

Actinium
Pharmaceuticals, Inc.

Iomab-B SIERRA Trial

Phase 3 Results

February 18, 2023

ATNM: NYSE AMERICAN

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Today's Speakers & Agenda



Sandesh Seth
Chairman & CEO

Introduction and
Closing Remarks



Dr. Madhuri Vusirikala
VP, Clinical Development,
BMT & Cellular Therapy

Iomab-B Phase 3
SIERRA Results



Dr. Avinash Desai
Chief Medical Officer

Significance
of SIERRA Results
and Next Steps



Caroline Yarbrough
Chief Commercial Officer

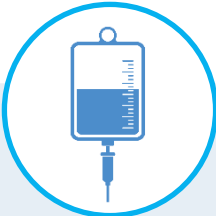
Iomab-B Market
Positioning and
Opportunity

SIERRA Results Support Iomab-B Becoming a New Standard of Care



Strong SIERRA Results

Met primary endpoint, doubled overall survival



Unprecedented BMT Access with Iomab-B

Patients got to BMT in half the time with Iomab-B, all engrafted



Improved Outcomes with Iomab-B and BMT

Improved sepsis, acute GVHD, and improved long-term survival



Large Underserved R/R AML Patient Segment

Addressed by Iomab-B



Favorable Commercial Dynamics

Patients, providers, payors benefit, no competition, concentrated centers

Iomab-B has paradigm changing and practice expanding potential

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
- Serves 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)

SIERRA: Positive Efficacy, Safety, and Long-Term Outcomes in R/R AML

	Trial Endpoints and Metrics	Results
✓ Primary	6-month durable Complete Remission (dCR)	p<0.0001
✓ Secondary	Event-Free Survival (EFS)	EFS Hazard Ratio of 0.22, p<0.0001
	Overall Survival (OS)	100% Increase over control arm
✓ Long-term Outcomes	2-year survival in patients achieving dCR	60% in lomab-B patients vs. 0% in control arm patients
✓ Key Safety & Tolerability Metrics	Sepsis	4x lower with lomab-B
	GVHD	Clinically meaningful lower rate of GVHD with lomab-B

SIERRA results support the potential for lomab-B to become the new standard of care for BMT conditioning in R/R AML

AML Fast Facts

AML is an aggressive disease that can progress rapidly despite treatments

≈21,000
AML patients
annually¹

68 years
Median age at
diagnosis¹

10 drugs
approved for
AML patients
since 2017

Older patients have
limited treatment
options and poor
outcomes



Develop R/R
disease²



of AML patients
access BMT³

BMT is the only
potential curative
treatment
for R/R AML,
but only younger or fit
patients can access it

1) SEER database; 2) Gyurkocza et al. Allogeneic hematopoietic cell transplantation in patients with AML not achieving remission: potentially curative therapy. Bone Marrow Transplantation (2017), 1-8; 3) Auletta JJ et al. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR US summary slides, 2021.

Challenges to Achieving Cures in AML

Patients must be able to overcome several challenges related to curative BMT

➔ Challenge #1

Need to attain a complete remission (CR)

➔ Challenge #2

Tolerate and survive effective BMT conditioning

Access

➔ Challenge #3

- Achieve BMT engraftment
- Achieve post-BMT CR

➔ Challenge #4

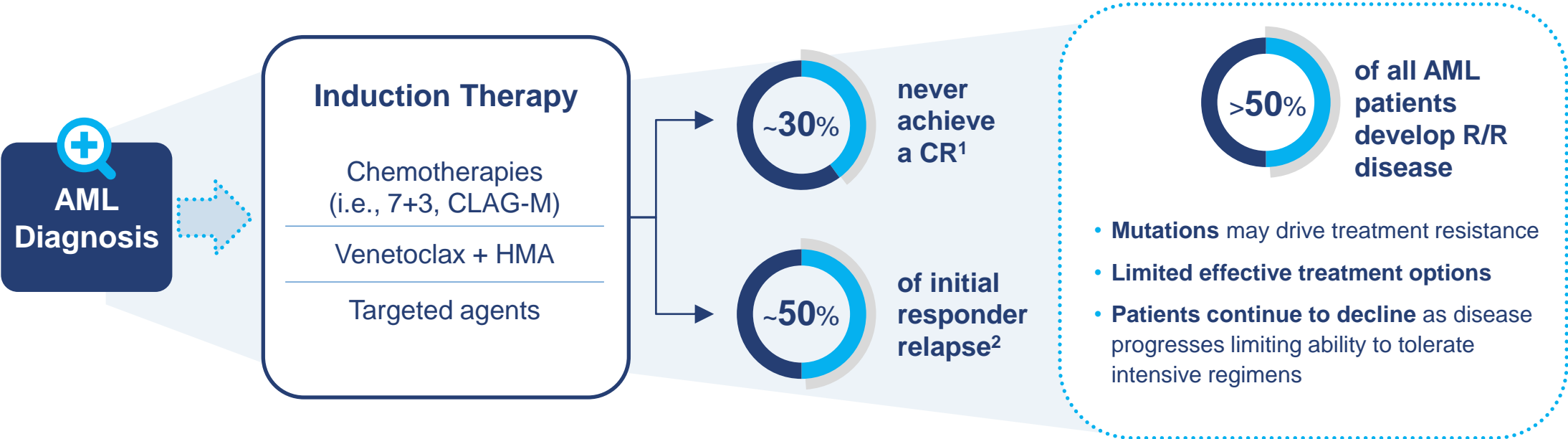
- Surmount BMT related complications
 - Graft failure
 - Side effects: sepsis, GVHD

Outcomes

Overcoming these challenges can result in long-term survival and curative outcomes

Challenge 1: Need to Achieve a CR

Current paradigm – existing therapies produce limited CRs

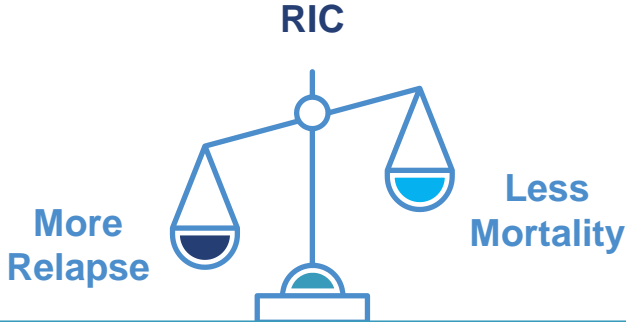


CRs are difficult to achieve once patients have R/R disease

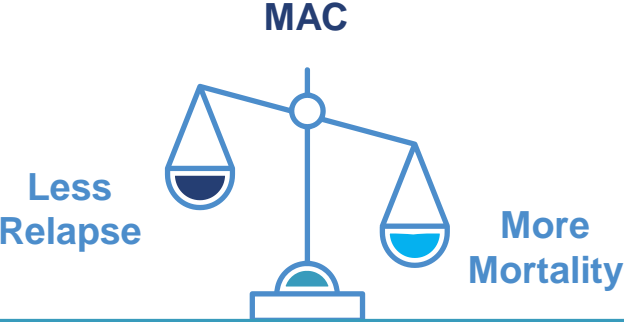
1) Ferguson, et al. An operational definition of primary refractory acute myeloid leukemia allowing early identification of patients who may benefit from allogeneic stem cell transplantation. *Haematologica*. 2016 Nov; 101(11): 1351–1358.
2) Gyurkocza et al. Allogeneic hematopoietic cell transplantation in patients with AML not achieving remission: potentially curative therapy. *Bone Marrow Transplantation* (2017), 1-8.

Challenge 2: Tolerate and Survive BMT Conditioning Regimens

BMT conditioning requires the patient to be subjected to and survive another round of non-targeted chemotherapy (± radiation)



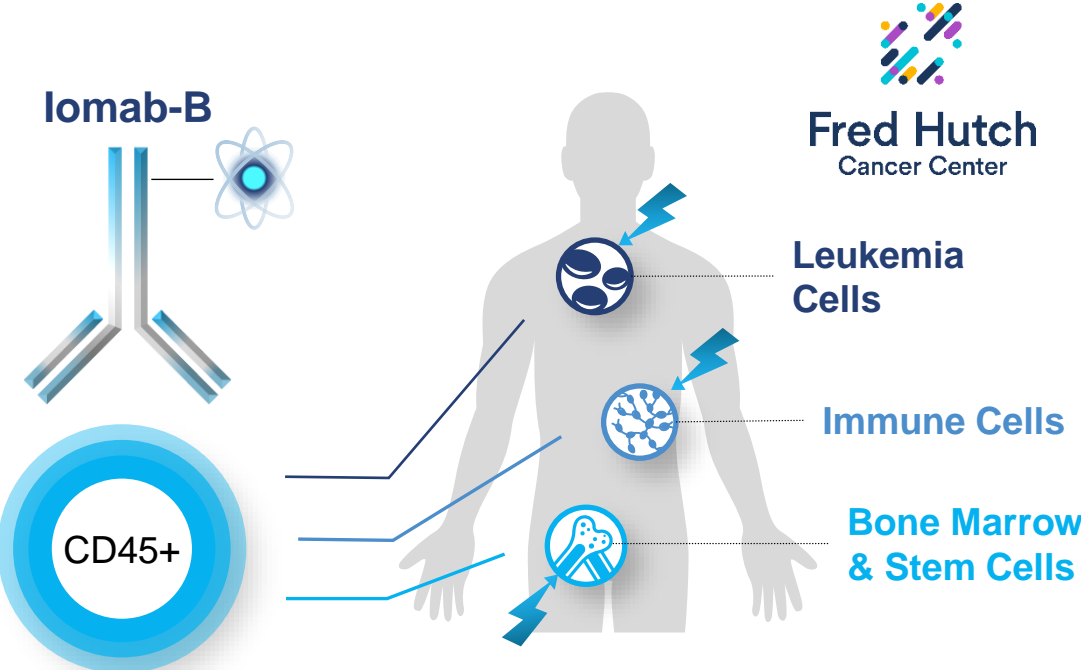
Reduced intensity chemotherapy (RIC) conditioning is “too cold” and is associated with in **higher risk of disease relapse due to residual disease**



