

# Oncology Leadership in Pretargeted Radioimmunotherapy Platform and Antibody-based Therapies

January 2025



## Disclaimer

This presentation contains forward-looking statements within the meaning of the US Private Securities Litigation Reform Act of 1995. The forward-looking statements involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements about: our business model, preliminary estimated financial results and expectations for the year ended December 31, 2024, including estimated net revenue; implied and express statements regarding the future of the Company's business; and the Company's strategies, development, regulatory, commercialization and product distribution plans are forwardlooking statements. Words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "goal," "guidance," "hope," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forwardlooking statements contain these identifying words. Our product candidates and related technologies are novel approaches to cancer treatment that present significant challenges. Actual results may differ materially from those indicated by such forward-looking statements as a result of various factors, including but not limited to: risks associated with our financial condition and need for additional capital; the risk that our reported results may differ materially from our preliminary estimated DANYELZA net product revenue results as a result of the completion of year-end closing procedures, final adjustments, and other developments arising between now and the time that our financial results are finalized; risks associated with our development work; cost and success of our product development activities and clinical trials; the risks of delay in the timing of our regulatory submissions or failure to receive approval of our drug candidates; the risks related to commercializing any approved pharmaceutical product including the rate and degree of market acceptance of our product candidates; development of our sales and marketing capabilities and risks associated with failure to obtain sufficient reimbursement for our products; the risks related to our dependence on third parties including for conduct of clinical testing and product manufacture; risks related to our ability to enter into partnerships; the risks related to government regulation; risks related to market approval; risks associated with protection of our intellectual property rights; risks related to employee matters and managing growth; risks related to our common stock; risks associated with ongoing geopolitical conflicts; and other risks and uncertainties affecting the Company including those described in the "Risk Factors" section included in our Annual Report on Form 10-K for the year ended December 31, 2023, our Quarterly Reports on Form 10-Q for the guarters ended March 31, June 30, and September 30, 2024, and in our other SEC filings. Any forward-looking statements contained in this presentation speak only as of the date hereof, and the Company undertakes no obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.





At Y-mAbs, our mission is to deliver innovative therapeutic solutions for life's most threatening diseases, helping to improve and extend people's lives

# Growing Base Business with Potential High Value RIT Platform

#### Next-Generation Novel Platforms



Self-Assembly DisAssembly Pretargeted Radioimmunotherapy ("SADA PRIT") Platform

Monoclonal Antibodies

#### Established Commercial Capabilities



DANYELZA (naxitamabgqgk), Anti-GD2 Approved for R/R High-Risk Neuroblastoma

U.S. Commercial Footprint; Ex-U.S. through partnerships, NPPs

#### Radiopharmaceutical Leadership



Deep bench of industry leadership and expertise in developing and commercializing radiopharmaceutical oncology therapeutics

#### **Broad Pipeline Potential**



SADA PRIT's proven mechanism of pre-targeted approach carries therapeutic potential beyond oncology



## 2024 Achievements

#### **COMMERCIAL PROGRESS**

DANYELZA remains an important anti-GD2 therapy for patients with HR R/R NB

MSK presented DANYELZA osteosarcoma data at CTOS

Increased DANYELZA vial demand in ex-U.S. markets including China, Brazil and Mexico; NPPs in Europe, Turkey

#### SADA PRIT ADVANCEMENT

Proof-of-concept of SADA PRIT platform achieved in GD2-SADA Phase 1 trial (Trial 1001)

Activated 4 sites for CD38-SADA Phase 1 trial (Trial 1201)

#### **FINANCIAL**

Preliminary estimated unaudited FY2024 total net revenue of ~\$88M within final guidance range\*

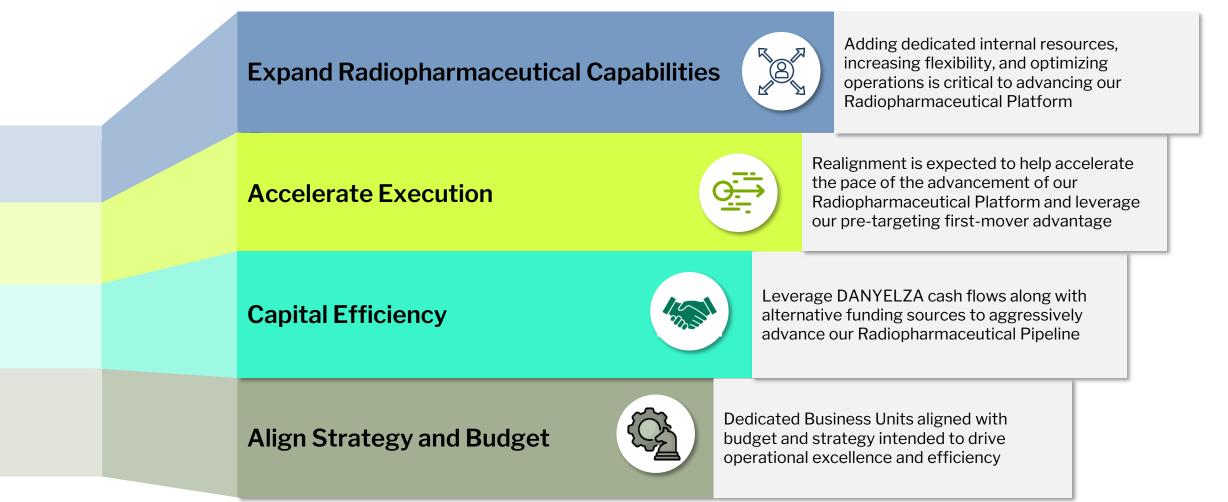
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Capital efficient with sound financial structure allowing us to invest in the future



\*Preliminary results are unaudited and based on management's initial review of the Company's results as of and for the year ended December 31, 2024, and are subject to revision based upon the Company's year-end closing procedures and the completion of the audit by the Company's external auditors of the Company's December 31, 2024 financial statements; Previously announced guidance range during Q3 2024 earnings report.

