

# NANOBIOTIX



## CORPORATE PRESENTATION

April 2024

Developing disruptive physics-based  
nanotherapeutics to transform  
outcomes for millions of patients



# IMPORTANT NOTICE REGARDING FORWARD-LOOKING STATEMENTS

IMPORTANT: You must read the following before continuing.

References herein to this presentation (the "Presentation") shall mean and include this document, the oral presentation accompanying this document provided by Nanobiotix SA (the "Company" and, together with its subsidiaries, the "Group"), any question and answer session following that oral presentation and any further information that may be made available in connection with the subject matter contained herein. This Presentation has been prepared by the Company and is provisional and for information purposes only. The information has not been subject to independent verification and is qualified in its entirety by the business, financial and other information that the Company is required to publish in accordance with the rules and regulations applicable to companies listed on the Nasdaq Global Select Market and the regulated market of the Euronext in Paris and the requirements of the U.S. Securities and Exchange Commission (the "SEC") and the French Financial Markets Authority (Autorité des Marchés Financiers -- the "AMF"), including the risk factors described in the Company's most recent universal registration document filed with the AMF and the most recent Annual Report on Form 20-F filed with the SEC, as updated from time to time by the Company's other public reports including the most filed recent half-year report (together the "Report"), which are available free of charge on the Company's website ([www.nanobiotix.com](http://www.nanobiotix.com)) and the respective websites of the AMF ([www.amf-france.org](http://www.amf-france.org)) and the SEC ([www.sec.gov](http://www.sec.gov)).

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- our ability to successfully develop and commercialize NBTXR3, including through the License Agreement by and between Janssen Pharmaceutica NV and Nanobiotix, dated July 7 2023 (the "Janssen Agreement");
- 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 in a timely manner;
- 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 complete applicable pre-marketing regulatory requirements and/or 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;
- our ability about the initiation, timing, progress and results of our preclinical studies and clinical trials, including those trials to be conducted under our collaborations with the MD Anderson Cancer Center of the University of Texas ("MD Anderson");
- our ability to obtain raw materials and maintain and operate our facilities to manufacture our product candidates, to market and distribute our products upon successful completion of applicable pre-marketing regulatory requirements, specifically NBTXR3;
- our reliance on Janssen to conduct the NBTXR3 co-development and commercialization activities in accordance with the Janssen Agreement, including the potential for disagreements or disputes; the risk that Janssen may exercise its discretion in a manner that limits the resources contributed toward the development of NBTXR3; and the ability of Janssen to exercise its termination rights under the Janssen Agreement without cause;
- our ability to obtain funding for our operations.

In light of the significant uncertainties in these forward-looking statements, these statements should not be regarded or considered as a representation or warranty by the Company or any other person that the Company will achieve its objectives and plans in any specified time frame or at all. Even if the Company's performance, including its financial position, results, cash-flows and developments in the sector in which the Company operates were to conform to the forward-looking statements contained in this Presentation, such results or developments cannot be construed as a reliable indication of the Company's future results or developments. The Company expressly declines any obligation to update or to confirm any prospective information in order to reflect an event or circumstance that may occur after the date of this Presentation. The Presentation and any information do not constitute an offer to sell or subscribe or a solicitation to purchase or subscribe for securities, nor shall there be any sale of these securities in the United States or any other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. No public offering of securities may be conducted in any member state of the European Economic Area (including France) prior to the publication in the relevant member state of a prospectus that complies with the provisions of Regulation 2017/119.

The Presentation includes information on the use of the Company's products and its competitive position. Some of the information included in the Presentation is from third parties. While this third-party information has been obtained from sources believed to be reliable, there is no guarantee of the accuracy or completeness of such data. In addition, certain of the industry and data comes from the Company's own internal research and estimates based on the knowledge and experience of the Company's management. While Nanobiotix believes that such research and estimates are reasonable and reliable, they, and their underlying methodology and assumptions, have not been verified by any independent source for accuracy or completeness and are subject to change without notice. Accordingly, undue reliance should not be placed on any of the industry, market or competitive position data contained in the Presentation.

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.

The Presentation should be read with the understanding that the Company's actual future results may be materially different from what is expected. The Company qualifies all of the forward-looking statements by these cautionary statements. All persons accessing the Presentation are deemed to agree to all the limitations and restrictions set out above.

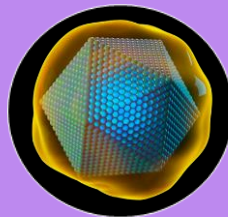
# 20 Years Pioneering Nanophysics Based Therapeutics to Impact the Lives of Millions of Patients

3 platforms leading to multiple products, from Phase 3 to preclinical stage

## NBTXR3

Nano-radioenhancer to help millions of patients receiving Radiotherapy

- 60% of oncology patients receive radiation therapy
- Randomized Ph 3, POC, several indications in clinical development
- Late-stage pipeline in a product with Ph 3 and Ph 2 catalyst
- \$2.5 billion collaboration with J&J



## Curadigm

Nanoprimer turning off the liver to prevent clearance of therapeutics

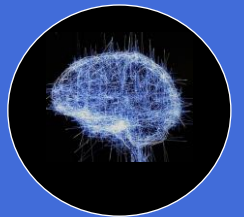
- Multiple indications and product applications: nanomedicine, RNA & DNA based products, oncolytic viruses, ...
- Preclinical POC established with multiple partners: Sanofi, NCL, MIT, ...
- In-house products and multiple partnership opportunities



## Oocuity

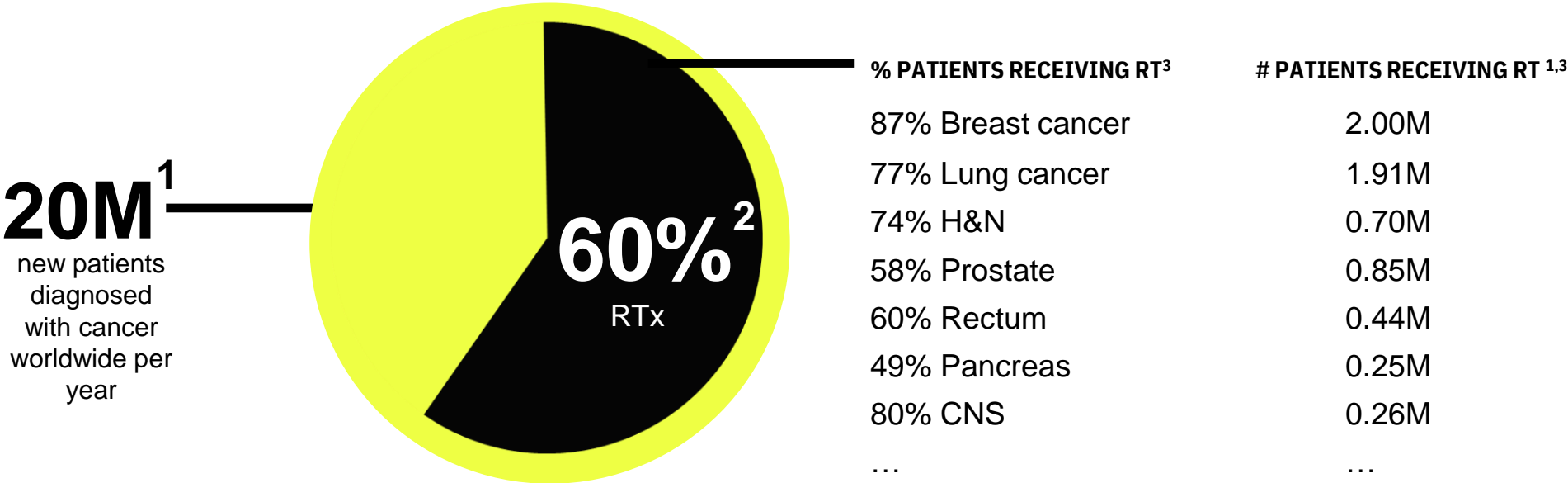
Nanoparticles rewiring of the brain

- CNS products for Parkinson, Alzheimer, Dementia...
- Custom-designed nanoparticles physics-based MOA to adjust neuronal activity
- Neuropathic pain is one of first potential applications



# 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





# NBTXR3: A First-In-Class Radioenhancer

Aqueous suspension of inorganic crystalline **hafnium oxide** ( $\text{HfO}_2$ ) nanoparticles

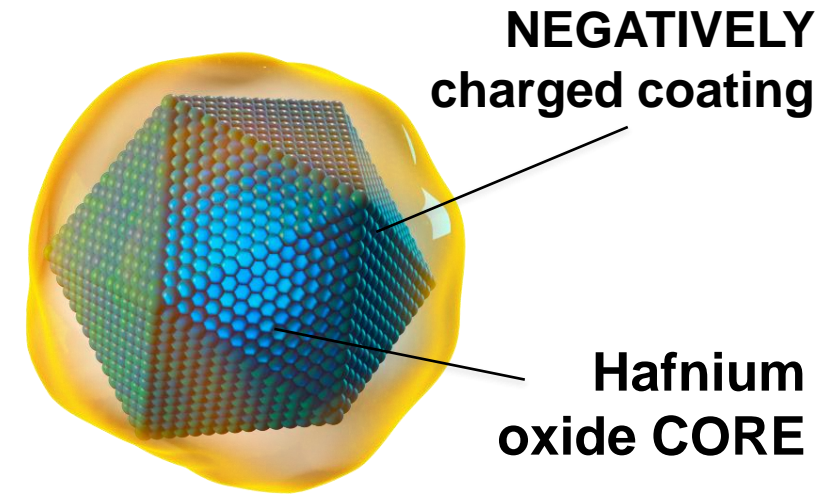
High atomic number ( $Z=72$ ) and electron density

**Inert** in the absence of ionizing radiation: “Off” status  
Activated by **ionizing radiation**: “On” status

**One-time intratumoral** administration, remains in tumor

Efficacy and safety demonstrated in a **randomized Phase 2/3 trial** in locally advanced soft tissue **sarcoma**<sup>1</sup>

Universal mode of action targeting all solid tumors



**Negative surface charge** for stability at neutral pH in aqueous medium  
+ **Nanometer scale** to fit inside cell



Facilitates entry into tumor cells

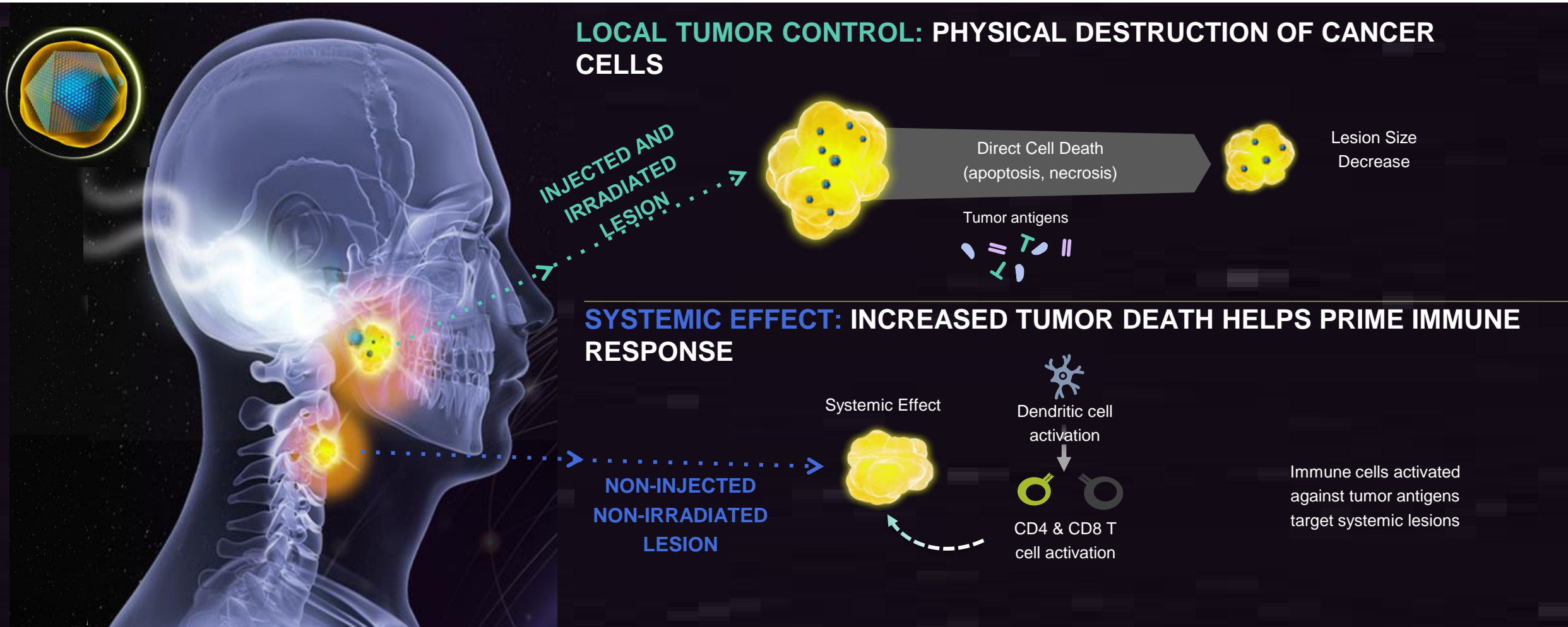
**High atomic number (72) and high  $e^-$  density**



Increased local absorption of ionizing radiation

# Local Cell Destruction Induced by NBTXR3 Activates Immune Priming

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





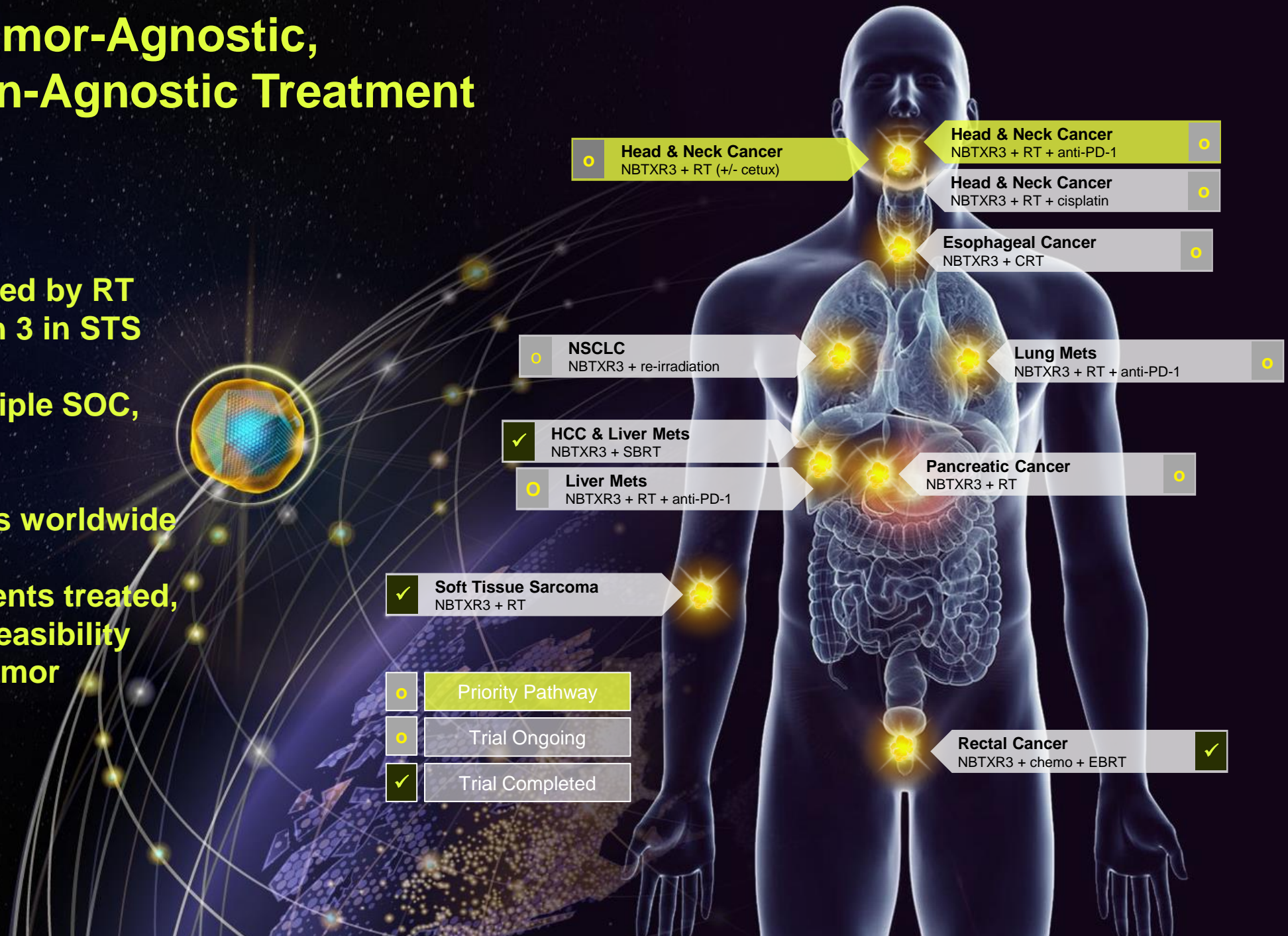
# Potential Tumor-Agnostic, Combination-Agnostic Treatment