High intensity, myeloablative conditioning (MAC) is “too hot”, making it **difficult to tolerate**, and has **high mortality rates**

RIC or MAC conditioning limits BMT access and results in poor outcomes in the majority of older, R/R AML patients

Iomab-B: A Next Generation Approach to Improve BMT Access, Outcomes



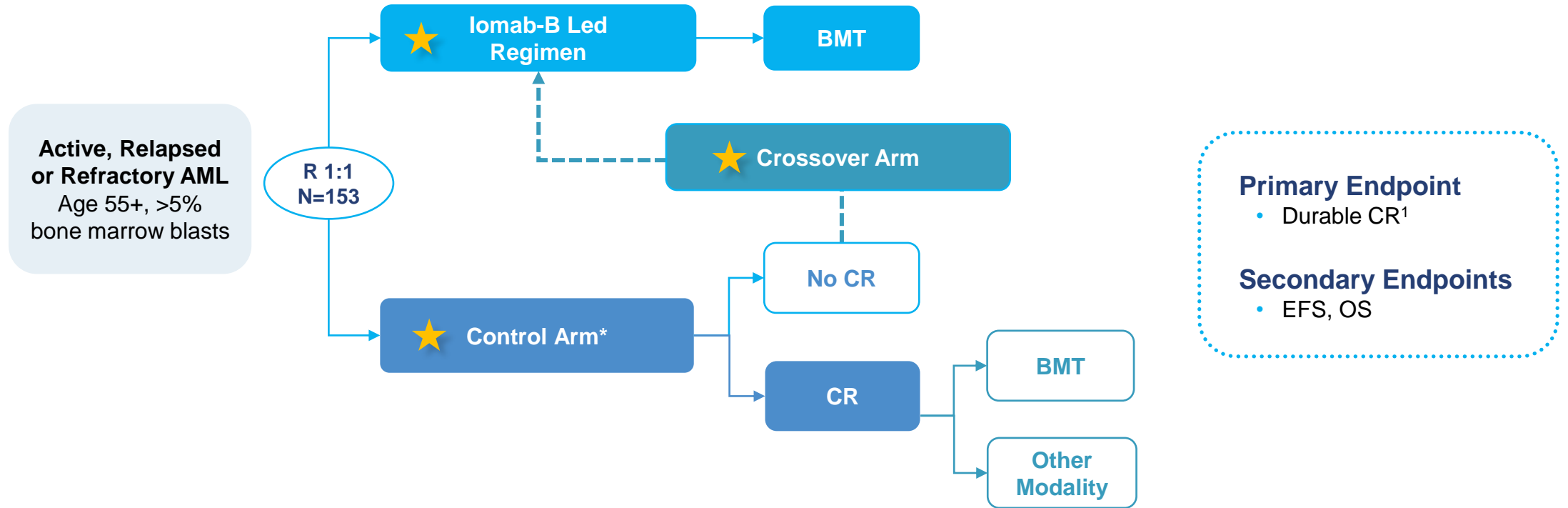
-  **400+** patients
-  **12** clinical trials
-  **6 diseases** (AML, MDS, MM, ALL, NHL/HL)
-  **Improved survival and curative outcomes**

- Iomab-B targets CD45, which has high expression only in AML immune and stem cells, thereby sparing organs and increases tolerability
- Enables high amounts of radiation to be delivered to radiation sensitive AML and immune cells
- Induction and conditioning by simultaneously eliminating targeted cells
- Allows patients with active disease to go directly to BMT rapidly via a single infusion

Challenges Addressed: Iomab-B in the SIERRA Trial

- Challenges 1 and 2: Improved Access - CR not needed, effective disease control and targeted myeloablation
- Challenges 3 and 4: Improved outcomes - better post-BMT engraftment, CR and lower complications

SIERRA: A Novel, Pivotal Phase 3 Study of Iomab-B in R/R AML



3 Novel Components of SIERRA Design

Iomab-B
Patients with active disease can go immediately to BMT

Control
≈20 agents that include CT/targeted therapies allowed – anything to get patient to CR and subsequent BMT

Crossover
Patients with treatment failure can be rescued on Iomab-B arm

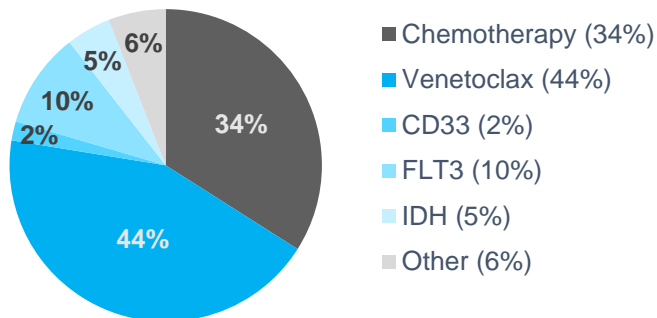
First Randomized Trial with Goal to Transplant R/R AML Patients

Patients enrolled in SIERRA have poor expected survival

SIERRA Designed to Evaluate if Iomab-B + BMT Can Improve the Outcomes of Active R/R AML Patients

R/R after Frontline Therapy ¹	Median OS (months)
Venetoclax + HMA	2.3
Intensive Chemo	3.6

SIERRA Patients Had Significant and Diverse Prior Therapy Representative of Current AML Treatment



SIERRA Trial: Iomab-B Arm Patient Characteristics

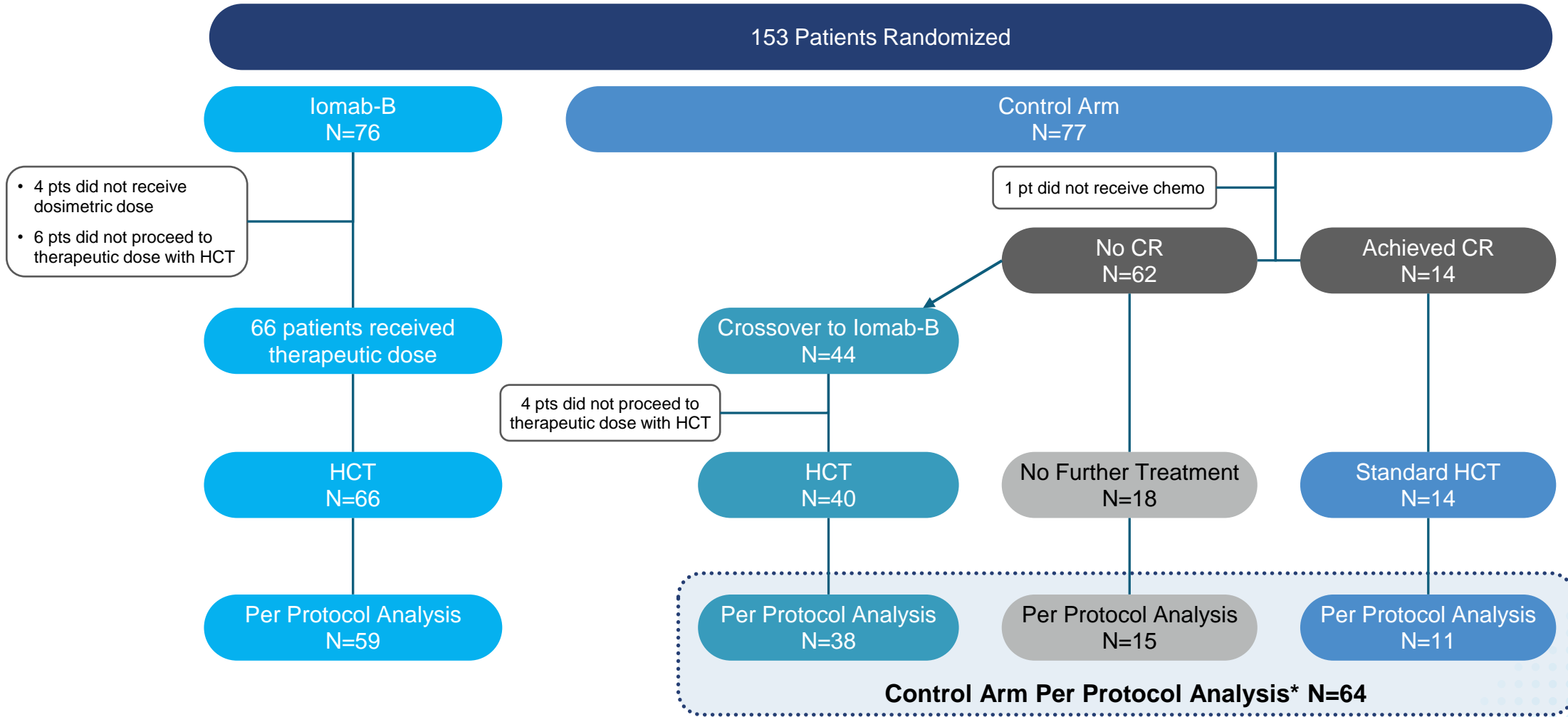
- Active R/R disease
- Median age: 64 (55-77)
- Intermediate and adverse cytogenetics and molecular risk: >90%
- Majority of patients had primary induction failure or first early relapse: 78%
- Median blast count: 30%
- Prior lines of treatment: 3 (1-8)

