

Actinium
Pharmaceuticals, Inc.



ATNM: NYSE AMERICAN

June 2021

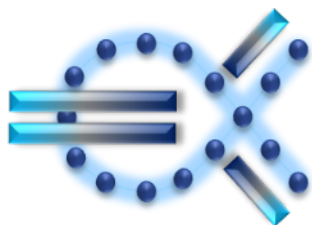
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Company Highlights

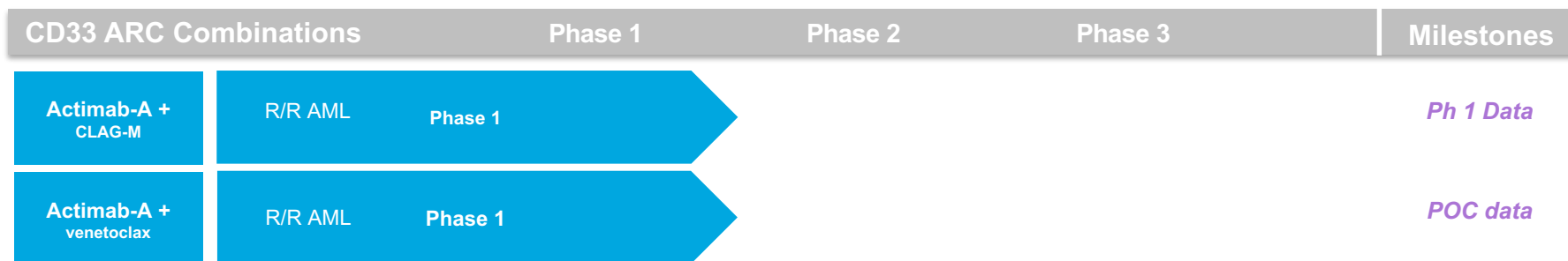
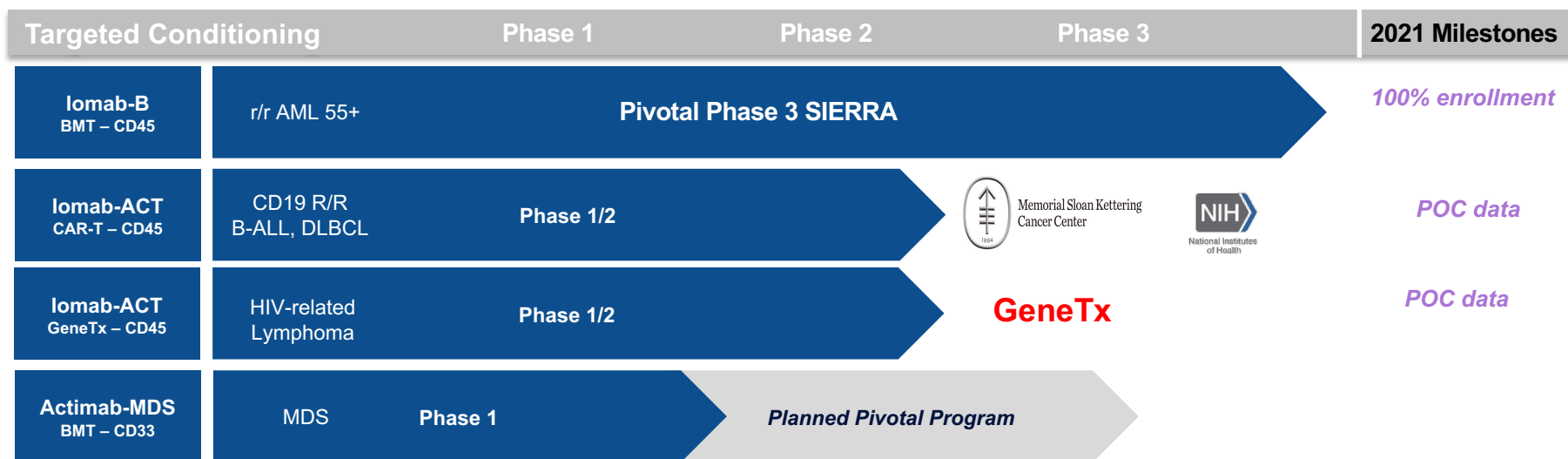
Late-stage, diverse Antibody Radiation-Conjugate (ARC) pipeline is maturing and progressing toward topline pivotal, POC trial and platform data amidst growing interest for targeted radiotherapies



- Pivotal Phase 3 SIERRA trial for lead program, lomab-B, showing clear value proposition for BMT conditioning through 75% enrollment
- Leading next-generation targeted conditioning clinical-stage pipeline for Bone Marrow Transplant (BMT), CAR-T and GeneTx
- Actimab-A, CD33 targeting ARC advancing in multiple R/R AML combination trials including with CLAG-M and venetoclax, PoC data could set the stage for one or more pivotal trials
- AWE technology platform drives innovation and partnerships including renewed collaboration with Astellas in solid tumors/theranostics and NIH/MSKCC in next-generation conditioning for CAR-T
- Strong balance sheet with ~\$72 million* enables multiple clinical and corporate milestones including completion of SIERRA enrollment, topline data, POC data from multiple Actimab-A combination trials and expanded AWE platform R&D

AWE Platform Powers Our Pipeline of ARCs

Deep pipeline of potent Antibody Radiation-Conjugates with significant therapeutic and combination potential in hematology and oncology



AWE Platform Collaborations & Preclinical Programs



Ac-225 + Undisclosed
Astellas Targeting Agents
Solid Tumor Theranostics

Ac-225 ARCs

Ac-225-
Daratumumab (CD38)



AML – Acute Myeloid Leukemia, MDS – Myelodysplastic Syndrome, MM – Multiple Myeloma, ALL – Acute Lymphoblastic Leukemia, NHL / HL – Non-Hodgkin's / Hodgkin's Lymphoma, HIV = Human Immunodeficiency Virus

AWE Platform Drives Pipeline, Enables Future Opportunities

Our AWE technology platform allows us to create ARCs for multiple areas of clinical development