PoC when activated by RT alone, positive Ph 3 in STS

Potential for multiple SOC, including IO

100+ Clinical sites worldwide

Hundreds of patients treated, showing safety, feasibility and consistent tumor response

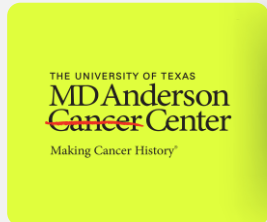


# Leveraging Strategic Collaborations to Advance and Expand NBTXR3 Opportunity With Optimal Efficiency

**Janssen\***

**Global collaboration to drive NBTXR3 substantial near- and long-term value in oncology indications with an initial focus on head and neck and lung cancers**

- Success-based payments of \$1.8 billion\*\*, \$650M in total for potential new indications developed by Janssen, \$220M for each potential new indication developed by Nanobiotix, and double-digit royalties



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

- 5 ongoing studies: 3 Phase 1 (Pancreatic, Esophageal, NSCLC), 1 Phase 1/2 (advanced cancers) and 1 Phase 2 (H&N R/M reRT+IO)

\* Janssen: Janssen Pharmaceutica NV, a Johnson & Johnson company. \*\* Excluding milestones for additional Janssen and Nanobiotix indications



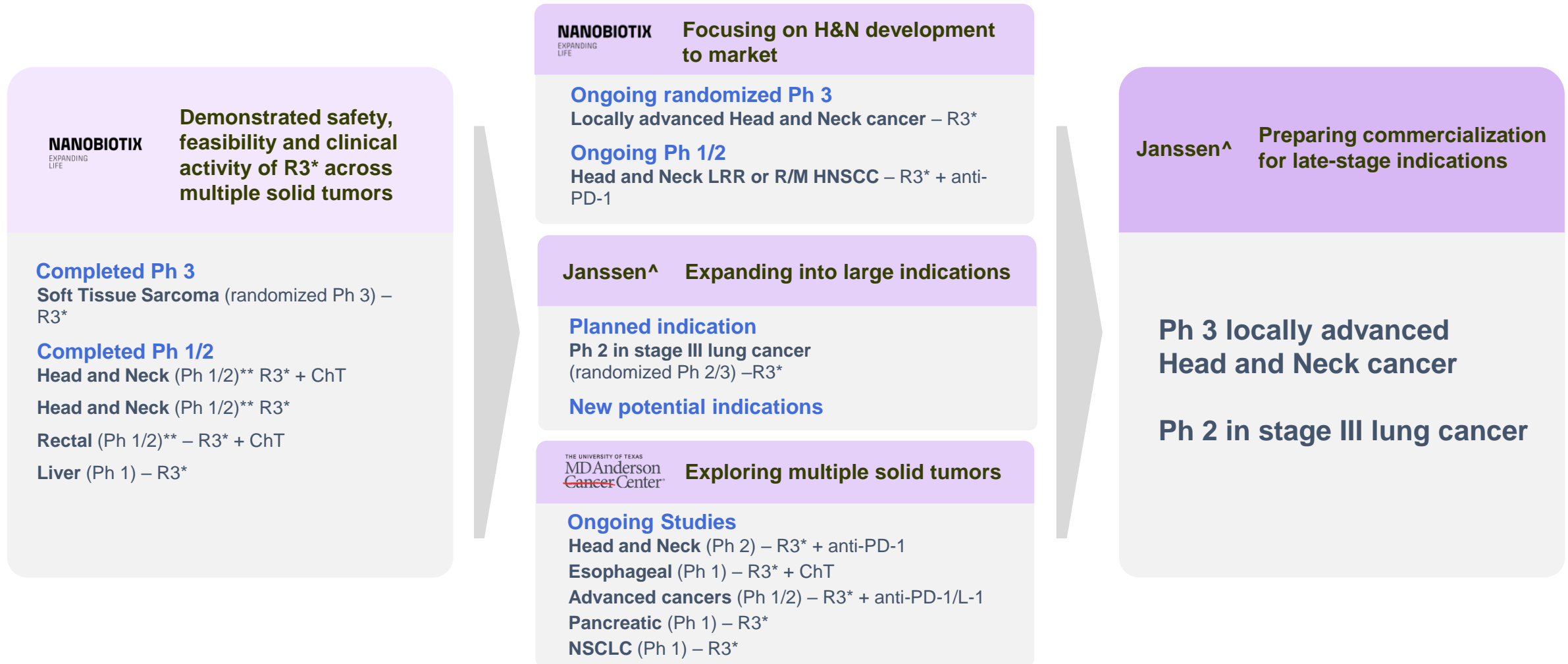
# Nanobiotix and Janssen\* Advance NBTXR3 Together

<b>Nanobiotix and Janssen collaborate on advancing NBTXR3 for oncology indications</b>	<b>Leverages the strengths of each organization</b>
Head and neck and lung cancers first and potentially others	Nanobiotix contributes NBTXR3, focused development, manufacturing expertise and innovation engine
Designed to accelerate and broaden the potential of NBTXR3 in the treatment of patients	Janssen contributes its substantial development support, regulatory and commercial capabilities

Upfront and in-kind support	Up to \$60 million
Development, regulatory and sales milestones**	Up to \$1.8 billion
Additional regulatory and development milestones for new indications Janssen may develop	Up to \$650 million
Additional regulatory and development milestones for new indications Nanobiotix may develop	Up to \$220 million per new indication
<hr/>	
Tiered Royalties	Low 10s to low 20s

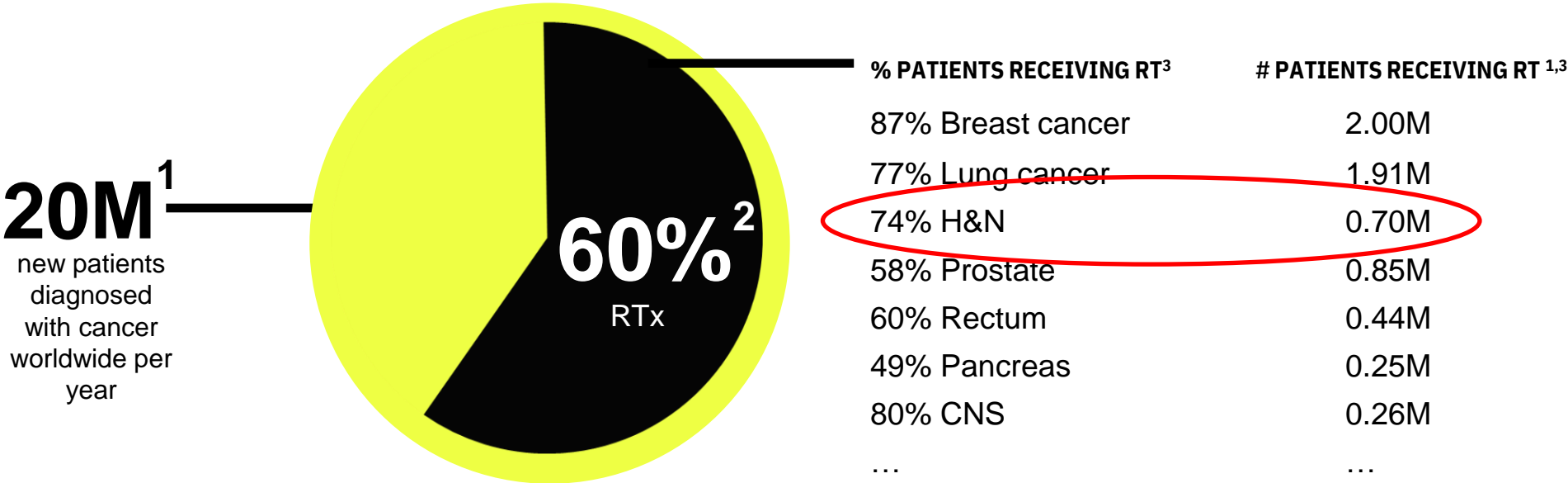
# Leveraging Strategic Collaborations to Advance and Expand NBTXR3 Opportunity With Optimal Efficiency

Pipeline-in-a-product strategy



# 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

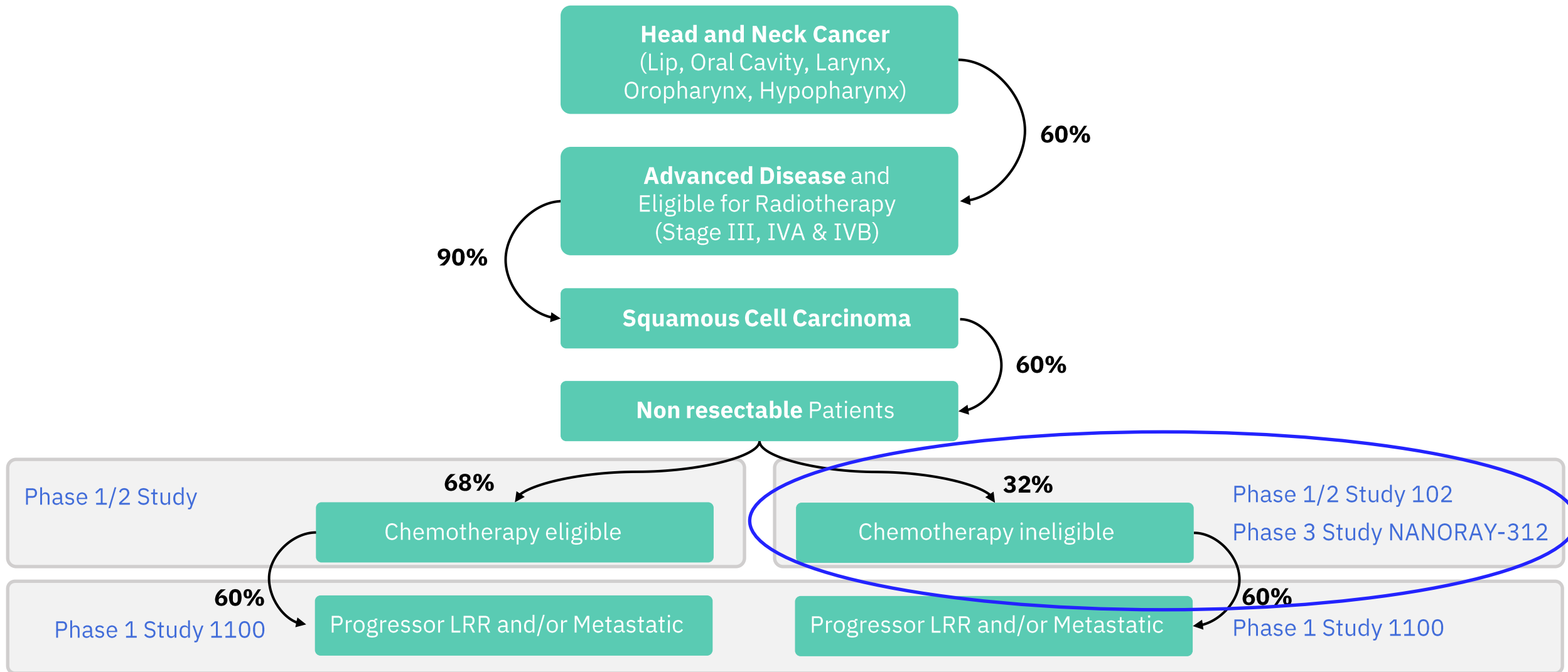


**20M<sup>1</sup>**  
new patients  
diagnosed  
with cancer  
worldwide per  
year

**60%<sup>2</sup>**  
RTx

# Potential \$6.2B HNSCC Market by 2029<sup>1</sup>

With 830,000 new patients diagnosed per year in the US, Europe and Asia<sup>2</sup>

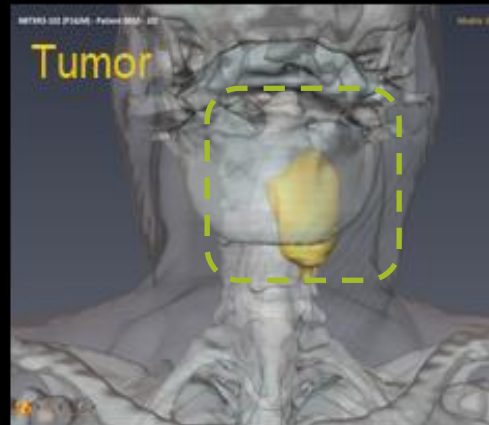




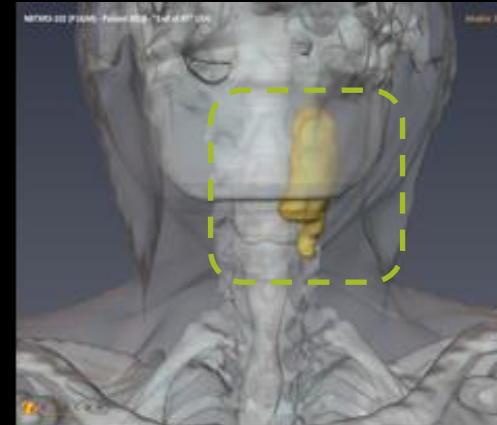
# NBTXR3 Demonstrated Curative Potential

Provides strong clinical rationale for pursuing registration

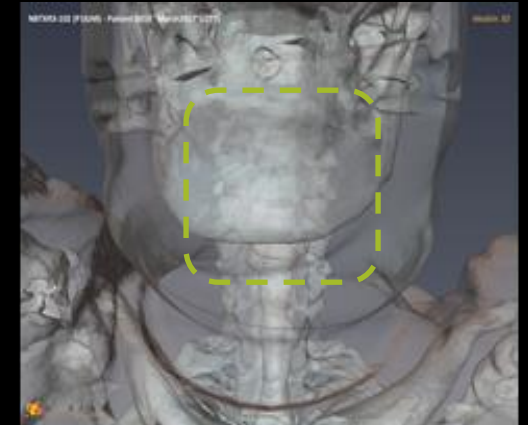
Complete Response  
and >55 months survival  
after treatment with  
NBTXR3 + RT