Patients Are Heavily Pre-treated With Active Disease

Baseline patient and disease characteristics were balanced between study arms

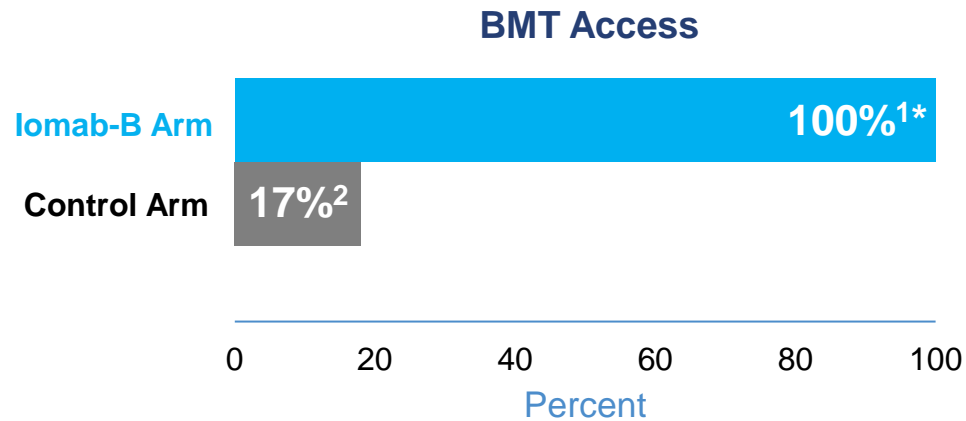
	Iomab-B (n=76)		Control Arm (n=77)		Crossover (n=44)	
Median Age	64 (55-77)		66 (55-76)		64 (55-76)	
Cytogenetics and Molecular Risk¹	Favorable:	5 (6.6)	Favorable:	2 (2.6)	Favorable:	1 (2.3)
	Intermediate:	27 (35.5)	Intermediate:	31 (40.3)	Intermediate:	21 (47.7)
	Adverse/Poor:	43 (56.6)	Adverse/Poor:	43 (55.8)	Adverse/Poor:	21 (47.7)
Disease Status at Randomization	Primary Induction Failure:	43 (56.6)	Primary Induction Failure:	40 (51.9)	Primary Induction Failure:	24 (54.5)
	First Early Relapse:	16 (21.1)	First Early Relapse:	22 (28.6)	First Early Relapse:	11 (25.0)
	Relapse/Refractory:	10 (13.2)	Relapse/Refractory:	10 (13.0)	Relapse/Refractory:	7 (15.9)
	2 nd + Relapse:	7 (9.2)	2 nd + Relapse:	5 (6.5)	2 nd + Relapse:	2 (4.5)
% Marrow Blasts at Randomization	30% (2-97) ²		20% (3-97) ²		35% (2-89) ² at crossover	
Prior Lines of Treatment	3 (1-8)		3 (1-8)		3 (1-8)	

Patient Disposition



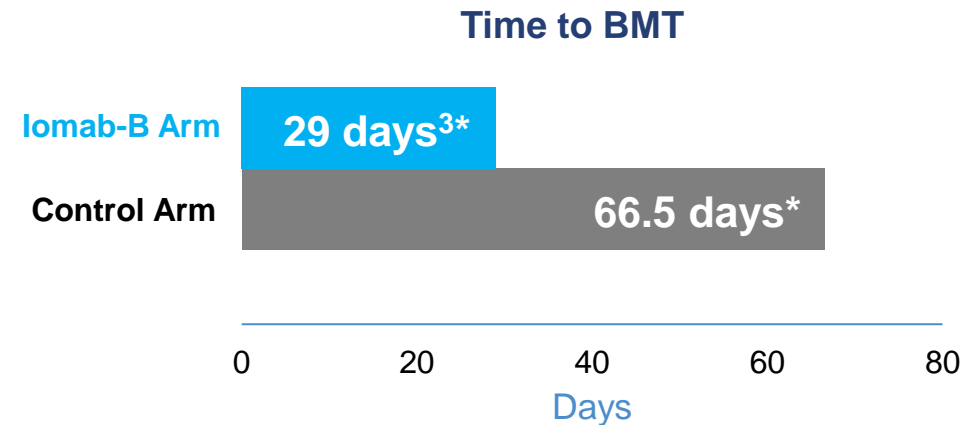
Challenge 1 & 2 Addressed: Unprecedented Access to BMT in Half the Time

Unprecedented Access to BMT



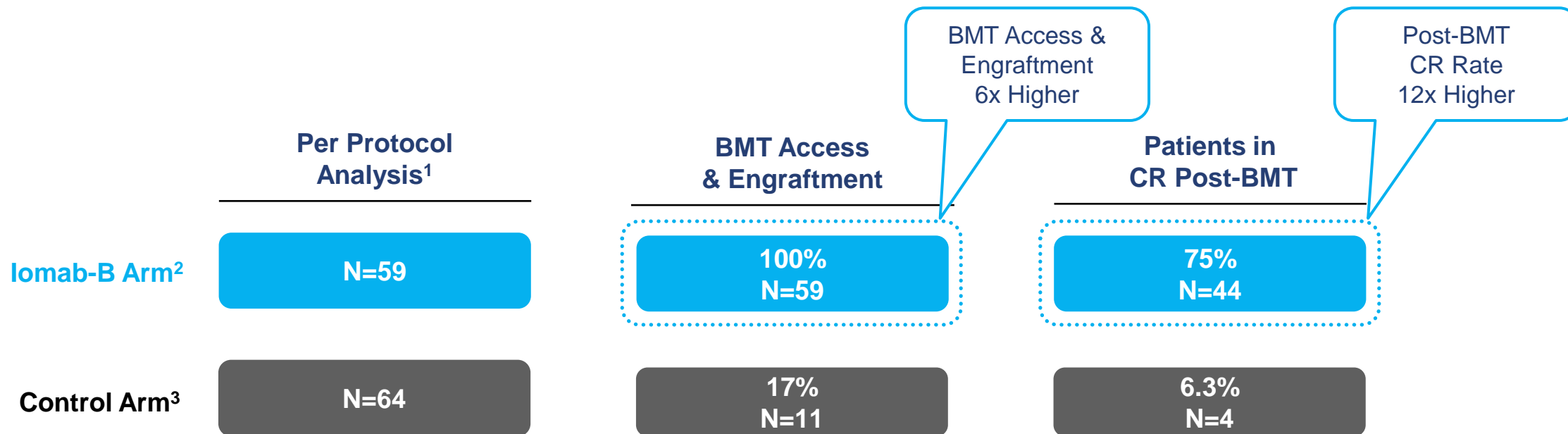
- **Targeted nature of Iomab-B** results in effective myeloablation with improved tolerability
- **Less than 20%** of patients on the control arm achieved CR vs. 100% on Iomab-B

Access to BMT in Less Than Half the Time



- **With Iomab-B there is no need to achieve a CR**; patients with active disease can go to directly to BMT in days and engraft successfully
- **1 – 2+ cycles of chemotherapy** required to attain CR if CR can even be produced

Challenge 3 Addressed: Unprecedented BMT Access & Engraftment and High Post-BMT CR