AWE Technology Platform

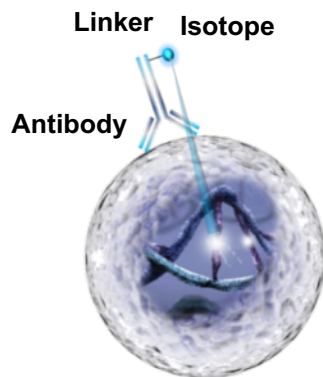
Scientific Founders



Memorial Sloan Kettering
Cancer Center



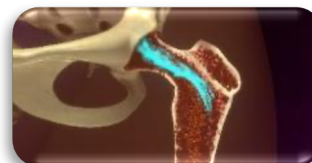
Collaborators



Strong, Growing IP Portfolio of 140+ Patents

Areas of Focus

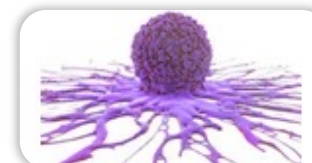
Targeted Conditioning



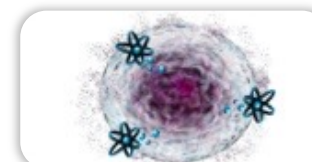
ARC Therapeutics and Combinations



Solid Tumors



Next-Generation ARCs



Multiple Targets

CD45

Leukemia, Lymphoma
and immune cells

CD33

AML, MDS
and MM

CD38

MM and
leukemia cells

Undisclosed

Solid tumor
theranostics

Multiple Isotopes⁽¹⁾

Iodine-131

Range: 2.3 mm
Energy: 0.6 MeV

Actinium-225

Range: .048 mm
Energy: 5.8 MeV

Lutetium-177

Range: 1.8 mm
Energy: 0.50 MeV



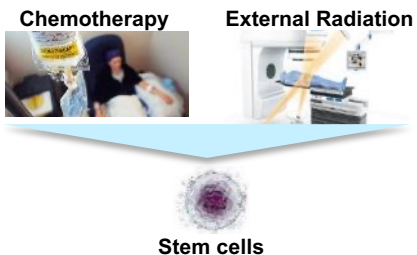
Enhanced R&D Infrastructure & Capabilities



Why Conditioning Matters

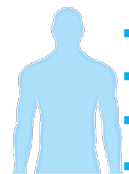
Conditioning is critical for BMT, ACT and GeneTx to be successful, but these potentially curative therapies currently depend on non-targeted chemotherapy and external radiation

Conditioning: Needed to deplete stem cells in the bone marrow to facilitate engraftment of new cells



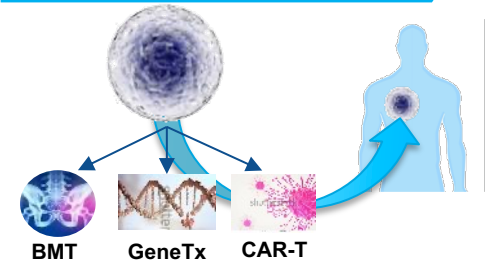
- Non-targeted
- Limits patient access
- Acute and chronic toxicities
- High-risk of failure/mortality

Diseases/Disorders



- Cancer (heme/solid)
- Genetic disorders
- Immune disorders
- Rare diseases

**BMT, ACT & GeneTx:
Potential Cures**



Significant need for new conditioning regimens to replace non-targeted approaches to increase patient access and improve outcomes

**Myeloablative Conditioning -
High-Dose Chemotherapy**



Limitation:
Too toxic, many patients cannot tolerate

Result:
Restricted access and high Treatment Related Morality

**Reduced Intensity Conditioning -
Low-dose chemo/radiation**



Limitation:
Can't eliminate all cancer and produce CR

Result:
High Relapse Rates

176,200 patients diagnosed with cancers treatable with BMT⁽¹⁾

Only ~23,000 BMTs in 2018⁽²⁾

**>150,000
Patients**

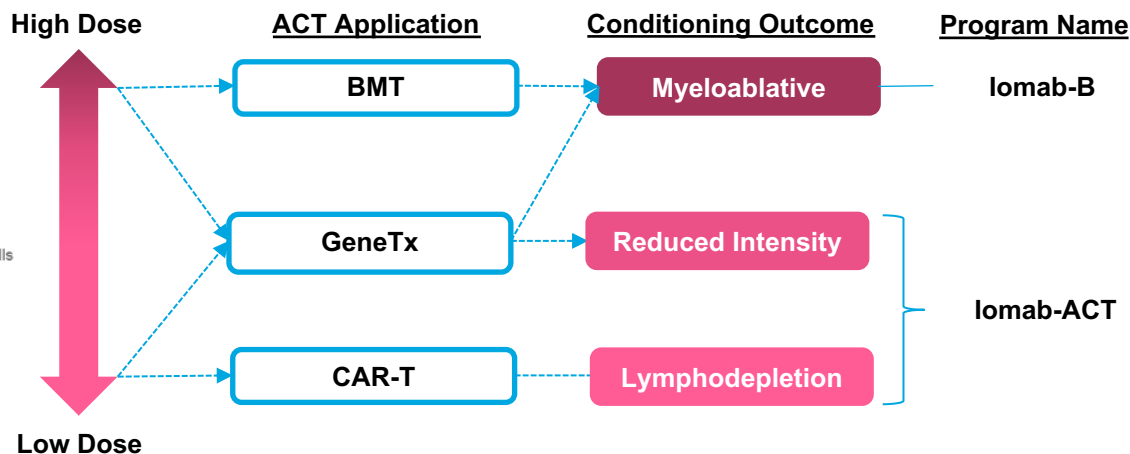
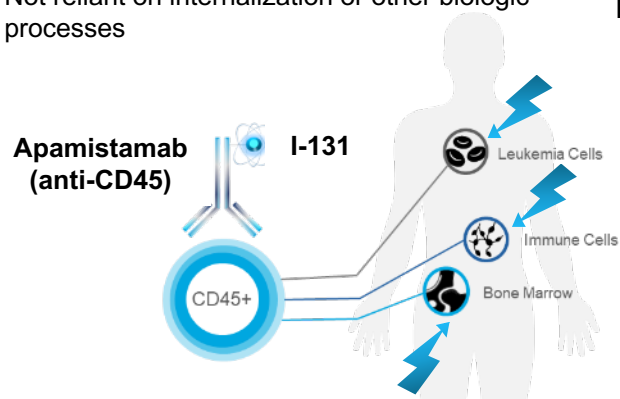
that could potentially benefit from a BMT that do not receive one today