Post IT injection



Post radiotherapy



7 months after RT

CT scan presented at MHNCS 2020 – Ph1 study 102

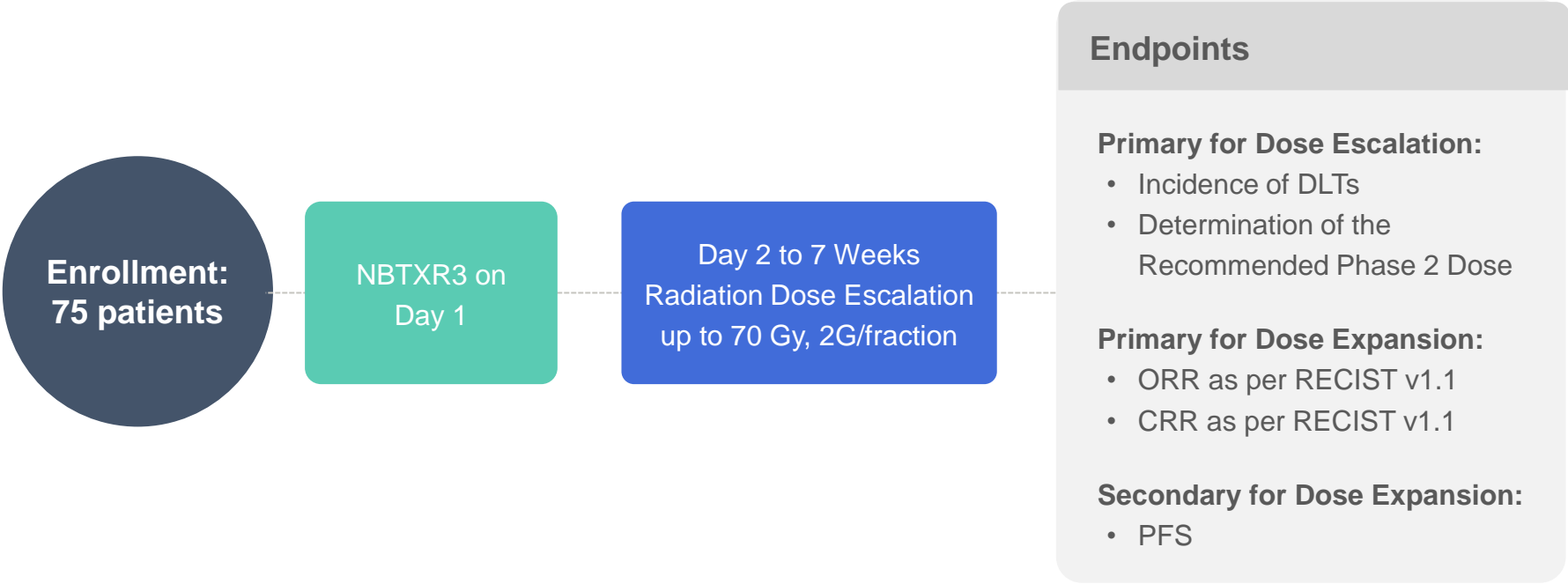
# Key Inclusion Criteria

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

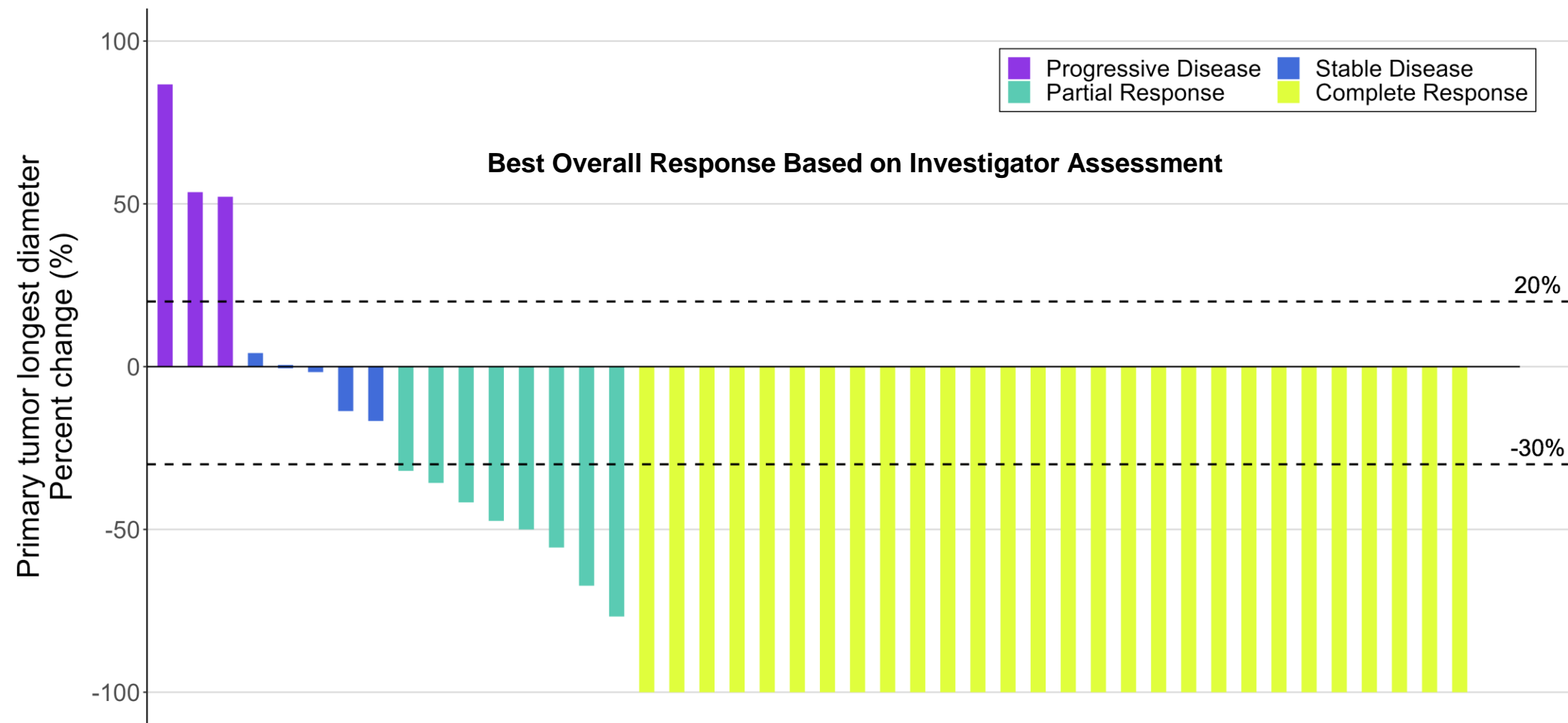
Phase 1 dose escalation and dose expansion evaluation of NBTXR3-RT\* in locally advanced head and neck cancers



Final Data

\*NBTXR3-RT: NBTXR3 activated by radiotherapy

# RT-Activated NBTXR3 Associated With Locoregional Control 81.8% ORR Including 63.6% CR

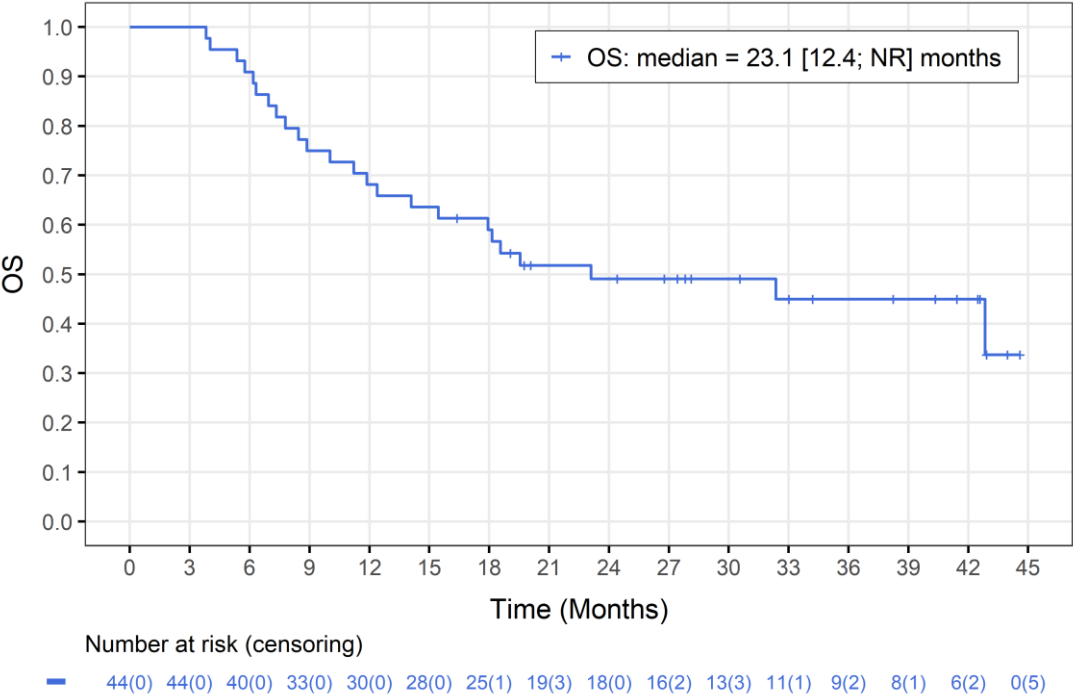


**Evaluable patients for Objective Tumor Response:** Underwent at least one post-treatment assessment, and received at least 80% of the planned dose of NBTXR3 and 60 Gy of IMRT  
**12 patients were non-evaluable:** i) not received 60 Gy of IMRT: 4 patients (3 TEAE, 1 consent withdraw), ii) No post treatment assessment: 8 early deaths

