit of Anti-PD-1 Resistant And Naïve Patients



Head and neck cancers

- Inoperable LRR or R/M HNSCC
- Tumor in previously irradiated field
- Amenable to re-irradiation
- Anti-PD-1 naïve or non-responder



Lung mets

- Cancer metastasized to the lung
- Tumor not previously irradiated
- Indicated to receive anti-PD-1
- Anti-PD-1 naïve or non-responder



Liver mets

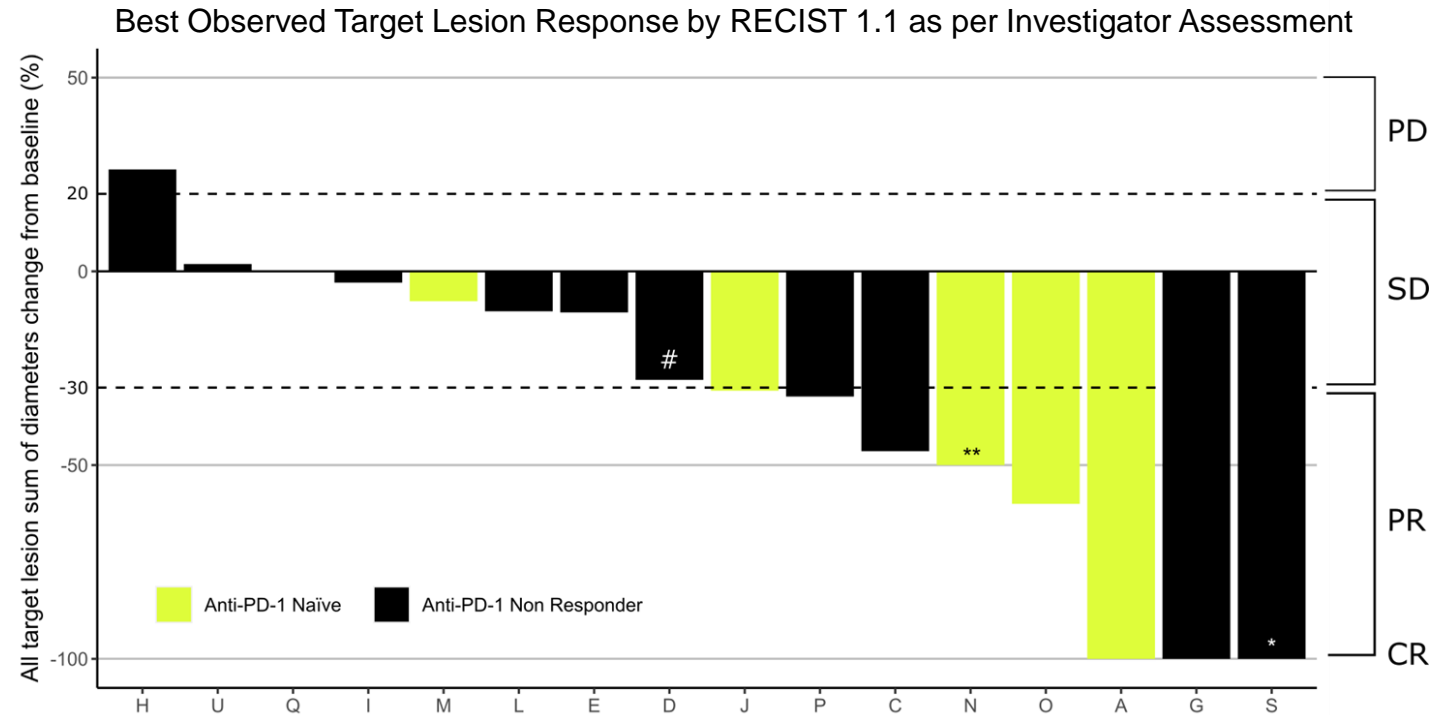
- Cancer metastasized to the liver
- Tumor not previously irradiated
- Indicated to receive anti-PD-1
- Anti-PD-1 naïve or non-responder



Best Overall Objective Response Rate of 56% Regardless of Prior Anti-PD-1 Exposure