CD45 Targeted Conditioning Asset and Program

Only clinical stage Targeted Conditioning program with applications in BMT, GeneTx, CAR-T and other adoptive cell therapies

ARC Advantages:

- Delivers a greater amount of validated radiation directly to target cells than external radiation
- Single infusion, rapid conditioning in days
- Less toxicities and better tolerated, stronger patient for BMT, GeneTx & ACT
- Not reliant on internalization or other biologic processes




CD45 Advantages:

- Expressed on leukemia and lymphoma cancer cells
- Expressed on immune cells, including bone marrow stem cells
- Enables simultaneous tumor/disease and stem cell ablation
- Not expressed outside the hematopoietic system
- High expression rates ~200,000 copies per cell, low internalization rates ~10%(1)

Iomab-B Value Proposition: Enhanced Access, Improved Outcomes

Transplant becomes a viable option for older patients with active, relapsed or refractory disease

Prior Clinical Experience



300+ patients



12 clinical trials



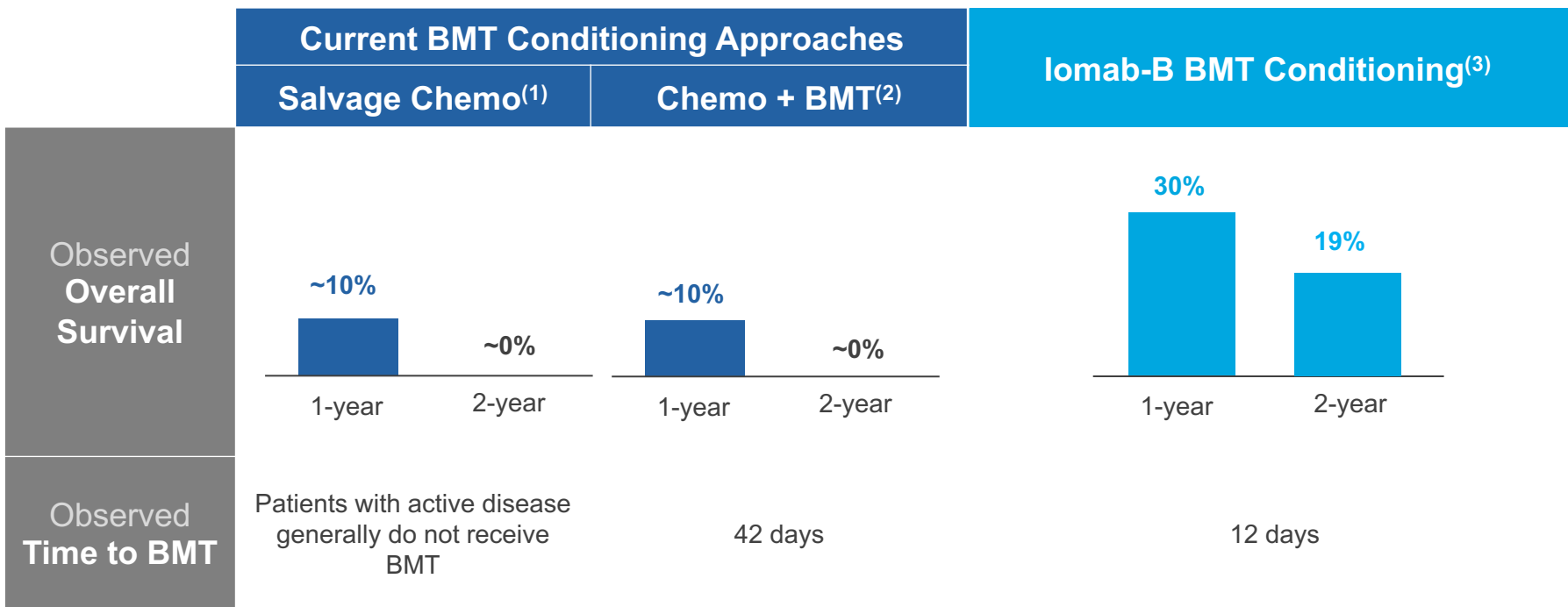
6 diseases
(AML, MDS, MM,
ALL, NHL/HL)



Improved
survival and
curative
outcomes



AML – Current Situation vs. POC Results

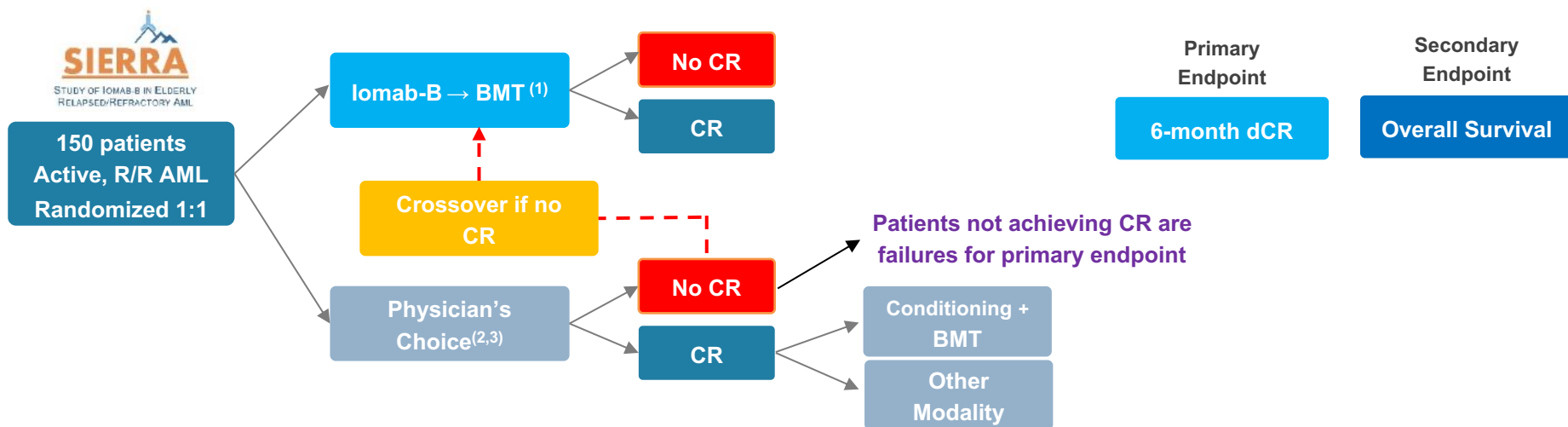


1) Roboz et al. J Clin Oncol 32:1919-1926 (2014) Intl Randomized Phase III Study of Elacytarabine Versus Investigator Choice in Patients with Relapsed/Refractory Acute Myeloid Leukemia (N=381) 2) Armistead et al. Biol Blood Marrow Transplant 15 :1431-1438 (2009) MD Anderson outcomes analysis. (Chemo + BMT N=19) 3) Pagel et. al. Blood 114:5444-5453 (2009) and additional data on file (N=36)

