

# Iomab-ACT Commercial CAR-T Trial

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## KOL Webinar

May 20, 2024

ATNM: NYSE AMERICAN

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# Today's Speakers & Agenda

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**Sandesh Seth**  
Chairman & CEO

Opening  
& Closing Remarks



**Dr. Madhuri Vusirikala**  
VP, Clinical Development  
Transplant & Cell  
Therapy

Iomab-ACT: Next  
Generation Cell  
Therapy Conditioning



**Dr. Farrukh Awan**  
Professor, Internal  
Medicine, UTSW

Iomab-ACT: Phase  
1B/2 Commercial CAR-  
T Trial



# Opening Remarks

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# Executive Summary

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- Actinium is pleased to invite **Dr. Farrukh Awan**, Professor of Internal Medicine - Division of Hematology Oncology at University of Texas Southwestern (UTSW), for today's KOL webinar:
  - Dr. Awan specializes in the treatment of patients with **leukemia and lymphoma including CAR-T therapy and bone marrow transplantation**; Dr. Awan will serve as principal investigator for this study that is led by UTSW
  - KOL webinar to highlight recently announced lomab-ACT trial with leading FDA-approved commercial CAR-T cell therapy
- Actinium has wide-ranging experience, differentiated radiotherapeutic programs, robust intellectual property portfolio, and critical know-how to anchor our vision of building a specialty radiotherapeutics company focused on targeted conditioning and hematological malignancies
- lomab-ACT program is a next generation conditioning program for rapidly growing CAR-T therapies with the potential to improve overall access and outcomes for patients who need these therapies:
  - lomab-ACT triggers targeted depletion of CD45+ cells in overcoming limitations of flu/cy conditioning; lomab-ACT is expected to address critical unmet needs related to CAR-T toxicities and CAR-T durability and persistence
  - Validity of approach is supported by an ongoing MSKCC NIH trial demonstrating lower rates of CRS and ICANS toxicities following lomab-ACT conditioning; an improved conditioning agent could bring CAR-T therapies to more patients in need
- Expansion of the lomab-ACT program into this current trial, which if successful will enable a pivotal trial, and open up a potential billion-dollar market in lymphodepletion for commercial CAR-Ts
- We look forward to an engaging and productive webinar

# Innovation Focused R&D Yields Differentiated, High-Value Programs

## Robust Experience Across Multiple Validated Cancer Targets & Isotopes

**CD45**  
Leukemia, Lymphoma  
and immune cells

**CD33**  
AML, MDS  
and MM

**Undisclosed**  
Solid tumor  
theranostics

**CD38**  
MM and leukemia  
cells


**ICI**  
Solid tumors and  
blood cancers


**Iodine-131**  
Range: 2.3 mm  
Energy: 0.6 MeV

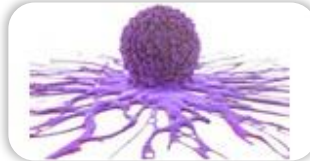
**Actinium-225**  
Range: .048 mm  
Energy: 24 MeV

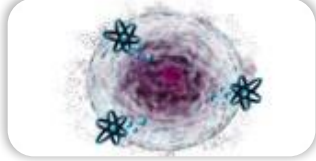
**Lutetium-177**  
Range: 1.8 mm  
Energy: 0.50 MeV

## Broad Areas of Focus Leveraging Significant Clinical Development Experience

**Hematology**  


**Targeted Conditioning**  


**Solid Tumors**  


**Next-Generation Radiotherapies**  




## Strong, Growing IP Portfolio of 230+ Patents

**Iomab-ACT's IP**

**Composition of Matter/ Formulation**


**Methods of Use**

**GRANTED PATENTS**





**EXPIRATION**






**2037**



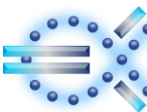
**2040**  
*(For gene-edited HSCs)*

**PENDING APPLICATIONS**





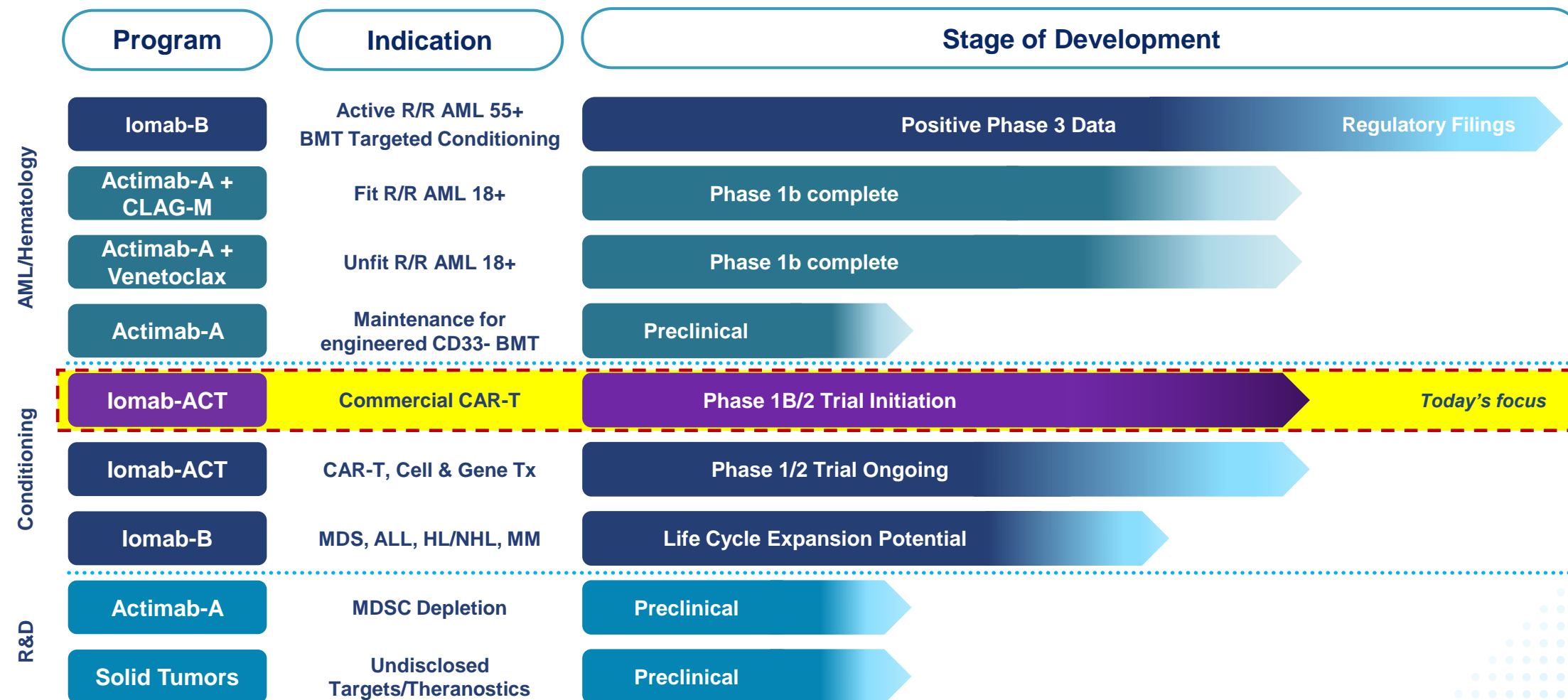
✓ **Multiple Patent Families Ensure Robust IP Protection**

**Actinium  
Pharmaceuticals, Inc.**

ICI: Immune checkpoint Inhibitors  
Actinium-225 linear energy transfer includes daughter emissions