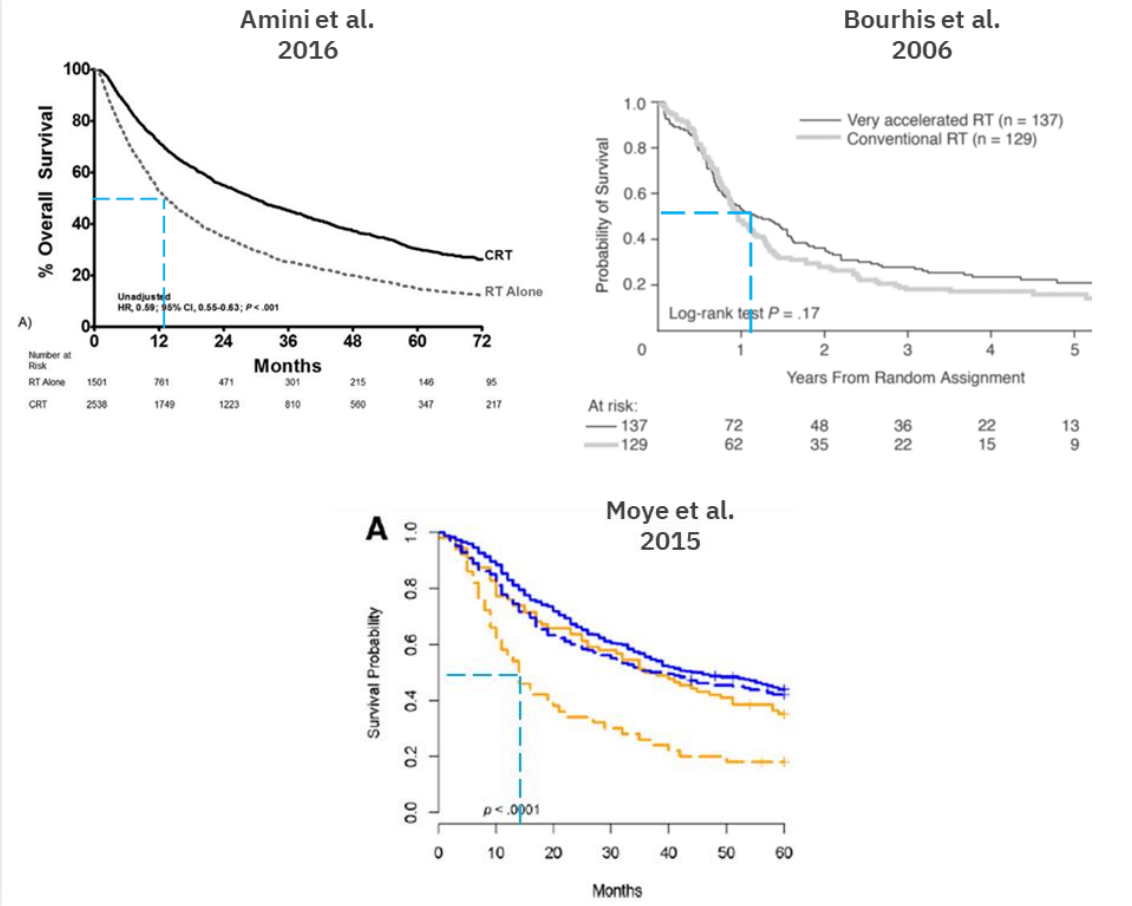
# Overall Survival

Cut-off date Jan 20, 2023

**Median OS: 23.1 months**  
Evaluable Population, n=44



**Median OS: ~ 12 months (historical control)**





Key Inclusion Criteria

Age ≥65 years

Eligible for definitive RT

At least one measurable and IT injectable tumor

Ineligible for platinum-based chemotherapy

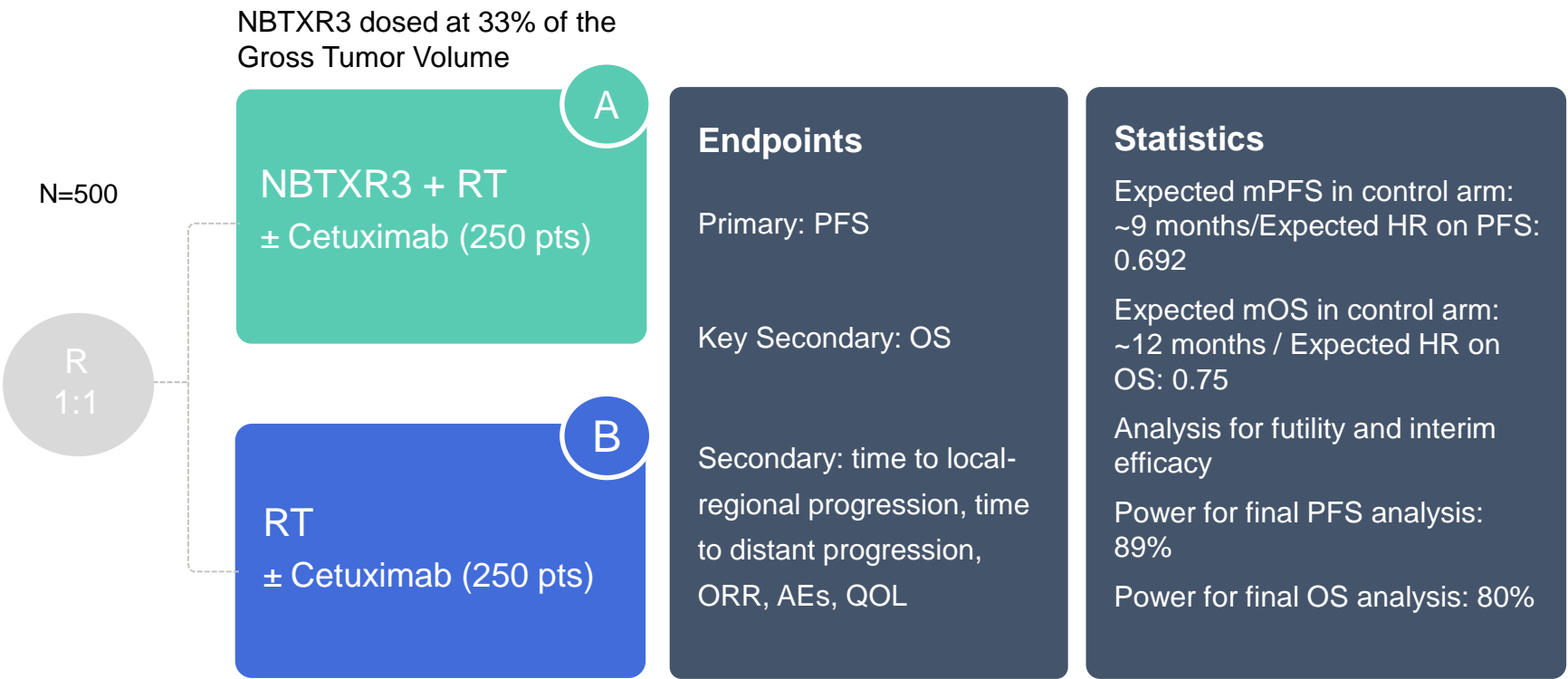
No prior systemic Rx or RT

Life expectancy ≥ 6 months

NANORAY-312

Ongoing Global Phase 3 registration trial locally advanced HNSCC

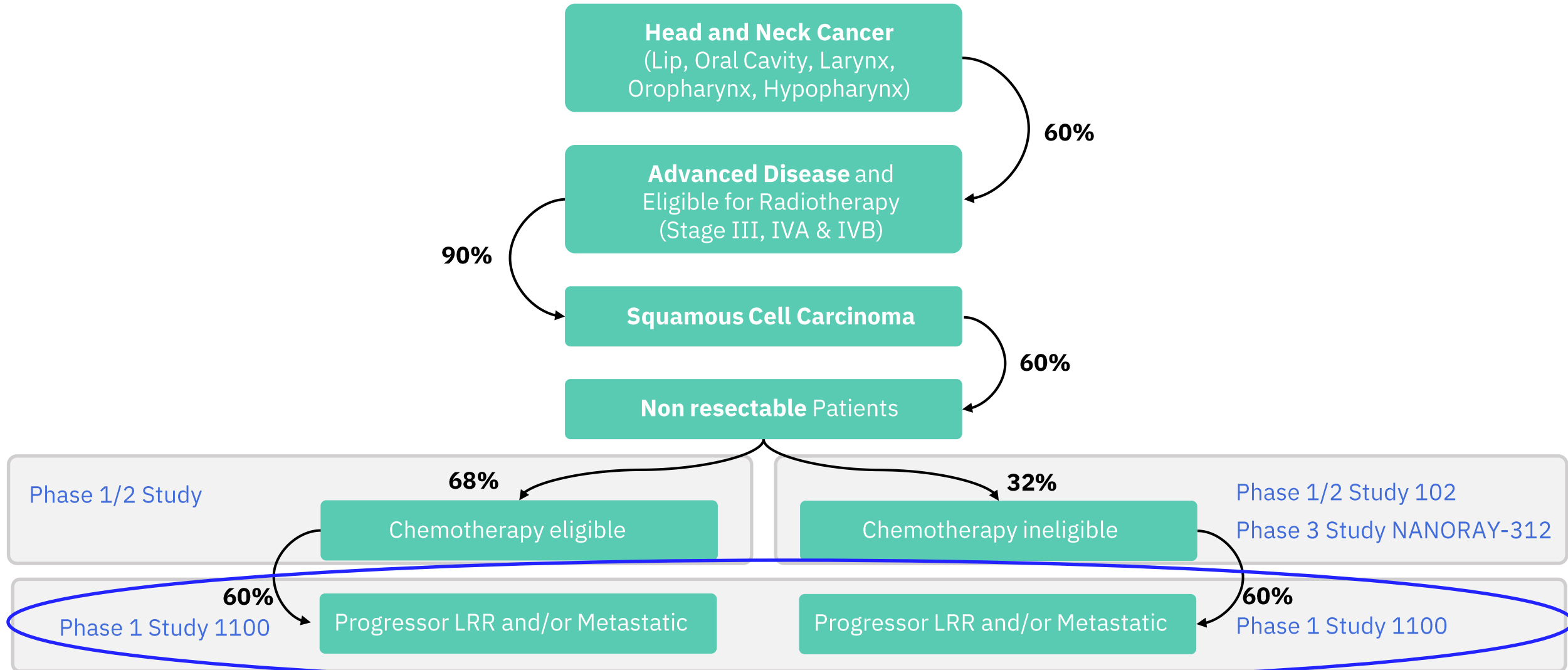
Designed to provide robust evidence for survival superiority



Stratification: mCCI, HPV status, cetuximab usage, geography

# Potential \$6.2B HNSCC Market by 2029<sup>1</sup>

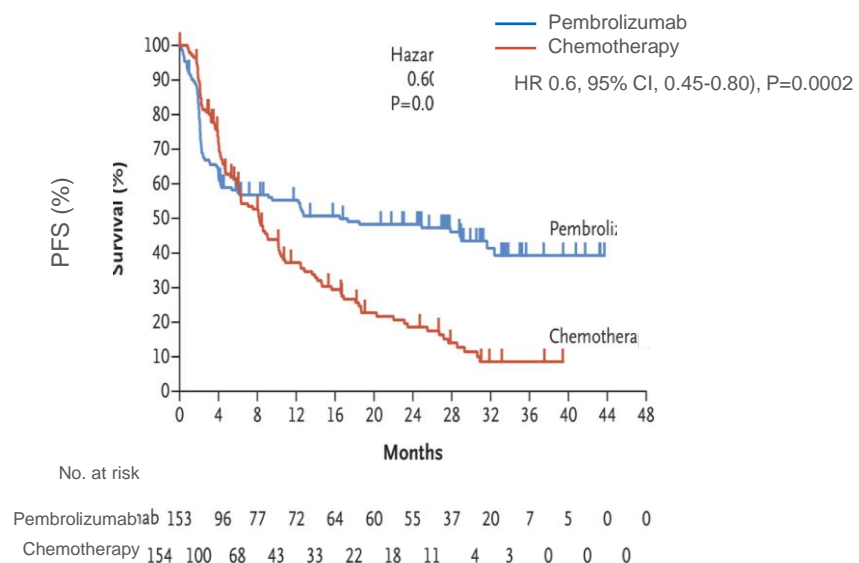
with 830,000 new patients diagnosed per year in the US, Europe and Asia<sup>2</sup>



# The Promise and Limitations of Immuno-Oncology Agents

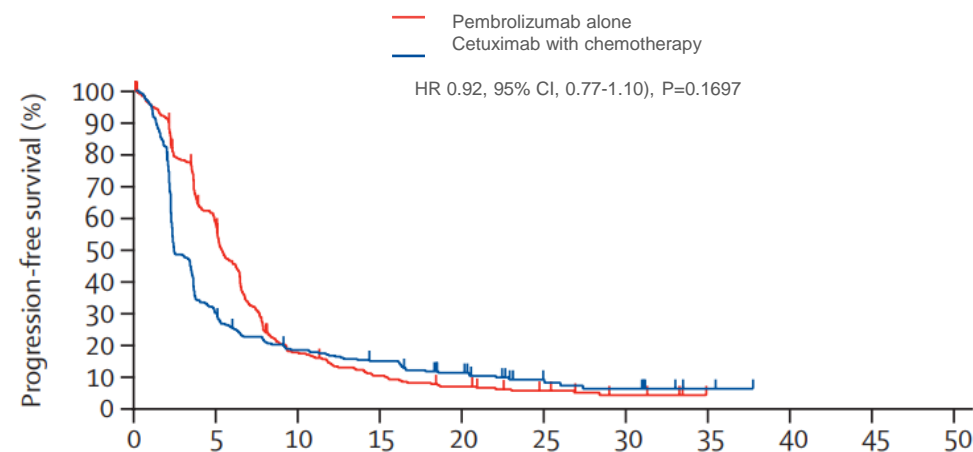
**IO has been practice changing and life changing for many patients with cancer...**

**KEYNOTE-177 in mMSI-H/dMMR CRC<sup>1</sup>**



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

**KEYNOTE-048 in R/M HNSCC<sup>2</sup>**

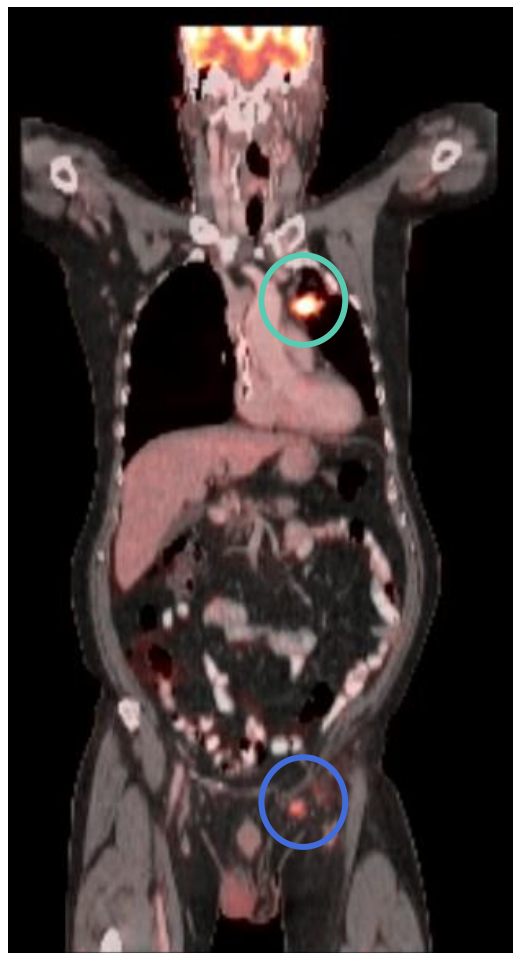


1. André et al. NEJM 2020; 2. Burness et al. Lancet 2019

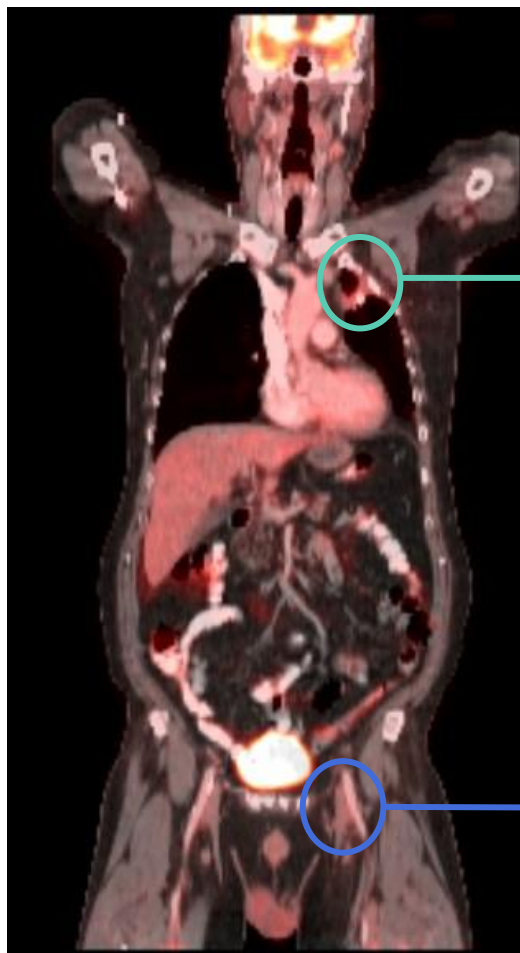
# Assessing Change in Target & Non-Target Lesions