Ongoing Pivotal Phase 3 SIERRA Trial for Iomab-B

The only randomized Phase 3 trial investigating a BMT option for patients older than 55 years with ACTIVE, relapsed or refractory AML

- 150 patients total, 75 patients per arm
 - Primary Endpoint:** Durable Complete Remission (dCR) at 6 months
 - Secondary Endpoint:** Overall Survival (OS)
- Need to show a 2x difference in dCR primary endpoint at full enrollment

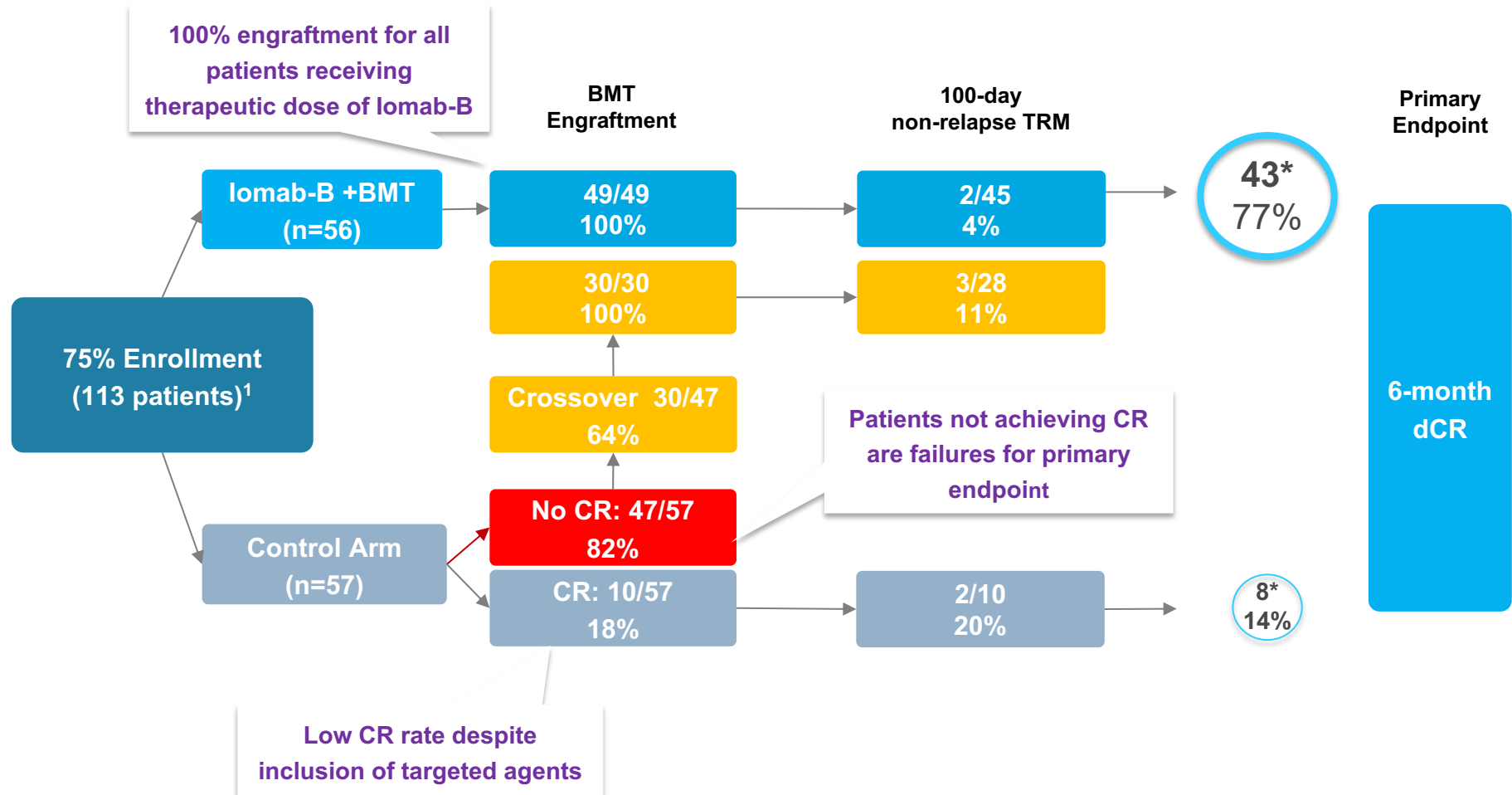


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75% Enrollment: Universal BMT and Engraftment Continues