# Realignment into 2 Business Units Intended to Accelerate Development in Radiopharmaceuticals and Maximize Value of DANYELZA







# **SADA PRIT Platform**

Novel Self-Assembly DisAssembly Pre-targeted Radioimmunotherapy Technology Platform

## Current Radiopharmaceutical Industry Challenges Negatively Impact Patient Care





## Novel SADA PRIT Platform Aims to Address Key Improvements over Traditional Radiopharmaceuticals

#### **Traditional Radioimmunotherapy**



Limited dose-to-tumor due to off-target radiation



Prone to drug shortages / supply issues with single-isotope only capabilities



Limited administration sites with licensed nuclear medicine oncologist



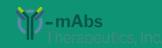
High investment needed for specific infrastructure and manufacturing

#### SADA PRIT Platform Potential Capabilities

- Pre-targeting tumor potentially minimizes toxicity and potentially enhances rapid clearing of unbound protein
- ✓ Potential to work with short  $T_{1/2}$  isotopes
- Potentially broader site options with protein doses administered by Medical Oncologist

#### Potential COGS improvements

\* Pending successful development and approval



## Two-Step GD2-SADA PRIT Designed to Selectively Delivers Cytotoxic Radiation to GD2+ Tumor Cells

#### PRIT Step 1

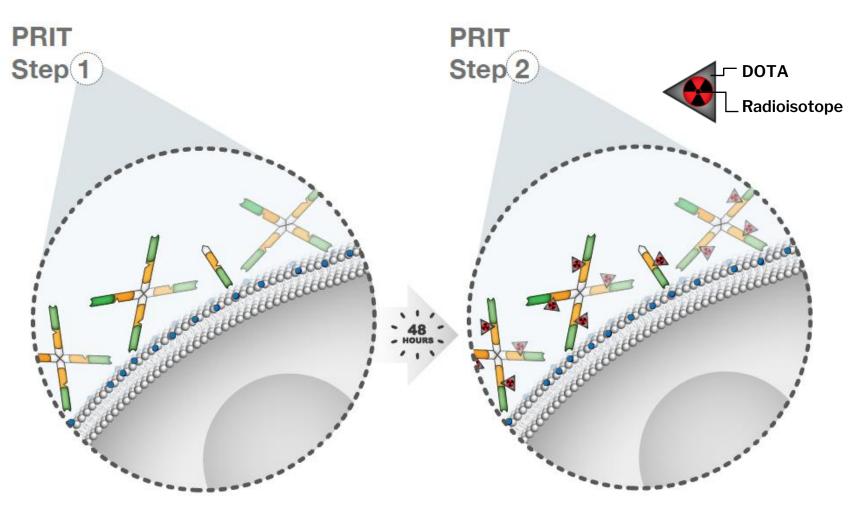
Non-radiolabeled SADA protein is administered at a concentration that favors tetramer formation<sup>1,2</sup> and binds with high avidity to targeted tumor cells<sup>1,2</sup>

Over time, unbound SADA protein disassembles into monomers that are renally cleared<sup>1-3</sup>

#### **PRIT Step 2**

Chelated radioisotope<sup>4</sup> binds to the anti-DOTA domain of SADA protein on tumor cells, causing radiation-induced damage<sup>1,2</sup>

Unbound radioisotope is cleared by the kidneys,<sup>1,3</sup> limiting exposure to the blood/marrow compartment





DOTA, dodecane tetraacetic acid, tetraxetan; GD2, disialoganglioside; Ln, lanthanide metal; PRIT, pretargeted radioimmunotherapy; SADA, self-assembly and disassembly. 1. Santich BH et al. *Clin Cancer Res* 2021;27:532-541. 2. Santich BH et al. *Cancer Res* 2022;82(12 suppl):3309. 3. Capala C, Kunos CA. *Clin Cancer Res* 2021;27:377-379 4. Cheal SM et al. *Eur J Nucl Med Mol Imaging* 2016;43:925-937.



# SADA PRIT Platform GD2-SADA Program Update

# GD2-SADA Phase 1 Clinical Trial (Trial 1001): Part A Ongoing

Theranostic approach using a 30 mCi <sup>177</sup>Lu-DOTA imaging dose before exposing to therapeutic dose

**Trial Overview** 

- Solid tumors: SCLC, malignant melanoma, sarcomas, adult neuroblastoma
- Completed Cohorts 1 through 5; currently in Cohort 6\*
- 21 patients dosed\*
- 6 sites open\*
- No DLTs or serious instances of treatmentrelated AEs reported\*

Part ADetermine optimal, well-<br/>tolerated GD2-SADA<br/>protein dose and dosing<br/>interval between GD2-<br/>SADA and 177Lu-DOTAPart BDose ranging to