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

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



PET Baseline



PET Follow-Up Visit 1

**Target Lesion**

PR in injected and irradiated tumor

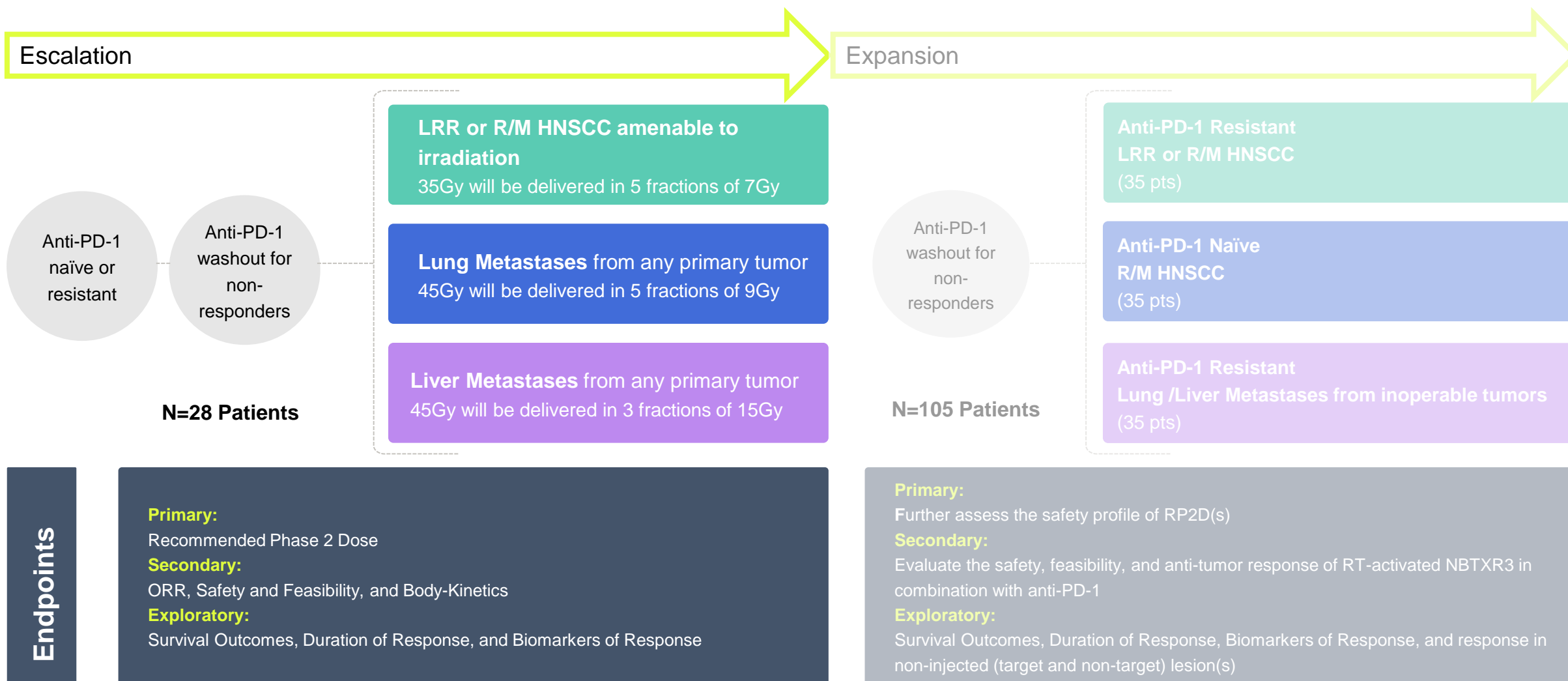
**Non-Target Lesion**

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



# Study 1100 Potential IO Combination

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

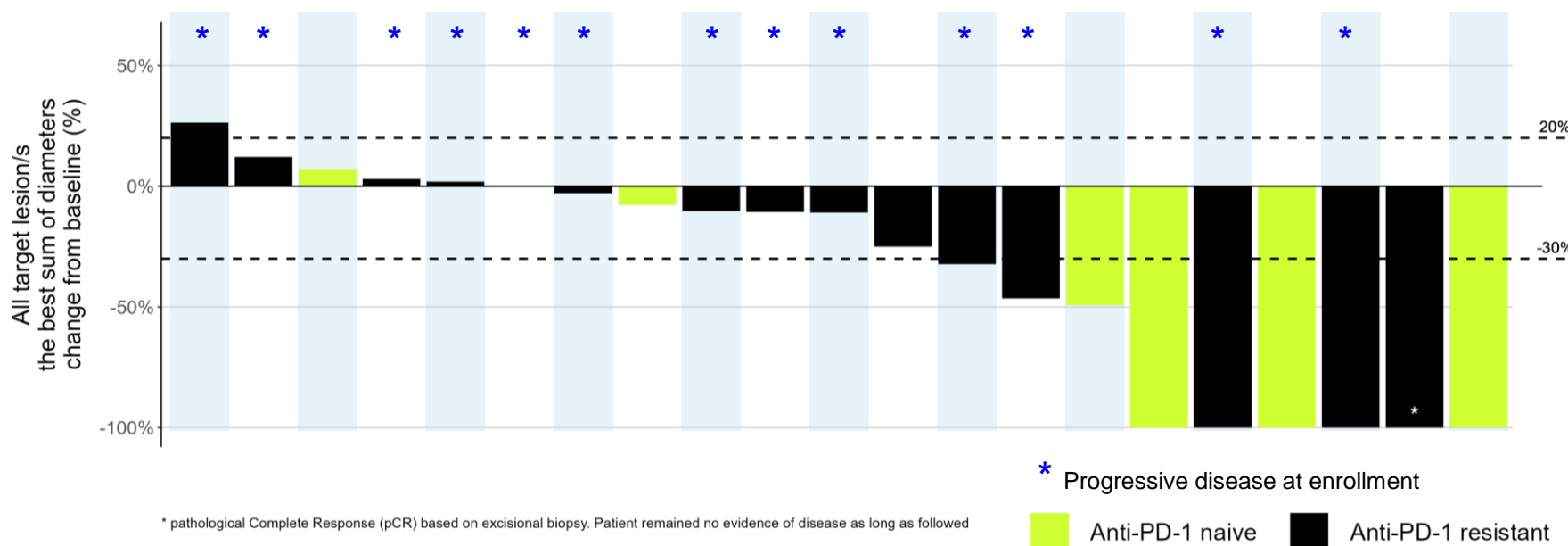


# Lesion/s Reduction Observed in Naïve and Anti-PD-1 Patients

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)

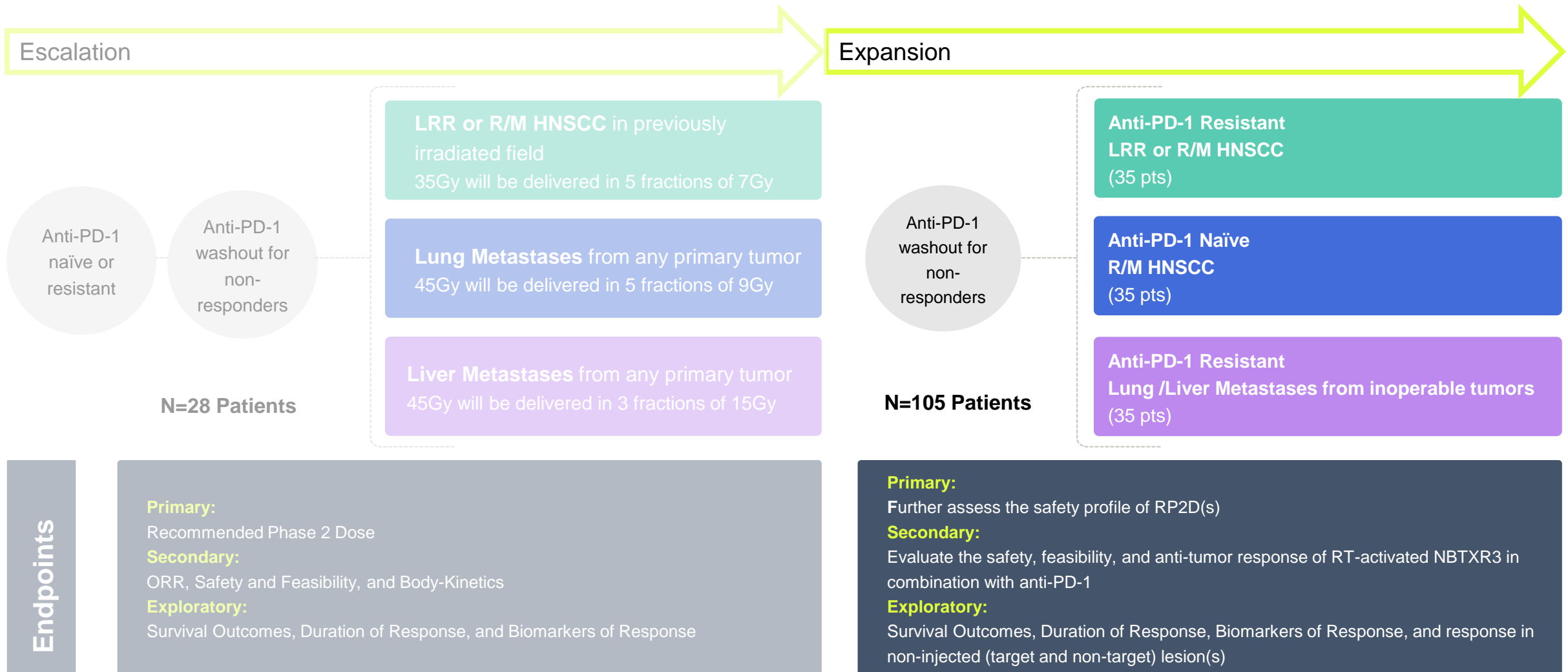


\* pathological Complete Response (pCR) based on excisional biopsy. Patient remained no evidence of disease as long as followed

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

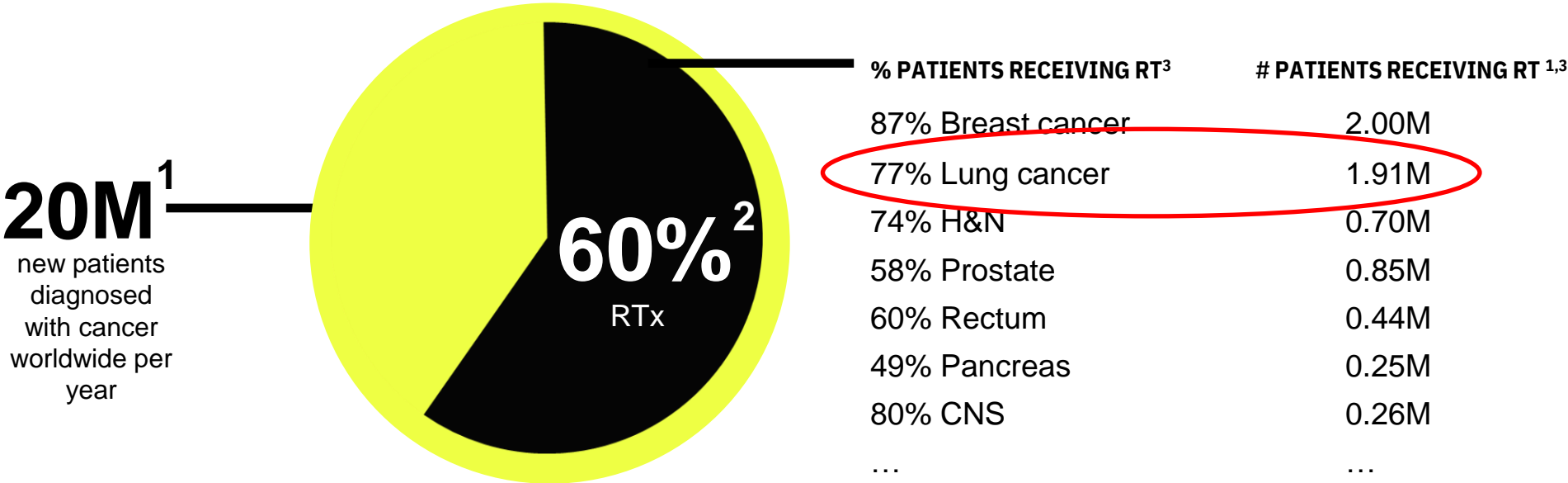
# Study 1100 Potential IO Combination

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



# Leveraging the Most Widely Used Cancer Treatment to Enhance Multiple Treatment Modalities

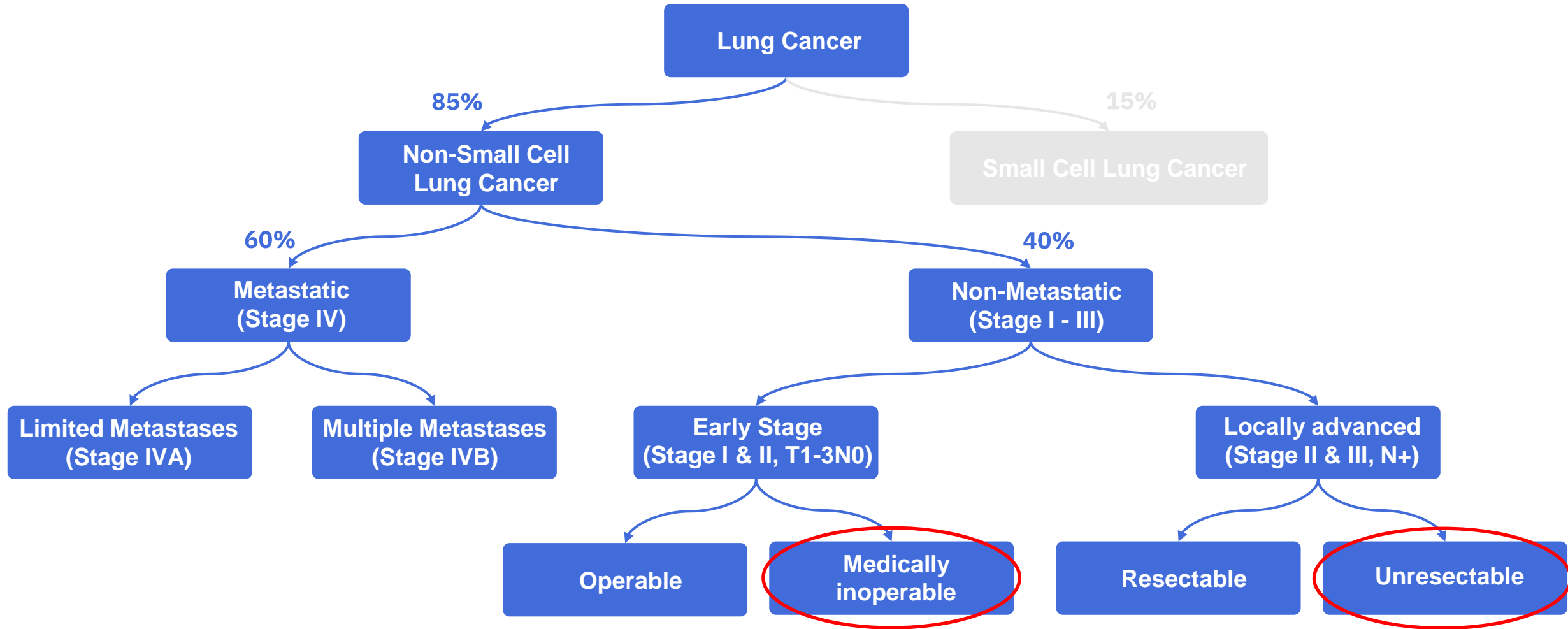
Radiotherapy is well-established, fully-integrated part of cancer treatment both alone and in combination with surgery, chemotherapy and systemic treatments





# Potential Lung Cancer Therapeutics Market \$54 Billion by 2030<sup>1</sup>

2,277,000 new lung cancer patients diagnosed per year in the US, Europe and Asia<sup>2</sup>



# Financial Summary

- **Cash runway extends into Q3 2025** (inclusive of \$20 million head and neck first development milestone from licensing agreement)
- **Cash\*\* as of December 31, 2023: €75.3M**
- **November 2023 equity raise gross proceeds €55.5M (\$58.7M)**
- **Principle received from key loans^ as of June 30, 2023:**
  - €30M credit facility from EIB
  - €10M from State-Guaranteed Loan (PGE)

**47,133,328 shares outstanding as of December 31, 2023**

Dual-listed: Euronext Paris (**NANO**)  
and Nasdaq Global Select Market (**NBTX**)

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

	For the full-year period ended December 31	
	2023	2022
<b>Revenue and other income</b>		
Revenue	30,058	—
Other income	6,150	4,776
<b>Total revenue and other income</b>	<b>36,207</b>	<b>4,776</b>
<b>Research and development expenses</b>	<b>-38,396</b>	<b>-32,636</b>
<b>Selling, general and administrative expenses</b>	<b>-22,049</b>	<b>-17,857</b>
Other operating expenses	-2,542	-985
<b>Total operating expenses</b>	<b>-62,986</b>	<b>-51,478</b>
<b>Operating income (loss)</b>	<b>-26,779</b>	<b>-46,702</b>
Financial income	2,002	3,533
Financial expenses	-14,803	-13,863
<b>Financial income (loss)</b>	<b>-12,801</b>	<b>-10,329</b>
Income tax	-120	-10
<b>Net loss for the period</b>	<b>-39,700</b>	<b>-57,041</b>
<b>Basic loss per share (euros/share)</b>	<b>-1.08</b>	<b>-1.64</b>
<b>Diluted loss per share (euros/share)</b>	<b>-1.08</b>	<b>-1.64</b>

\* JJDC: Johnson & Johnson Innovation, Inc.; \*\* Includes cash, cash equivalents and short-term investments; ^EIB and bank loans.