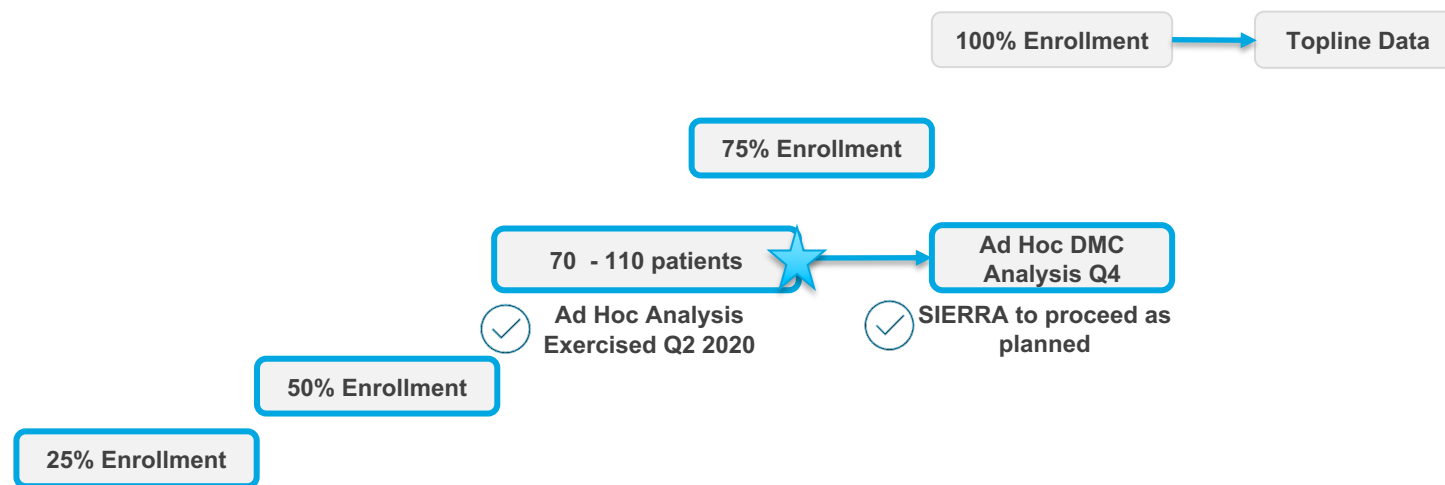
Universal BMT access and engraftment for all patients that received a therapeutic dose of lomab-B including 60% of patients that crossed over after salvage therapy



1) Gyurkocza et al. TCT 2021 Oral Presentation. Targeted Radioimmunotherapy with Anti-CD45 Iodine (131I) Apamistamab [lomab-B] in Older Patients with Active, Relapsed or Refractory (R/R) Acute Myeloid Leukemia Results in Successful and Timely Engraftment Not Related to the Radiation Dose Delivered *Patients potentially available for the primary endpoint of 6-month dCR

SIERRA Trial Status

Strong momentum following ASH 2020, Positive DMC Interim Analysis and TCT 2021 with 100% enrollment expected in 2021

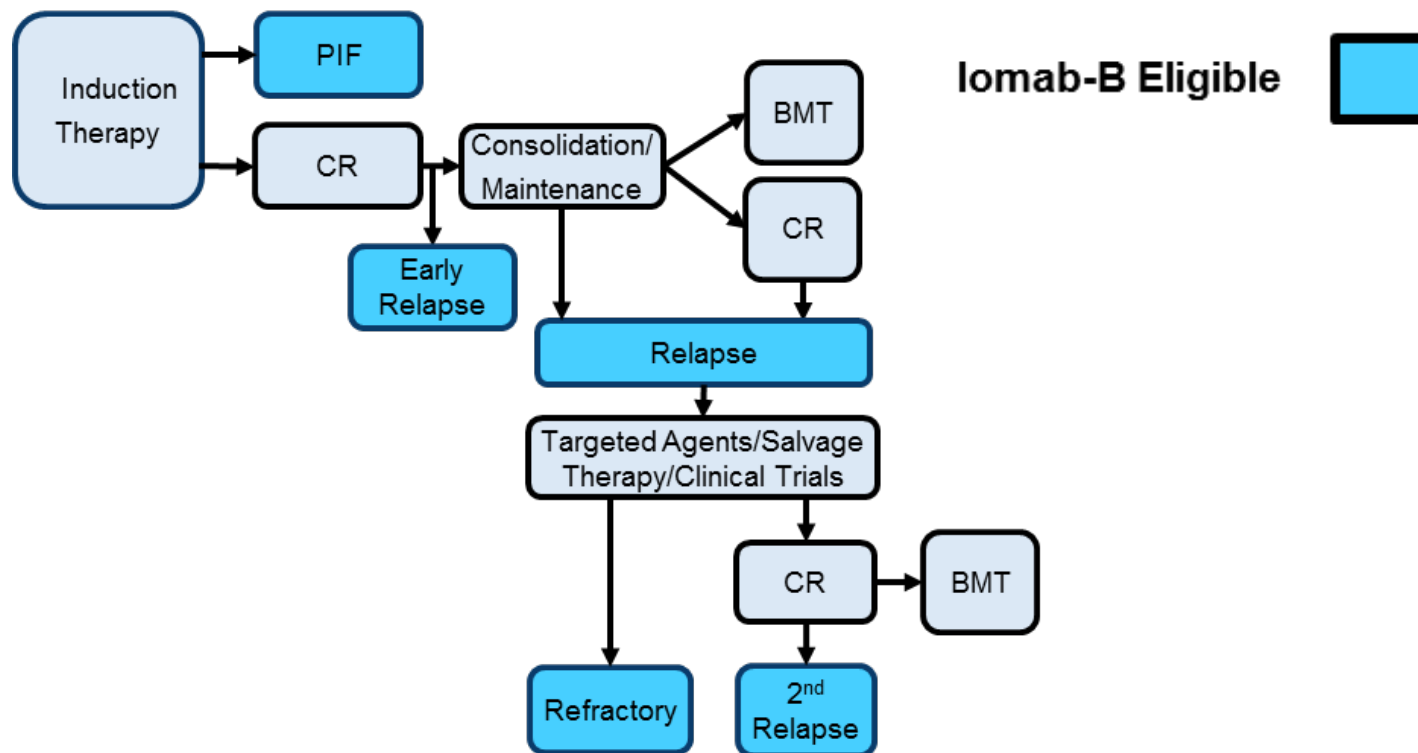


- SIERRA is over 75% enrolled
- Universal engraftment and positive safety results reported at 25%, 50% and 75% enrollment, engraftment predictive of long-term outcomes
- DMC recommended that SIERRA proceed as planned to full enrollment, no safety concerns raised
- Minimal alpha spend with ad hoc interim analysis, p-value threshold of 0.046 at full enrollment (150 patients)
- Actinium did not receive primary and secondary endpoint data that the DMC evaluated

Iomab-B's Highly Differentiated Position in AML

Despite 9 AML drug approvals, none are curative and a significant patient population remains where Iomab-B has a clear and compelling value proposition as it is the only path to a potentially curative BMT in relapsed/refractory AML

Iomab-B would represent a paradigm change in conditioning as it is both an induction and conditioning agent unlike currently used agents. Iomab-B potentially enables patients to go directly to a BMT without being in remission.

