

NANOBIOTIX



CORPORATE PRESENTATION

November 2022

Developing disruptive physics-based
nanotherapeutics to treat locally advanced and
metastatic cancers

IMPORTANT NOTICE REGARDING FORWARD-LOOKING STATEMENTS

IMPORTANT: You must read the following before continuing.

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- our ability to complete clinical trial NANORAY-312 within the expected time-frame due to a number of factors, including delays in patient enrollment or in manufacturing sufficient quantities of NBTXR3 necessary to conduct the trial or in supplying NBTXR3 in a timely manner ;
- our ability to successfully develop and commercialize NBTXR3;
- our ability to expand our product pipeline by developing and commercializing NBTXR3 in additional indications, including in combination with chemotherapies or I-O treatment;
- our ability to maintain regulatory approvals and certifications for our products and product candidates and the rate and degree of market acceptance of our product candidates, including NBTXR3;
- the expected timeline of our clinical trial completion, including our ability, and the ability of third-party collaborators, to successfully conduct, supervise and monitor clinical trials for our product candidates;
- our ability to manufacture, market and distribute our products upon successful completion of applicable pre-marketing regulatory requirements, specifically NBTXR3;
- our ability to obtain funding for our operations.

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Caution should be exercised when interpreting results from separate trials involving separate product candidates. There are differences in the clinical trial design, patient populations, and the product candidates themselves, and the results from the clinical trials of distinct product candidates may have no interpretative value with respect to our existing or future results. Similarly, caution should be exercised when interpreting results relating to a small number of patients or individually presented case studies.

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NANOBIOTIX: Applying universal properties of physics to develop nanotherapeutics targeting the biological complexities of disease

Focused and Differentiated Pipeline



NBTXR3 is a **first-in-class radioenhancer** with paradigm breaking potential and **proven MOA in randomized Ph 3 trial**
Physics-based mechanism overcomes biological heterogeneity at indication and patient level, resulting in **consistent activity** across wide range of solid tumors

Expansive Market Opportunity



PoC when activated by RT alone, and **synergistic add-on potential to multiple SOC, including IO**
Prioritized **focus in head and neck cancers** with significant, **de-risked expansion opportunities**
> 75 clinical sites worldwide, ~300 patients treated, >12 clinical trials completed or ongoing

Multiple Late-Stage Catalysts



Clear clinical path; Fast track designation; Potential for **accelerated approval**
Ongoing Ph 3 in locally advanced head and neck cancer with interim Ph 3 data expected in 2H 2024
Protocol submission for **2nd Ph 3 in combination with anti-PD-1** in R/M HNSCC expected in Q1 2023

Well-Capitalized







Development plan **funded into Q1 2024**

*R/M HNSCC: recurrent and/or metastatic head and neck cancer

Evaluating tumor agnostic, combination agnostic potential of NBTXR3 in solid tumors with an initial focus in HNSCC

Pipeline-in-a-product strategy

| Indication | Trial Name | Approach | Phase I | Phase II | Phase III | Expected Milestones |
|---|------------------------|---------------------------|---|----------|-----------|------------------------------------|
| Head and Neck Locally Advanced | NANORAY-312 | NBTXR3-RT* ± cetuximab |  | | | Interim Ph 3 data 2H 2024 |
| | Study 102 | NBTXR3-RT* |  | | | Final Ph 1 Data Mid-2023 |
| Head and Neck Recurrent and/or Metastatic | TBD <i>Planning</i> | NBTXR3-RT* + anti-PD-1 |  | | | FDA Protocol Submission Q1 2023 |
| | Study 1100 | NBTXR3-RT* + anti-PD-1 |  | | | Expansion Data Update TBD |

NANOBIOTIX
EXPANDING
LIFE

Demonstrated safety, feasibility and clinical activity of NBTXR3-RT* across multiple solid tumors

Completed Studies

Soft Tissue Sarcoma – NBTXR3-RT* Rectal** – NBTXR3-RT* + Chemo Tx
Head and Neck** – NBTXR3-RT* + Chemo Tx Liver – NBTXR3-RT*

THE UNIVERSITY OF TEXAS
MDAnderson
Cancer Center

Exploring safety, feasibility and efficacy of NBTXR3-RT* in solid tumors

Ongoing Studies

Head and Neck – NBTXR3-RT* + anti-PD-1 Pancreatic – NBTXR3-RT*
Esophageal – NBTXR3-RT* + Chemo Tx NSCLC – NBTXR3-RT*

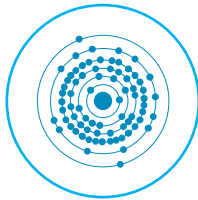
*NBTXR3-RT: NBTXR3 activated by radiotherapy; **Study terminated prior to completion as result of conclusion of collaboration, results presented at ASCO 22

NBTXR3: The universal radioenhancer for solid tumors

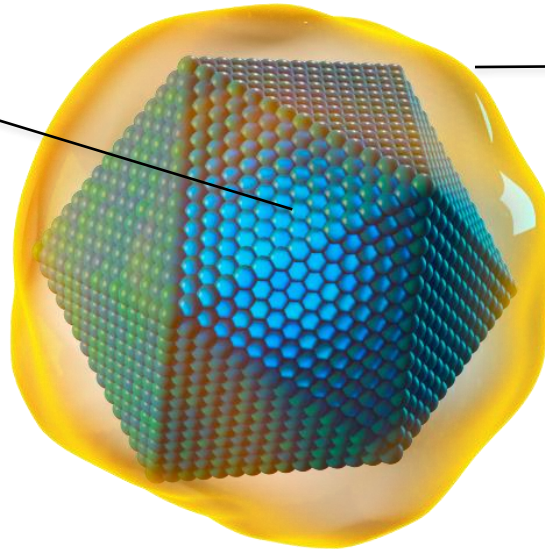
Suspension of metabolically inert nano-sized particles for intratumoral injection

Hafnium oxide CORE

High atomic number (72)
and high e^- density



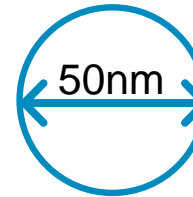
Increased local
absorption of ionizing
radiation



NEGATIVELY charged coating

Nanometer scale
to fit inside cell

Negative surface charge for
stability at neutral pH in
aqueous medium



Facilitates entry into
tumor cells

Hyper-focused delivery of enhanced radiation into cancer cells

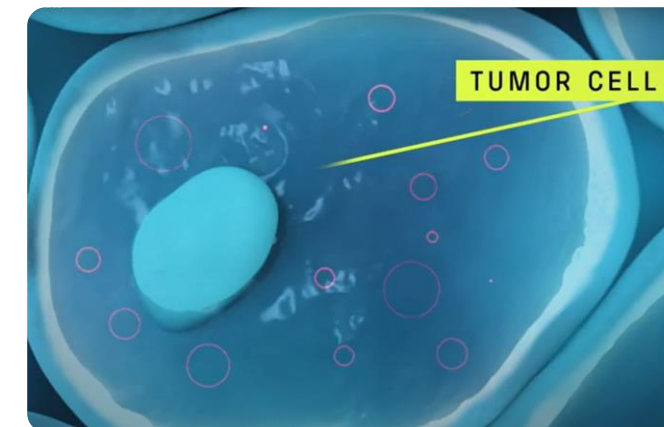
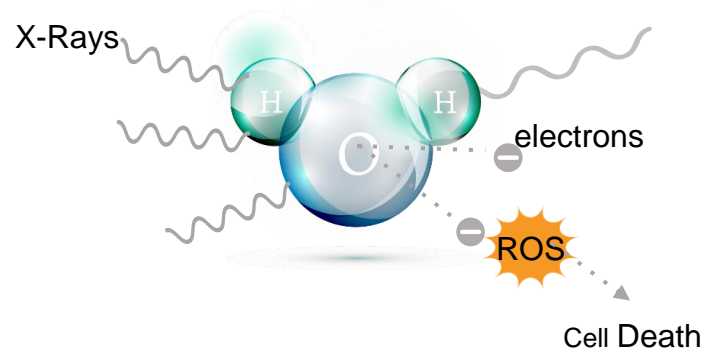
9x dose enhancement* of radiotherapy for selective and robust tumor killing

RADIOTHERAPY ALONE

X-rays interact with H_2O

Free electrons generated

Triggers cell death or damage

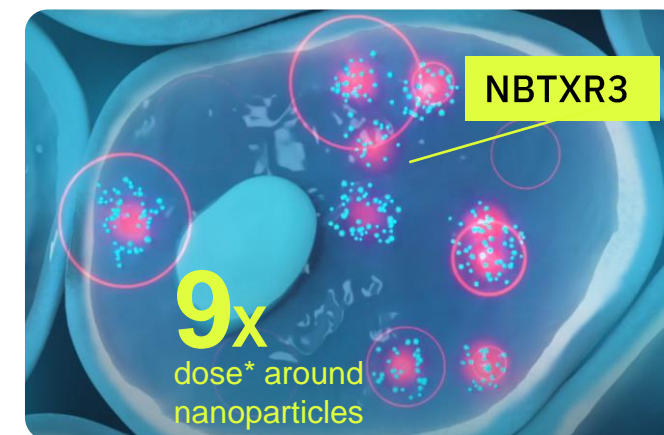
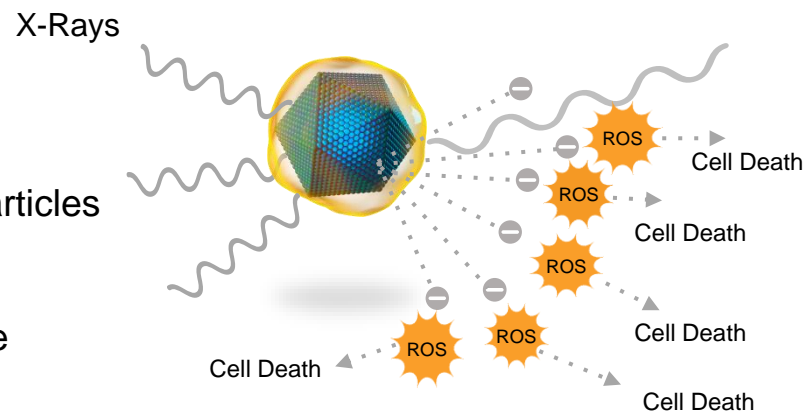