**Study 1100:
NBTXR3 +
Checkpoint
Inhibitors**

**Preliminary
Results
@
ASTRO
2021**



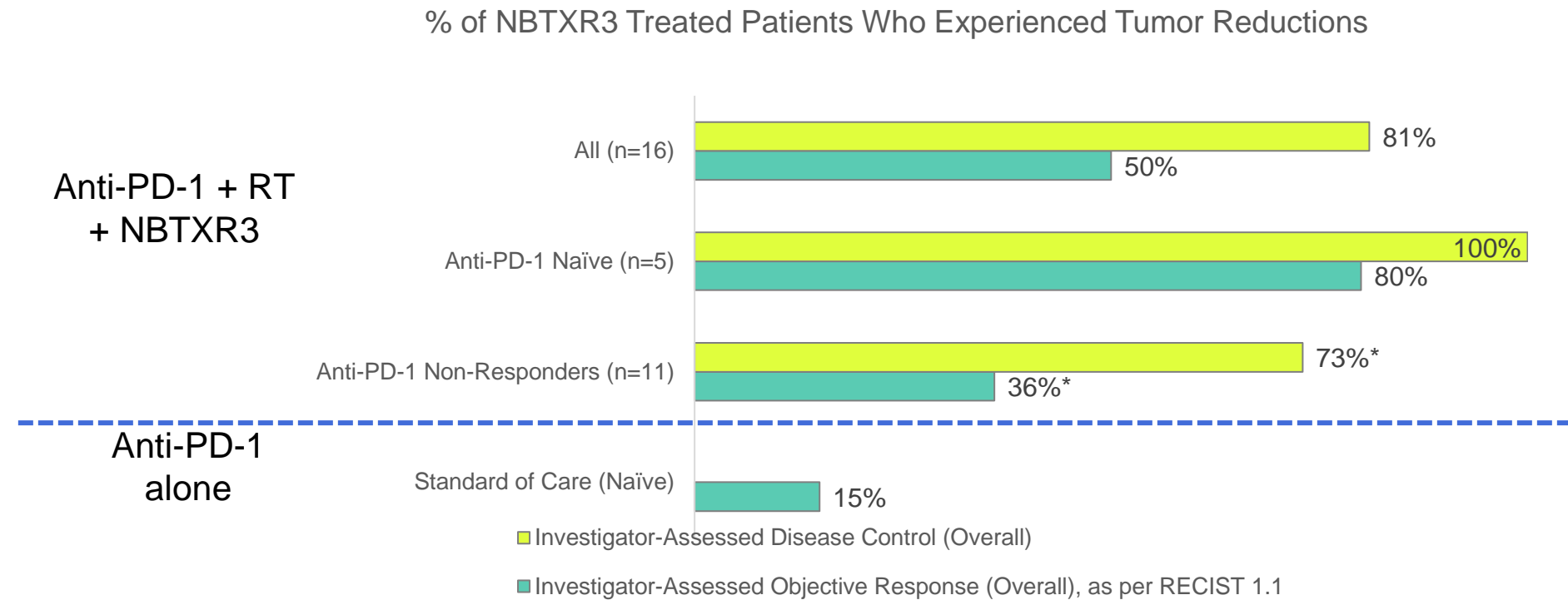
Patient D: pCR based on biopsy sample located in the target lesion
 * Patient S: Patient with unconfirmed complete response
 ** Patient N: Lymph node size is 8mm; complete response as per RECIST 1.1

Source: NBTXR3-1100 - Cut-off date:3Sep2021

Correlation between local and systemic response regardless of prior anti-PD-1 Exposure

Study 1100: NBTXR3 + Checkpoint Inhibitors

Preliminary Results @ ASTRO 2021



*Of which 1 pCR based on biopsy sample located in the target lesion (patient D) and 1 unconfirmed CR (patient S)

1. Ott PA, Bang YJ, Piha-Paul SA, Razak ARA, Bennouna J, Soria JC, et al. T-Cell-Inflamed Gene-Expression Profile, Programmed Death Ligand 1 Expression, and Tumor Mutational Burden Predict Efficacy in Patients Treated With Pembrolizumab Across 20 Cancers: KEYNOTE-028. J Clin Oncol. 2019;37(4):318-27. 2. Gong J, Chehrizi-Raffle A, Reddi S, Salgia R. Development of PD-1 and PD-L1 inhibitors as a form of cancer immunotherapy: a comprehensive review of registration trials and future considerations. J Immunother Cancer. 2018;6(1):8.