Dose ranging to determine maximum tolerable activity of <sup>177</sup>Lu-DOTA

Repeat dosing to determine (RP2D); early efficacy signals

Part C

#### Part A Data Anticipated to be Presented in Q2 2025

- × Optimal and safe GD2-SADA protein dose
- Dosing interval between GD2-SADA and <sup>177</sup>Lu-DOTA
- PK dosimetry
- Rate of excretion
- Concentration in tissue
- Tumor burden
- PET/CT scan images

\*As of January 12, 2025



## Trial 1001: Demonstrated Proof-of-Concept in GD2-SADA Across Various Tumor Types

Overview of patients who showed tumor uptake

	<b>Cohort 2</b> (2-day interval)	<b>Cohort 3</b> (5-day interval)	<b>Cohort 3</b> (5-day interval)	<b>Cohort 3</b> (5-day interval)	<b>Cohort 4</b> (5-day interval)	<b>Cohorts 5</b> (4-day interval)	<b>Cohort 6</b> (3-day interval)	<b>Cohort 6</b> (3-day interval)	<b>Cohort 6</b> (3-day interval)
Patient Number	3	5	8	9	11	16	18	19	21
Diagnosis	Osteosarcoma	Osteosarcoma	Synovial Sarcoma	Uveal Melanoma	Leyomyosarc oma	Uveal Melanoma	Melanoma	Uveal Melanoma	Melanoma
Dose level (mg/kg)	0.3	1.0	1.0	1.0	3.0	1.0	1.0	1.0	1.0
Tumor uptake	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Total Number of Patients by Tumor Type (N = 21)						
Sarcoma	11					
Melanoma	8					
Small Cell Lung Cancer (SCLC)	1					
Neuroblastoma (NB)	1					

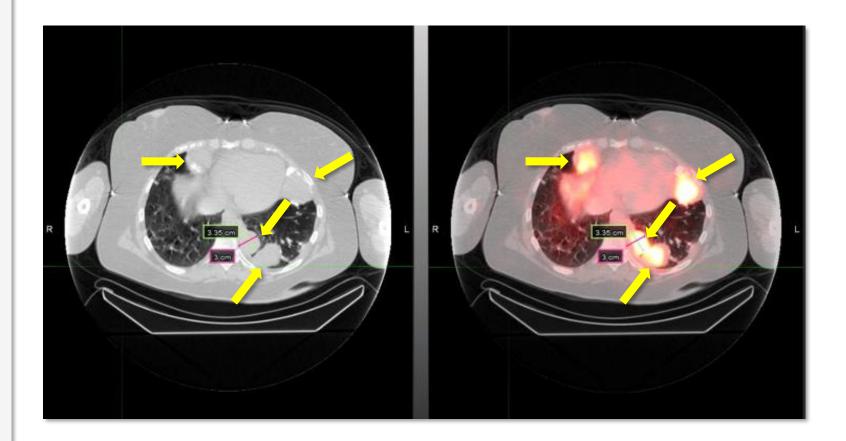
Data cut as of January 6, 2025. These early results are not complete and are not necessarily indicative of the full results or ultimate success of the SADA development program which is in early development with no guaranty of approval.



# Trial 1001: SPECT/CT Scan on Osteosarcoma Patient Demonstrating Positive Tumor Uptake After Exposure\*

Shared patient scan shows:

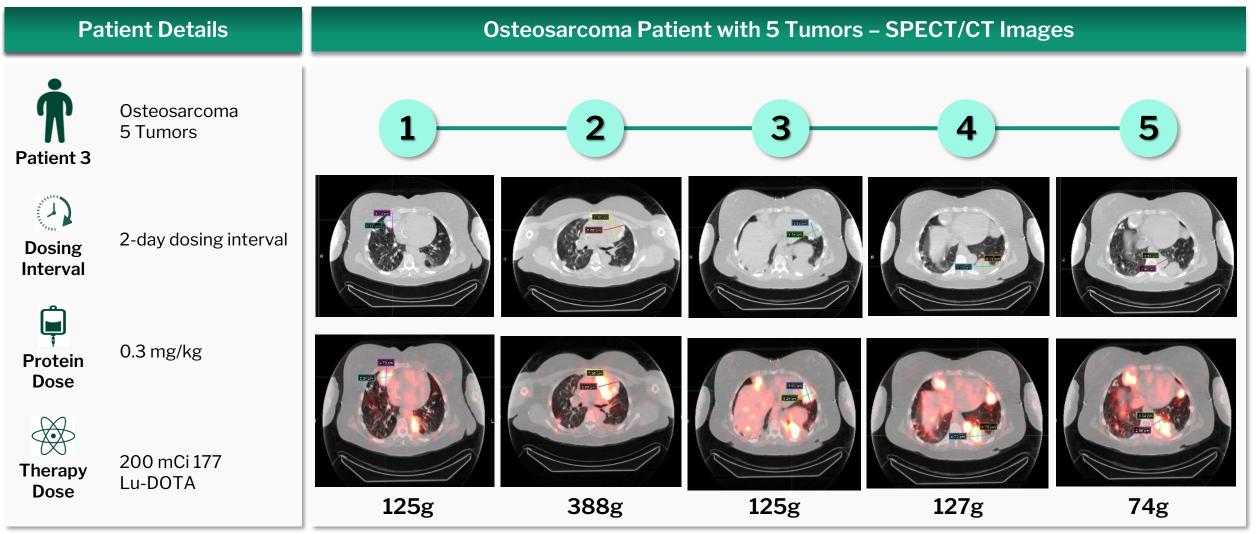
- Patient treated with 0.3 mg/kg GD2-SADA, followed by 200 mCi <sup>177</sup>Lu-DOTA (lowest therapeutic radionuclide dose) 48-hours later
- Scan performed 24 hours after radionuclide administration
- 4 target lesions marked on CT scan (left image) – all targeted by <sup>177</sup>Lu-DOTA SADA (right image)



<sup>\*</sup>These early results are not complete and are not necessarily indicative of the full results or ultimate success of the SADA trials or the SADA development program, which is in early development with no guaranty of approval. Limitation: Patient-level data are for descriptive purposes and should not be considered indicative of typical product efficacy or duration; interpret with caution.