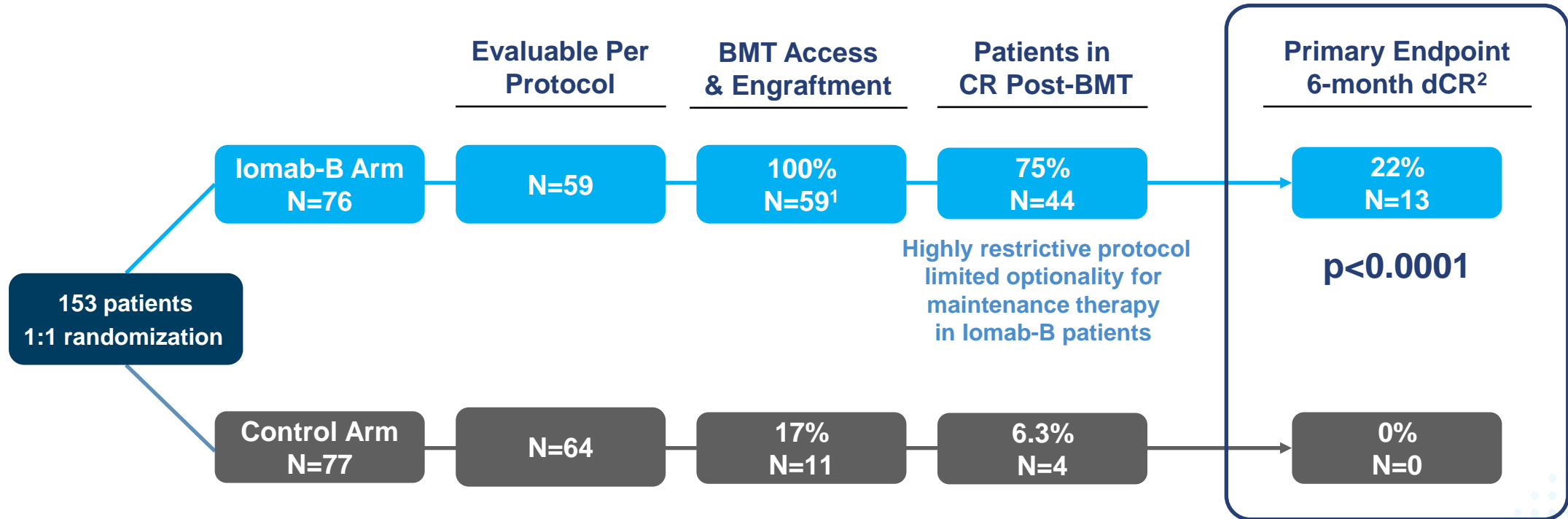
Challenge 4 Addressed: Excellent Safety of Targeted Radiotherapy

Iomab-B side effects are meaningfully lower, implying less complexity (and cost) post-transplant

Adverse Event* (%)	Iomab-B Arm N=66	Control Arm N=14
Sepsis ¹	6.1%	28.6%
Febrile Neutropenia	43.9%	50.0%
Mucositis ²	15.2%	21.4%
Acute GVHD (Gr II-IV) ³	26.1%	35.7%

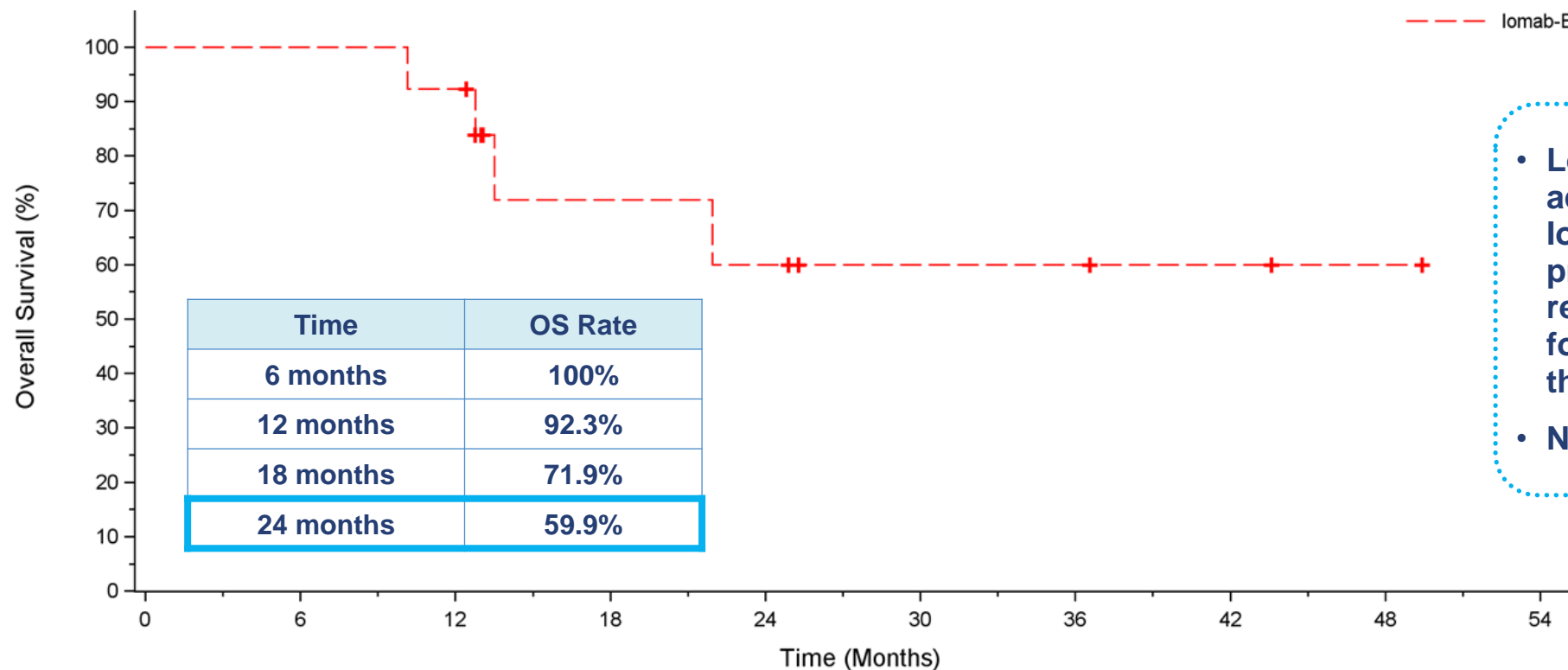
SIERRA Results: Iomab-B Overcomes Key BMT Challenges

Primary endpoint met with high significance: High rates of post-BMT remissions resulted in significantly higher durable remissions with Iomab-B



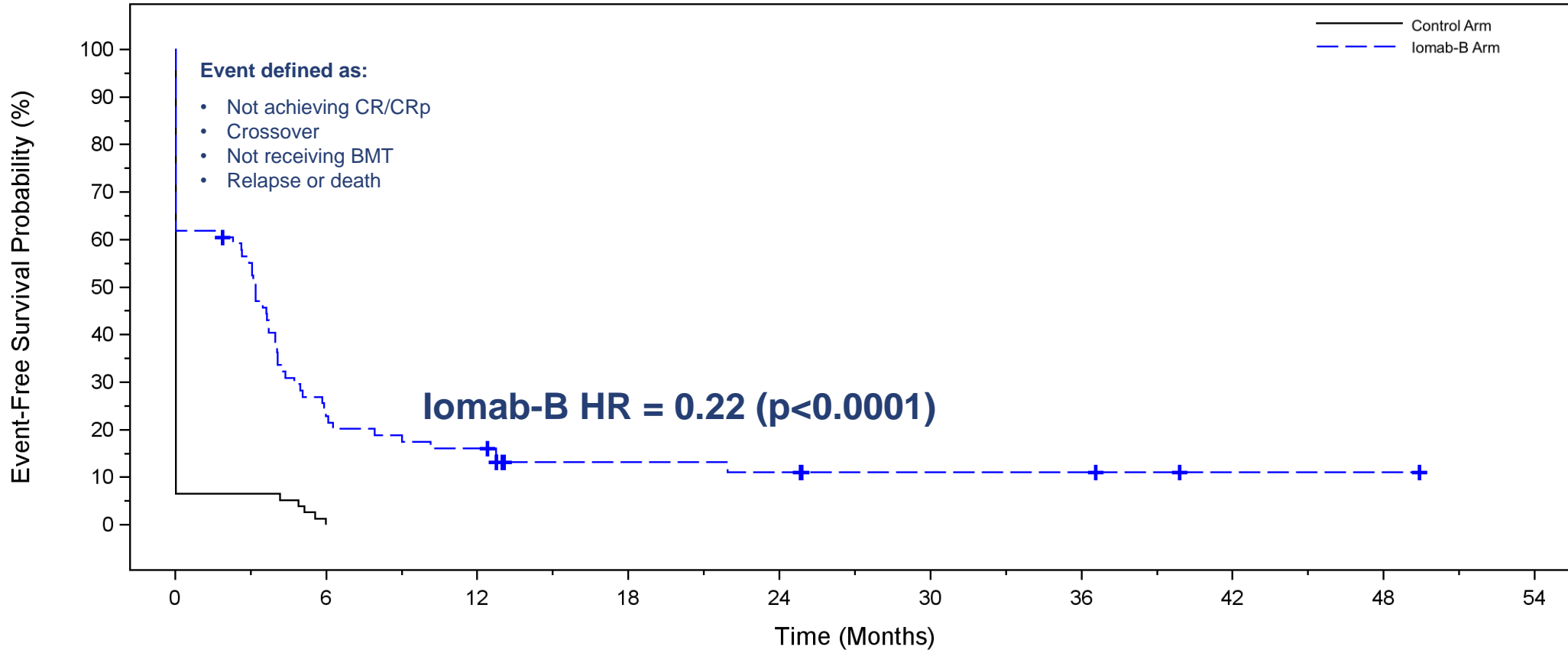
Long-Term Survival in Patients Achieving the Primary Endpoint

Median OS not reached; 2-year survival highly indicative of long-term outcomes including potential cure



- Long-term survival achieved even though lomab-B patient protocols had highly restrictive optionality for maintenance therapy post-BMT
- Not the norm