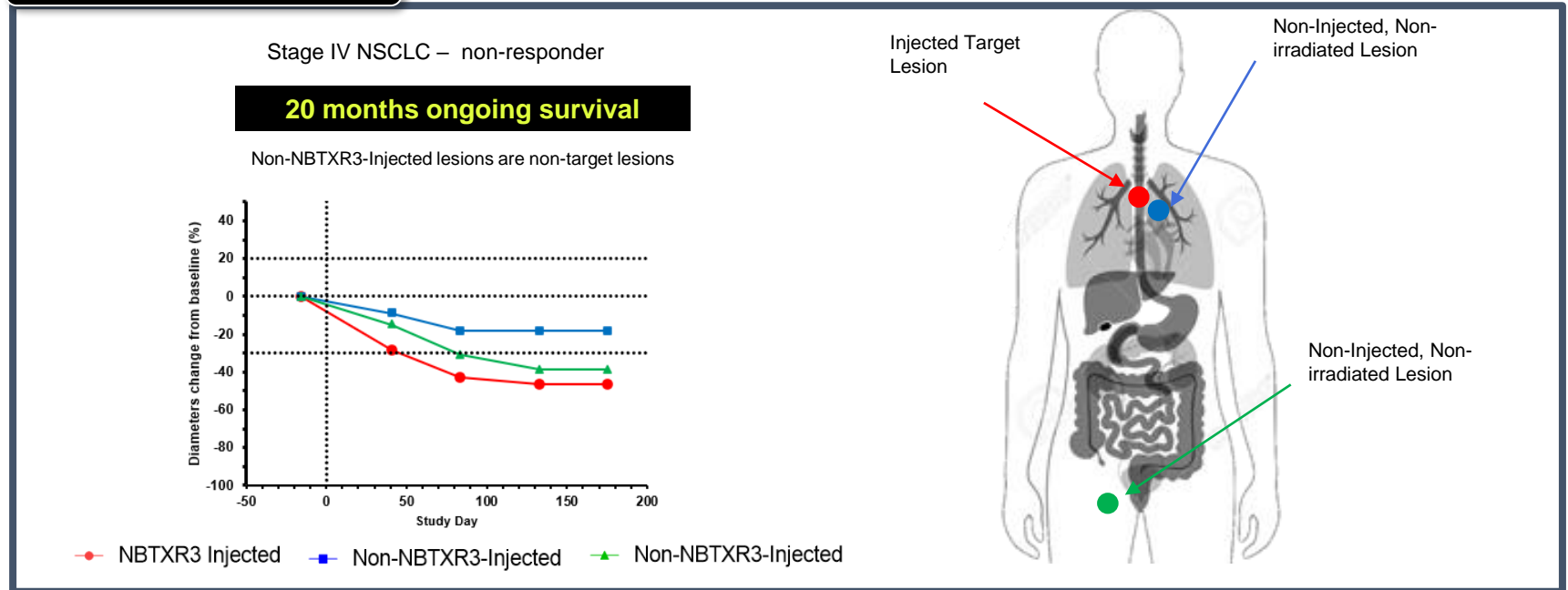
Source: NBTXR3-1100 - Cut-off date: 3Sep2021

Evidence of Both Local and Systemic Control: Possible Immune Response and Distant Tumor Control in Multiple Anti-PD-1 Non-Responder Patients*