# Trial 1001: Further Example of Osteosarcoma Patient Demonstrating Positive Tumor Uptake Across All 5 Tumors After <sup>177</sup>Lu-DOTA SADA Dose

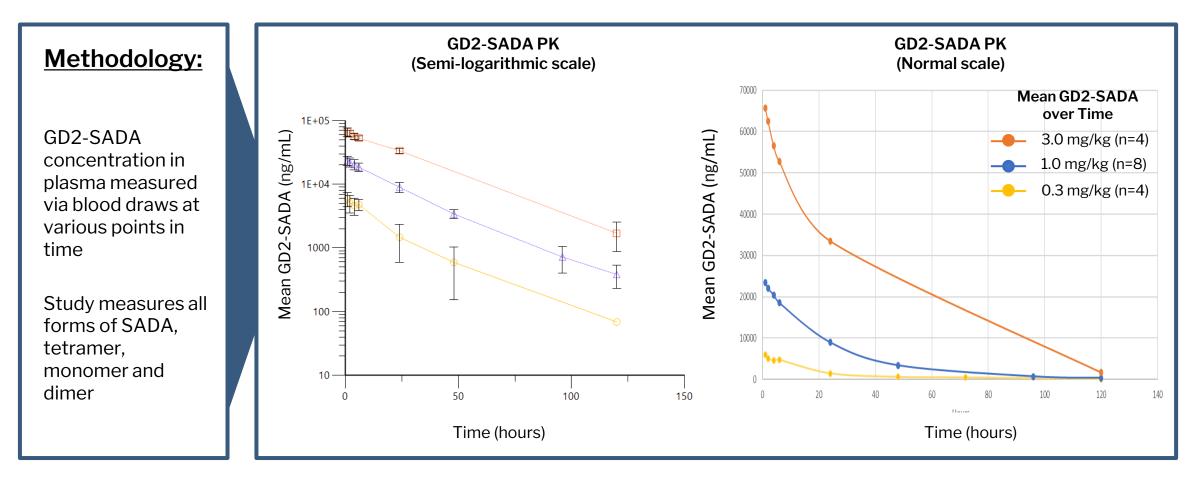


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# Mean Blood PK Values Indicates Clearance Rates Similar with Different Dose Levels, as Predicted, in Preliminary Data

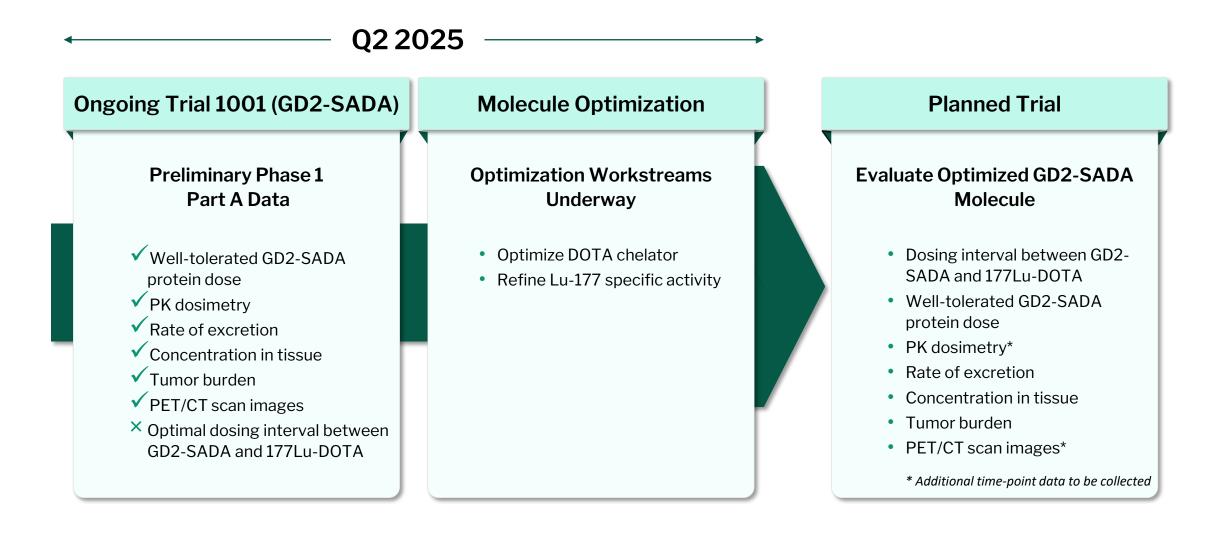
#### Trial 1001: Blood Pharmacokinetic for GD2-SADA (mean values)