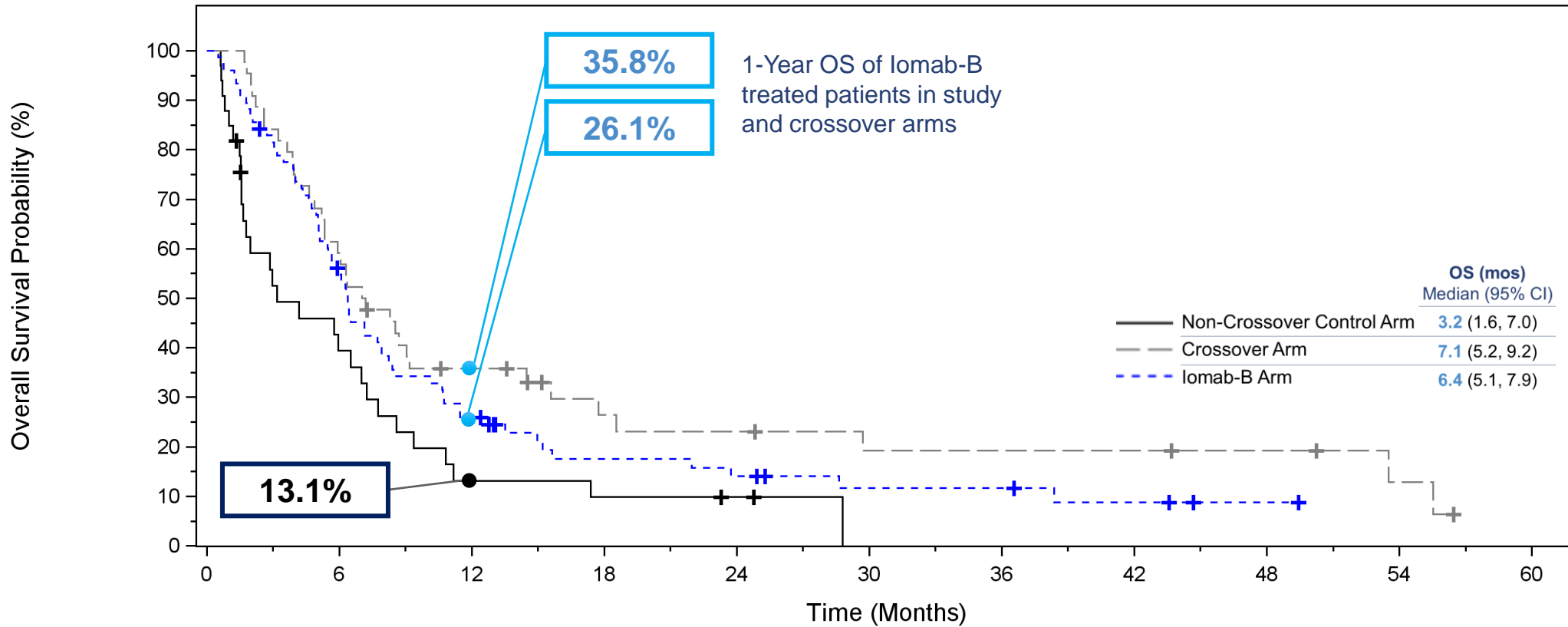
Iomab-B Reduced the Probability of an Event by 78%



EFS HR of 0.22 (p<0.0001) compared to control arm clearly supports the use of Iomab-B in this high-risk population

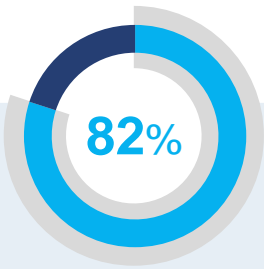
Iomab-B Demonstrates Clear Survival Benefit

Iomab-B doubled 1-year overall survival rates and median overall survival



Crossover Results Support Iomab-B Value Proposition

Iomab-B treatment yielded access and improved outcomes for crossover patients despite their failing an additional line of therapy



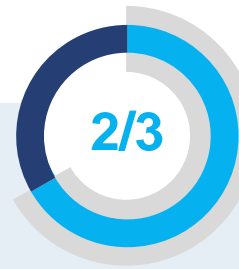
82% of control arm patients did not

achieve a remission and could not proceed to BMT



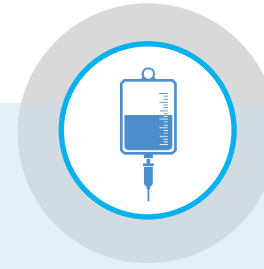
No viable treatment options for control arm failures

best supportive care or hospice



2/3 of control arm failures crossed over

and were rescued with Iomab-B



100% BMT & engraftment in crossover patients

receiving therapeutic dose of Iomab-B

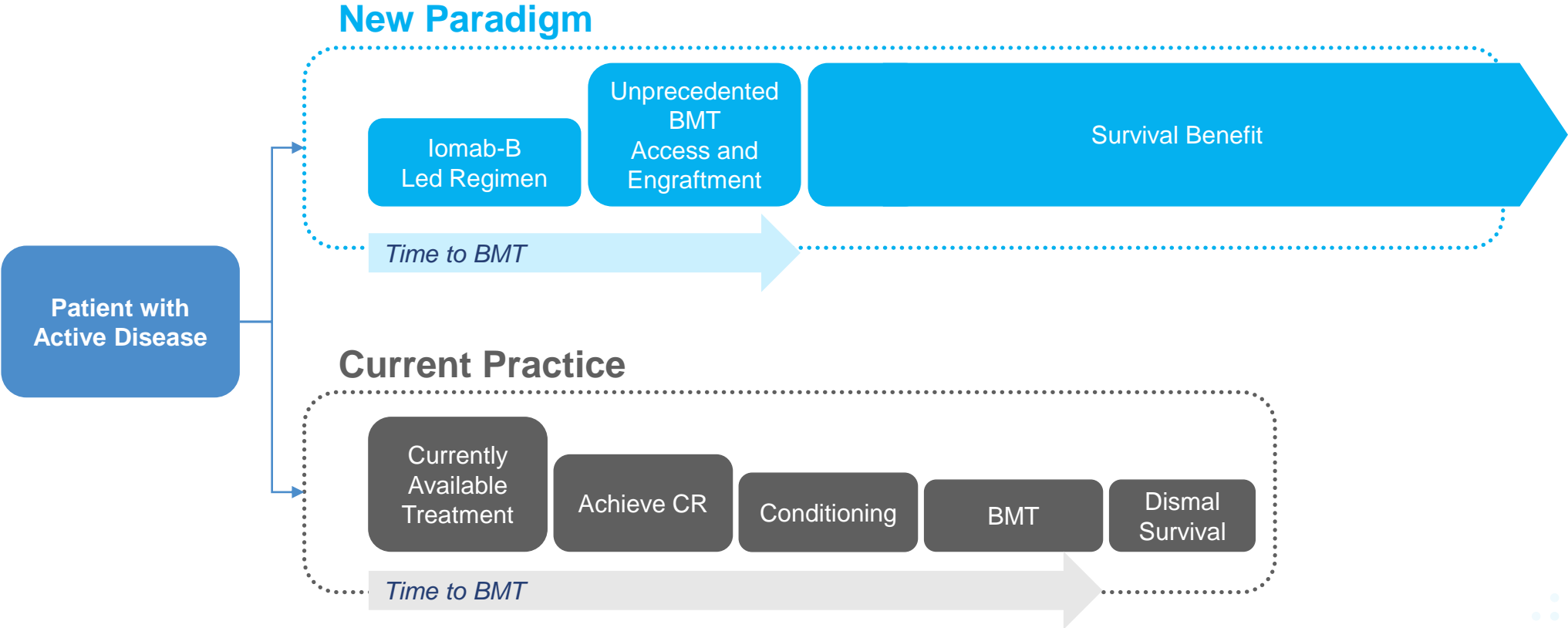


Crossover patients also achieved improved survival

via Iomab-B and BMT

Iomab-B Represents a New Paradigm

Clear separation in access and outcomes favor Iomab-B utilization



Dr. Avinash Desai, Chief Medical Officer



Johnson & Johnson

GSK

 **DARZALEX**[®]
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

 **VELCADE**[®]
(bortezomib)

- Joined Actinium in November 2020 and promoted to Chief Medical Officer in 2021
- 27 years of biopharmaceutical experience in clinical development and medical affairs
- Joined Actinium from GSK where he was Vice President, Head of U.S. Medical Affairs - Oncology, launching 3 oncology products in 15 months
- Previous experience at Janssen Pharmaceuticals (Johnson & Johnson), Eli Lilly & Co. Takeda, Inc. and Sanofi
- Contributed to the development and supported multiple blockbuster products including Darzalex and Velcade at Janssen
- Participated in multiple successful NDA submissions, launch readiness strategies and execution and life cycle management plans