Study 1100:
NBTXR3 +
Checkpoint
Inhibitors

Preliminary
Results
@
ASTRO
2021

Case study: Patient C



Patient experienced tumor reduction in lesions that did not receive NBTR3

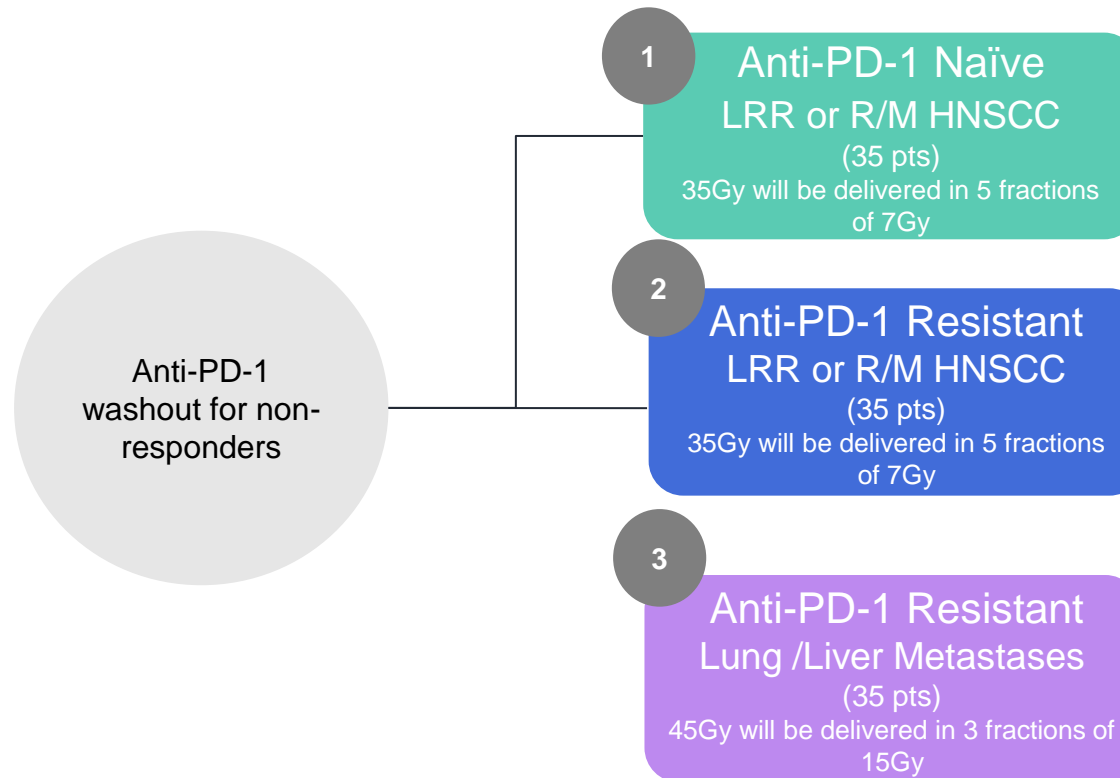
Source: NBTR3-1100 - Cut-off date:3Sep2021

*While such observations support further evaluation of this potential response, in light of the small number of enrolled patients and because certain local lesions in these patients potentially received low-dose radiation due to their vicinity to target treatment areas, such data should not be interpreted as statistically significant evidence of any result.

Study 1100 Expansion Phase: Phase I Basket Trial of NBTXR3 in Combination with Anti-PD-1 Checkpoint Inhibitors

Key Inclusion Criteria

- Anti-PD-1 Naïve; or
- Anti-PD-1 Resistant:
 - meets criteria consistent with anti-PD-1 primary resistance , or
 - meets criteria consistent with anti-PD-1 secondary resistance



Endpoints

- **Primary:** further assess the safety profile of RP2D(s)
- **Secondary:** Evaluate the safety, feasibility, and anti-tumor response of RT-activated NBTXR3 in combination with anti-PD-1
- **Exploratory:** Survival Outcomes, Duration of Response, Biomarkers of Response, and response in non-injected (target and non-target) lesion(s)

Study 1100: transforming non-responders into responders

Study 1100: NBTXR3 + Checkpoint Inhibitors

Preliminary Results @ ASTRO 2021

Study suggests that the combination of NBTXR3/RT and anti-PD-1 may **produce a sustained response in both anti-PD-1 naïve patients and patients having progressed** on prior anti-PD-1 therapy

NBTXR3/RT has demonstrated potential to **stimulate an immune response and to turn anti-PD-1 non-responders into responders**

These data support **continued development of NBTXR3/RT in combination with anti-PD-1 across tumor types regardless of prior anti-PD-1 exposure**

Preliminary feedback from FDA suggests a single randomized, controlled trial including a pre-specified comparative analysis of **overall response rate (ORR) may be suitable to support an accelerated approval, with verification of clinical benefit based on overall survival (OS)** results from the same trial

Expanding NBTXR3 Opportunity With World-Class Partners

Leveraging Strategic Partners To Advance and Expand NBTXR3 Opportunity

Advance



Develop and commercialize NBTXR3 across tumor types and therapeutic combinations in China and other Asian markets