# Multiple Potential Value Inflection Points Expected in 12-24 Months

Indication	Trial Name <i>Approach</i>	2023	2024		2025	
		2H	1H	2H	1H	2H
Head and Neck Locally Advanced	NANORAY-312 NBTXR3-RT* ± cetuximab			Futility analysis		Interim analysis
	Study 102 NBTXR3-RT*	Final data				
Head and Neck Recurrent and/or Metastatic	TBD NBTXR3-RT* + anti-PD-1	Plans under discussion with partners				
	Study 1100 NBTXR3-RT* + anti-PD-1		Dose expansion update			
Lung	Johnson & Johnson-led programs	Stage III Ph2				
Other Solid Tumor Indications	MD Anderson-led programs	Ph 1 PDAC data	Ph 1b/2 esophageal data, RP2D NSCLC, PDAC expansion enrollment complete			

# NANOBIOTIX: Applying Universal Properties of Physics to Develop Nanotherapeutics Targeting the Biological Complexities of Disease

## Focused and Differentiated Pipeline



NBTXR3 is a potential **first-in-class radioenhancer** with paradigm breaking potential and **proven MOA in randomized Ph 2/3 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**  
Clinical sites worldwide, hundreds of patients treated, >12 clinical trials completed or ongoing  
**Expansion of development and commercial preparation through global licensing with J&J / \$2.5B**

## Multiple Clinical Catalysts



**Clear clinical path**; Fast track designation; Potential for **accelerated approval**  
**NANORAY 312** Ph 3 interim data expected mid 2025  
Start of Lung stage III randomized trial (J&J) 2024  
IO Study 1100 data expected by 1H 2024  
Updated data from MD Anderson led studies (Pancreas, Lung, ...) expected in 2024

# Appendix

# Hyper-Focused Delivery of Enhanced Radiation Into Cancer Cells

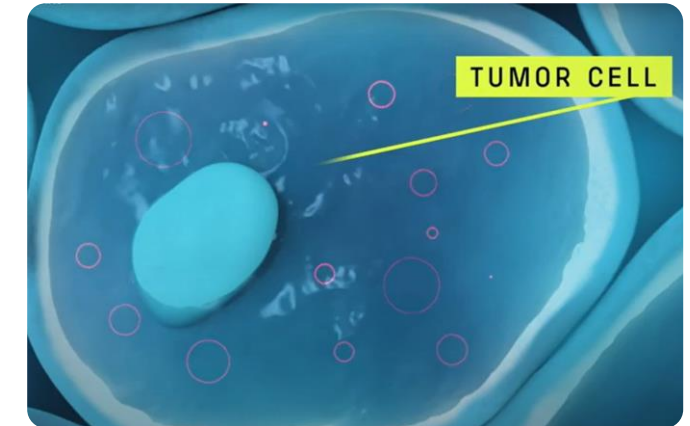
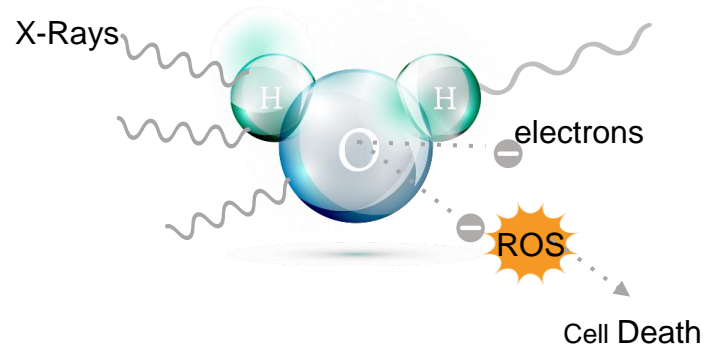
9x dose enhancement\* of radiotherapy for selective and robust tumor killing

## RADIOTHERAPY ALONE

X-rays interact with  $H_2O$

Free electrons generated

Triggers cell death or damage

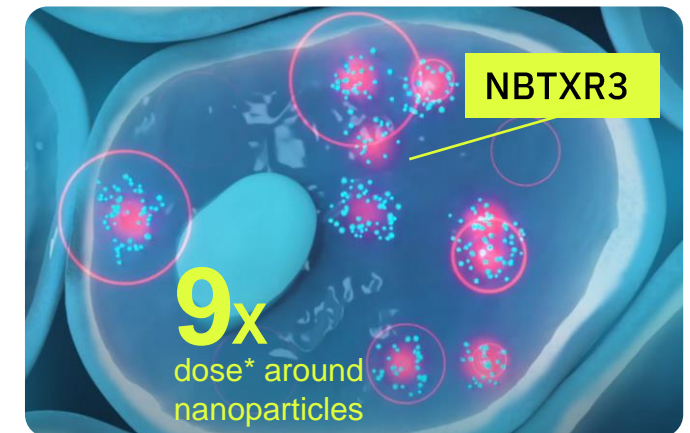
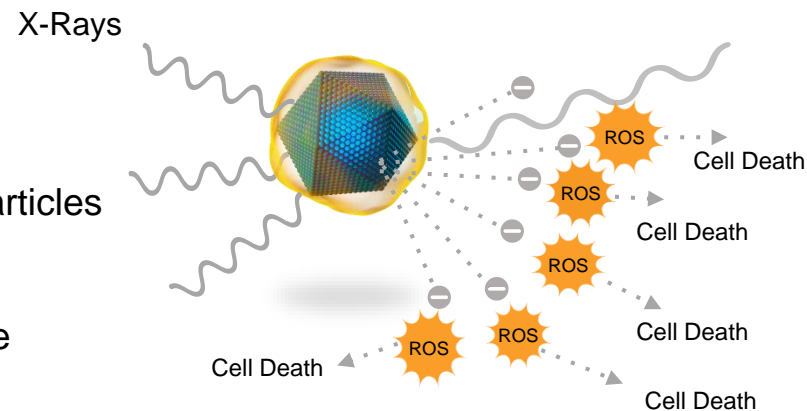


## RADIOTHERAPY + NBTXR3

X-rays interact with high electron density nanoparticles

Amplified generation of free electrons

Triggers more robust tumor cell death or damage

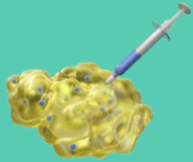


\*Note: Dose enhancement determined by monte carlo simulation (CEA Saclay, France)



# NBTXR3: Key Value Drivers of Clinical Differentiation

Designed to disrupt outcomes without disrupting clinical practice



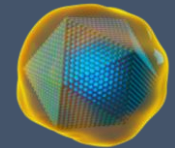
## Single Treatment

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 Activity

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



## 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

# 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 1	Phase 2	Phase 3
Head and Neck Locally Advanced	NANORAY-312	R3* ± cetuximab			
	Study 102 - <i>Terminated</i>	R3*			
Head and Neck Recurrent and/or Metastatic	TBD	R3* + anti-PD-1			
	Study 1100	R3* + anti-PD-1			

**NANOBIOTIX** EXPANDING LIFE **Demonstrated safety, feasibility and clinical activity of R3\* across multiple solid tumors**

## Completed Studies

**Soft Tissue Sarcoma** (Ph 2/3) – R3\*  
**Head and Neck** (Ph 1/2)\*\* R3\* + ChT  
**Rectal** (Ph 1/2)\*\* – R3\* + ChT  
**Liver** (Ph 1) – R3\*

THE UNIVERSITY OF TEXAS  
**MD Anderson Cancer Center** **Exploring safety, feasibility and efficacy of R3\* in solid tumors**

## Ongoing Studies

**Head and Neck** (Ph 2) – R3\* + anti-PD-1  
**Esophageal** (Ph 1) – R3\* + ChT  
**Advanced cancers** (Ph 1/2) – R3\* + anti-PD-1/L-1  
**Pancreatic** (Ph 1) – R3\*  
**NSCLC** (Ph 1) – R3\*

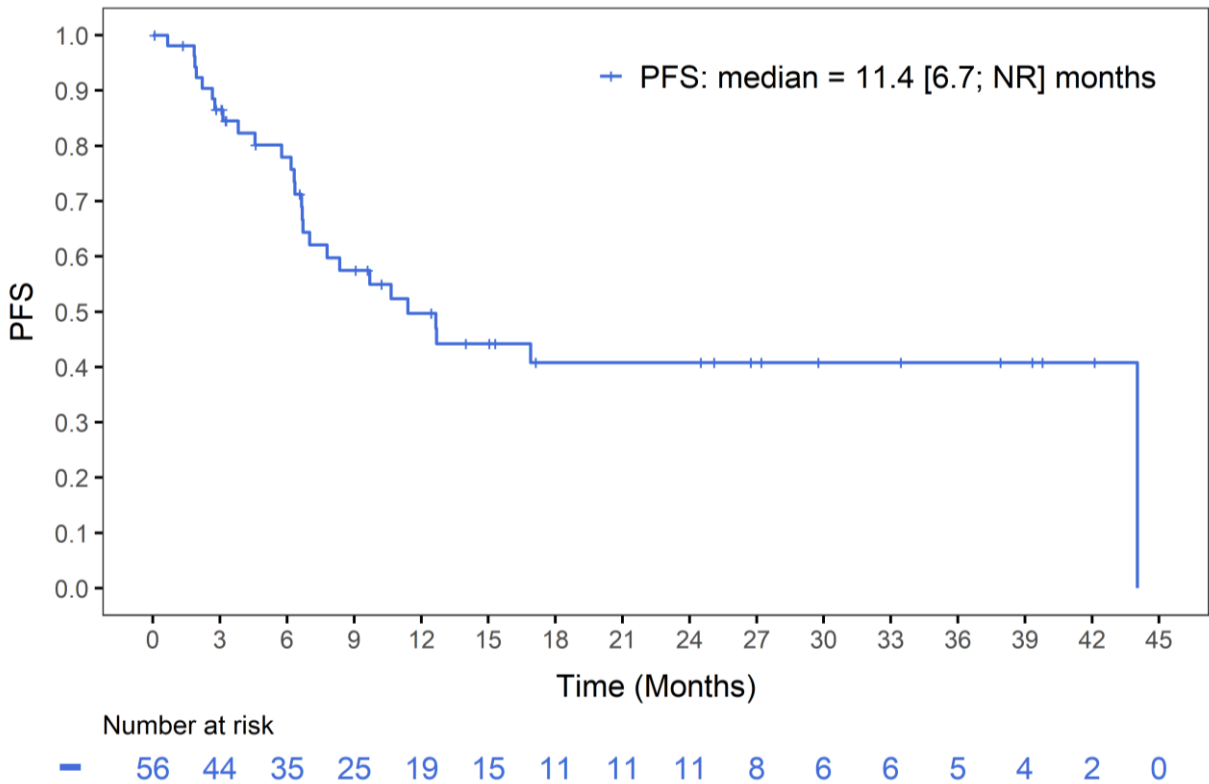
**Janssen<sup>^</sup>** **Expanding into large indications**

**Planned indication**  
 Ph 2 in stage III lung cancer  
**New potential indications**  
 TBD

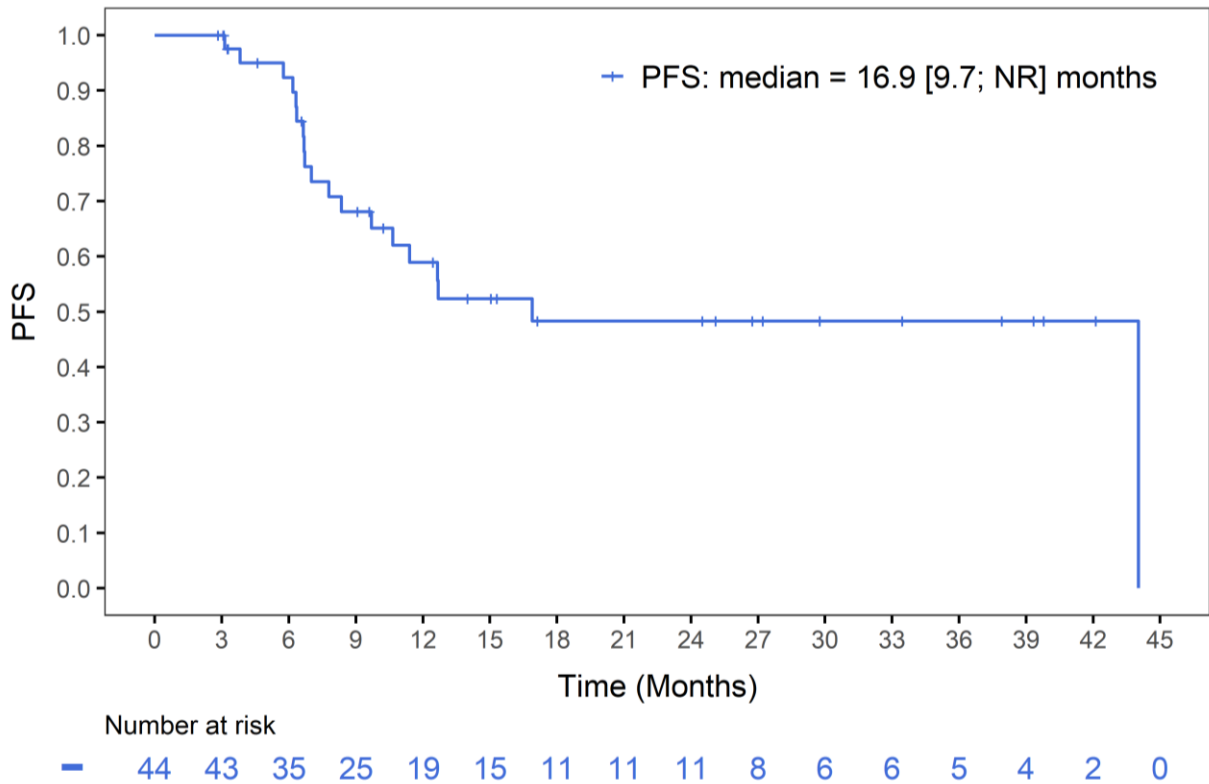
# Median PFS of 16.9 Months in Evaluable Patients

By Independent Central Review

All Treated Population N=56



Evaluable Population\* N=44



Among the 12 patients who were non-evaluable for objective tumor response, 9 had severe comorbidities (ACCI≥4)

~30% of HNSCC patients > 70 years old and have poor outcomes (PFS ~9 months<sup>3</sup>; OS ~12 months<sup>3,4,5</sup>)

# Phase 1 Study 102 Informs Higher Confidence in NANORAY-312 Phase 3

## Study 102 vs NANORAY 312

### Study 102 – Expansion Cohort

- ~64% CR in evaluable patients
- 16.9 months mPFS in evaluable patients
- 23 months mOS in evaluable patients
- 67% of all patients ACCI  $\geq 4$
- Lymph nodes not injected

### NANORAY-312

- Same burden of disease but with lower ACCI
- Lymph nodes potentially injected
- Final analysis assumptions:
  - mPFS: 9 vs 13 months
  - mOS: 12 vs 16 months

### Power for final PFS analysis

Delta vs 9 months	Power
4 months	89.2
6 months	98.2
8 months	99.7

# Study 1100 POC Forms Basis For 2<sup>nd</sup> Potential HNSCC Registration Study

NBTXR3-RT\* + anti-PD-1 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

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

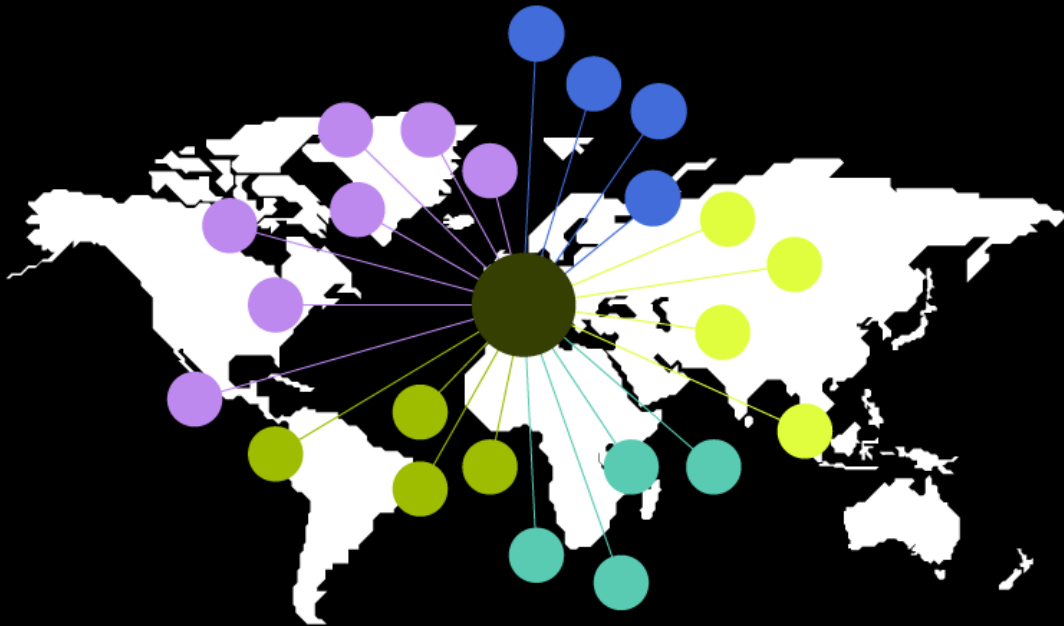
### Global randomized Phase 3:

- Continued development of NBTXR3-RT\* in combination with anti-PD-1
- Potential for accelerated approval based on interim ORR analysis
- Next steps in discussion with partners

\*NBTXR3-RT: NBTXR3 activated by radiotherapy

# 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**

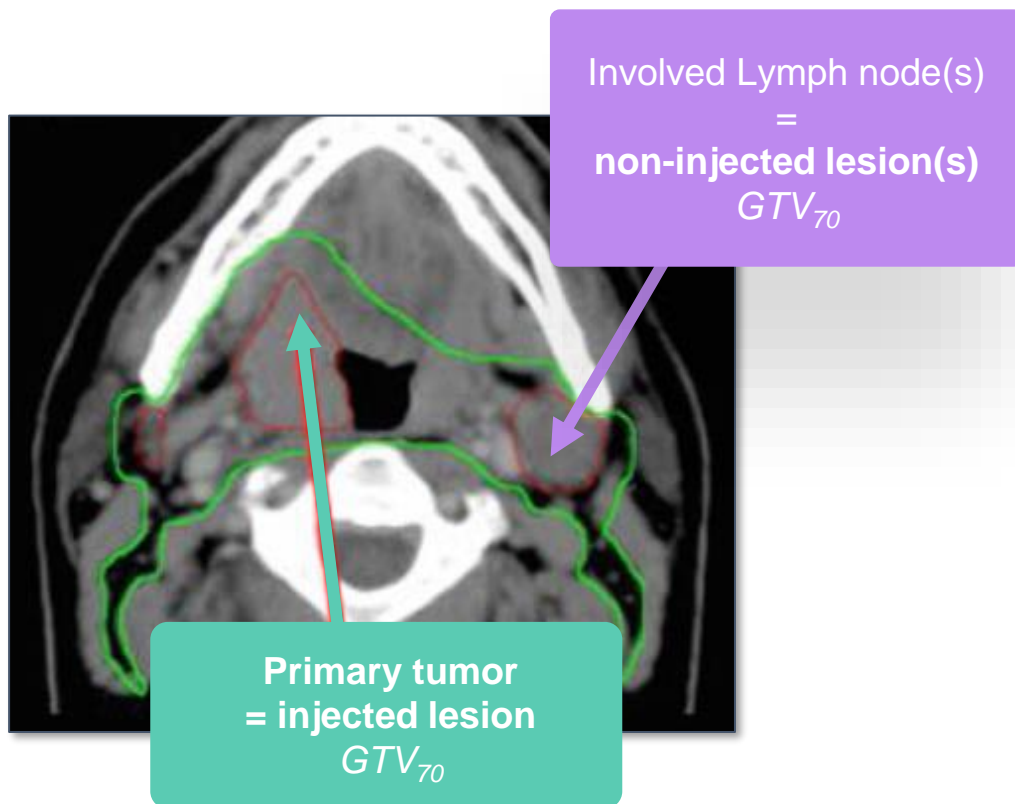
Built to scale, validated process with ability to accommodate initial commercial demand

**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



# Locoregional Control and Duration of Response



## Duration of Objective Response

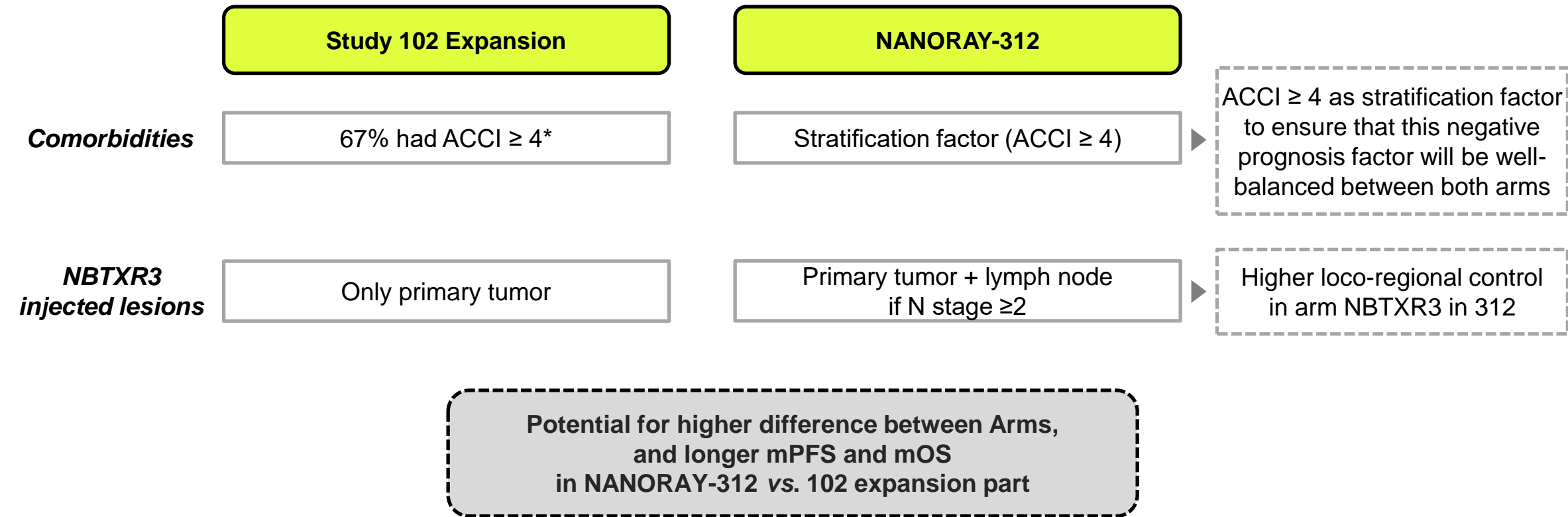
### NBTXR3-injected lesion (n=36)

Median [95%CI], months      Not Reached [7.2, NR\*]

### Injected and non injected lesion (n=35)

Median [95%CI], months      12.4 [6.6, NR\*]

# Differences Between Study 102 Expansion and NANORAY-312



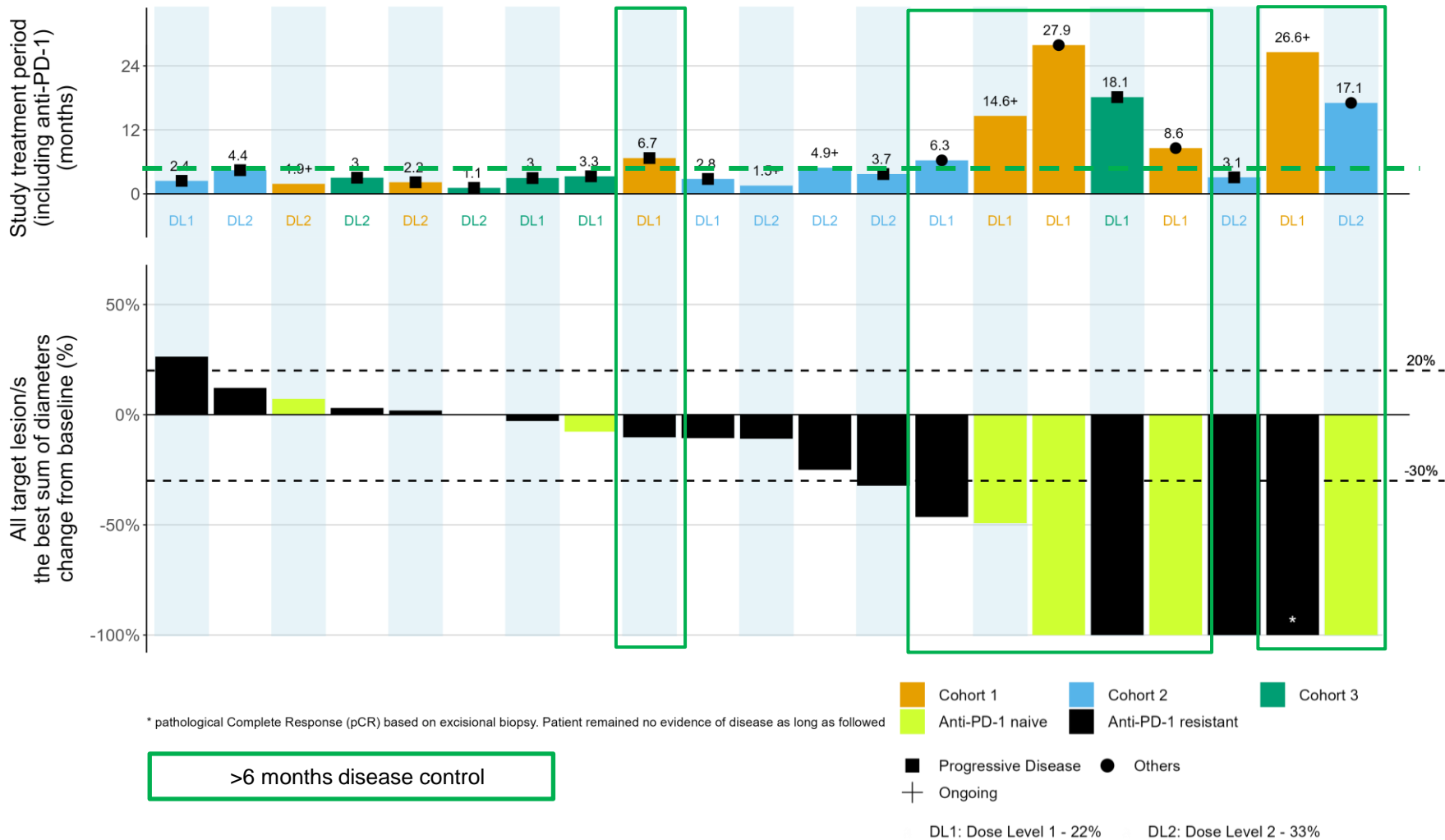
# Objective Reductions, Long-term Control in Anti-PD-1 Naïve & Resistant

SITC 2022: All target lesions

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

8 patients with > 6 months disease control

5 patients with >12 months disease control

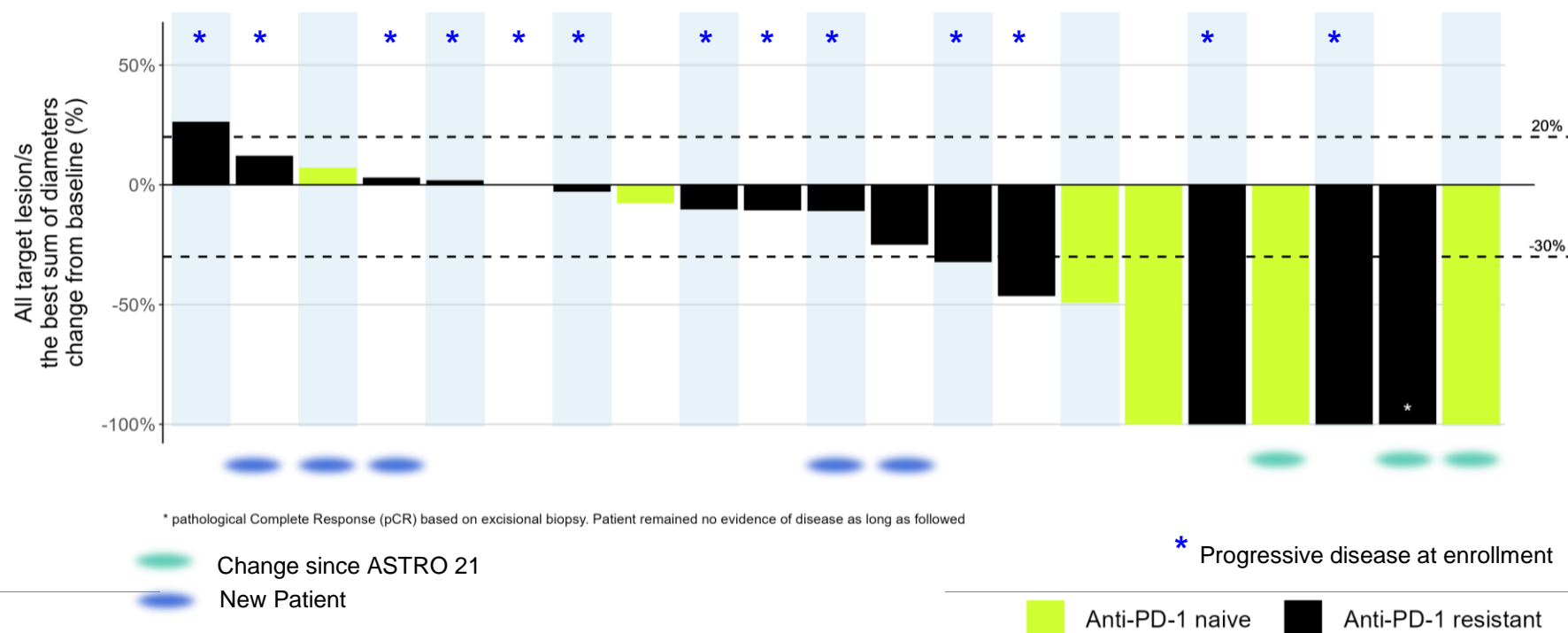


# Objective Reduction Target Lesion/s in Previously Progressing Patients

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

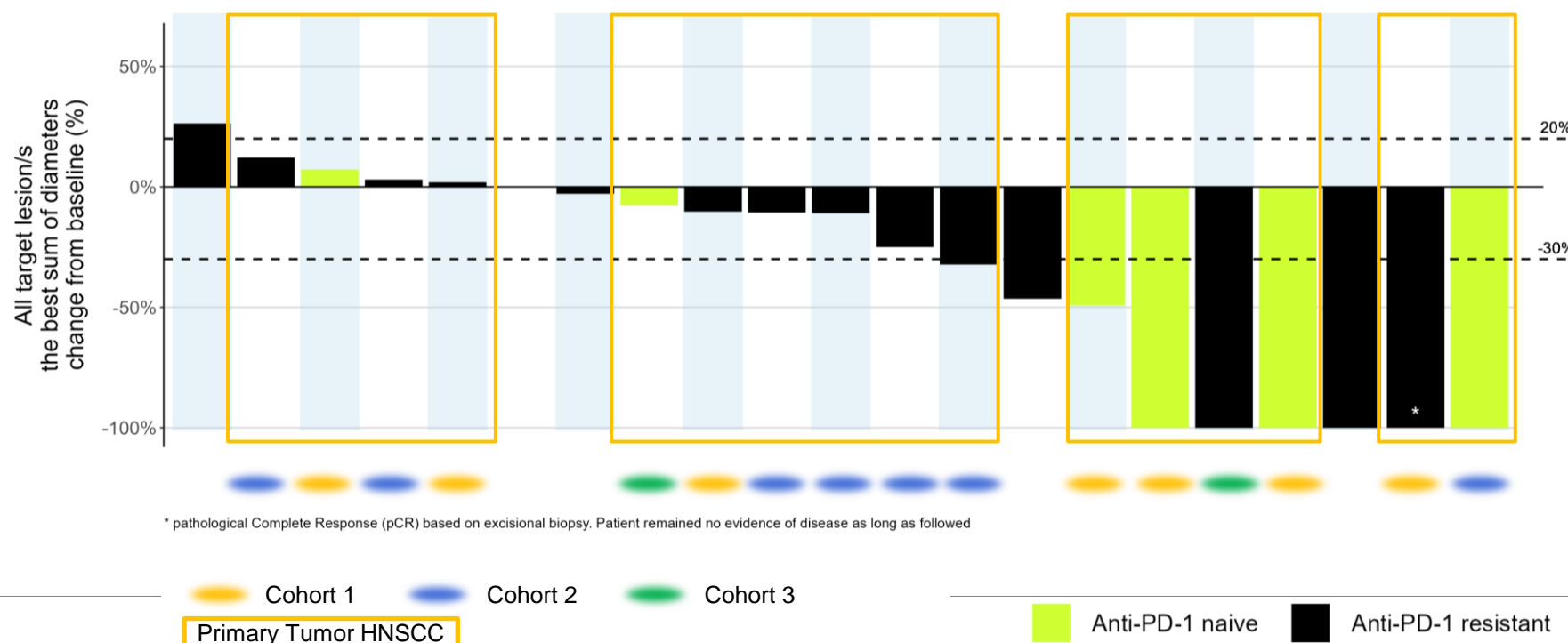
SITC 2022: All [target lesions](#)