6

# Pipeline: Transformative Potential in AML, Cell & Gene and Solid Tumors

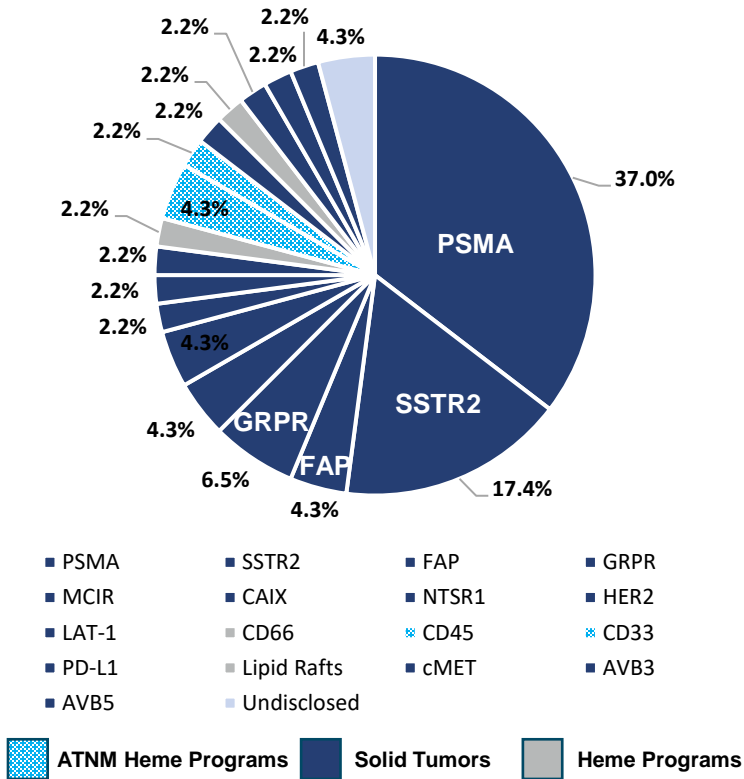




# Actinium: Differentiated by Late-Stage, Hematology-Focused Programs

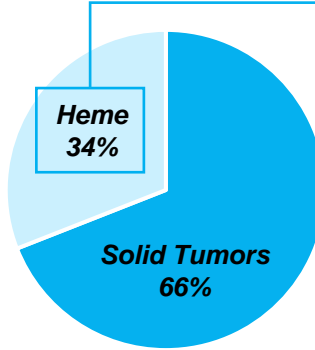
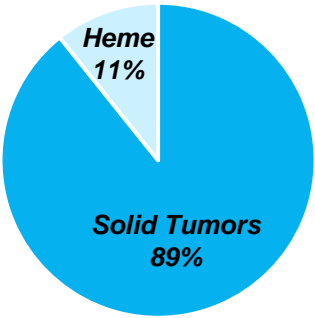
90% of the radiopharma industry pipeline focused on solid tumors, ~65% concentrated on 4 targets

4 of the top 10 cancer drugs are for hematology indications



2024 Expected Cancer Incidences<sup>2</sup>

Percentage of 2023 Global oncology drug sales<sup>2</sup>



Drug	2023 (\$USD,B) <sup>2</sup>
Keytruda®	25.012
Darzalex®	9.744
Opdivo®	9.009
Revlimid®	6.097
Tagrisso®	5.799
Ibrance®	4.753
Perjeta®	3.768
Tecentriq®	3.76
Imbruvica®	3.60
Pomalyst®	3.441



# Iomab-ACT's Strong Value Proposition for CAR-T Conditioning

Unprecedented opportunity to shift outcomes in cell and gene therapy conditioning and access existing patient in the multi-billion-dollar CAR-T markets with Iomab-ACT program



## Novel Radiotherapeutic Applications

Iomab-ACT represents the first radiotherapy for targeted cell and gene therapy conditioning



## Strong Scientific Rationale

Strong scientific pedigree and significant support for CD45 target for conditioning



## Deep Clinical Experience

Clinical data from MSKCC NIH trial supports advancement to commercial CAR-Ts



## Pathway to Large Markets

UTSW trial creates pathway to pivotal trial, which if successful, can open up a large addressable market opportunity with existing commercial CAR-Ts



# Iomab-ACT: Next-Generation Cell Therapy Conditioning

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# Dr. Madhuri Vusirikala, VP, Clinical Development BMT & Cell Therapy



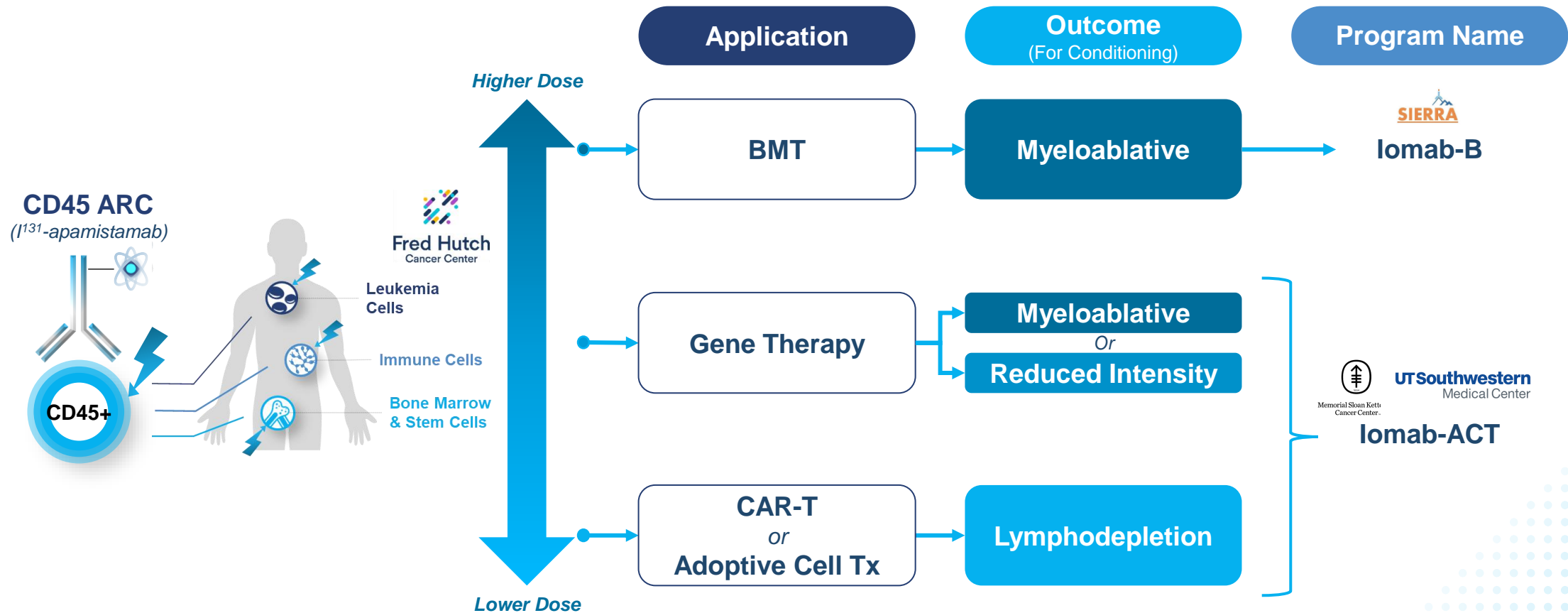
**UT Southwestern**  
Medical Center



- Joined Actinium in October 2022 as Vice President, Clinical Development, Transplant & Cellular Therapy
- Over 20 years of clinical experience specializing in adult allogeneic bone marrow transplant
- Most recently, Director of the Allogeneic Stem Cell Transplant Program at University of Texas – Southwestern (UTSW) and Professor of Medicine in the Division of Hematology and Oncology
- Served on several national committees including the National Comprehensive Cancer Network (NCCN) panels for Hematopoietic Stem Cell Transplantation and Acute Lymphoblastic Leukemia, BMT Infonet, and the MDS/Aplastic Anemia Foundation
- Fellowship in Bone Marrow Transplant at Vanderbilt University
- Fellowship in Hematology-Oncology at the University of Pittsburgh
- Residency at SUNY Syracuse
- Medical Training at Lady Hardinge College (India)