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# Preliminary Part A Data and Anticipated GD2-SADA 2025 Milestones





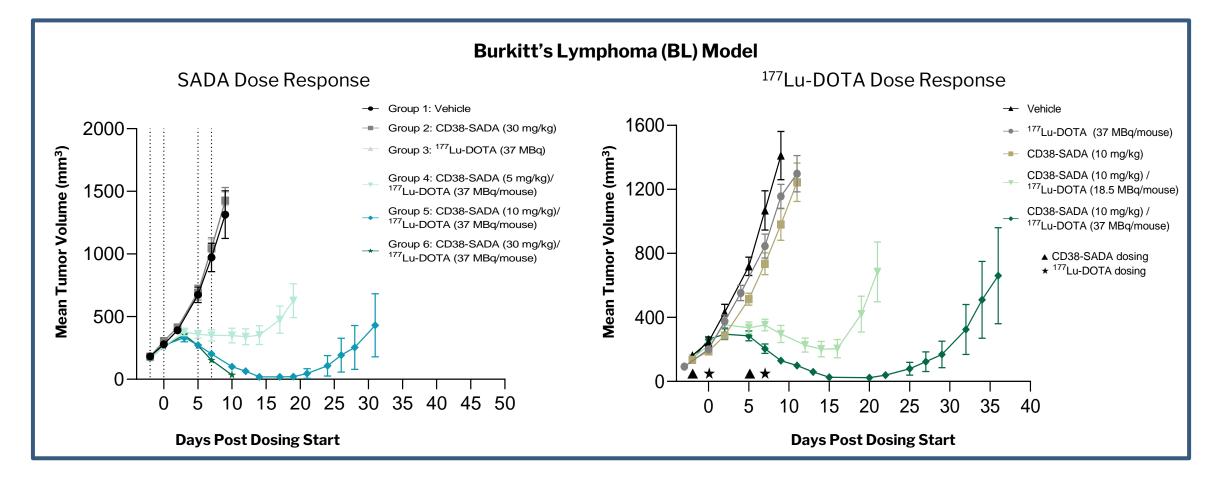


# **SADA PRIT Platform**

CD38-SADA Program in Circulating Tumors

## CD38-SADA Demonstrated Dose-dependent Anti-tumor Activity Against CD38-positive Tumors

Anti-Tumor Response of CD38-SADA (two preclinical models)

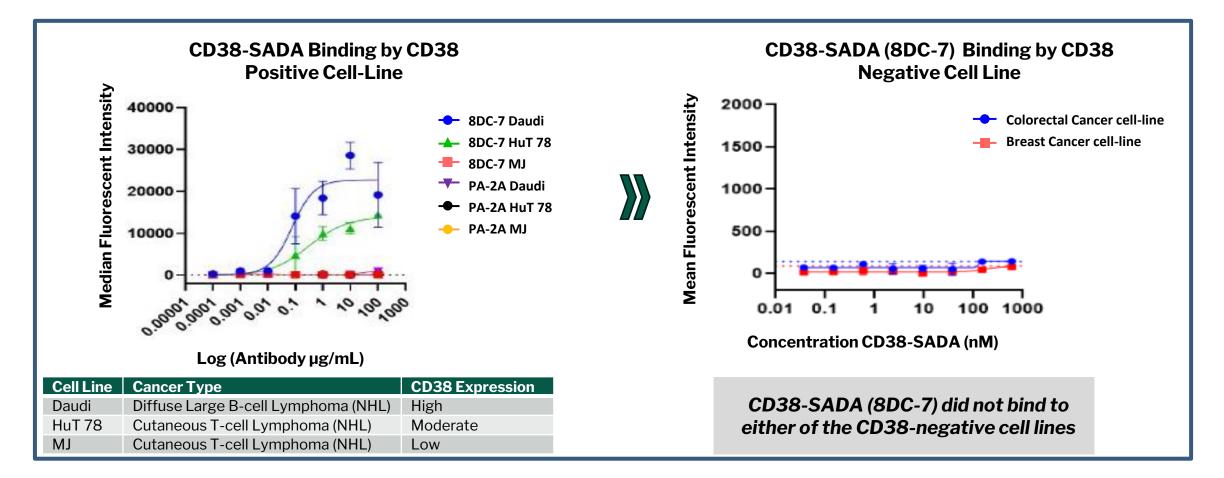


Santich, et al. CD38-SADA, a Self-Assembling and Dis-Assembling Bispecific Fusion Protein for Two-Step Pretargeted Radioimmunotherapy of Non-Hodgkin Lymphoma. Poster Presentation. American Society of Hematology. 5 November 2024. San Diego, California.



# CD38-SADA Binds Well to CD38-positive Cell-lines While Not Binding to Negative Cell-lines

Binding Characteristics of CD38-SADA in Preclinical Model



Santich, et al. CD38-SADA, a Self-Assembling and Dis-Assembling Bispecific Fusion Protein for Two-Step Pretargeted Radioimmunotherapy of Non-Hodgkin Lymphoma. Poster Presentation. American Society of Hematology. 5 November 2024. San Diego, California.