RADIOTHERAPY + NBTXR3

X-rays interact with high electron density nanoparticles

Amplified generation of free electrons

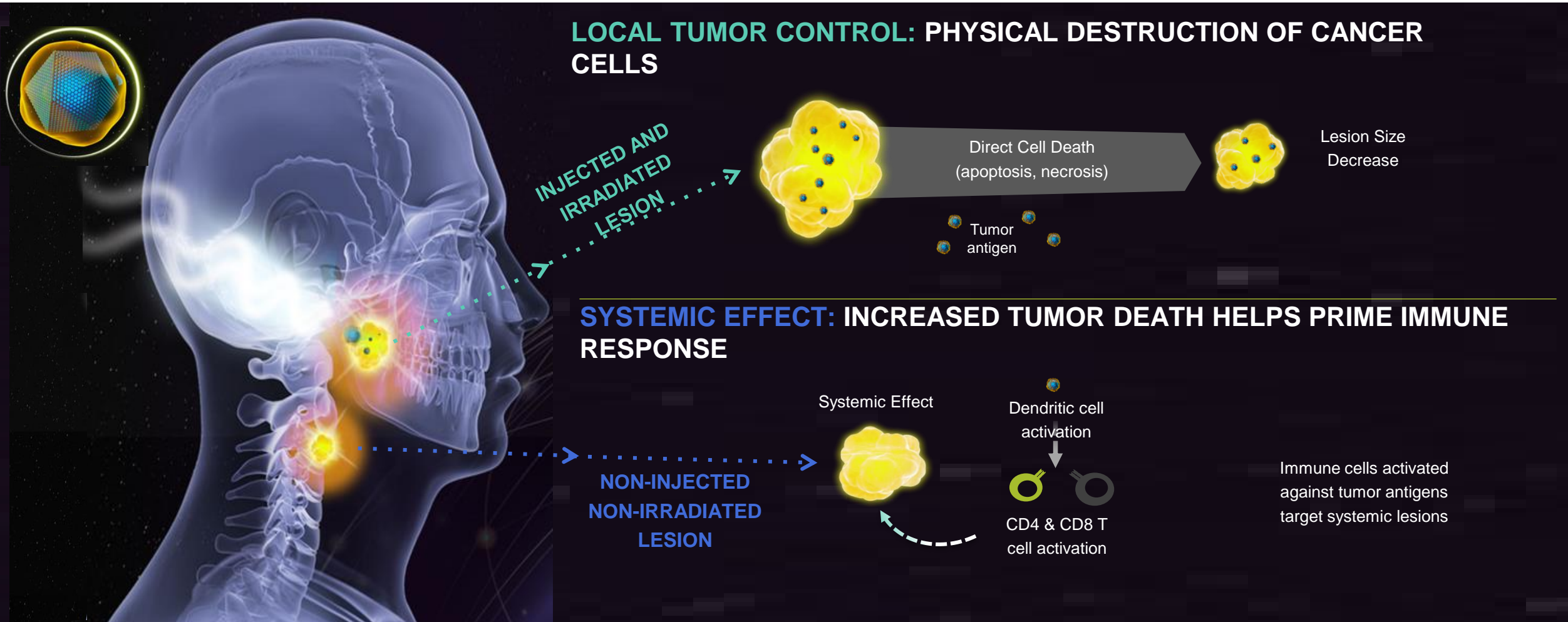
Triggers more robust tumor cell death or damage



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

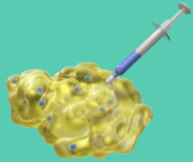
Local cell destruction induced by NBTXR3 activates immune priming

Local and systemic benefits through cell death and immune activation against tumor antigens



NBTXR3: Key value drivers of clinical differentiation

Designed to disrupt outcomes without disrupting clinical practice



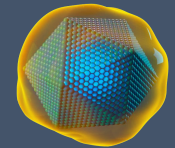
Single Treatment

One-time intratumoral administration
Significantly enhances therapeutic index of radiotherapy



Easily Integrated into Patient Flow

Activated by any form of radiotherapy using standard equipment
Adds +1 visit to ~50 visits in typical patient flow
Combinability with targeted therapies, chemotherapy and surgery



Well-Tolerated With Consistent Efficacy

Consistent overall response rate across all solid tumor indications evaluated to date
Does not change safety and tolerability of RT or immune checkpoint inhibitors
Over 300 patients with cancer treated to date

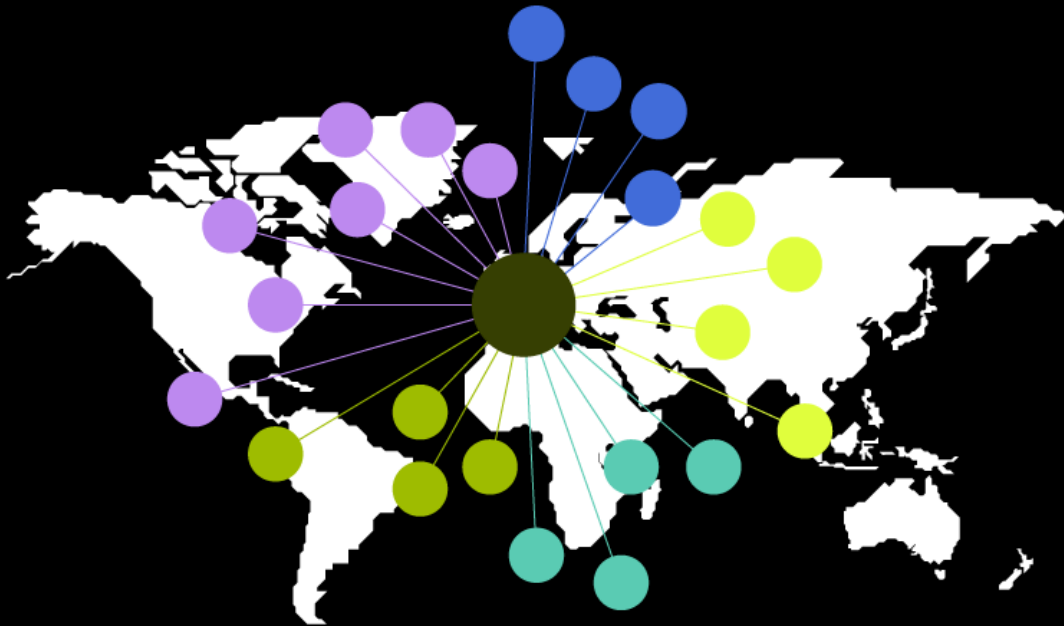


Broad Application

Universal application across all solid tumors
More than 60% of all cancer patients are treated with RT
Potential to expand and create new market opportunities in combination with targeted therapeutics

Proprietary commercial manufacturing capability and robust IP

Composition, quality, and performance are highly dependent on the manufacturing processes



In-house, GMP compliant, scalable drug substance manufacturing established in 2017

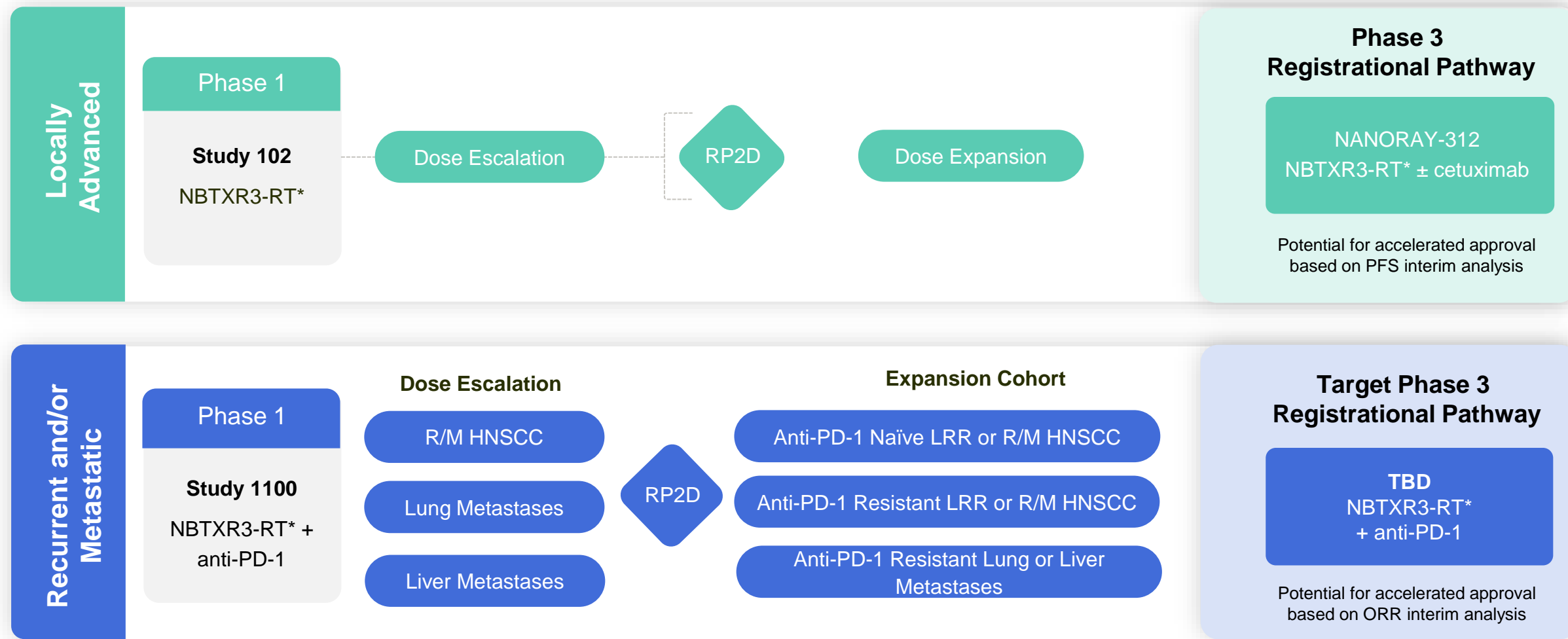
Built to scale, validated process with ability to accommodate commercial demand

Over 400 issued or pending patents and patent applications across the world

Includes concepts, products and uses of nanoparticles activated by ionizing radiation through NBTXR3 technology and for new applications in nanomedicine

Focusing on late-stage development opportunities in head and neck cancer

Based on Phase 1 proof-of-concept studies NBTRXR3-RT is well-positioned for two Phase 3 registrational opportunities



Potential \$4.5 billion HNSCC global market¹ despite significant limitations

Among the deadliest malignant tumors, with ~700,000 new patients diagnosed per year and a 5-year survival rate of roughly 50%²

Radiation therapy ± chemotherapy

primary treatment modality for unresectable head and neck cancer

74%

HNSCC Patients Receive RT³

Limited by dose-dependent toxicities, damage to healthy tissue, patient tolerability and lower quality of life

~12-14% of LA-HNSCC are ineligible for platinum-based chemotherapy⁴

Erbitux (cetuximab)

generally used with radiation in HPV-HNSCC where comorbidities limit use of chemotherapy

~\$320M

Peak Sales HNSCC⁵

13% ORR in the monotherapy setting⁶ and 36% ORR in combination with chemotherapy⁷

primary and acquired resistance mechanisms considerably limit the clinical benefit

pembrolizumab and nivolumab

approved for recurrent or metastatic HNSCC and pembrolizumab as primary treatment for unresectable disease

~\$1.8B

HNSCC 2021⁵

>80% of eligible HNSCC patients do not respond to immune checkpoint inhibitors⁸

primary and acquired resistance mechanisms considerably limit the clinical benefit