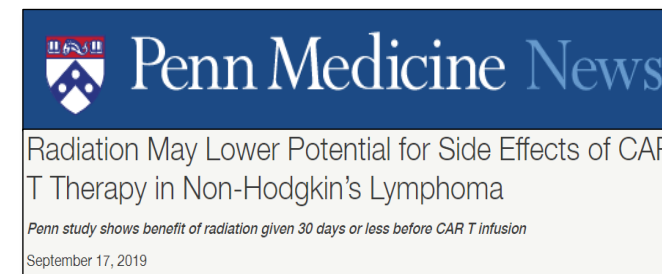
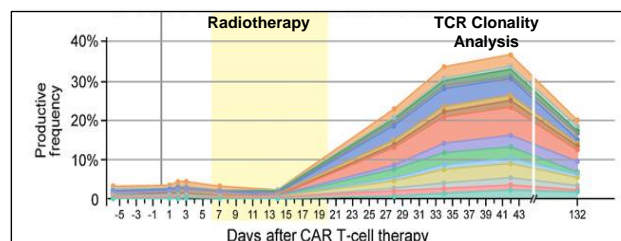
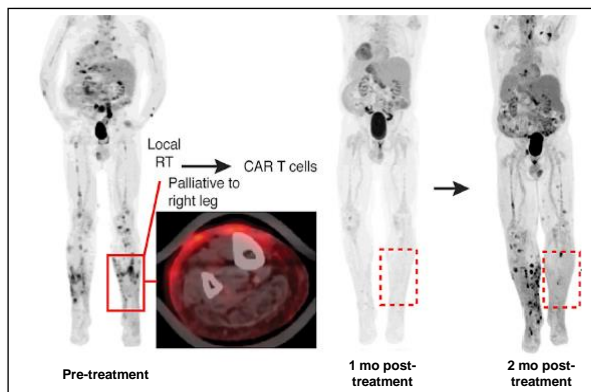
# Multiple Applications with Actinium's CD45 ARC Conditioning

CD45 ARC is the only clinical-stage targeted conditioning program with applications in bone marrow transplant, gene therapy, CAR-T, and other adoptive cell therapies



# Strong Rationale for Combining Radiotherapy with CAR-T Therapies

Radiotherapy can be leveraged to safely and effectively improve CAR-T patient outcomes



Radiation **sensitizes** tumor cells to TRAIL-dependent killing by CAR-T and improves durability of tumor clearance<sup>1</sup>



Radiotherapy combined with BCMA-CAR-T resulted in **expansion** of TCR repertoire and **abscopal effect**<sup>2</sup>

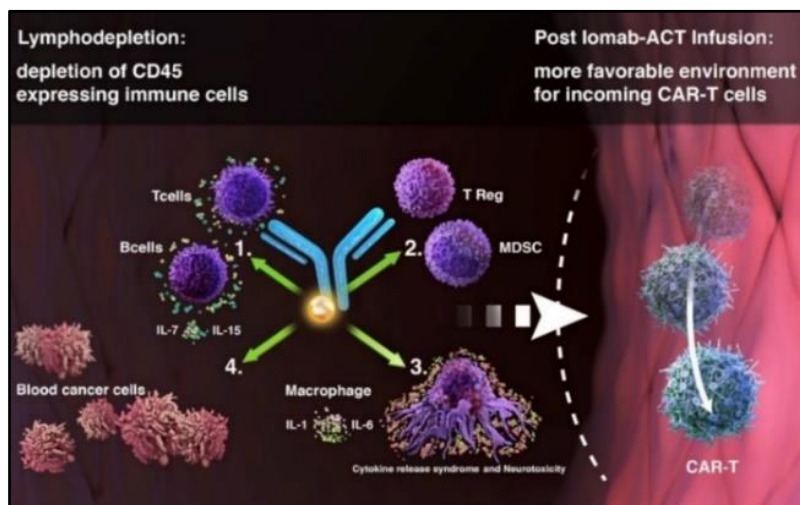


Patients receiving radiation prior to CAR-T experience **lower rates of CRS** and **neuro-toxicities**<sup>3</sup>

# Actinium's Iomab-ACT as a Lymphodepleting Agent for CAR-T

Iomab-ACT can potentially improve overall response to CAR-T cell therapy by promoting cell expansion, enhancing persistence and reducing side effects through targeted CD45 depletion

## Mechanism of Action:



## CD45+ Immune Cells Ablated:

1

### Lymphocytes

Iomab-ACT can reduce lymphocyte cytokine sinks creating a receptive immune microenvironment<sup>2</sup>

2

### T<sub>reg</sub> cells and MDSCs

Iomab-ACT can deplete immunosuppressive cells that promote a hostile tumor microenvironment against CAR-Ts<sup>3,4</sup>

3

### Blood cancer cells

Iomab-ACT targets CD45 found on leukemia and lymphoma

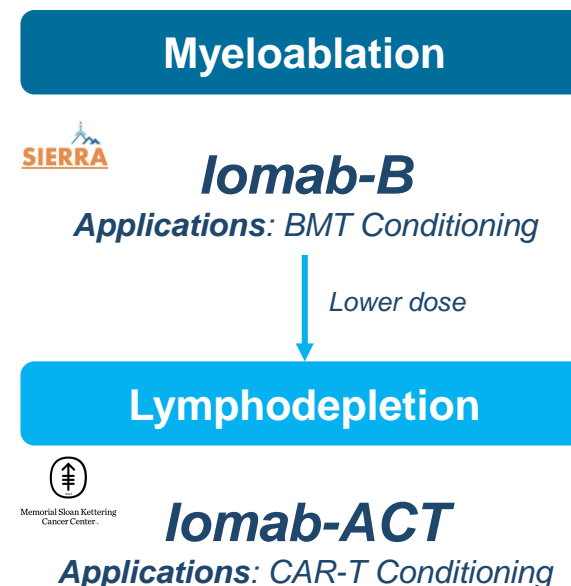
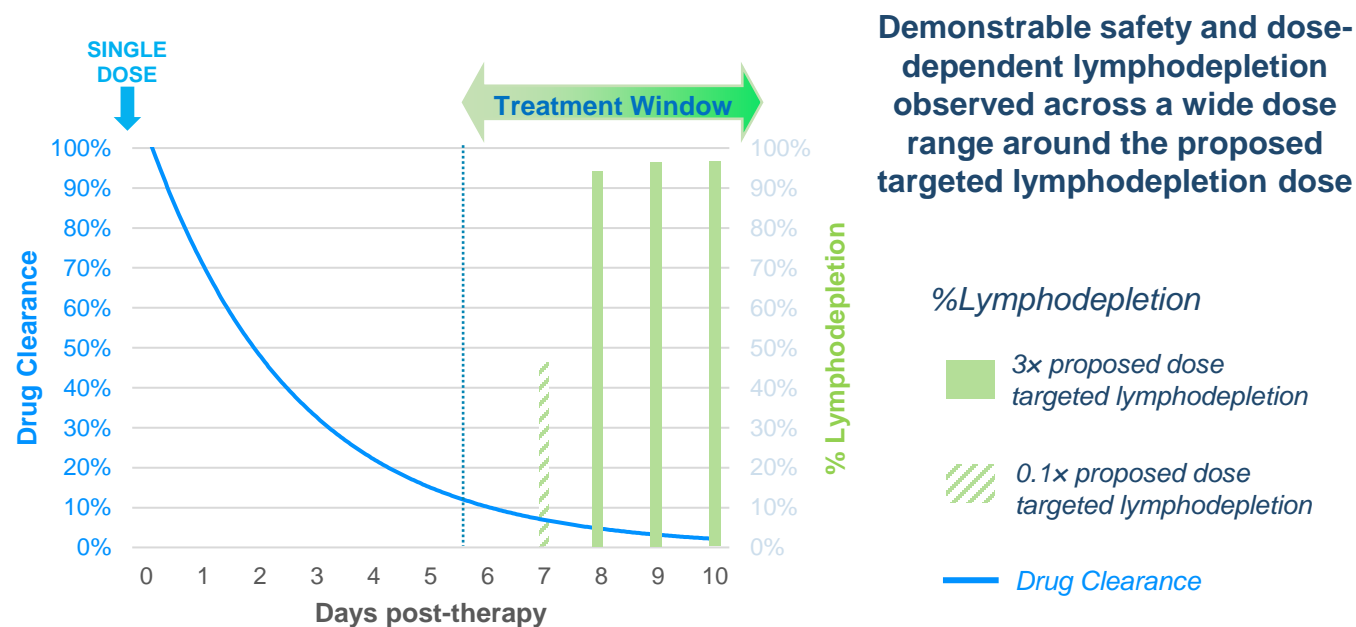
4