# CD38-SADA Phase 1 Clinical Trial (Trial 1201): Trial Design

Theragnostic approach using IHC validated CD38 positive tumors and <sup>177</sup>Lu-DOTA organ dosimetry before dosing in patients with relapsed or refractory non-Hodgkin Lymphoma

		Part A	Part B	
		N = 12 – 15	N = 12 – 15	
Inclusion Criteria				TRIAL UPDATE
R/R non-Hodgkin Lymphoma and ineligible/ exhausted standard therapeutic options	DESIGN	CD38-SADA dose- escalation with fixed imaging and therapeutic <sup>177</sup> Lu-DOTA doses	<sup>177</sup> Lu-DOTA therapeutic dose escalation with the CD38-SADA dose determined in Part A	<ul> <li>&gt; IND cleared by U.S. FDA in Q4 2023</li> <li>&gt; First 6 sites selected; 4 sites activated*</li> </ul>
Fluoro-deoxyglucose (FDG)-avid lymphoma with measurable disease				UPCOMING CATALYSTS
ECOG performance status score of 0, 1, or 2 CD38+ tumor	OUTCOME	Tumor imaging and occurrence of DLTs during evaluation period	Occurrence of DLTs during evaluation period	<ul> <li>Anticipate dosing the first patient in Q1 2025</li> </ul>

#### \*As of January 12, 2025



# Novel SADA PRIT Platform Potentially Provides Simplicity and Enhanced Precision for Physicians and Patients<sup>\*</sup>



#### Ongoing GD2-SADA Phase 1 Trial (Trial 1001)

- > Evidence of tumor uptake
- No DLTs observed to date
- Demonstrated PoC that GD2-SADA targets and binds to tumor in humans



#### CD38-SADA Phase 1 Trial

#### (Trial 1201)

- First-in-human trial in patients with R/R non-Hodgkin Lymphoma
- > Anticipate dosing first patient in Q1 2025



GD2-SADA Phase 1 Part A data, optimization data and new high-value targets expected to be presented in Q2 2025



Potential to shift radioimmunotherapy treatment paradigm for patients and physicians with simplicity and enhanced precision of novel SADA PRIT platform

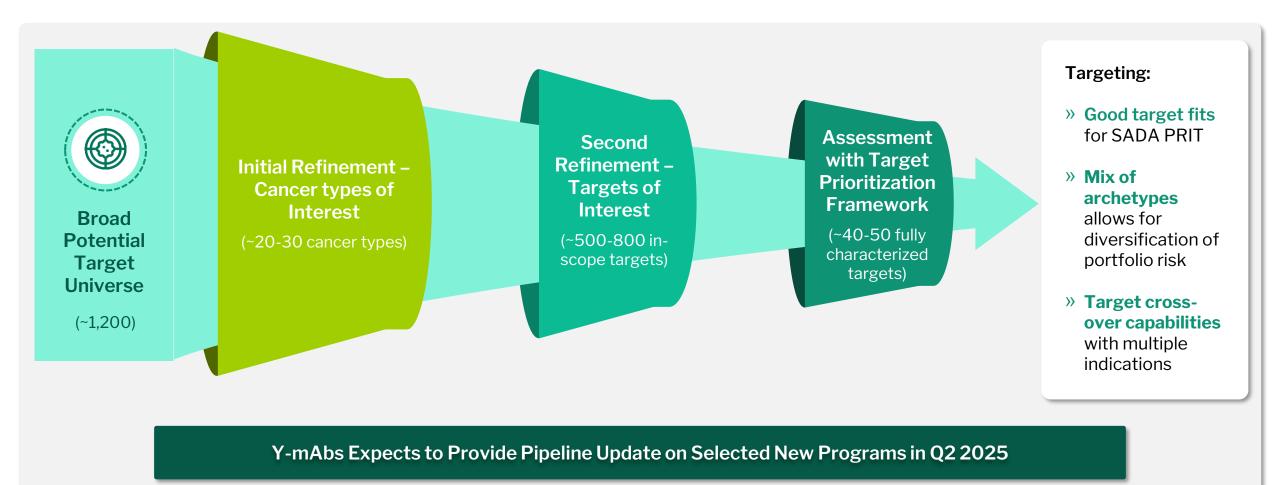
\*These early results are not complete and are not necessarily indicative of the full results or ultimate success of the SADA trials or the SADA development program which is in early development with no guaranty of approval





# Radiopharmaceutical Pipeline Expansion Plans

# Selection Process Potentially Leading to High-Value Targets for Future Development





# Y-mAbs' Comprehensive Radiopharmaceutical Target Identification Process

#### Next Cohort of Potential High-Value Oncology Targets for Development with SADA PRIT

#### Selection to determine suitability for targeting with SADA PRIT Platform in Mind

#### Key target considerations

- Clinical validation (especially via ADCs)
- Extracellular localization
- High tumor expression (ideally with applicability across tumor types)
- Low healthy tissue expression

#### Key commercial considerations

- Commercial landscape and competitive intensity
- Potential speed to PoC
- Organizational capabilities

Prioritized target archetypes for different development strategies

#### Good fit, good validation

Targets with ADC / RLT validation and niche commercial opportunity

#### **Novel target, high-value** Targets with less clinical validation and significant commercial opportunity

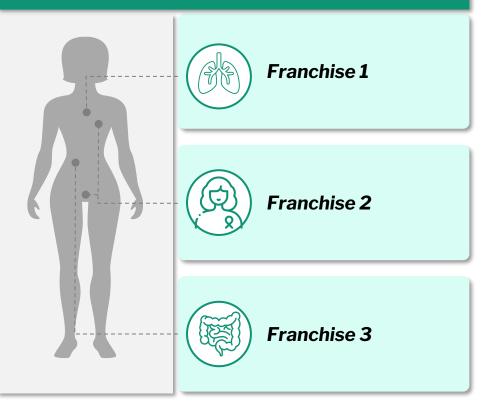
#### High-risk, high-reward

Targets with strong clinical validation but with a high degree of competition

#### Validation

Targets used as benchmarks against current RLTs

Targets are diversified across tumor types, but also offer vertical franchise opportunities