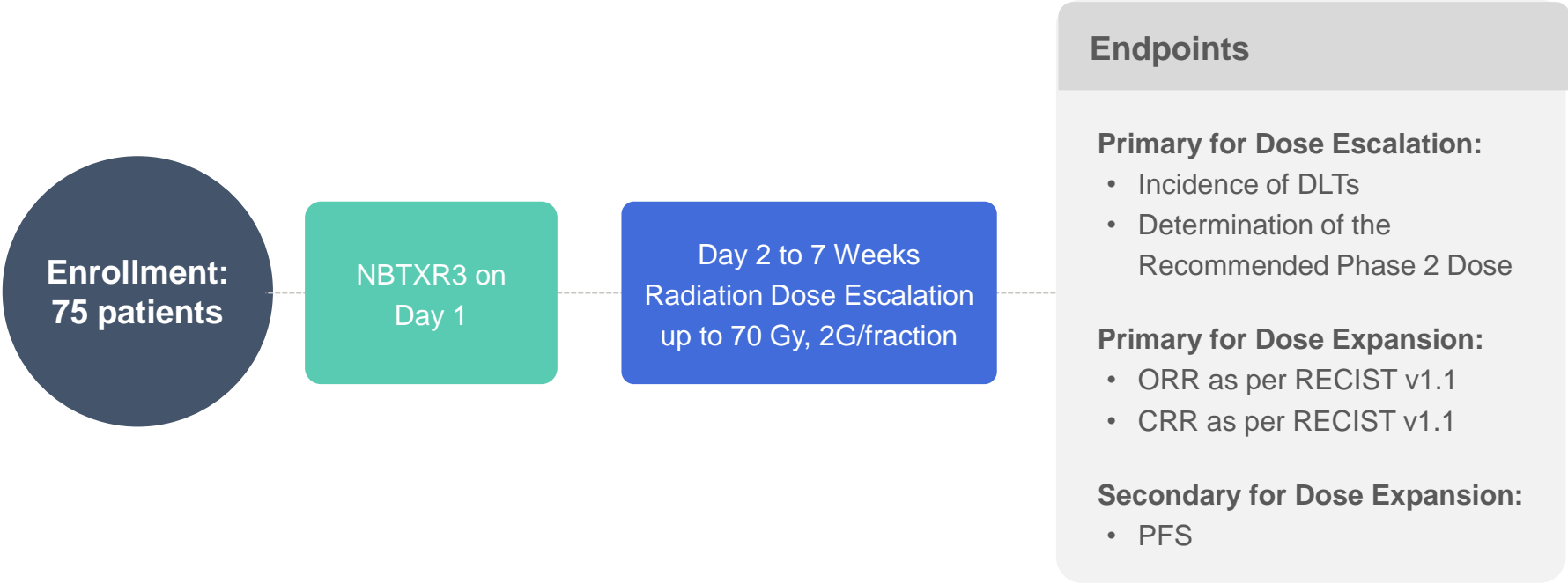
Key Inclusion Criteria

Diagnosed with Locally Advanced Head and Neck Squamous Cell Carcinoma
Cetuximab Ineligible

>70 years of age or >65 but <70 and cisplatin ineligible or Cisplatin contraindicated or intolerant to cisplatin or cetuximab

Study 102:

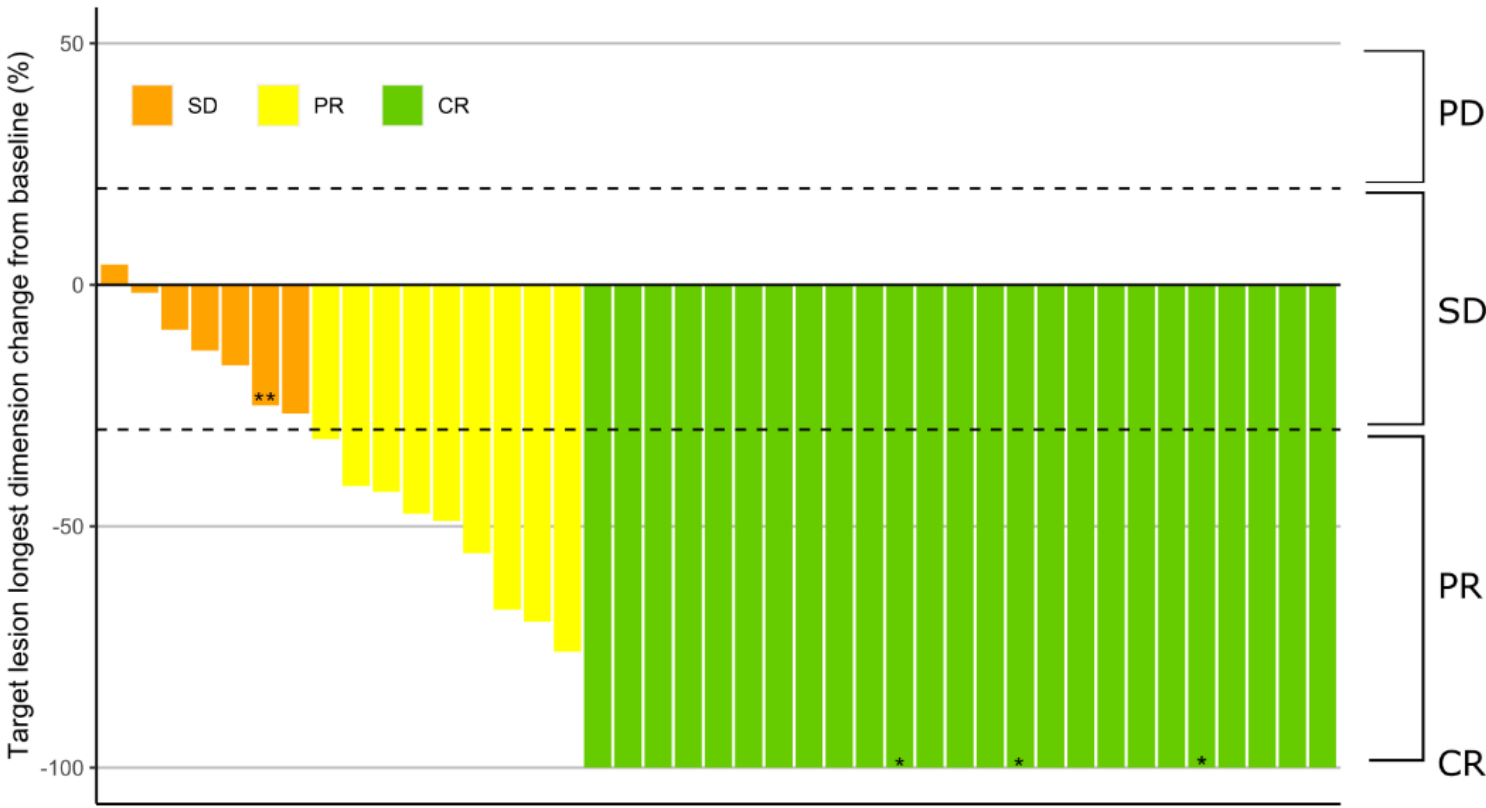
Phase 1 dose escalation and dose expansion evaluation of NBTXR3-RT* in locally advanced head and neck cancers



Enrollment Complete | Final data expected mid-2023

85% of patients achieved a response to NBTXR3-RT* as per Investigator Assessment

Median follow up of 9.5 months



63%

achieved a Complete Response**

Dose expansion
N= 41 evaluable patients

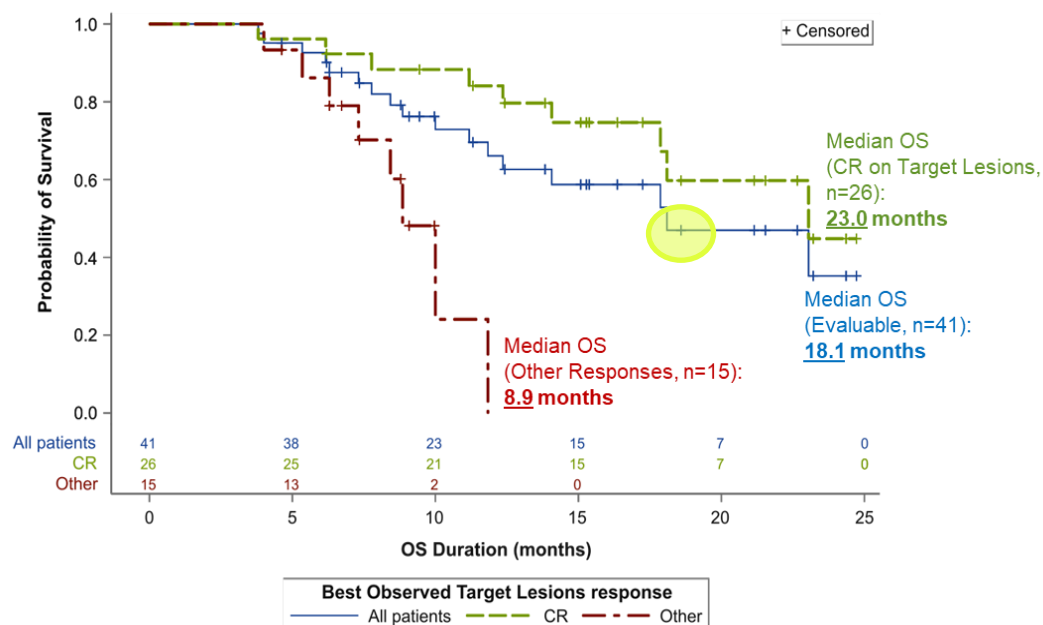
*NBTXR3-RT: NBTXR3 activated by radiotherapy **Study 102 ASTRO 2021; Data cut-off date: September 2021

High response rate correlates with improved OS and PFS

ASTRO 21 update, September 2021 Data Cut-off

Median OS: 18.1 months

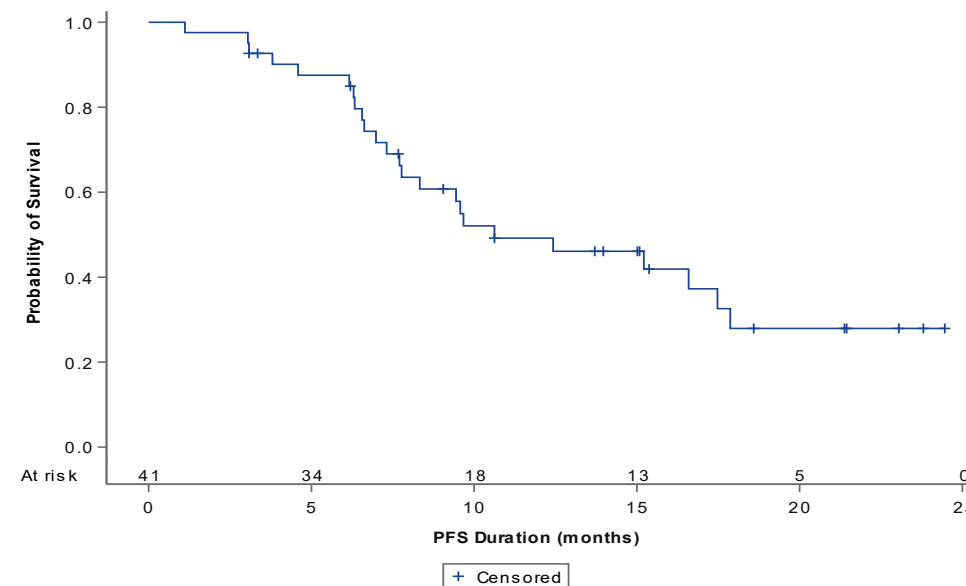
Evaluable population (n=41)