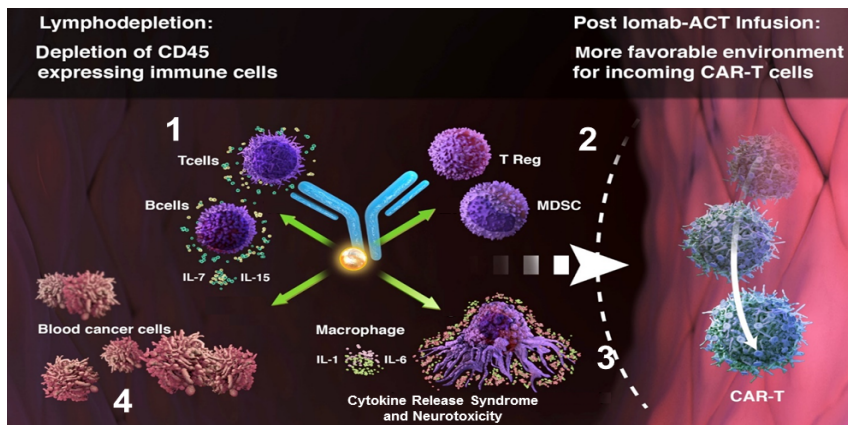


Iomab-ACT: NIH Funded CAR-T Clinical Collaboration

MSK's 19-28z CAR-T's strong efficacy but challenging CRS and neurotoxicity profile ideal for collaboration

- CD45 positive immune cells are implicated in major CAR-T side effects; cytokine release syndrome (CRS) and neurotoxicity
- Iomab-ACT intended to selectively target and deplete these immune cells to reduce severity and incidence of toxicities
- Iomab-ACT is a single infusion, outpatient administration compared to current chemotherapy that requires multiple infusions
- Phase 1/2 trial will enroll up to 39 DLBCL and B-ALL patients
- Patient enrollment initiated; POC data expected from Phase 1 portion of study in 2021

Iomab-ACT enables targeted depletion of multiple immune cells implicated in CAR-T toxicities

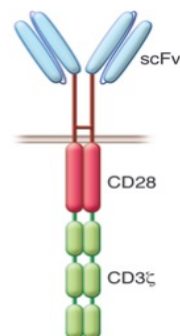


Robust data with MSK 19-28z provides clear benchmark to evaluate Iomab-ACT's impact

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NIH
National Institutes
of Health
SBIR/STTR

The NEW ENGLAND
JOURNAL of MEDICINE

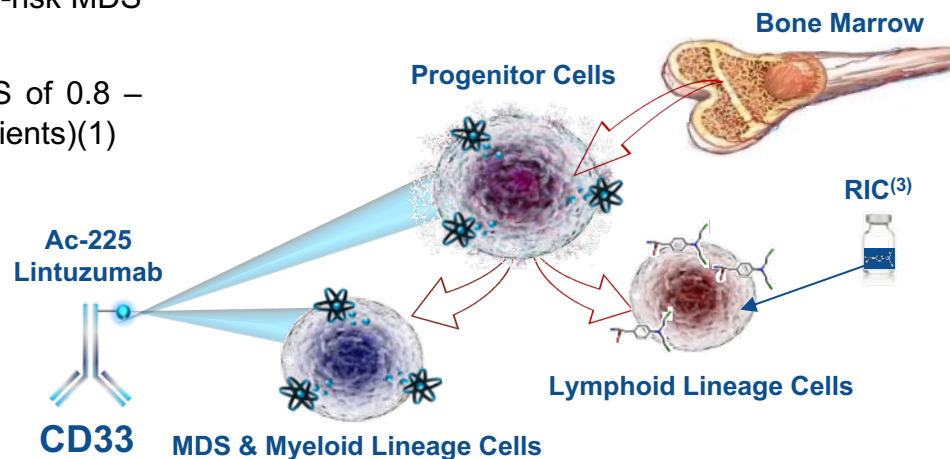


- 83% CR rate in B-ALL compares favorably with CR rates of approved CD19 CAR-T¹
- 20-26% Grade 3 CRS rates¹
- 42-67% Grade 3&4 neurotoxicity¹

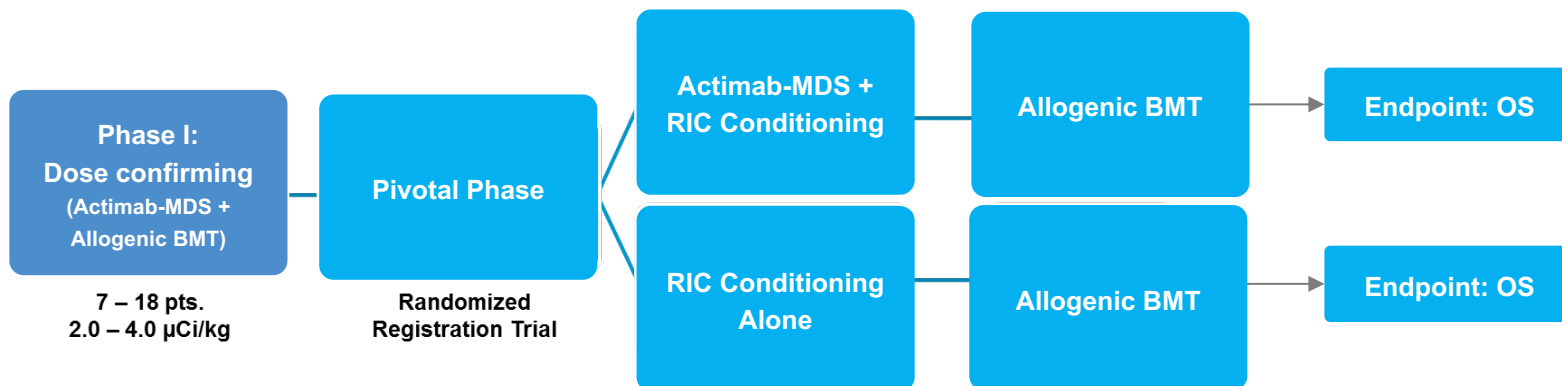
Actimab-MDS: Targeted Conditioning Franchise Expansion