### Macrophages

Iomab-ACT can reduce incidences of CRS through depletion of cells that release proinflammatory IL-6 and IL-1<sup>5</sup>

# Single Dose Iomab-ACT Lymphodepletion and Clearance for CAR-T

Favorable pharmacokinetics and effective lymphodepletion observed with Actinium's targeted lymphodepleting technology which can be optimized for use with CAR-T



✓ Actinium believes a low dose of targeted lymphodepletion with Iomab-ACT represents a promising strategy to achieve safe and transient lymphodepletion prior to CAR-T

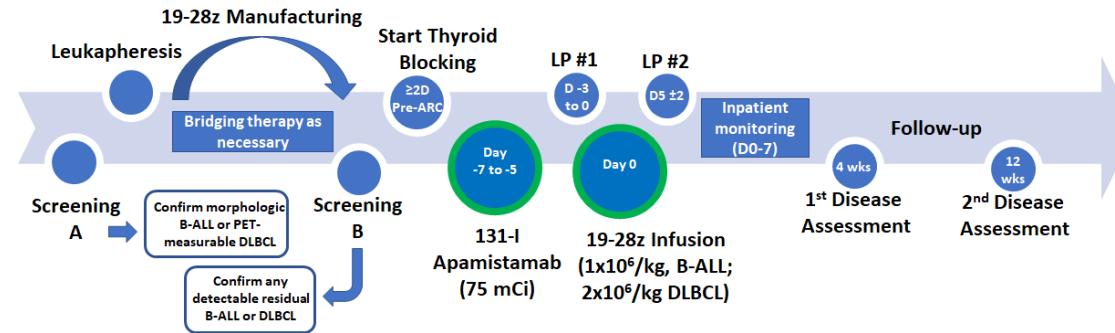


# A Pilot Clinical Study of Iomab-ACT Prior to CAR-T Therapy

Iomab-ACT lymphodepletion results in a favorable safety profile for patients receiving CAR-T therapies



Design



Disclosed  
Results

Pt ID	Sex/Age (y) at Treatment	Malignancy	Prior AlloHCT	Prior CAR-T	Max Grade CRS	Max Grade ICANS	DLT	Protocol-Defined Response
1	F/34	R/R B-ALL	Y, x2	N	0	0	N	No response
2	M/51	R/R DLBCL (RS)	Y, x1	Y, x2	0	0	Y	CR
3	F/69	R/R DLBCL	N	Y, x1	1	0	N	POD
4	M/42	R/R DLBCL (RS)	N	N	0	0	Eval Ongoing	CR



Safety

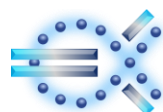
✓ **Favorable safety profile** with no Gr 3.+ incidences of CRS and ICANS; **only Gr 1.**



Efficacy

✓ **N=2 (50%) patients achieved CR**, with N=1 DLT observed (myelosuppression)

*Heavily pretreated patients display minimal levels of CRS or ICANS*



Actinium  
Pharmaceuticals, Inc.

Source: [ClinicalTrials.gov, Abstract #216](#) – Tandem Meetings Transplantation and Cellular Therapy of ASTCT and CIBMTR; AlloHCT – Allogeneic Hematopoietic Stem Cell Transplant; CRS – Cytokine Release Syndrome; ICANS – Immune Cell-Associated Neurotoxicity Syndrome; DLT – Dose Limiting Toxicities; MDSC – Myeloid Derived Suppressor Cell; R/R DLBCL – Relapse/Refractory Diffuse Large B-Cell Lymphoma

# Iomab-ACT has Clear Use as a CAR-T Conditioning Agent



✓ Selective targeting of immune cells implicated in CRS and ICANS



✓ Combat tumor microenvironment and reduce tumor burden



✓ Favorable pharmacokinetics with flexibility to optimize lymphodepletion



✓ Ease of administration with a single dose at an outpatient setting



✓ Expansion of patient access with a targeted and safe profile



✓ Technology primed for collaboration with commercial CAR-T products

# Iomab-ACT: Phase 1B/2 Commercial CAR-T Trial

Farrukh Awan, MD – Professor of Internal Medicine – UTSW Medical Center



# Farrukh Awan, MD

Professor of Internal Medicine – UTSW Medical Center



**UTSouthwestern**  
Medical Center



- Joined the UT Southwestern faculty in 2018 with over 20 years of clinical experience specializing in stem cell transplant, cellular therapies and evaluation of novel therapies for the treatment of patients with lymphoid malignancies and chronic lymphocytic leukemias
- Member of the Division of Hematology and Oncology at UTSW's Harold C. Simmons Comprehensive Cancer Center where he serves as the Clinical Director of the Section of Hematologic Malignancies, Transplantation and Cellular Therapies
- Certified by the American Board of Internal Medicine, the American Board of Medical Oncology, and the American Board of Hematology
- Member of several professional organizations, including the American Medical Association, the American Society of Clinical Oncology, and the American Society of Hematology
- Fellowship - Ohio State University Hospital, Hematology Oncology
- Residency - University of Pittsburgh Medical Center, Internal Medicine
- Medical Training - University of Pittsburgh Graduate School of Public Health
- Medical Training - Aga Khan University (Pakistan)



# Setting the Standard for Commercial CAR-T Therapy

UT Southwestern Medical Center has been at the forefront in the delivery of CAR-Ts for its patients



## Hundreds of Commercial CAR-T Procedures Conducted

▶ **~570-600 new lymphoma** cases annually; Annual growth rate of ~15%

▶ **Successful administration of 250+ CAR-T** procedures over the last 5 years

▶ **~70-90 CAR-T procedures** conducted at center/year; ~95% CAR-T procedures for myeloma or lymphomas

## UT Southwestern Medical Center



## Experienced Use of Commercial CAR-Ts

▶ Commercial CAR-T treatments **started from 2018**

▶ **Consistent manufacturing and accessibility** of commercial CD19 CAR-Ts from center experience