- Development commitment includes 5 registration studies
- Enrolling 100 of 500 patients targeted for NANORAY-312
- Solely responsible for all regulatory and commercial costs in territory
- \$20M upfront, \$220M in milestones, tiered low double-digit royalties

Expand

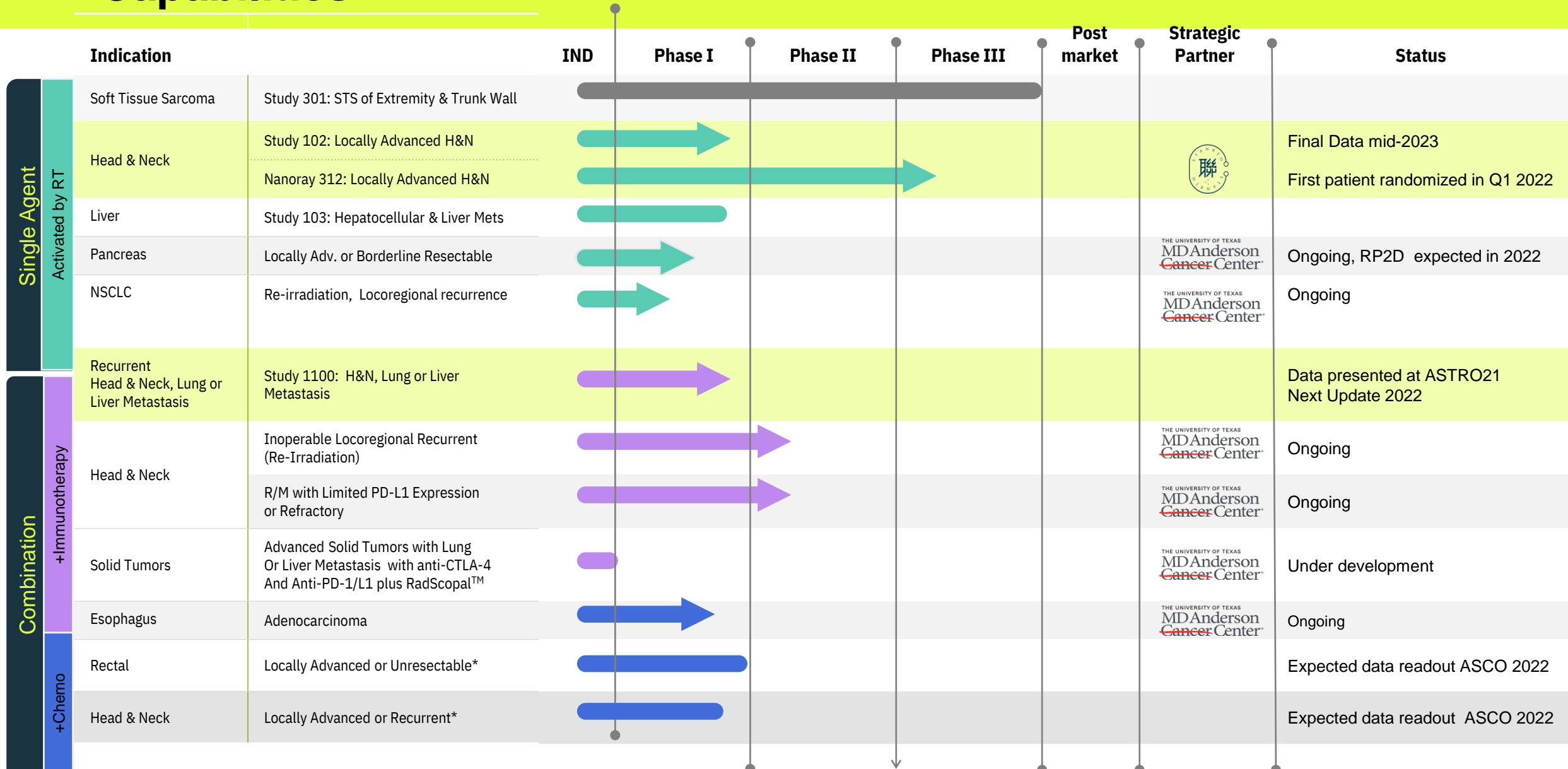


Large-scale, comprehensive clinical research collaboration to expand the therapeutic breadth and flexibility of NBTXR3