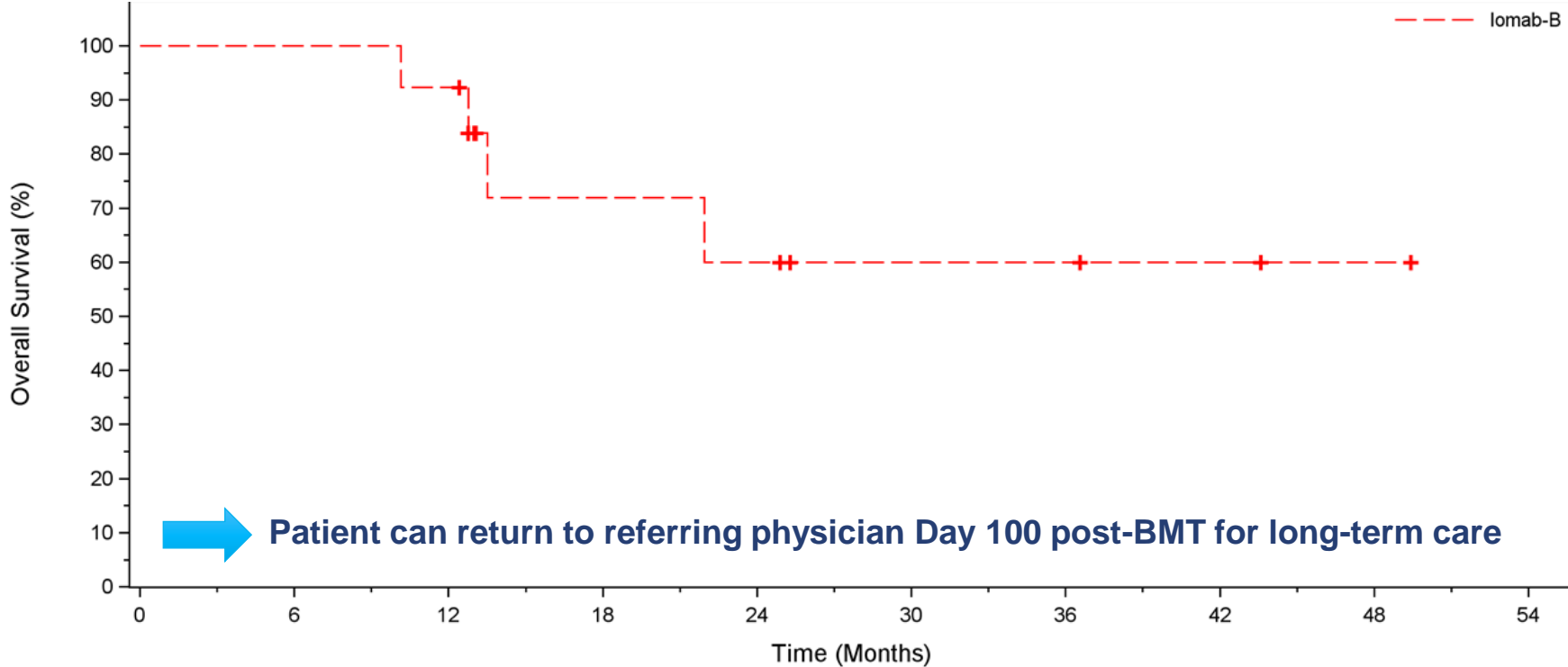
Iomab-B Represents a Practice Expanding Opportunity

Iomab-B offers the promise of transplant outcomes in the patient population for those cannot access a transplant today

Unprecedented Access

Improved Outcomes

Improved Safety & Tolerability



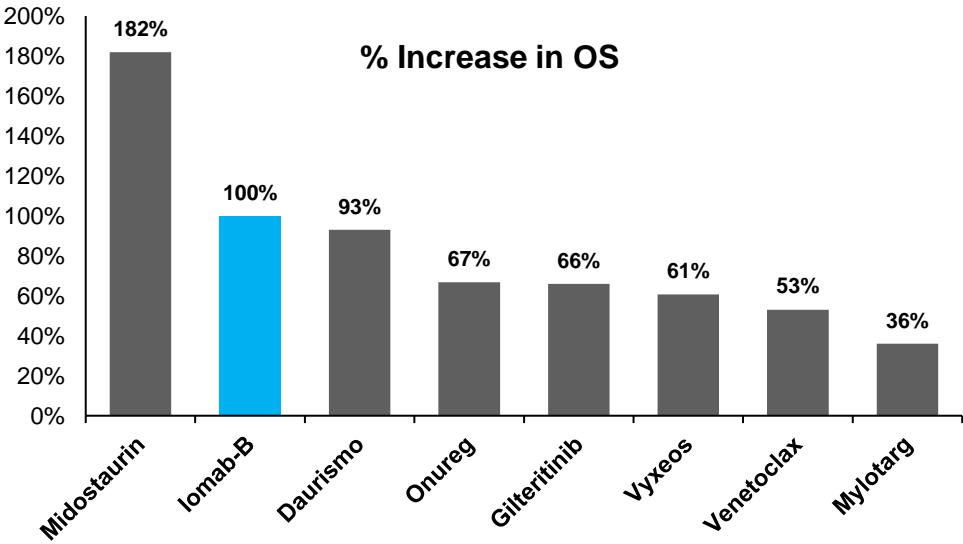
These results open the entire universe of R/R patients for transplant

Iomab-B Results Stand Out in Most Difficult AML Patient Segment

Iomab-B Had Strongest P-Value for Primary Endpoint Compared to Approved AML Drugs¹

Drug	P-Value ²
Iomab-B	<0.0001
Daurismo	0.0002
Gilteritinib	<0.001
Venetoclax	<0.001
Onureg	<0.001
Mylotarg	0.005
Vyxeos	0.005
Midostaurin	0.009

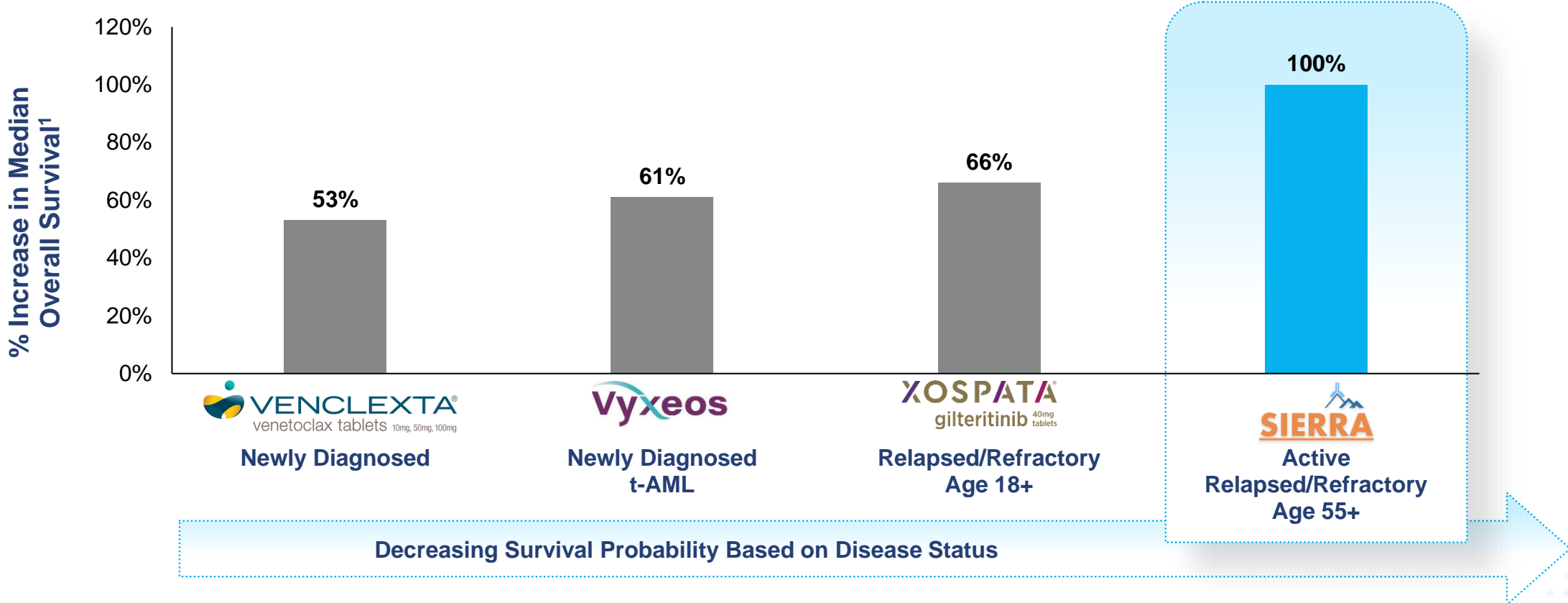
Iomab-B Produced Large Increase in OS Relative to AML Drugs³



Results demonstrate the ability of Iomab-B to produce outcomes that other approaches did not in their respective treatment settings

1) Includes approved therapies with comparator arms with a reported p-value for overall survival or event-free survival. *AML therapies have been approved on OS, EFS, response rates and duration of response endpoints; 2) Company Research, FDA approval labels; 3) Company research, market reports, publications