All patients treated (n=54) at **14.1 months**

Median PFS: 10.6 months

Evaluable population (n=41)



All patients treated (n=54) at **9.4 months**

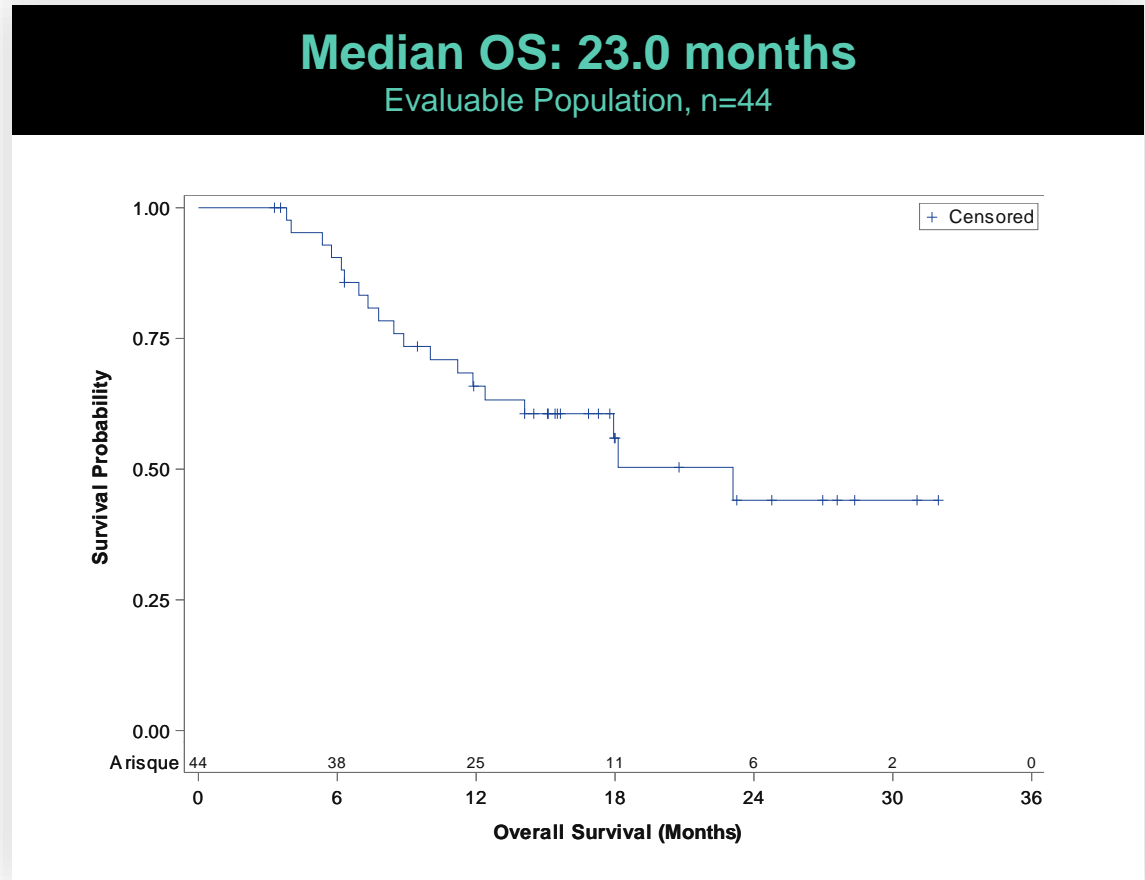
~12 months median OS Overall LA-HNSCC population¹

7.3 months median PFS Overall LA-HNSCC population²

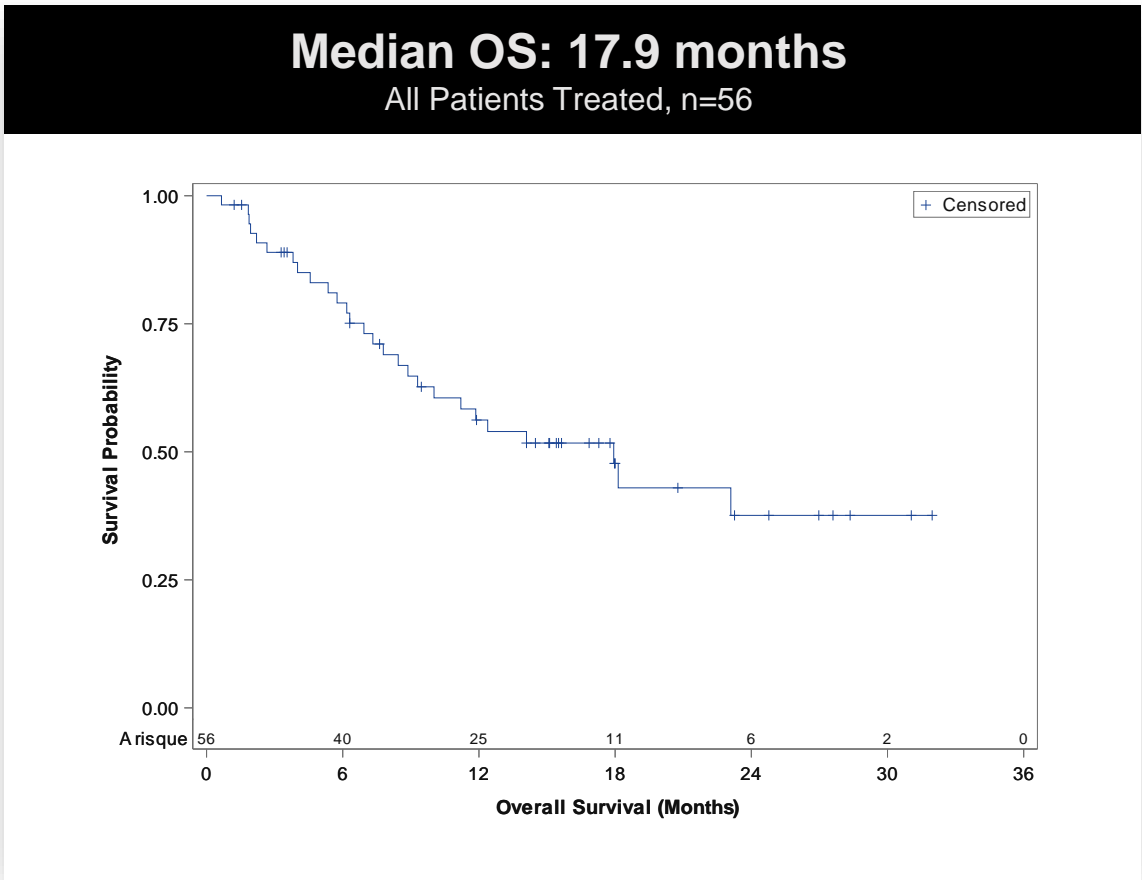
Source: NBTXR3-102 - Cut-off date: Sep. 03, 2021

Continued increase in mOS

Cut-off date 22 Feb 2022



Enrollment Complete



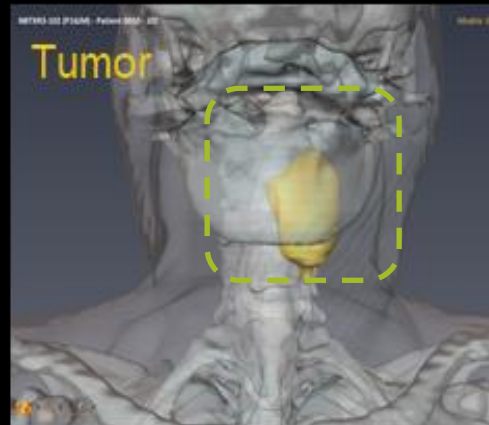
Final data expected mid-2023

Source: NBTXR3-102 - Cut-off date: Feb. 22, 2022

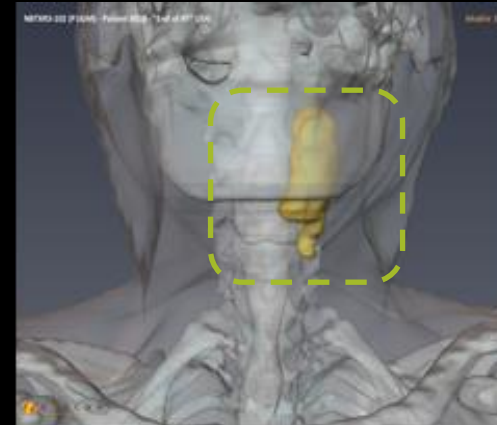
NBTXR3 demonstrated curative potential

Provides strong clinical rationale for pursuing registration

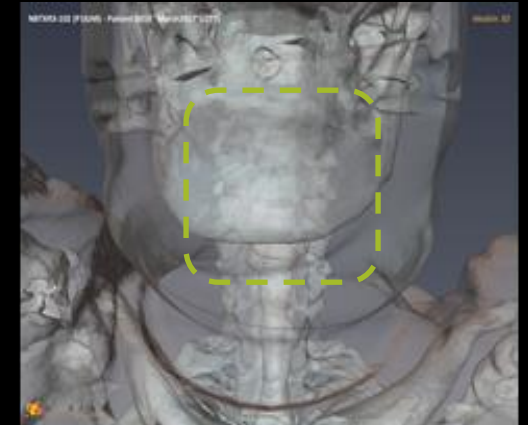
Complete Response
and >55 months survival
after treatment with
NBTXR3 + RT



Post IT injection



Post radiotherapy



7 months after RT

Moving from successful Phase 1 to Phase 3 registration trial

Study 102 supports global randomized NANORAY-312 Phase 3 trial

Study 102: Cetuximab Ineligible

Phase 1 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 3 (~500 patients):

- Target patient population carries same burden of disease but with fewer co-morbidities
- Fast Track designation
- Potential for accelerated approval based on interim analysis
- First patient randomized in January 2022

*Calculation in expansion part includes one patient marked * in chart on slide 14 recorded as unconfirmed Complete Response by principal investigator

NANORAY-312:

Global Phase 3 registration trial locally advanced HNSCC

Designed to provide robust evidence for survival superiority

Key Inclusion Criteria

Age ≥65 years

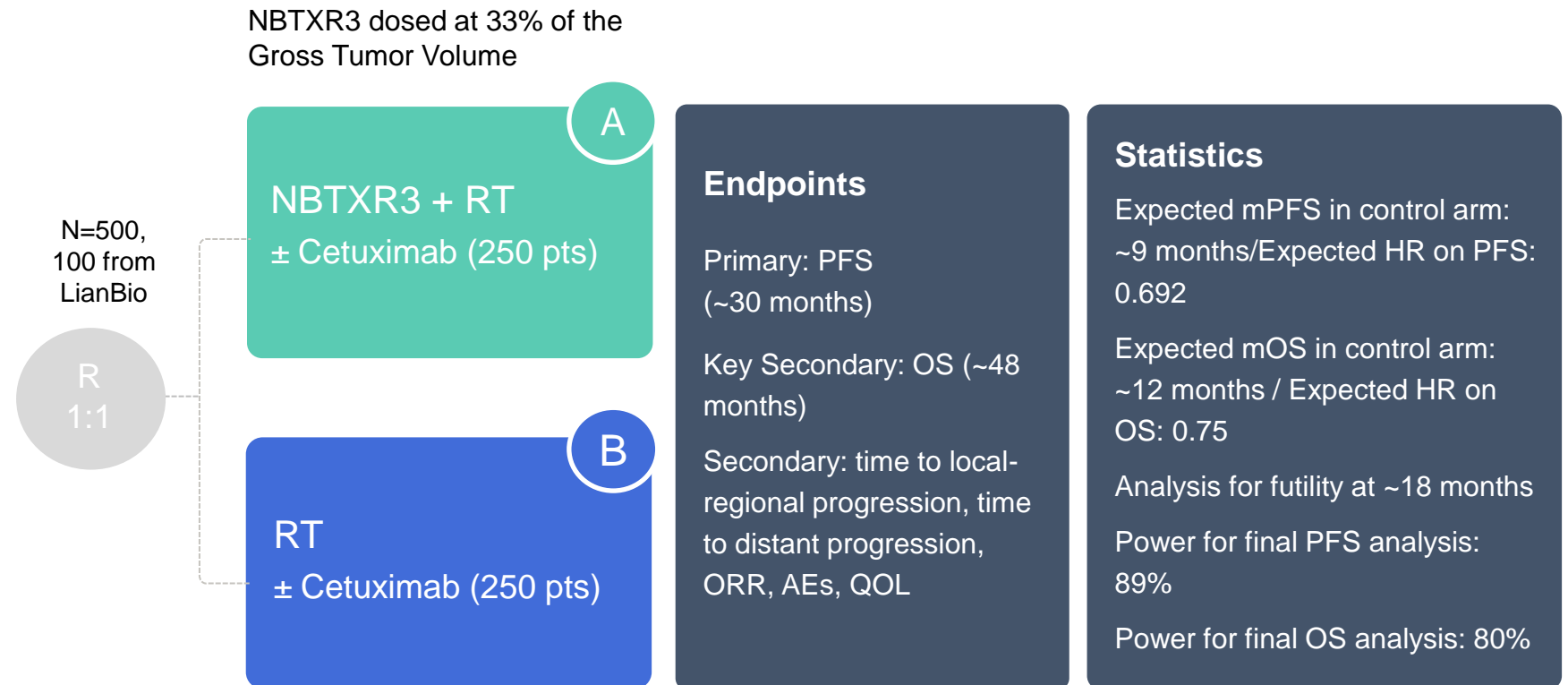
Eligible for definitive RT

At least one measurable and IT injectable tumor

Ineligible for platinum-based chemotherapy

No prior systemic Rx or RT

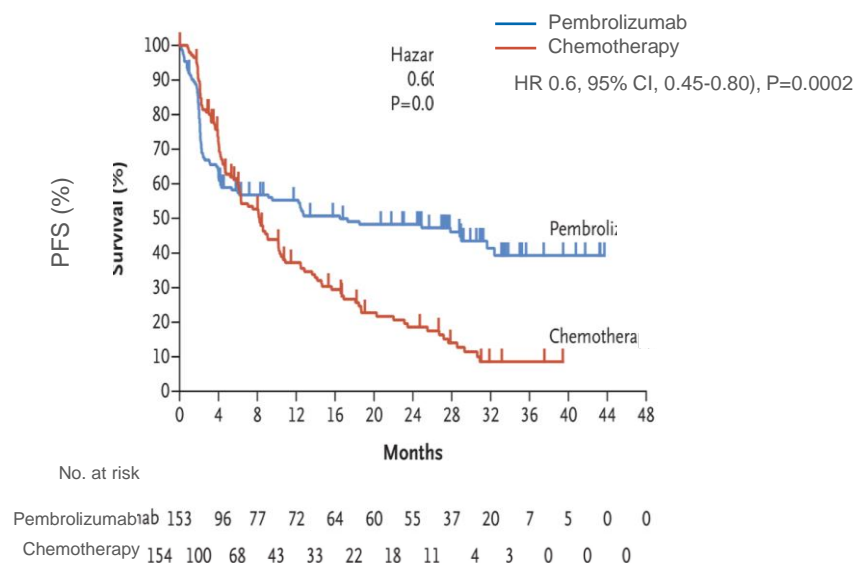
Life expectancy ≥ 6 months



The promise and limitations of immuno-oncology agents

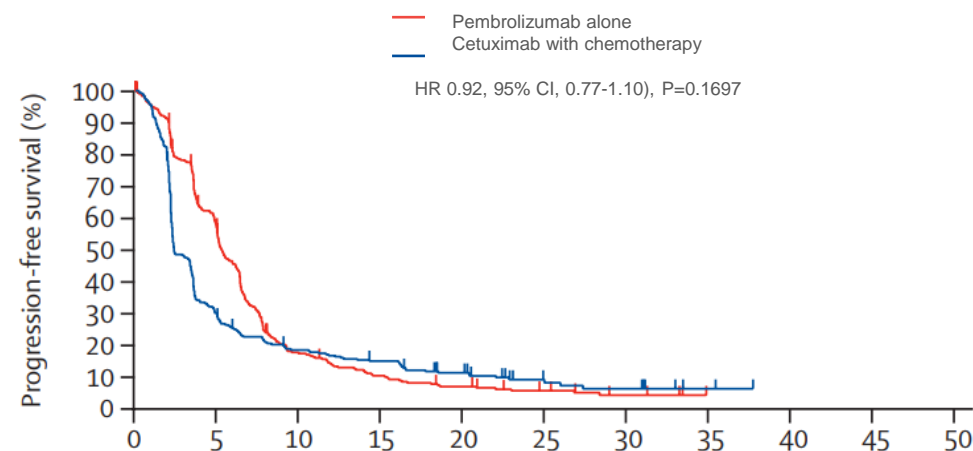
IO has been practice changing and life changing for many patients with cancer

KEYNOTE-177 in mMSI-H/dMMR CRC¹



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

KEYNOTE-048 in R/M HNSCC²



(1) André et al. NEJM 2020; (2) Burness et al. Lancet 2019

Key Inclusion Criteria

Anti-PD-1 Naïve; or

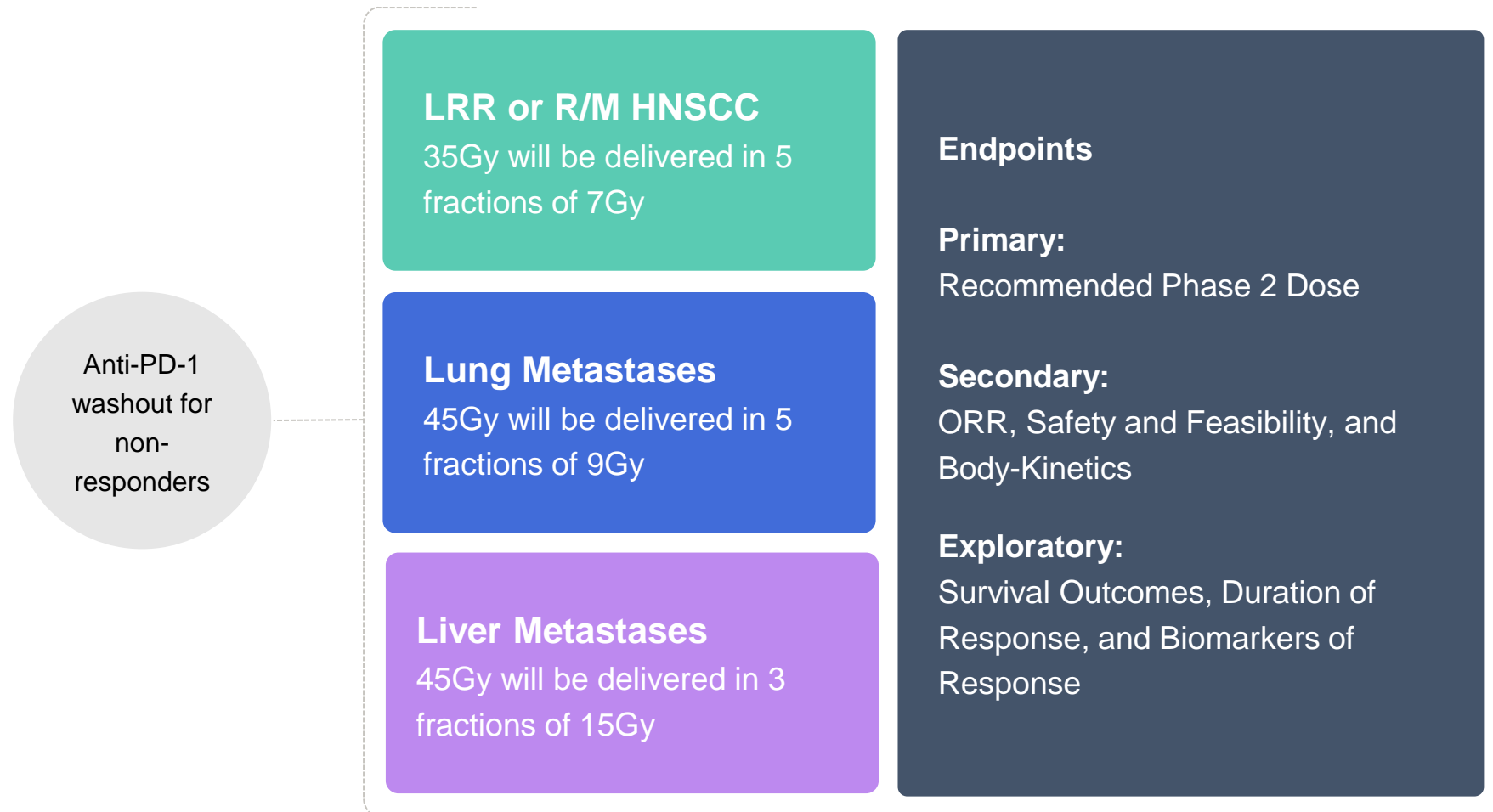
Anti-PD-1 Resistant:

Dose escalation cohorts:

- LRR or R/M HNSCC in a previously irradiated field
- Lung metastases from any primary cancer eligible for anti-PD-1 therapy
- Liver metastases from any primary cancer eligible for anti-PD-1 therapy

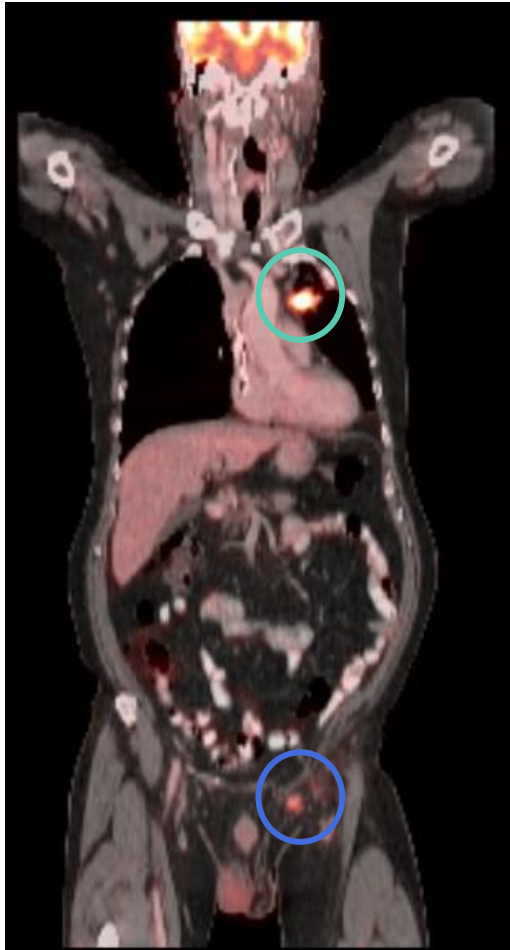
Study 1100: Dose escalation

Phase 1 evaluation of NBTXR3-RT* ± immune checkpoint inhibitors for recurrent and/or metastatic HNSCC