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

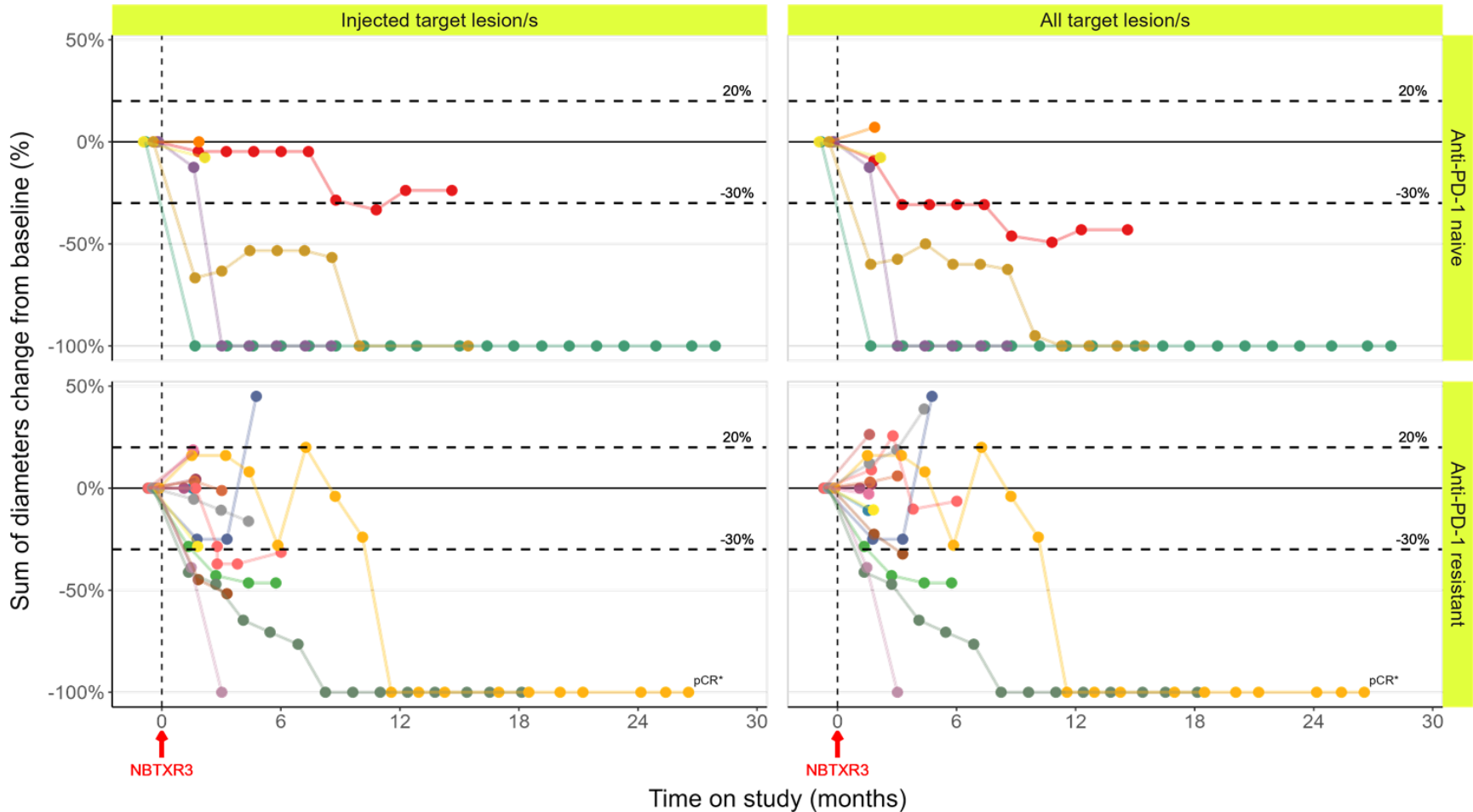


# % Change From Baseline Over Time: Injected Lesion Vs All Target Lesion/s

SITC 2022: All target lesions

Local control in injected lesions occurred in all patients and remained in all patients except 1

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





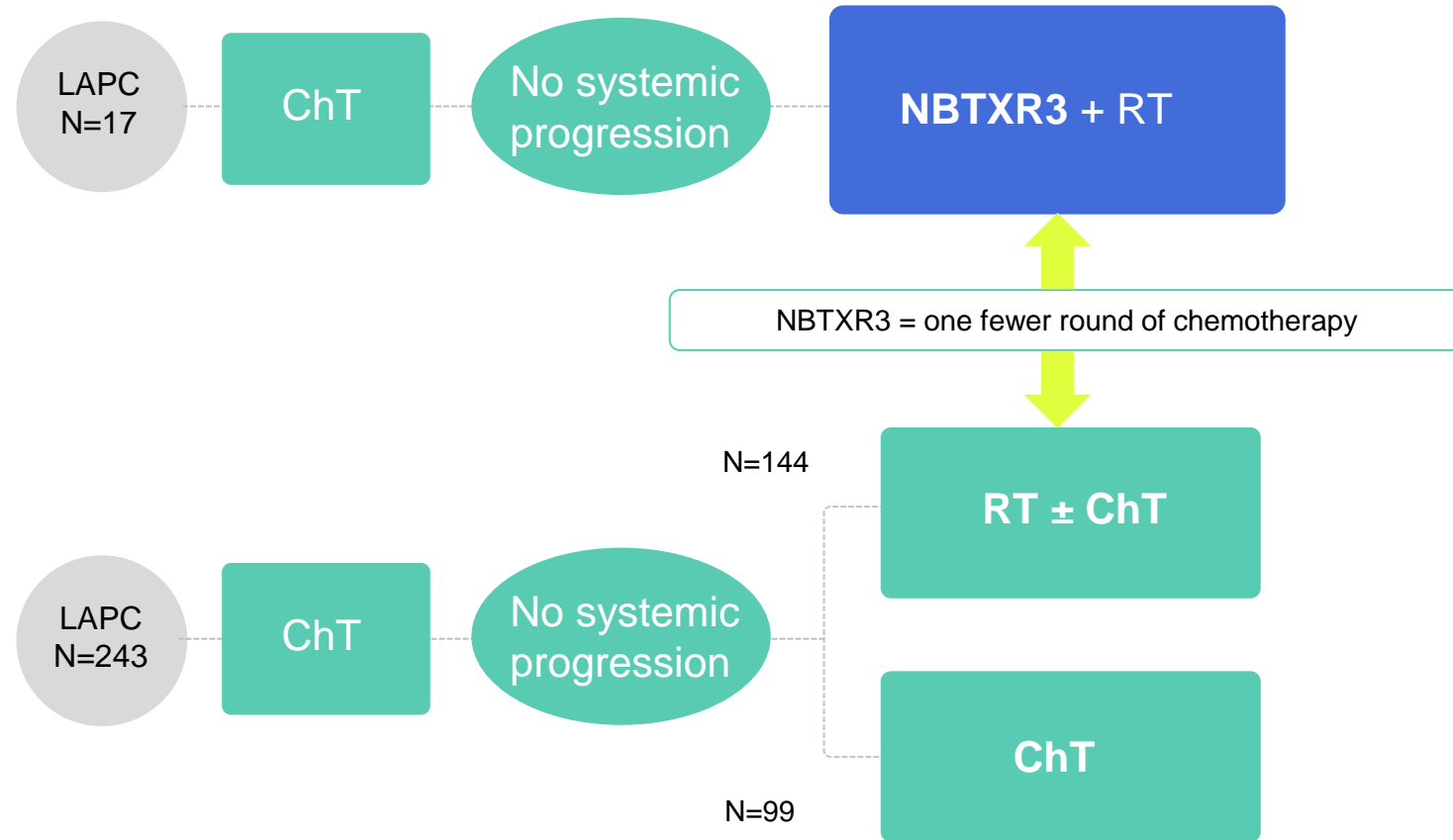
RT activated NBTXR3 in  
LAPC, MD Anderson-led  
trial

Historical review of 243  
patients with LAPC at the  
same MD Anderson center

LAPC: Locally Advanced  
Pancreatic Cancer  
ChT: Chemotherapy  
RT: Radiotherapy

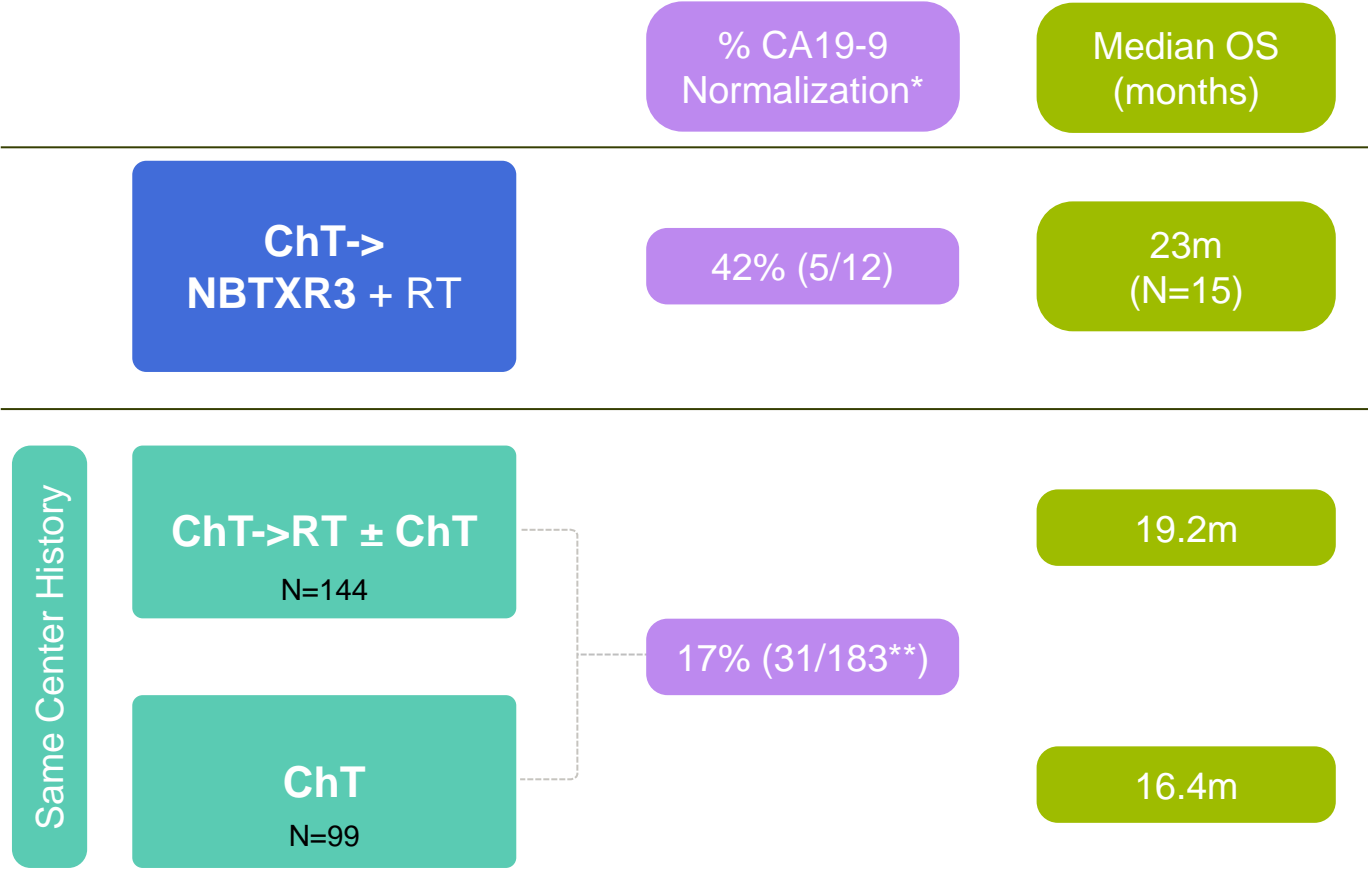
# Phase 1 Study Design

RT-activated NBTXR3 after chemotherapy for patients with LAPC



# NBTXR3+RT Achieved 23 Months mOS With One Fewer Course of Chemo

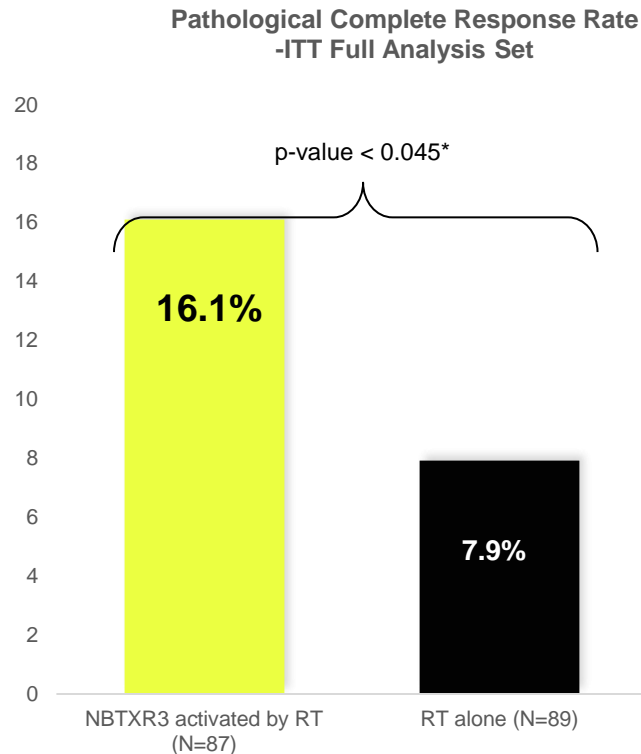
MD Anderson clinical trial for the treatment of locally advanced or borderline-resectable pancreatic cancer



\*Normalization vs elevated levels at diagnosis; \*\*Of the 183, 109 received chemo followed by chemo RT and 74 received chemo only. ChT: Chemotherapy, RT: Radiotherapy

# Proof-of-concept Established in Randomized PII/III, EU 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 Tanguy, Antonio Casado Hernandez, Alessandro Gronchi, Lucile Mangin, Teresa Sy-Ostin, Peter Hohenberger, Thierry de Baat, Axel Le Cesne, Sylvie Huguier, Emma Soussi-Bouaid, Aneta Borkowska, Rodica Anghel, Ann-Cu, Michael Gebert, Guy Kuster, Angel Montoro, Herbert H Long, Ramona Vargiu, Lore Leprie, Scott Dine, Gabriel Kacou, Lyn Arian, Laurence Mourou-Zabotto, Vincent Servais, Eva Wardemann, Philippe Terrier, Alexander J Lazar, Judith VM G Bovic, Cécile Le Pichoux, Zsuzsanna Papp*

### 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 (HfO<sub>2</sub>) 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)

\* ITT FAS = Intention to Treat Full Analysis Set; statistically significant at a threshold of 0.04575.