# **Commercial Progress**

DANYELZA® (naxitamab-gqgk)

GD2 Antibody for R/R High-Risk Neuroblastoma

# DANYELZA: Only FDA-Approved Medicine for R/R HR NB Patients

#### FDA Approval for R/R HR Neuroblastoma (NB)

- Differentiated therapy:
  - > Humanized antibody
  - Rapid infusion, modest toxicity
  - Administered in outpatient treatment setting
- U.S. addressable market:
  - > 2L NB: **300** patients
  - > 40% of NB patients are HR



#### Neuroblastoma

- NB forms in certain types of nerve tissue, most frequently starting from adrenal glands; can also develop in the neck, chest, abdomen or spine
- NB is the most common cancer in infants

#### Global Commercial Launch Performance

- Preliminary estimated unaudited FY 2024 net sales of approx. \$88.0 million\*
- **68 sites** across the U.S. have utilized DANYELZA\*\*
- Ex-U.S. commercial ramp progressing in China, Brazil and Mexico
- Strong demand through NPP in Europe and Turkey\*\*\*

#### Solid Drivers of Market Uptake

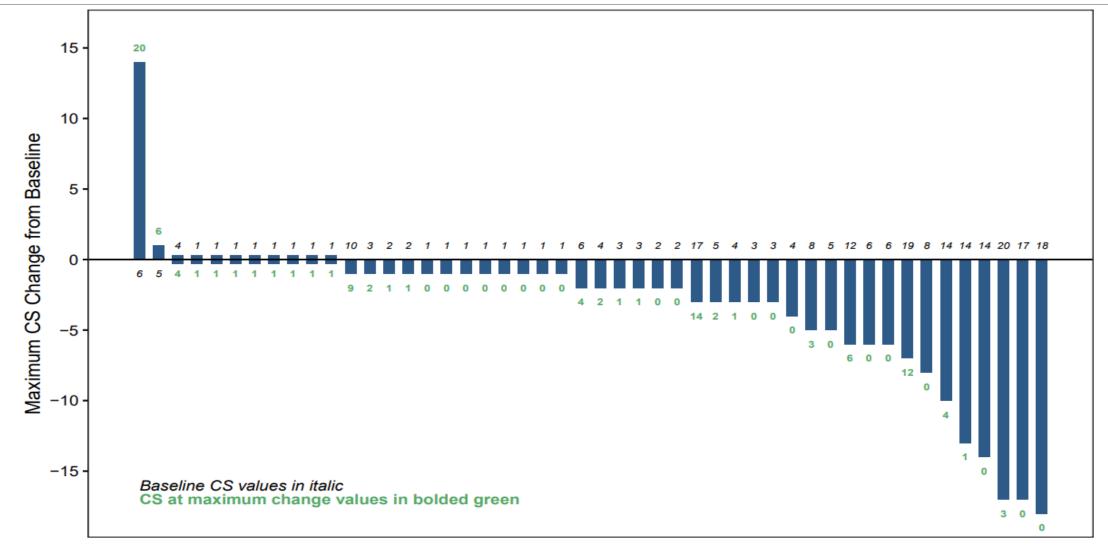
- DANYELZA added to 48
   hospital formularies since initial launch in 2021\*\*
- **113 HCPs** prescribed
   DANYELZA since launch<sup>+</sup>
- DANYELZA remains an important therapy in U.S. anti-GD2 market



This indication is approved under accelerated approval. Continued approval for this indication contingent upon verification and description of clinical benefit in a confirmatory trial(s).

\* Unaudited, as of January 12, 2025 \*\* As of November 8, 2024 \*\*\* Named Patient Program Preliminary results are unaudited and based on management's initial review of the Company's results as of and for the year ended December 31, 2024, and are subject to revision based upon the Company's year-end closing procedures and the completion of the audit by the Company's external auditors of the Company's December 31, 2024 financial statements.

### Pivotal Study 201 Data: Waterfall Plot of Change in Curie Score in <u>all</u> Relapsed/Refractory Patients with Bone Disease (n = 48)



# Ongoing and Potential New Studies for Naxitamab: Exploring Expansion of Usage in New Indications

Cancer Indications		Treatable Patient Population (U.S.)	GD2 Expression	2022 2023 2024 2025 2026		
High-Risk	Relapsed / Refractory	300	~ 99-100%	R/R HRNB Confirmatory Study 201*		
Neuroblastoma	Front-line Induction	450	00 100/0	1st line Induction1st line Induction RCTBCC-018 Phase 2BCC study		
<b>Osteosarcoma</b> Relapsed/Recurrent		200	~ 88%	Relapsed Osteosarcoma MSKCC Study 15-096 Pivotal RCT**		
<b>Soft-Tissue Sarcomas</b> Including Ewings		2,900 (1 <sup>st</sup> -line population)	> 90%	ISS – Ongoing Phase 2 (Ewings)		
<b>Breast Cancer</b> Triple Negative / Advanced		8,900 (2 <sup>nd</sup> line & 3 <sup>rd</sup> line +)	> 50%	ISS – Ongoing Phase 2		
<b>Melanoma</b> Newly Unresectable and Metastatic		11,400 (2 <sup>nd</sup> line & 3 <sup>rd</sup> line +)	> 50%	ISS – Area of Interest		

\* This indication is approved under accelerated approval. Continued approval for this indication contingent upon verification and description of clinical benefit in a confirmatory trial(s). \*\* Subject to data readout of MSKCC study 15-096.