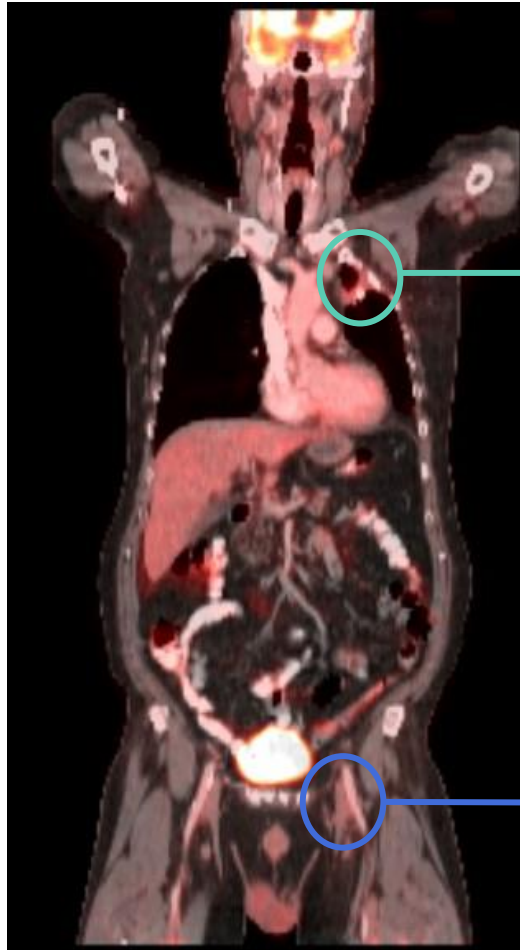


Assessing change in target & non-target lesions

SITC 2022: Anti-PD-1 resistant patient case study



PET Baseline



PET Follow-Up Visit 1

Target Lesion

PR in injected and irradiated tumor

Patient progressing at enrollment after ~ 1-year anti-PD-1 treatment

Local control (PR) achieved in target lesion in anti-PD-1 resistant patient

Distant control (CR) in non-injected, non-irradiated, non-target lesion

Non-Target Lesion

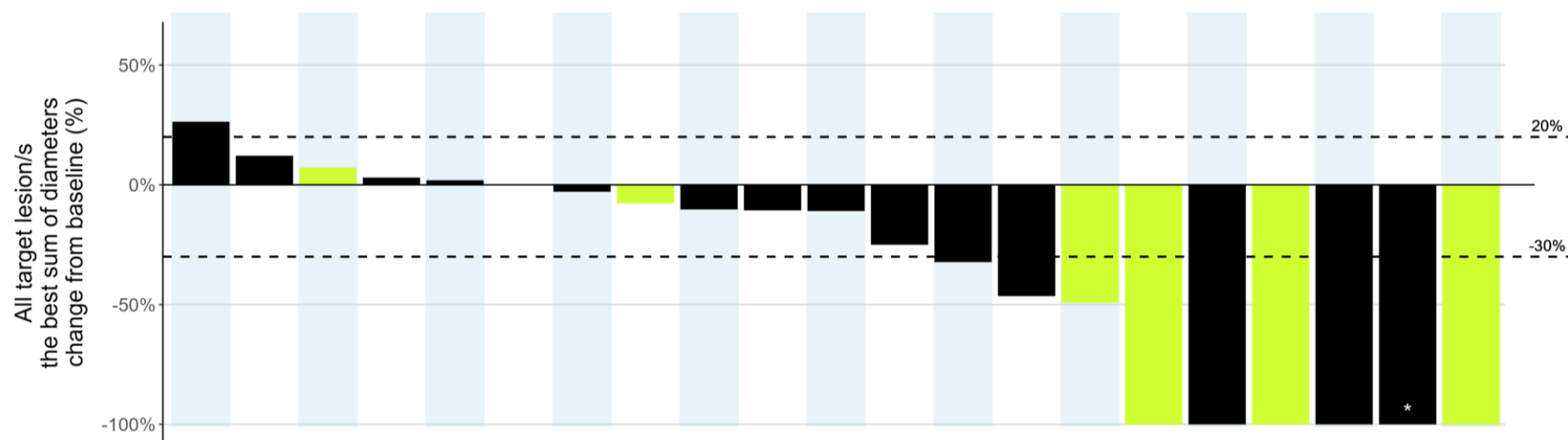
CR in non-injected and non-irradiated distal lesion suggesting systemic response

Lesion/s reduction observed in naïve and anti-PD-1 patients

SITC 2022: All target lesions

Objective reduction in target lesion/s from baseline was observed in:

- **71.43 %** of evaluable patients (15/21)
- **67.00 %** of anti-PD-1 resistant (10/15)
- **83.00 %** of anti-PD-1 naïve (5/6)



* pathological Complete Response (pCR) based on excisional biopsy. Patient remained no evidence of disease as long as followed

Notes: - If a Lymph node involved normalizes to less than 10 mm, the change from baseline for this lesion is set to -100%
- The best sum of diameters change is defined as the biggest decrease, or smallest increase if no decrease

Anti-PD-1 naïve Anti-PD-1 resistant

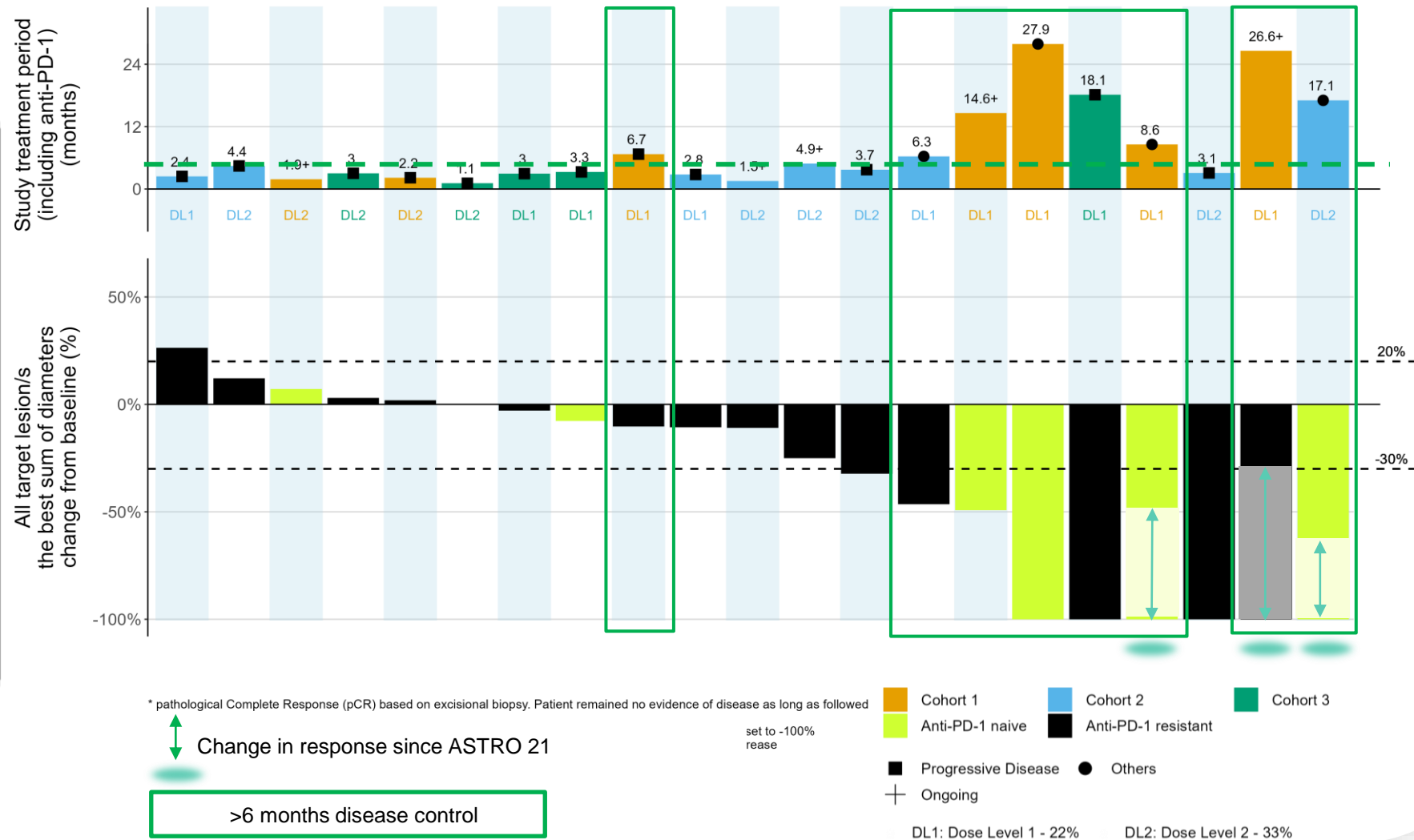
Objective reductions with long-term control in both anti-PD-1 naïve & resistant patients

SITC 2022: All target lesions

Objective reduction in target lesion/s resulted in long term control in both naïve and resistant lesions- regardless of site of injection

8 patients with > 6 months disease control

5 patients with >12 months disease control



SITC 2022: All target lesions

In 8/21 patients
this resulted in
disease control
of 6 months or
longer



Study 1100: Dose expansion

Phase 1 evaluation of NBTXR3-RT* ± immune checkpoint inhibitors for recurrent and/or metastatic HNSCC