▶ Authorized treatment center for all currently **approved CAR-T products**

# UT Southwestern – Innovative Leader in CAR-T Cell Therapy

Experience with various CAR-T products and clinical trials underscores commitment to changing outcomes for patients



## Multiple CAR-T Products Delivered to Patients

*Non-exhaustive*



## Deep CAR-T Clinical Experience

✓ First CAR-T clinical trials **initiated in 2017**

✓ **Active trial engagement** of CAR-T products for solid tumors and non-malignant conditions

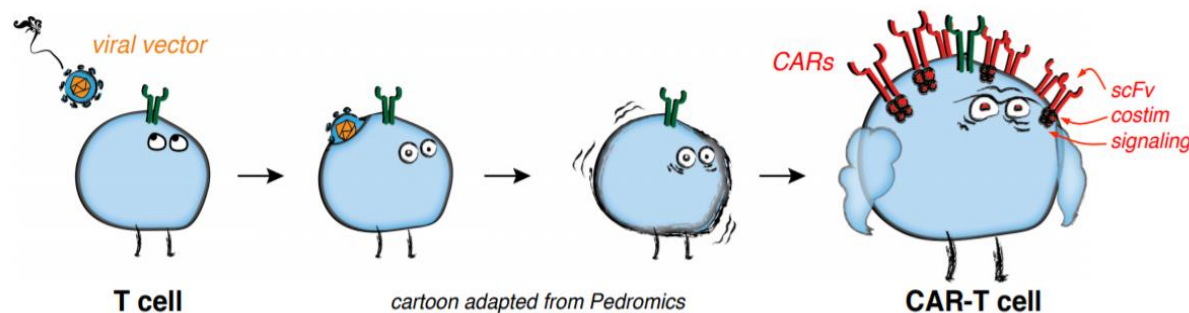
✓ **Lead accruing site** for important CAR-T trials including KarMMA and CARBON trials

# CAR-T Cell Therapy – Groundbreaking Cancer Immunotherapies

Landmark cellular therapies that have changed outcomes in various hematological malignancies



## Overview



Patient's T-cells extracted, engineered to display **Chimeric Antigen Receptor (CAR)** to target tumor antigens, re-administered to patients, and eliminate tumor cells

## Approved Indications:

**Acute Lymphoblastic Leukemia**

**Non-Hodgkin's Lymphoma**  
(e.g., DLBCL, Follicular, Mantle Cell)

**Multiple Myeloma**

## FDA-Approved CAR-T Products

### CD19 Targeted:

**YESCARTA**<sup>®</sup>  
(axicabtagene ciloleucel) Suspension for IV infusion  
First Approved: 2017

**KYMRIAH**<sup>®</sup>  
(tisagenlecleucel) Suspension for IV infusion  
First Approved: 2017

**TECARTUS**<sup>®</sup>  
(brexucabtagene autoleucel) Suspension for IV infusion  
First Approved: 2021

**Breyanzi**<sup>™</sup>  
(lisocabtagene maraleucel) Suspension for IV infusion  
First Approved: 2021

### BCMA Targeted:

**Abecma**<sup>™</sup>  
(idecabtagene vicleucel) Suspension for IV infusion  
First Approved: 2021

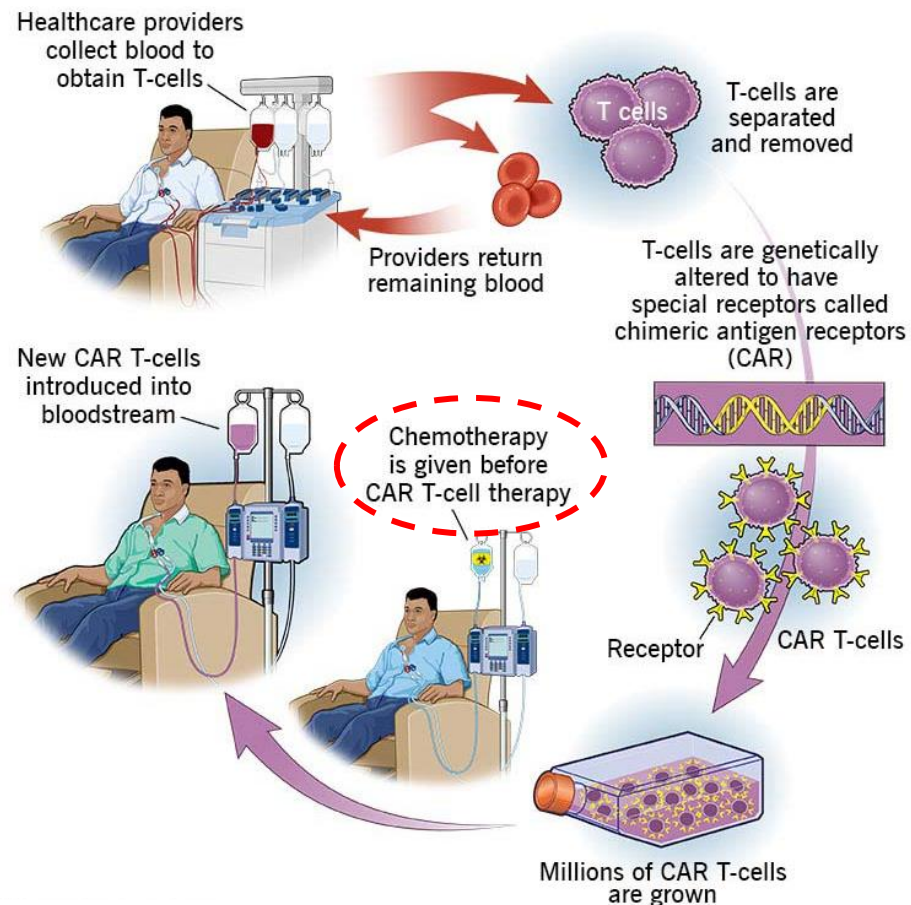
**CARVYKTI**<sup>™</sup>  
(ciltacabtagene autoleucel) Suspension for IV infusion  
First Approved: 2022



# Lymphodepletion Critical to Ensure Successful CAR-T Outcomes

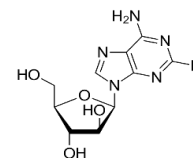


## CAR-T Typical Patient Journey

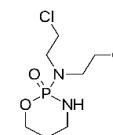


## Principles of Lymphodepletion

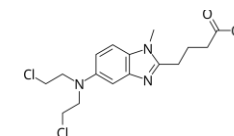
### Typical Agents



Fludarabine (Flu)



Cyclophosphamide (Cy)



Bendamustine

- **Reduce endogenous lymphocytes** to prepare a niche for engraftment of CAR-T infusions and to support their long-term activity
- **Ablate tumor cells** to avoid exhaustion of CAR-T
- **Prepare and reprogram microenvironment** and soluble factors to ensure optimal engraftment, homing and survival of CAR-T

# Standard Flu/Cy Lymphodepletion Chemotherapy is Not Ideal

Multiple critical unmet needs exist with the current lymphodepletion (e.g., flu/cy) practices