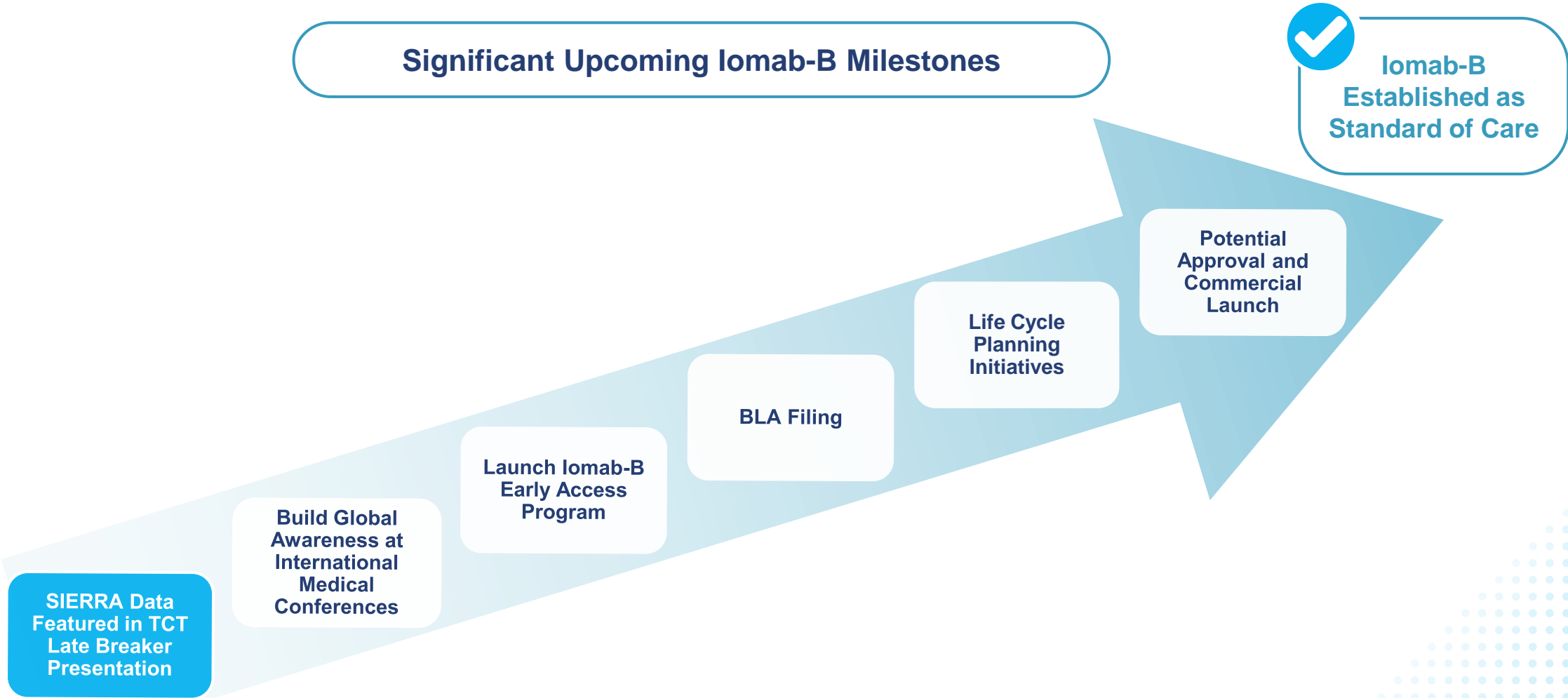
SIERRA Results Provide Compelling Foundation for Commercialization



Iomab-B provides patients and physicians hope for better outcomes where there is a clear unmet need and no visible competition

1) Company research and calculations, FDA approval labels market reports, publications

Clear Pathway to Establishing Iomab-B as Standard of Care



SIERRA Sets Foundation to Leverage Robust Iomab-B Data

Life cycle management and indication expansion opportunity supported by significant body of data with Iomab-B



400+ patients



12 clinical trials



6 diseases
(AML, MDS, MM,
ALL, NHL/HL)



Improved survival
and curative
outcomes

- Extensive data and consistent results from more than 400 patients including Fred Hutchinson Cancer Center studies demonstrate high BMT access and engraftment and improved outcomes in patients with MDS, younger AML, ALL, HL/NHL and MM
- These indications represent tens of thousands of patients with R/R disease having similar unmet needs to the AML patients in SIERRA
- These data, together with the strong results from the pivotal Phase 3 trial will be leveraged to execute our comprehensive life cycle management strategies to further expand Iomab-B's role in these variety of malignant and non-malignant hematological disorders
- Patients are treated by BMT physicians in the same concentrated, high-volume centers, most of which are SIERRA sites

Strong Foundation From Positive Results and Operational Excellence

**SIERRA experience at leading high-volume BMT positions
Iomab-B favorably for commercialization**

**Core Competencies Developed During
Execution of the SIERRA Trial**

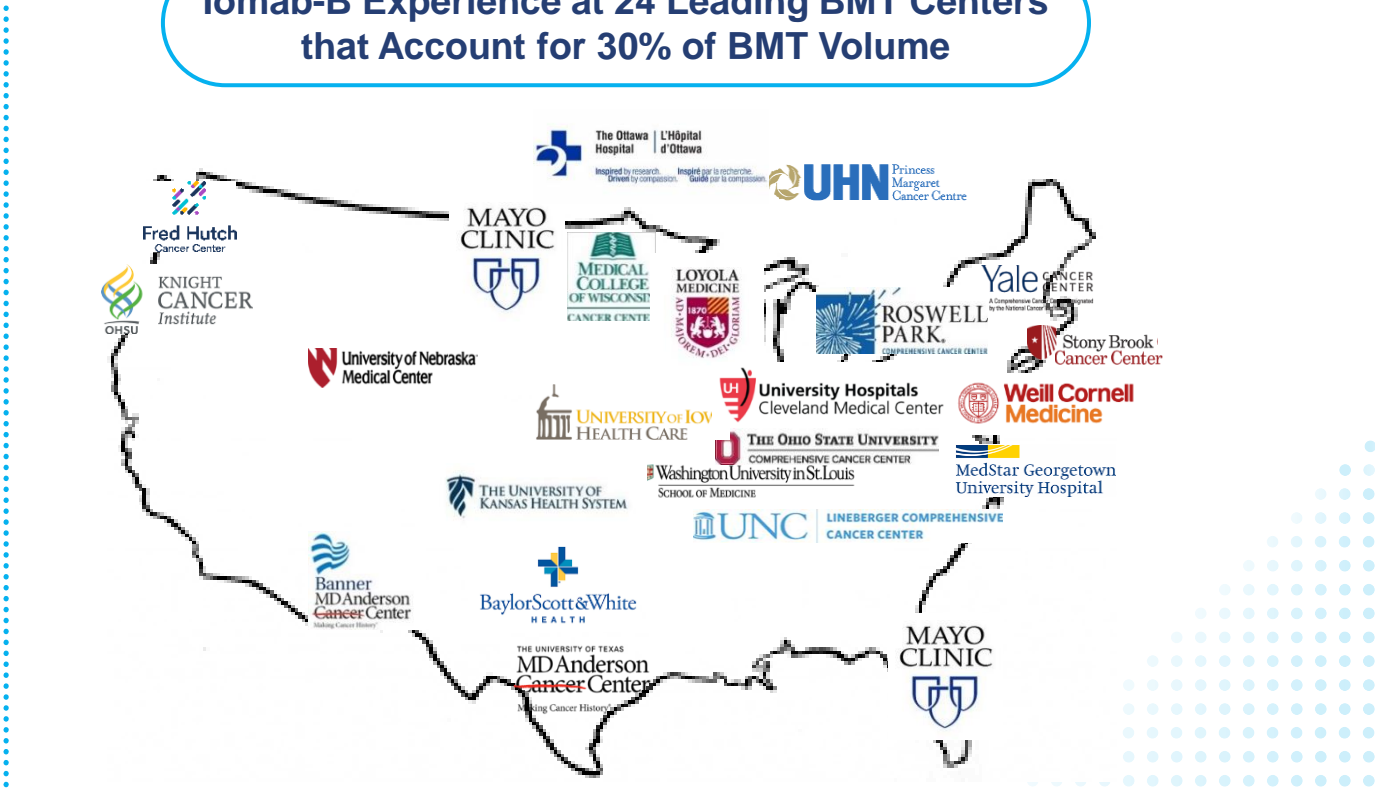
Robust Supply Chain

Operational Excellence at the Point of Care

Strong KOL Relationships

Broad Reach Across Leading BMT Centers

**Iomab-B Experience at 24 Leading BMT Centers
that Account for 30% of BMT Volume**



Caroline Yarbrough, Chief Commercial Officer



- Joined Actinium in October 2022 with 25 years of BioPharma commercial experience
- Most recently, Portfolio General Manager, US Oncology at Novartis, a \$1+ Billion product portfolio
- Strong hematology experience from leading Novartis Chronic Myelogenous Leukemia (CML) portfolio including Scemblix and Tasigna
- Led strategic account management to support the launch of the first approved CAR-T therapy Kymriah
- Significant prior experience at GSK, BMS, Viropharma and Merck
- Deep understanding of the hematology market, CAR-T/BMT center dynamics, and experience with strategic planning and growing businesses in multiple oncology disease areas

Iomab-B Has a Paradigm Changing Profile

Iomab-B Checks All Boxes to Become New Standard of Care



Unprecedented Access to BMT



Excellent Safety and Tolerability



Meaningful Survival Benefit

Practice Expanding Potential that Will Allow BMT Physicians to Transplant More Patients