Actimab-MDS is Actinium's second pivotal program in targeted conditioning

- BMT is considered the only curative treatment option for high-risk MDS patients
- High-Risk MDS patients have dismal outcomes (Median OS of 0.8 – 1.6 years vs. 3.0 – 5.3 years for intermediate and low risk patients)(1)
- Current approaches to BMT largely similar to AML (Chemo based MAC or RIC conditioning)
- CD33 is expressed in a vast majority of MDS patients(2)
- At high doses (2.0 $\mu\text{Ci/kg}$) Actimab-A exhibited significant myelosuppression, a surrogate for conditioning, in Phase 2 single-agent trial at fractionated doses



Novel conditioning regimen, no other trial of this kind for patients with MDS



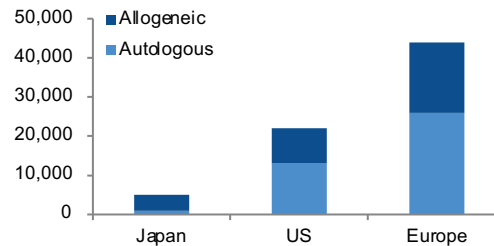
Targeted Conditioning: Compelling Market Opportunity

Concentrated market and growing addressable patient population that could be expanded with targeted conditioning

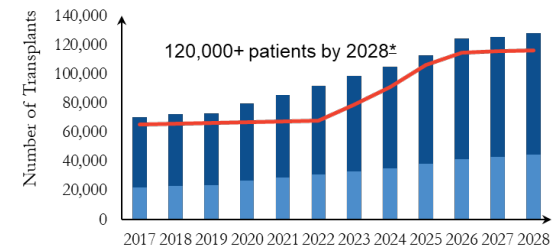
Major markets (US, EU, Japan) can be served effectively and efficiently with lean infrastructure



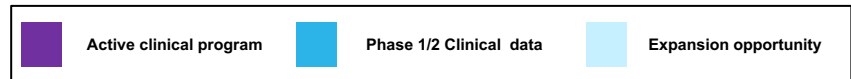
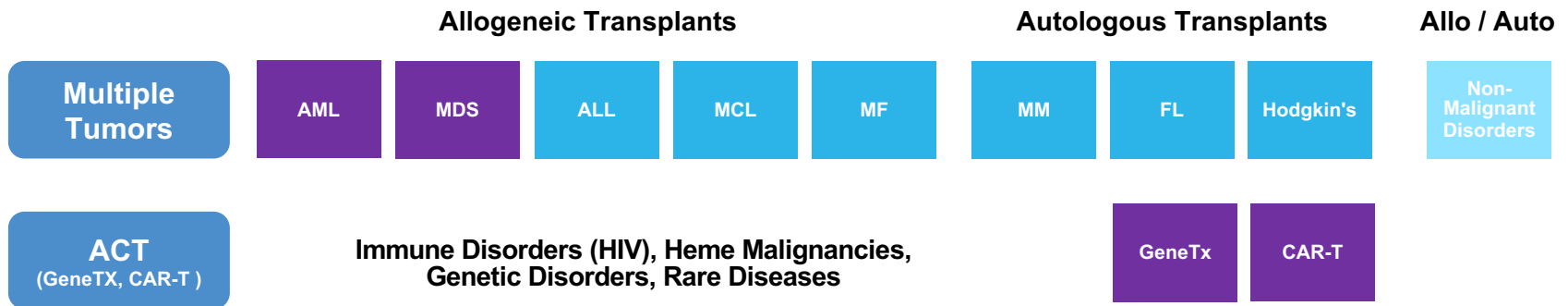
Over 70,000 transplant procedures performed in the US⁽¹⁾, EU⁽²⁾ and Japan⁽³⁾ in 2016



Targeted conditioning can enable significant expansion of the addressable patient population⁽⁴⁾



Distinct Opportunity For Comprehensive Portfolio Build-out



Highly Differentiated CD33-Alpha Program

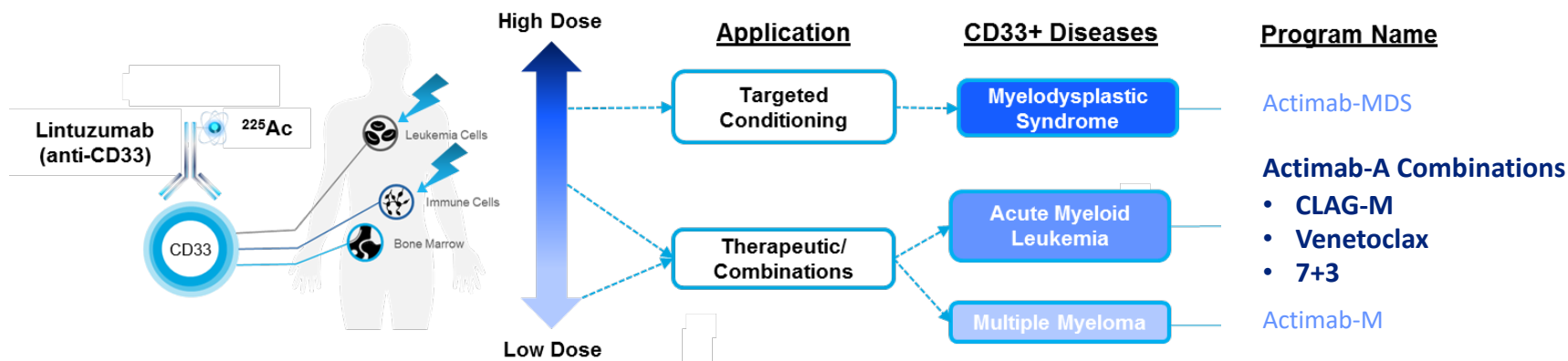
Development strategy being driven by clinical data and radioimmunobiology

- Clinical experience in 125+ patients in 6 clinical trials
- Minimal non-hematologic toxicities > grade 3 outside of myelosuppression in Phase 1/2 trial
- Clinical data driving high-dose targeted conditioning and low-dose combination development strategy
- Multiple opportunities to use Actimab-A in combination with chemotherapy, targeted agents and immunotherapy

Actimab-A Phase 1/2 Results

Dose Level ($\mu\text{Ci/kg/fraction}$)	Response Rate (%) (CR, CRp & Cri)
0.5 $\mu\text{Ci/kg}^1$	0%
1.0 $\mu\text{Ci/kg}^1$	17% (1 CR)
1.5 $\mu\text{Ci/kg}^2$	22% (3 CRp, 3 Cri)
2.0 $\mu\text{Ci/kg}^3$	69% (1 CR, 2 CRp, 6 Cri)