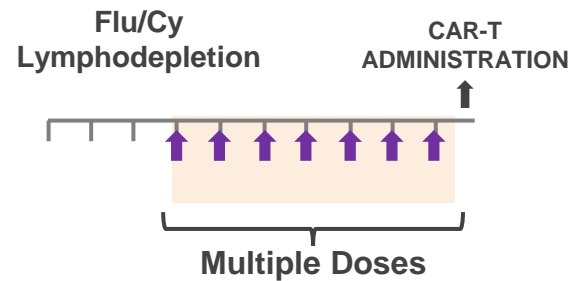
<b>Effectiveness</b>	<ul style="list-style-type: none"><li>• Flu/Cy is toxic, and not fully optimized for CAR-T programs</li></ul>
<b>Safety</b>	<ul style="list-style-type: none"><li>• Fatal toxicities such as CRS and ICANS remain significant with current lymphodepleting regimens; Multi-variable analysis identified Flu/Cy lymphodepletion prior to CAR-T as a risk factor for CRS, a major adverse event related to CAR-T therapy.<sup>1</sup></li><li>• The severity of CRS is related to the Flu/Cy administered and the dose of CAR-T cells.<sup>1</sup></li></ul>
<b>Pharmacoeconomics</b>	<ul style="list-style-type: none"><li>• Flu/Cy may contribute to CRS-related treatment costs associated with CAR-T</li></ul>
<b>Patient Convenience</b>	<ul style="list-style-type: none"><li>• Flu/Cy requires multiple administrations prior to CAR-T infusion</li></ul>
<b>Improved Utilization</b>	<ul style="list-style-type: none"><li>• Oncologists surveyed indicate that the toxicity profile of Flu/Cy + CAR-T is concerning and might limit the number of patients they would refer to treatment<sup>2</sup></li></ul>
<b>Intellectual Property</b>	<ul style="list-style-type: none"><li>• Patent US9855298 covering use of Flu/Cy as lymphodepletion therapy in preparation for CAR-T administration can impair freedom to operate</li></ul>
<b>Patient Access</b>	<ul style="list-style-type: none"><li>• Non-specific Flu/Cy lymphodepletion restricts access to a relatively robust patient population</li></ul>

# Advantages of Iomab-ACT Lymphodepletion

Iomab-ACT conditioning offers a potentially more targeted profile, enhanced outcomes, and improved convenience



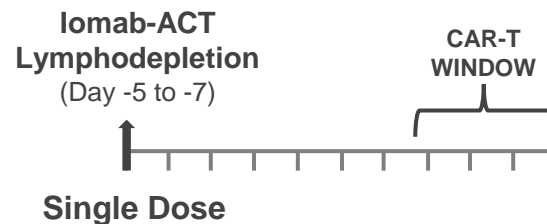
## Administration



## Limitations of Flu/Cy

- Multiple administrations needed
- Non-targeted chemotherapy engenders off-target Toxicities
- Doses and scheduling for lymphodepletion not well optimized for CAR-T
- Flu/Cy patents may limit optimization or use
- Identified as a risk factor for Cytokine Release Syndrome
- Limited patient access; not all patients may tolerate or respond to chemotherapy

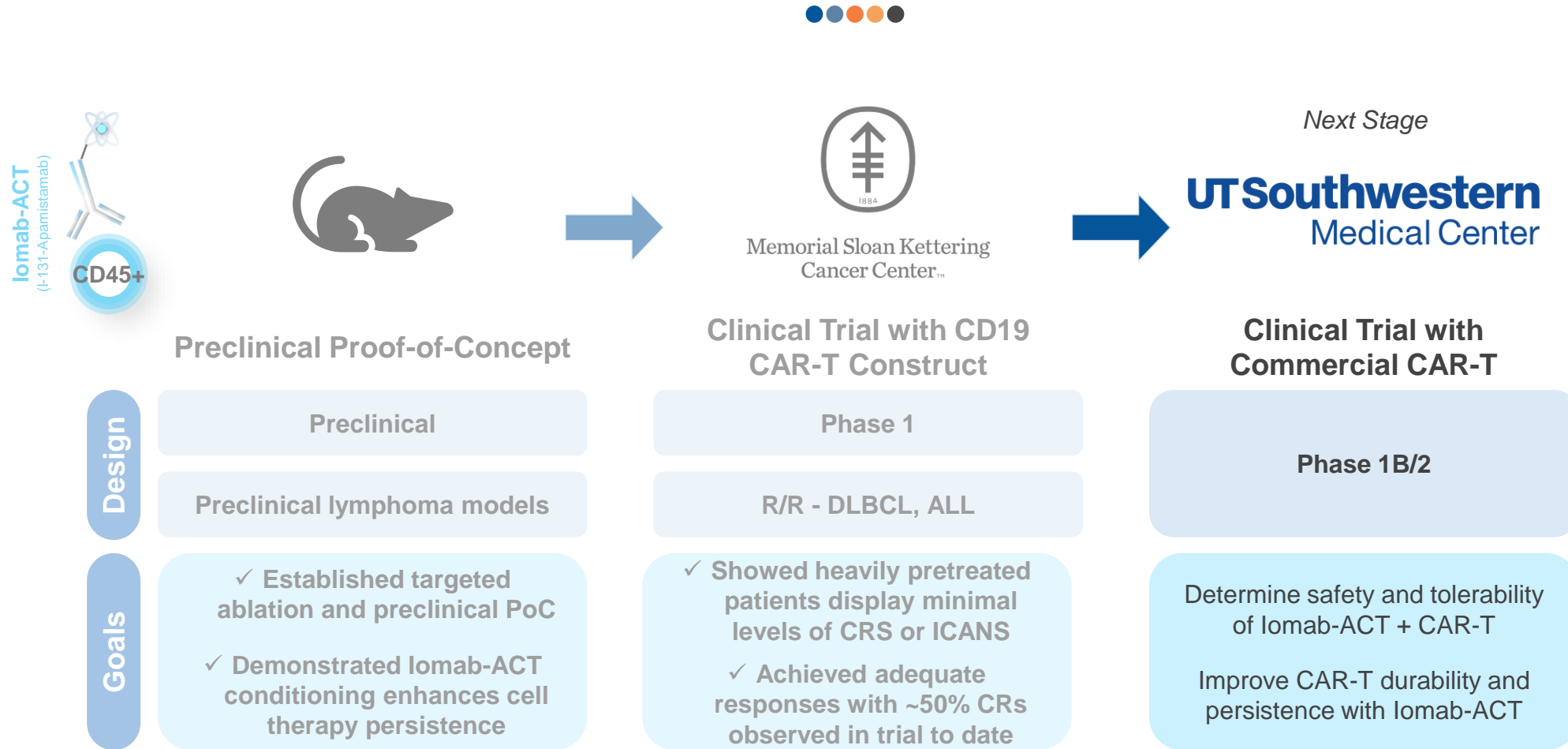
## Advantages of Iomab-ACT



- Single dose, outpatient administration
- Favorable pharmacokinetics; flexibility to optimize lymphodepletion step
- Selectively targets immune cells, including those implicated in CRS
- Potential for improved outcomes and reduced tumor burden
- Patient access expansion with a targeted, good safety profile