# DANYELZA Addresses Significant Unmet Needs in R/R High-Risk NB with Expansion Potential Across Broader Patient Populations



- Studies 12-230 and 201 formed primary basis of approval in November 2020
  - > Reached 100 patients in Study 201



- Granted ODD and BTD
  - > Frontline study ongoing



- U.S. commercialization in HR RR NB
- > Expanding ex-U.S. reach
  - Commercially available in China through partner SciClone, LATAM partner Adium in Brazil and Mexico
  - > EU and Turkey access via WEP



- > Multiple potential advantages over other anti-GD2 therapies:
  - Modest toxicity
  - > Shorter infusion time
  - Ability to be administered in outpatient setting





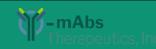
# Company Takeaways

## Advancing Focused Pipeline with Multiple Potential Value-Added Catalysts Ahead

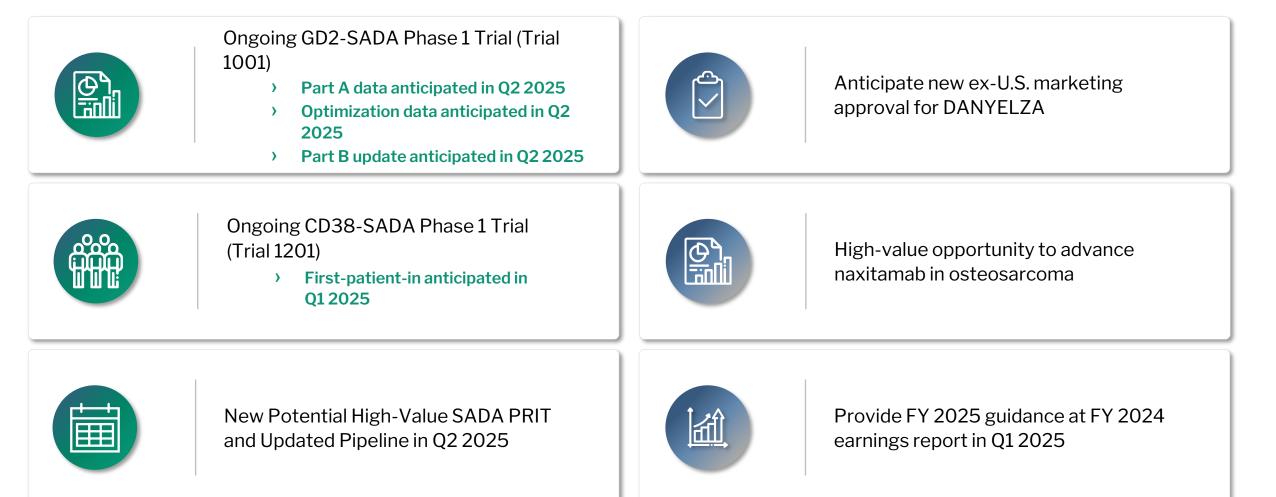
	Study Therapeutic Area		Preclinical	Phase 1	Phase 2/Pivotal	Approved	Trial Sponsor	Status
Lead Programs								
	201	Relapsed/Refractory High-Risk Neuroblastoma (Pediatric)	DANYELZA (naxitam	ab-gqgk) Confirm	natory Trial	$\checkmark$		U.S. FDA approved
	12-230	Relapsed/Refractory High-Risk Neuroblastoma (Pediatric)	DANYELZA (naxitam	ab-gqgk)		Ø	Memorial Sloan Kettering Cancer Center	U.S. FDA approved
	BCC018	Front-Line Induction in High-Risk Neuroblastoma (Pediatric)				1	Beat Childhood Cancer RESEARCH CONSORTIUM	Expect primary completion in 2026
Naxitamab-gqgk (Anti-GD2)	15-096	Relapsed Second-Line Osteosarcoma					Memorial Sloan Kettering Cancer Center	Potential pivotal trial
	17-251	Chemoimmunotherapy for Relapsed/ Refractory High-Risk Neuroblastoma					Memorial Sloan Kettering Cancer Center	Study completed
	Butterfly	Refractory Ewing's Sarcoma					Institute of Mother and Child	Expect completion in 2028
		Metastatic Breast Cancer				(	THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER	Trial initiated in Q2 2024
<b>SADA PRIT</b> (Radioimmunotherapy)	1001	GD2-SADA: Solid Tumors (SCLC, Malignant Melanoma, Sarcoma)						Ongoing Part A
	1201	CD38-SADA: Non-Hodgkin Lymphoma						Expect FPI in Q1 2025



#### Potential High-Value SADA PRIT Targets and Pipeline to be Presented in Q2 2025



## Anticipated 2025 Milestones





# Growing Base Business with Potential High Value RIT Platform

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Deep bench of industry leadership and expertise in developing and commercializing radiopharmaceutical oncology therapeutics

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# THANK YOU