Key Inclusion Criteria

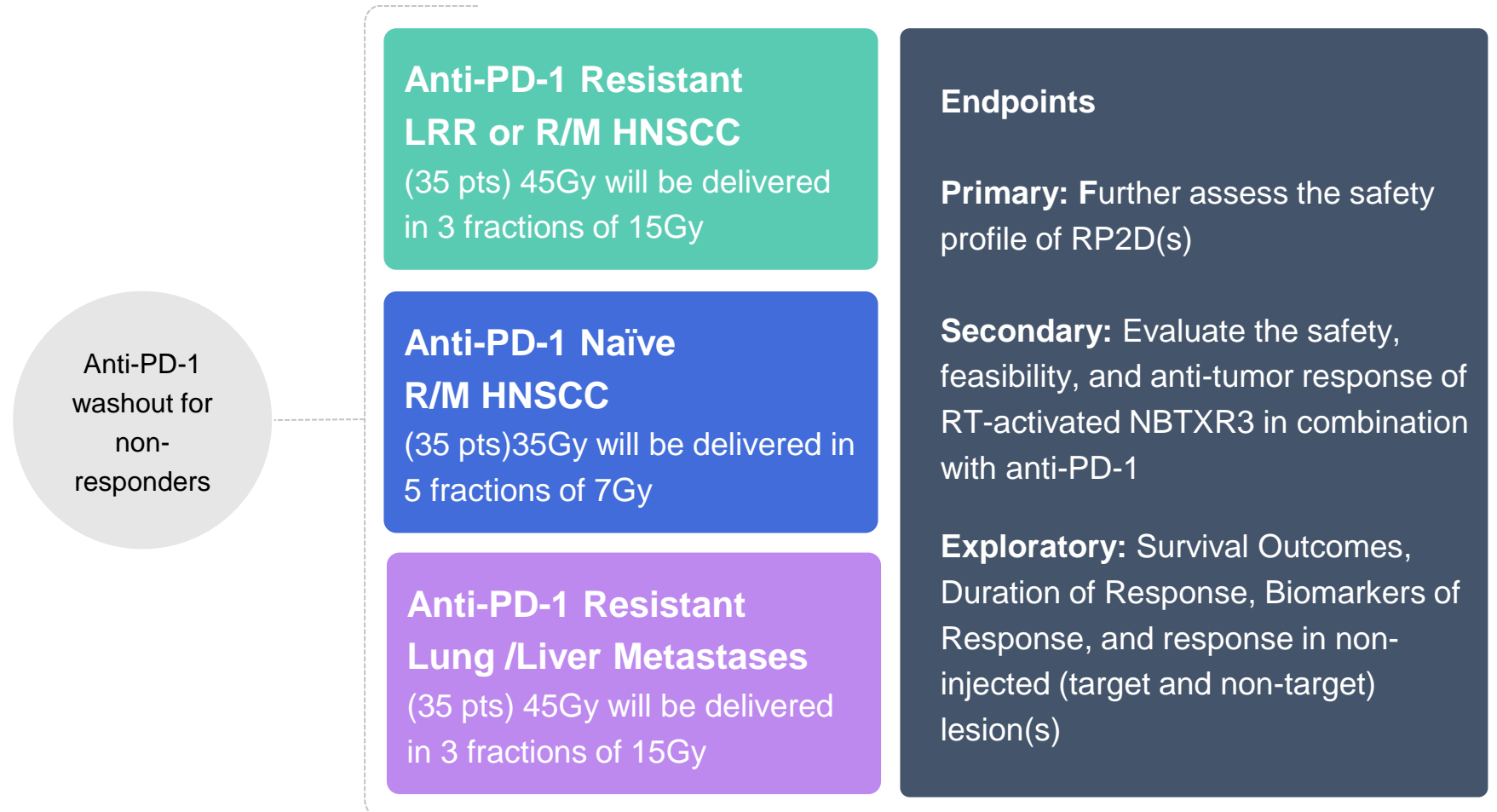
#1. LRR or R/M HNSCC with lesion H/N area or in lung or liver, resistant to anti-PD-1 therapy.

#2 Same as #1 Anti-PD-1 Naïve

#3 Inoperable NSCLC, malignant melanoma, HCC, RCC, urothelial cancer, cervical cancer or TNBC with metastases to lungs, liver or soft tissue resistant to anti-PD-1 therapy.

N=105 Patients

LRR: = Locoregional Recurrence
R/M = Relapsed or Metastatic
NSCLC = Non-small cell lung cancer
HCC = Hepatocellular Carcinoma
RCC = Renal Cell Carcinoma
TNBC = Triple Negative Breast Cancer



*NBTXR3-RT: NBTXR3 activated by radiotherapy

Study 1100 POC forms basis for 2nd potential HNSCC registration study

NBTXR3-RT* + anti-PD-1 inhibitor for recurrent and/or metastatic head and neck squamous cell carcinoma (R/M HNSCC)

Study 1100: Anti-PD-1 naïve & refractory in advanced solid tumors

Phase 1 escalation and expansion:

- Well tolerated
- Correlation between local effect and systemic response regardless of anti-PD-1 exposure
- 33% ORR
- Demonstrated potential to convert anti-PD-1 non-responders into responders

Planned registration pathway: Anti-PD-1 refractory in R/M HNSCC

Global randomized Phase 3:

- Continued development of NBTXR3-RT* in combination with anti-PD-1
- Potential for accelerated approval based on interim ORR analysis
- Protocol submission expected in Q1 2023

Leveraging strategic collaborations to advance and expand NBTXR3 opportunity with optimal efficiency

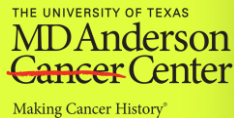
Advance



Develop and commercialize NBTXR3 across tumor types and therapeutic combinations in Greater China, South Korea, Singapore and Thailand

- Development commitment includes 5 registration studies
- Enrolling up to 100 of 500 patients targeted for NANORAY-312
- Exclusive commercial rights for NBTXR3 and sole responsibility for clinical development, regulatory and commercial costs in designated territory
- \$20M upfront, >\$200M in milestones, tiered low double-digit royalties

Expand



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

- 4 Phase 1/2 trials ongoing
- 3 Phase 1 Studies: Pancreatic, Esophageal, NSCLC
- 1 Phase 2 Study: H&N R/M reRT+IO
- ~\$12M for 340 patients over lifecycle of development

Key Financial Highlights

- Cash* as of Sept 30, 2022: €53.5M
 - Equity financing line provides flexible access to capital
 - Accessible capital resources expected to support development plan into first quarter 2024
- Debt as of September 30, 2022:
 - €30M credit facility from EIB
 - €10M from State-Guaranteed Loan (PGE)
- Dual-listed: Euronext Paris (**NANO**) and Nasdaq Global Select Market (**NBTX**)

34,875,872 shares outstanding as of June 30, 2022

(Amounts in thousands of euros, except per share numbers)

| | For the six-month period ended June 30, | |
|---|---|----------------|
| | 2022 | 2021 |
| Revenue and other income | | |
| Revenue | — | 10 |
| Other income | 1,329 | 1,309 |
| Total revenue and other income | 1,329 | 1,319 |
| Research and development expenses | -16,608 | -15,506 |
| Selling, general and administrative expenses | -9,635 | -10,176 |
| Other operating expenses | -963 | -5,414 |
| Total operating expenses | -27,206 | -31,096 |
| Operating income (loss) | -25,877 | -29,778 |
| Financial income | 2,465 | 2,511 |
| Financial expenses | -2,940 | -3,152 |
| Financial income (loss) | -474 | -640 |
| Income tax | -6 | -2 |
| Net loss for the period | -26,357 | -30,420 |
| Basic loss per share (euros/share) | -0.76 | -0.88 |
| Diluted loss per share (euros/share) | -0.76 | -0.88 |

Multiple, potential value inflection points expected in the next 12-24 months

| | | 2022 | | 2023 | | 2024 | |
|--|---------------------------------------|---------------------------------|---------------------------------------|---------------------------|----|-------------------|--|
| Indication | Trial Name <i>Approach</i> | 2H | 1H | 2H | 1H | 2H | |
| Head and Neck Locally Advanced | NANORAY-312 NBTXR3-RT* ± cetuximab | | | Futility analysis | | Interim Ph 3 data | |
| | Study 102 NBTXR3-RT* | | Final Ph 1 data | | | | |
| Head and Neck Recurrent and/or Metastatic | TBD NBTXR3-RT* + anti-PD-1 | | FDA protocol submission | | | | |
| | Study 1100 NBTXR3-RT* + anti-PD-1 | RP2D Initiate Dose Expansion | | Dose Expansion Update TBD | | | |
| Other Solid Tumor Indications | MD Anderson-led programs | Pancreas RP2D | Ph 1 Esophageal Ph 1 Pancreas Data | Ph 1 NSLC | | | |

Developing first-in-class nanotherapeutic with the potential to become integral part of cancer therapy

Opportunity to improve outcomes for patients with locally advanced & recurrent/metastatic disease

Strong Body of Evidence



Robust **preclinical and clinical datasets** supporting consistent clinical effect of **NBTXR3** to increase potency of **local treatment with immunostimulatory effect** potentially enhancing response to systemic therapy

Rational, De-risked Development Strategy Focused on Building HNSCC Franchise



Near-term commercial opportunity to enhance local control in LA-HNSCC
Ph 3 ongoing; Fast track designation and **potential for accelerated approval**

Near-term expansion opportunity **to overcome or circumvent resistance and increase overall response to immunotherapy** in R/M HNSCC
FDA protocol submission for Ph 3 in combination with anti-PD-1 expected in Q1 2023

Significant Expansion Opportunities



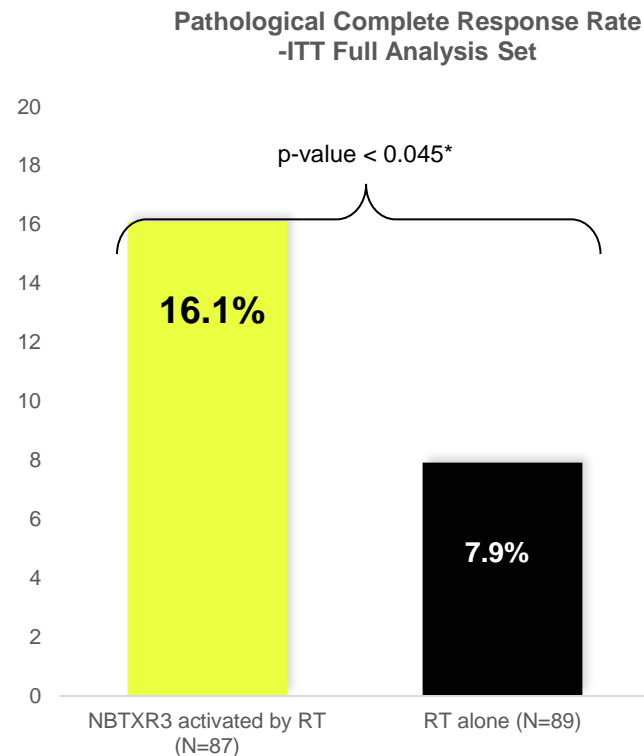
Large long-term potential to **expand across solid tumor indications and next generation therapeutic combinations** including anti-PD-1, LAG3, CTLA-4, TIGIT

*R/M HNSCC: recurrent and/or metastatic head and neck cancer

Appendix

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.