- 5 PI/II trials ongoing
- 3 Phase I Studies: Pancreatic, Esophageal, NSCLC
- 2 Phase II Studies: H&N R/M reRT+IO, H&N reRT+IO

Corporate Summary

Evaluating Tumor Agnostic, Combination Agnostic NBTXR3 Capabilities



*NANO-312 is a global Phase III clinical trial for elderly patients with locally advanced head and neck cancer who are ineligible for platinum-based (cisplatin) chemotherapy, will be initially activated in Europe and the United States as a Phase III trial. We expect U.S. site activation and enrollment to begin in 2023. For its evaluation of NANO-312, the FDA has accepted the available data from Study 102 Escalation. NBTXR3 for the treatment of locally advanced head and neck cancers received Fast Track designation from the FDA in February 2020. 1. LineBio controls the development / commercialization strategy for NBTXR3 in key countries in Asia. In addition, three NBTXR3 clinical trials conducted by our former collaborator, PharmaEngine, are currently being conducted in Asia and are in the process of being concluded or terminated. *Phase I/II Study initiated by former partner, PharmaEngine. In conjunction with the termination of the license and collaboration agreement, PharmaEngine will implement the early termination and wind-down of this clinical trial in accordance with good clinical practice guidelines. The trial will be deemed completed when all enrolled patients have reached "end-of-study" and PharmaEngine issues a final study report in accordance with good clinical practice guidelines.

Key Financial Highlights

- Cash* as of March 31, 2022: €70.6M
 - Equity financing line provides flexible access to capital
 - Accessible capital resources expected to support development plan into fourth quarter of 2023
- Debt as of December 31, 2021:
 - €30M credit facility from EIB
 - €10M from State-Guaranteed Loan (PGE)
- Dual-listed: Euronext Paris (**NANO**) and Nasdaq Global Select Market (**NBTX**)

34,825,872 shares outstanding as of December 31, 2021

	For the year ended December 31,	
	2021	2020
Revenues and other income		
Revenues	10	50
Other income	2,637	2,462
Total revenues and other income	2,647	2,512
Research and development expenses	(30,378)	(24,330)
Selling, general and administrative expenses	(19,434)	(14,611)
Other operating and income expenses	(5,414)	—
Total operating expenses	(55,226)	(38,941)
Operating income (loss)	(52,579)	(36,428)
Financial income	6,170	201
Financial expenses	(590)	2,646
Financial income (loss)	5,580	2,847
Income tax	(5)	(9)
Net loss for the period	(47,003)	(33,590)
Basic loss per share (euros/share)	(1.35)	(1.38)
Diluted loss per share (euros/share)	(1.35)	(1.38)

Key takeaways and upcoming milestones

Summary

- Potential First-in-Class Tumor Agnostic, Combination Agnostic Oncology Product
- Established Proof-of-Concept as a single agent in Soft Tissue Sarcoma Randomized Phase II/III trial
- Global Phase III Registration Trial Initiated In Head & Neck Cancer
- Clinical immuno-oncology combination data in anti-PD-1 refractory patients showing the potential to transform non-responders into responders
- World-Class Collaborative Partners

2022 Milestones

Advance Priority Pathways

Single Agent, Registration Program in Head & Neck Cancer

- ✓ NANORAY-312 pivotal PIII trial, first patient randomized in January 22
- ✓ US Site activation

Proof-of-Concept Combination: NBTXR3 + ICI

- ☐ Conclude dose escalation and report RP2D for each cohort
- ☐ Report updated Study 1100 Data
- ✓ Regulatory guidance on registration pathway

Leverage Strategic Partners to Advance Pipeline Development

Single Agent, Registration Program in Head & Neck Cancer

- ✓ LianBio to initiate NANORAY-312 pivotal PIII site in Asia

Report new collaboration data

- ☐ Conclude dose escalation and report RP2D for Phase I Pancreatic Cancer
- ✓ Report final data from Phase I Study in Combination with Concurrent Chemotherapy for Patients with Head and Neck Cancer
- ✓ Report final data from Phase I/II in Combination with Concurrent Chemotherapy for Patients with Locally Advanced or Unresectable Rectal Cancer

NANOBIOTI

NANO
LISTED
EURONEXT

NBTX
Nasdaq Listed