- Changes the paradigm by enabling R/R patients to go to BMT without physicians having to learn a “new trick”
- Continue to practice BMT the same way, but for more patients
- Opens up 50% of AML patients that are currently not treatable to potentially curative BMT
- Potential to produce long-term outcomes for patients who currently have 2-3-month survival
- Physician regains patients after BMT and gets to see their patients for long-term follow-up care

Iomab-B can address a high unmet need in AML while bringing value to patients and physicians

Highly Favorable Dynamics Support Iomab-B Commercial Prospects

3P's, 2C's: Key variables impacting commercial success align favorably toward Iomab-B

Patients

- Unprecedented access to potentially curative BMT in AML with favorable safety and tolerability

Physicians

- Increased opportunity to treat patients that previously had no other treatment options without disruption to current practice
- Referring physicians get their patient back post-BMT for follow-up and long-term care

Payors

- Strong pharmacoeconomic value proposition driven by Iomab-B product profile

Competition




- No direct or indirect visible competition for the next 5-10 years

Concentrated Market

- Top 50 centers perform 75% of BMTs; concentrated in metropolitan areas
- 12-15 account managers to cover BMT center footprint, 35-50-person commercial organization

Iomab-B Compares Favorably to High Value Hematology Therapies

Therapies that provide a meaningful clinical benefit to R/R patients with limited treatment options have seen strong commercial adoption

	 BLINCYTO [®] * (blinatumomab) for injection <small>35 mcg single-dose vial</small>	 YESCARTA [®] * (axicabtagene ciloleucel) Suspension for Intravenous Use	 Iomab-B
Indication	R/R ALL	R/R DLBCL	R/R AML
EFS HR	NA	0.40	0.22
OS Improvement	93% (7.7 vs 4.0 months)	NA	100% (6.4 vs 3.2 months)
Modality	Bi-specific	CAR-T	Targeted radio

* FDA prescribing label
DLBCL – Diffuse large B-cell lymphoma



Closing Remarks

Actinium Pharmaceuticals, Inc.



Key Iomab-B and SIERRA Takeaways



Addresses
Clear Unmet
Need

**Makes BMT Possible for Patients
with Active Disease**



Improved
Access

**Unprecedented BMT
Access & Engraftment**



Improved
Outcomes

**Increased 1-year and Median OS,
Long-term Survival**



Operational
Excellence

**Focused on Execution at the
Point of Care**













Highly
Favorable
Commercial
Dynamics in
US, Europe

**3P's, 2C's Align Toward Success,
Immedica EU Partnership
Provides Advantage**

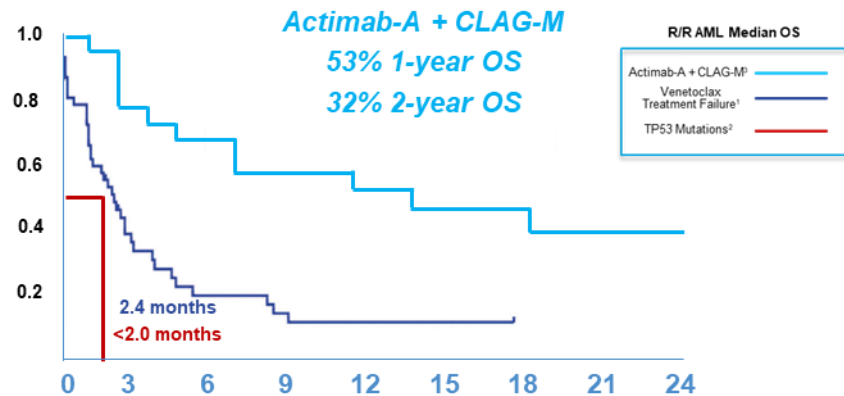
Iomab-B Compares Favorably Versus Other Radiotherapy Assets

Radiotherapies have commanded premiums based on scarcity of late-stage programs

	 Lutetium (¹⁷⁷ Lu) oxodotreotide	 Lutetium Lu 177 vipivotide tetraxetan INJECTION FOR INTRAVENOUS USE	 radium Ra 223 dichloride INJECTION	Iomab-B
Indication	GEP-NETs	mCRPC	mCRPC	Active, R/R AML age 55+
Developer		 ENDOCYTE	 ALGETA	
Stage of Development at Acquisition/Current Stage	Approved in EU, NDA filed with FDA	Phase 3	Approved	Phase 3
Acquirer/Sponsor of Phase 3	 NOVARTIS	 NOVARTIS	 BAYER	Independent
Initial Addressable U.S. Patient Opportunity	~4,900 ¹	~25,000 ²	~6,000 ³	~8,000 ⁴
Data Supporting Multi-Disease Potential	No	No	No	Yes
Potential Future Addressable U.S. Patient Opportunity	~12,000 ⁵	~27,000 ⁶	~4,000 ⁷	100,000+ Malignant + Non-Malignant Heme Patients ⁸
Justification for Updated Patient Opportunity	Improved diagnostics & awareness	Moving to 2 nd line treatment setting	Improved Therapeutic Options	Indication Expansion in BMT, Cell & Gene Therapy
Purchase Price/Market Cap	\$3.9 Billion	\$2.1 Billion	\$2.9 Billion	~\$350 million market cap ⁹

Actimab-A Development Bolstered By Recent NCI CRADA

NCI sponsored Actimab-A development to include Phase 1, 2 and 3 trials featuring with the potential to develop Actimab-A as a backbone of AML combination therapy



- Survival benefit in CLAG-M combination demonstrates potential in high-risk, heavily treated R/R patients
- 150 patients treated with Actimab-A as monotherapy or combination, most clinical experience with Ac-225 isotope
- Broad applicability – agnostic to mutations and cytogenetics enables broad utilization



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

February 08, 2023

**Announcement of Availability to Investigators
of Actimab-A (NSC 843488)**

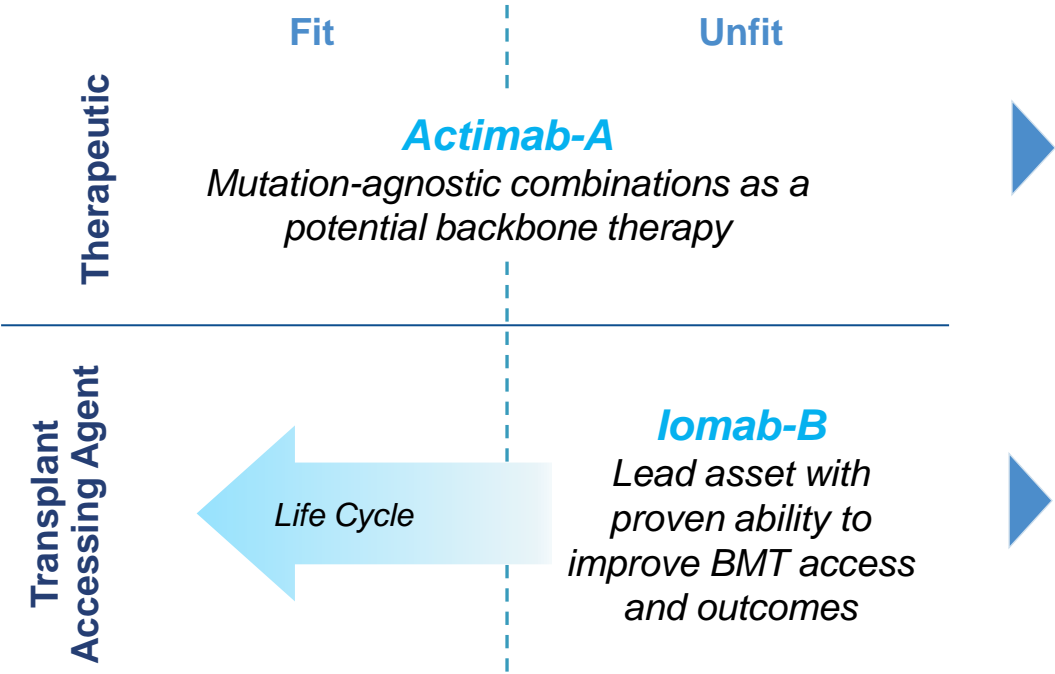
For Clinical and Nonclinical Study Proposals

- CRADA provides access to 2,000 clinical trial sites in Experimental Clinical Trial Network – ECOG, SWOG and Alliance and NCI's MyeloMATCH program
- Actinium to review and approve trials and protocols with NCI and has rights to all data
- Enables broad and aggressive development as single agent and combination-backbone

Balance sheet sparing with full rights to data – Actinium supplies Actimab-A while NCI covers all clinical trial execution and development expenses

Actinium's Opportunity to Transform Treatment Outcomes in AML

Iomab-B and Actimab-A together afford Actinium the unique opportunity to significantly modify the dismal status quo in AML in a complementary manner



- Companies Ability to Deliver on this Opportunity**
- Addressable patient population >50% R/R with dismal outcomes
 - Patient population largely treated in top 100 quaternary care centers
 - Favorable commercial dynamics for a successful Iomab-B launch with a lean commercial organization
 - Operational excellence at the point of care and efficient supply chain

Our mission is to deliver on the promise to modify AML outcomes and create a highly differentiated, specialty radiotherapeutics company focused on the large hospitals



Q&A

Actinium Pharmaceuticals, Inc.





Thank you

Actinium Pharmaceuticals, Inc.