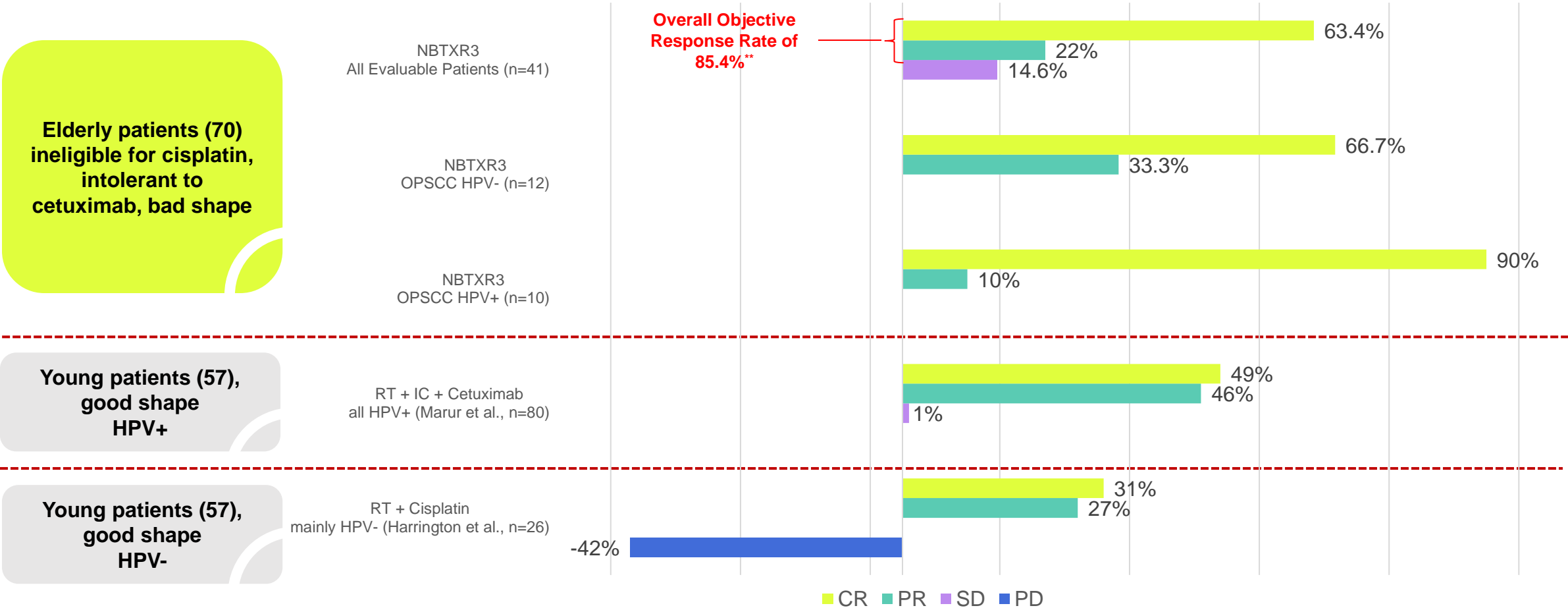
Sylvie Bonvalot, Piotr L Rutkowski, Juliette Thariat, Sébastien Camire, Anne Ducas, Marie-Pierre Sunyach, Peter Agostin, Angèle Hong, Augustin Mery, Marco Rastrelli, Victor Moreno, Rubi Kili, Béatrice Tchang, Antonio Casado Hernandez, Alessandro Gronchi, Lucio Margel, Teresa Sy-Ostin, Peter Hohenberger, Thierry de Baat, Axel Le Cesne, Sylvie Huguier, Emma Scaudo-Bouard, André Borkowski, Rodica Anghel, Anna Gu, Michael Gebert, Guy Kattan, Angel Montoro, Herbert H Long, Ramona Vargiu, Lore Legrand, Scott Dine, Gabriel Kacou, Lyn Arian, Laurence Mourou-Zabotto, Vincent Servais, Eva Wardemann, Philippe Terrier, Alexander J Lazar, Judith V M G Boer, 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
Published Online
July 8, 2019
[http://dx.doi.org/10.1016/S1473-3099\(19\)30266-2](http://dx.doi.org/10.1016/S1473-3099(19)30266-2)

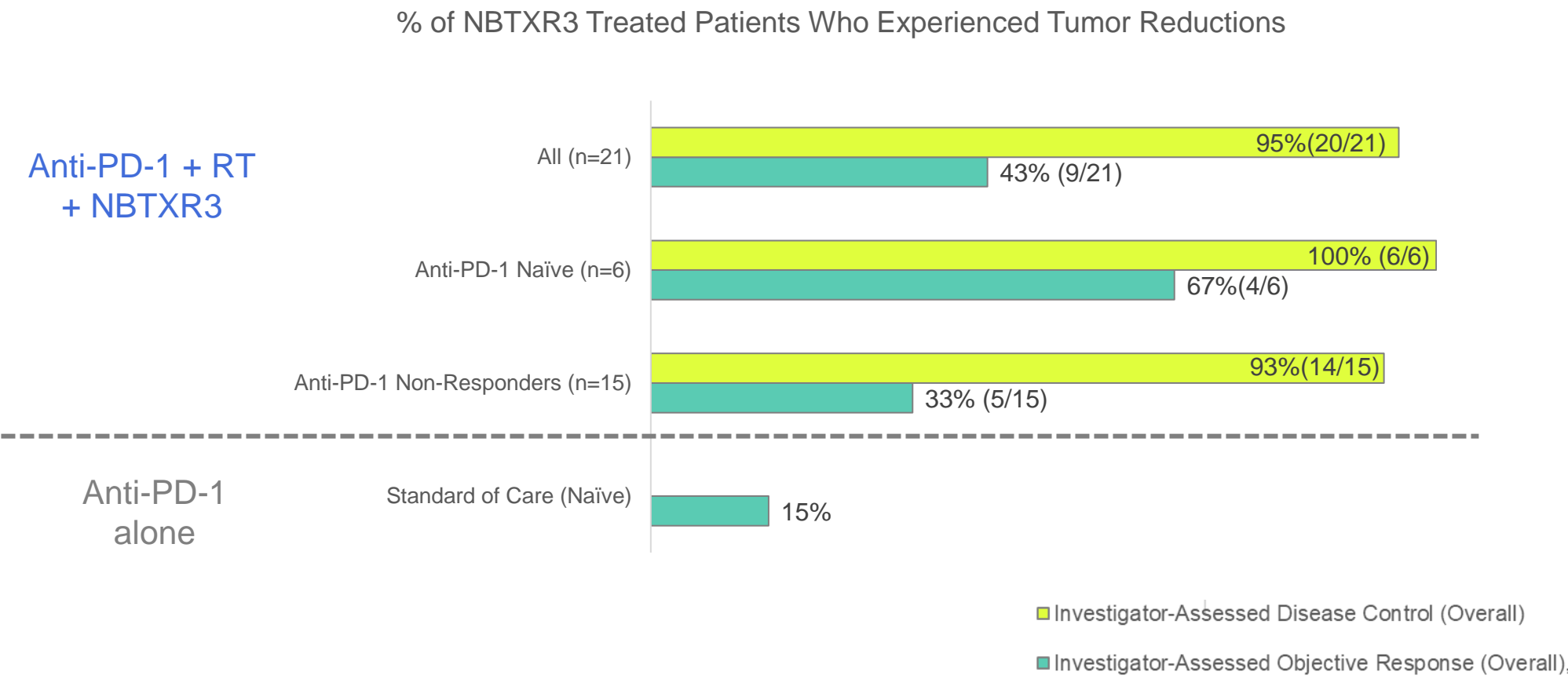
Study 102: High response rates evidence of improved local control in elderly, tough to treat LA-HNSCC



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

Local and systemic response regardless of prior anti-PD-1 exposure

SITC 2022

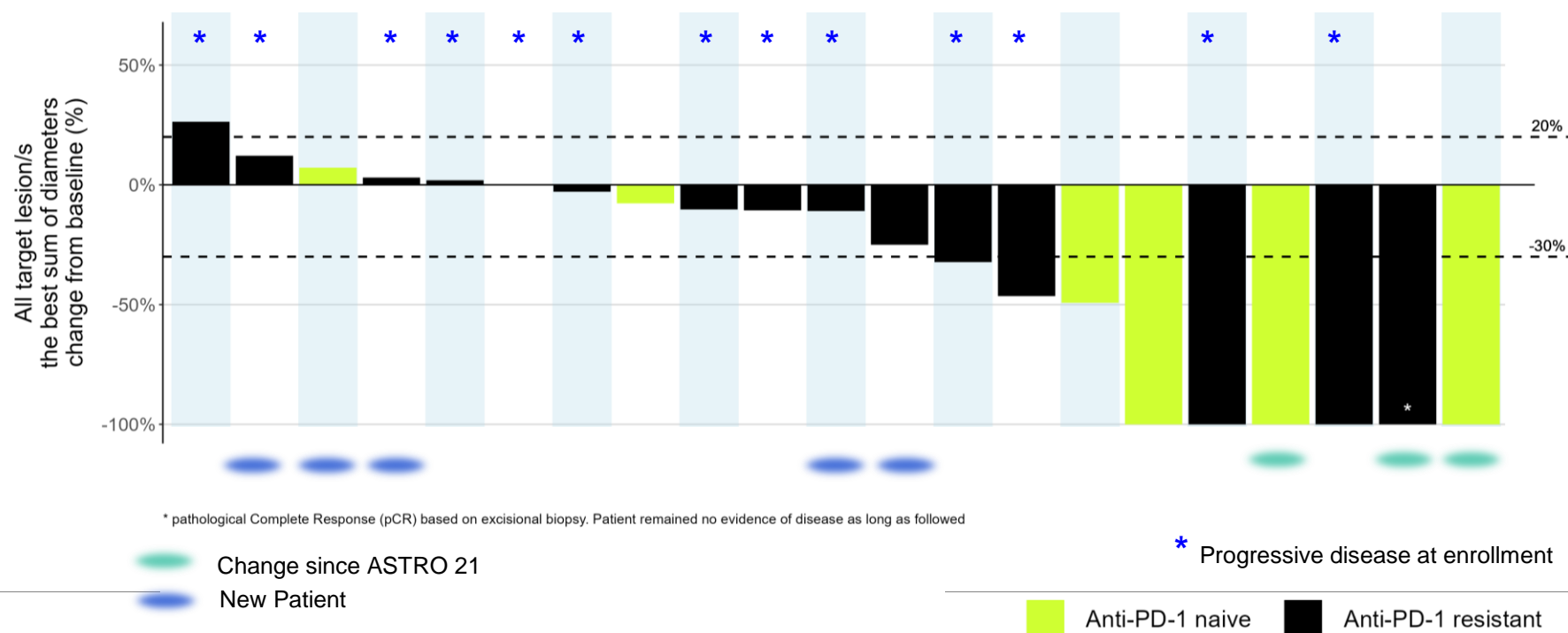


Objective reduction target lesion/s in previously progressing patients

SITC 2022: All [target lesions](#)

Out of the 15 evaluable anti-PD-1 resistant patients, 87% (13) had progressive disease when entering the study:

- **31%** (4/13) had a measurable reduction of at least 30% or more
- **15%** (2/13) experienced a complete reduction of the target lesions
- Only 1 patient experienced an increase of over 20% in measurable target lesions



Focusing on HNSCC: 16 of 21 evaluable patients with primary HNSCC

SITC 2022: All [target lesions](#)

Objective reduction from baseline in target lesion was observed in

- **75% patients with primary HNSCC:**
 - **70%** patients with primary HNSCC resistant to anti-PD-1
 - **83.33%** patients with primary HNSCC naïve to anti-PD-1

Objective **reduction of at least 30% or more** was observed in **43.75%** (7/16) all **HNSCC** patients

Complete reduction in target lesion was observed in **31.25%** (5/16) of all **HNSCC** patients