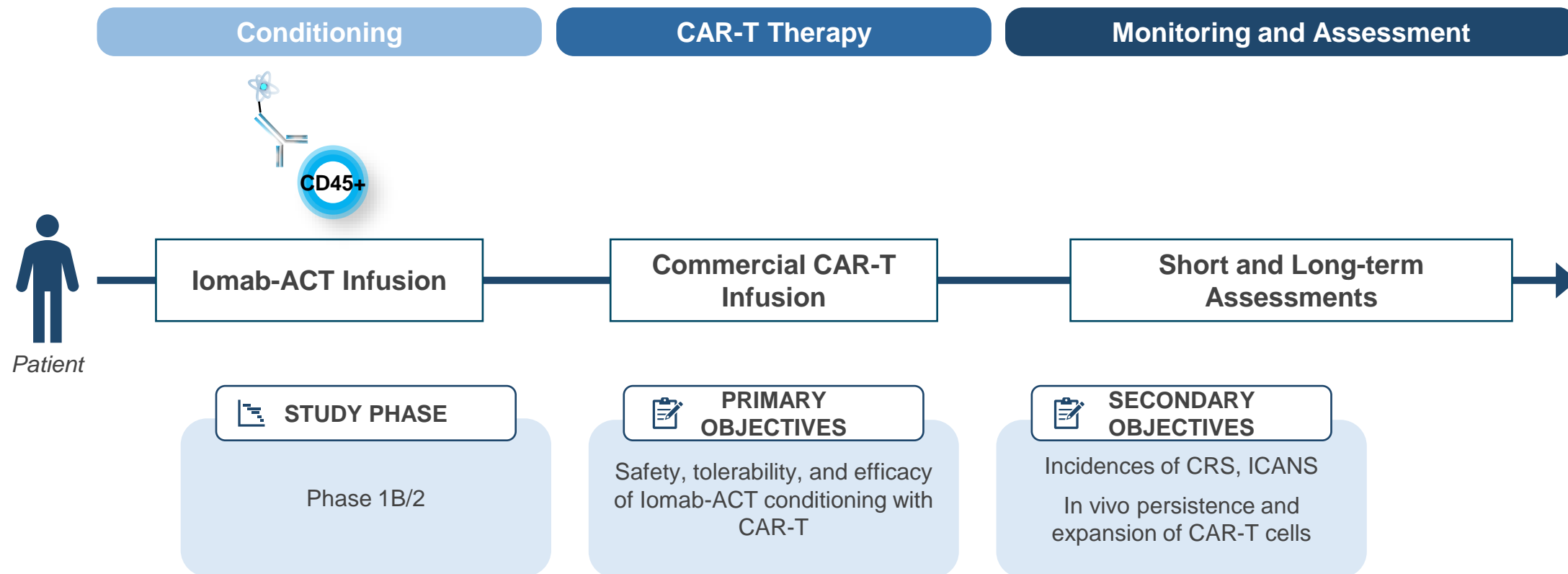
# Strong Rationale for Conditioning with Commercial CAR-T

Iomab-ACT experience to date is indicative that benefits of conditioning will translate into commercial CAR-T setting



# Study Design – Phase 1B/2 Commercial CAR-T study at UTSW

In a single-arm study, patients will receive lomab-ACT as a lymphodepletion regimen prior to commercial CAR-T infusion



For competitive reasons, Actinium will disclose lomab-ACT dose and CAR-T product by study readout

# Multiple Goals to Shift Paradigm for Commercial CAR-T Conditioning



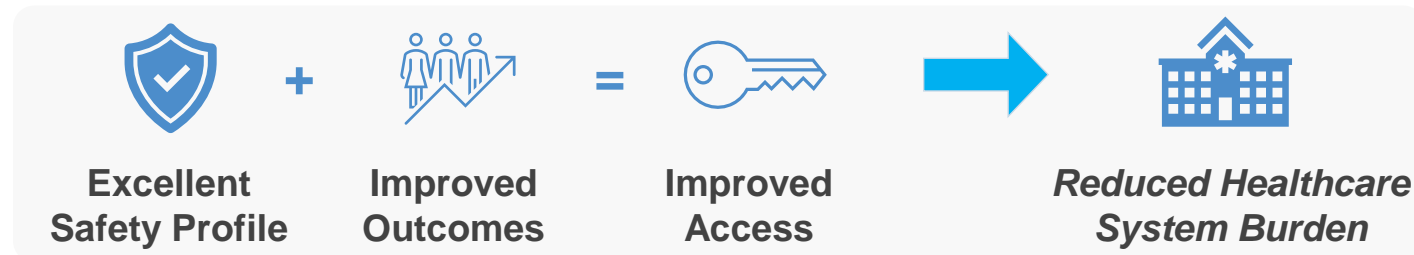
## Ensuring Safety

- ✓ **Reduce incidences of CRS and ICANS** with commercially available CAR-Ts
- ✓ **Mitigate myelosuppression** seen in CAR-Ts
- ✓ Expand patient eligibility and **enable more patients** to be treated by curative therapy



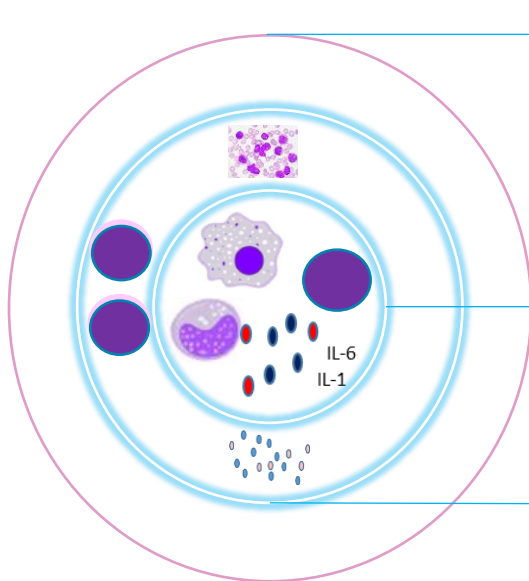
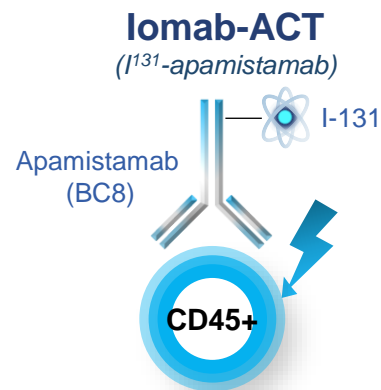
## Advancing Outcomes

- ✓ **Ensure long-term** durability and persistence of commercial CAR-T products
- ✓ **Decrease incidences** of post CAR-T cancer relapse and reduce burden upon patients
- ✓ **Minimize treatment related mortality** associated with standard of care lymphodepletion



# Iomab-ACT's Value Proposition to the CAR-T Paradigm

Using a proven modality to achieve optimized lymphodepletion to increase efficacy, reduce toxicities and expand access of CAR-T



## Depletes lymphocytes and reduces tumor burden

- Potentially lowers risk for CRS/Neurotoxicities
- CAR-T cells have greater ability to expand, resulting in potential for more efficacy
- Potential to increase CAR-T dose to improve responses and their duration

## Optimizes tumor microenvironment

- Depletes cells that exert negative effects on CAR-T
- Depletes macrophages lowering cytokines linked to CRS/NT

## Selective and Specific Targeting

- Stronger patient implies potentially greater access and or improved outcomes with CAR-Ts

✓ Targeted

✓ Single Dose

✓ Out-Patient

✓ Improved  
Outcomes

✓ Expanded  
Access



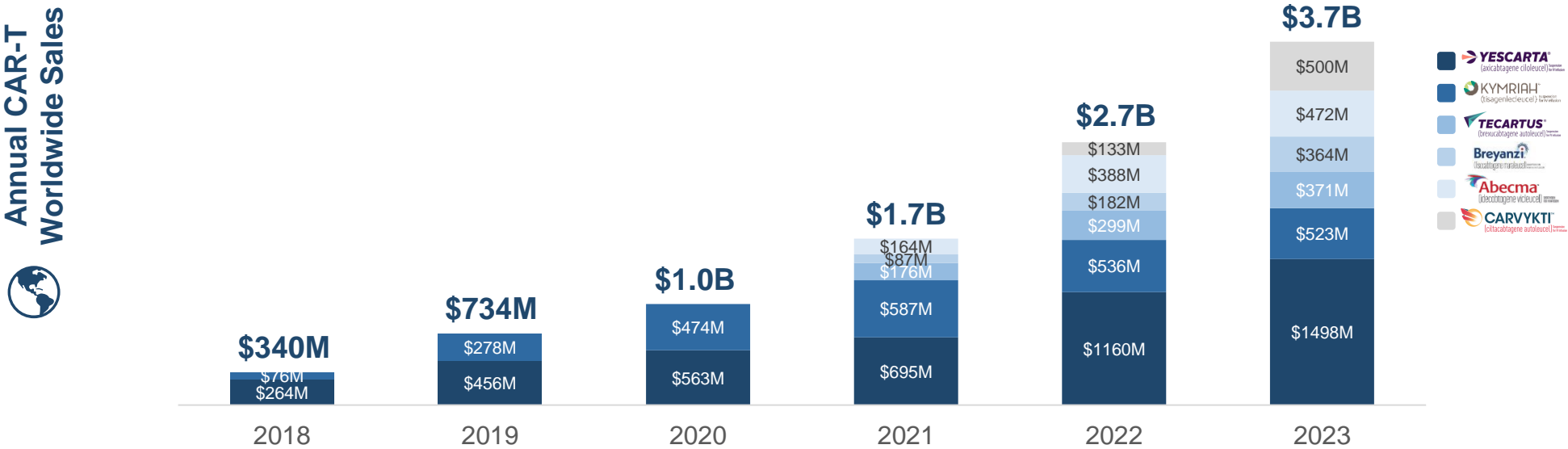


## Closing Remarks

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# Opportunity to Transform Existing Multi-Billion-Dollar Markets

>\$3.5B in annual CAR-T sales underscores blockbuster opportunity for Iomab-ACT conditioning



 Fast-expanding CAR-T market with expected approvals in various new indications and earlier treatment lines

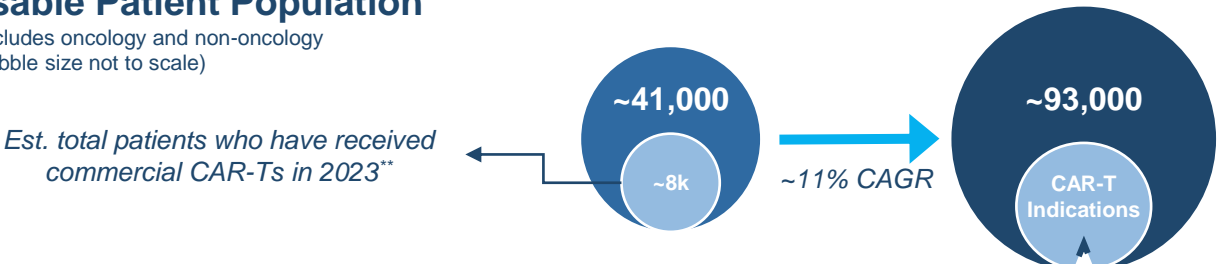
# Rapidly Expanding Market Highlights Potential Impact for Conditioning

New CAR-T indications and gene therapy approvals expected to significantly increase addressable market and catalyze uptake of Iomab-ACT conditioning

## Cell and Gene Therapy Market<sup>1,3</sup>

### Addressable Patient Population

(Illustrative, includes oncology and non-oncology indications, bubble size not to scale)



### CGT Projections by 2030:

**~60 Product Approvals**  
(Cumulative, range: 54 – 75)

**~93,000 Patients**  
(Total Addressable Market)

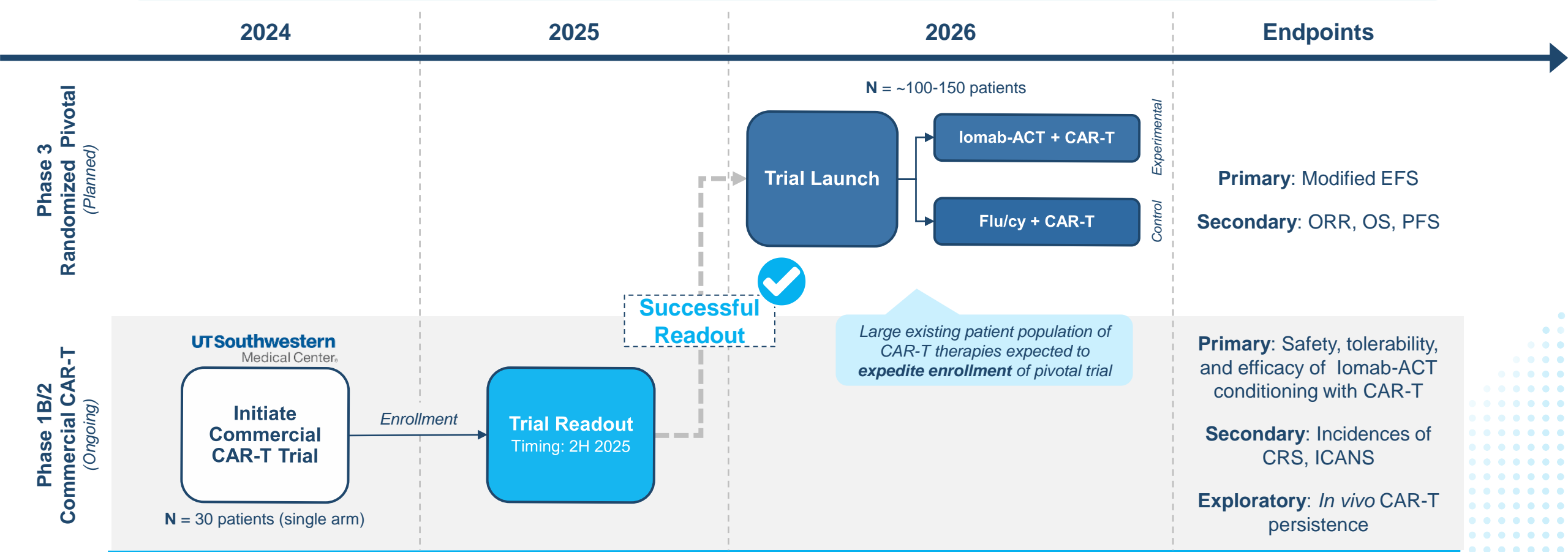
**~\$20B Total Market Size\***  
(Range: \$15-\$35B)

CAR-T Approvals <sup>1,2</sup>	Indications	2023	By 2030 (Anticipated)
	ALL and DLBCL (First approvals in 2017-2018)	✓	✓
	+ MM, MCL, CLL, and FL	✓	✓
	+ Solid Tumors and I&I		✓

Source: <sup>1</sup>Durable cell and gene therapy potential patient and financial impact: US projections of product approvals, patients treated, and product revenues; <sup>2</sup>McKinsey and Company – Driving the next wave of innovation in CAR-T cell therapies; <sup>3</sup>IQVIA – Strengthening Pathways for Cell and Gene Therapies: Current State and Future Scenarios; \*Based on pricing analogs from gene therapy (Luxturna and Zolgensma) and oncology (Kymriah and Yescarta); \*\*Estimated off \$3.7B annual CAR-T sales and list pricing of CAR-T products; ALL – Acute Lymphoblastic Leukemia; DLBCL – Diffuse Large B-Cell Lymphoma; MCL – Mantle Cell Lymphoma MM – Multiple Myeloma; CLL – Chronic Lymphocytic Leukemia; FL – Follicular Lymphoma; NHL – Non-Hodgkin’s Lymphoma; I&I – Immunology and Inflammation; CGT – Cell and Gene Therapy

# Upcoming Value-Creating Milestones for Iomab-ACT

Success of phase 1B/2 commercial CAR-T trial will inform pivotal study, paving a path for Iomab-ACT approval and launch





# Q&A

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**Actinium Pharmaceuticals, Inc.**



# Thank you

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