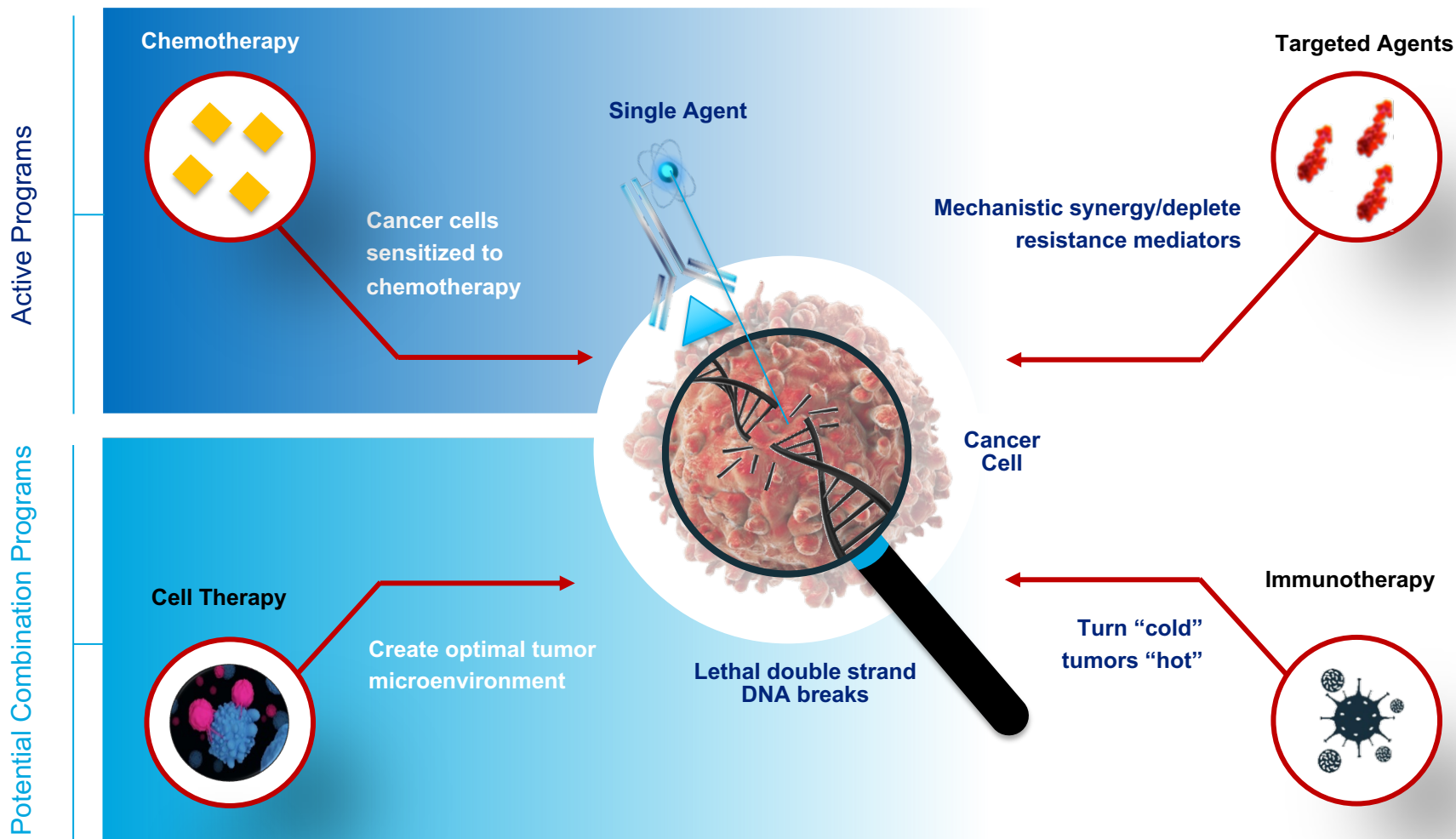
Actimab-A Development Strategy



1) Jurcic et al. ASH 2016. (N=9) 2) Atallah et al. Blood (2018) 132 (Supplement 1): 1457 (N=27) 3) Finn et al. Blood (2017) 130 (Supplement 1): 2638; (N=13)

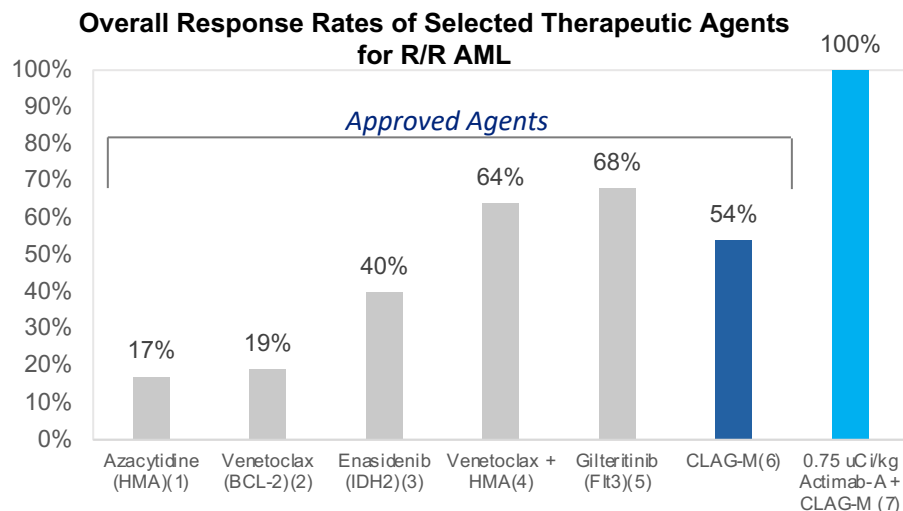
Potential Mechanistic Synergies Drive CD33 Program Expansion

Actinium has data demonstrating the potentiating and synergistic effect of targeted radiotherapy



Promising Phase 1 Results: Actimab-A + CLAG-M Combo

High remission rates vs approved agents from Actimab-A + CLAG-M combo in R/R AML



MRD Negativity Rate in R/R AML

	CLAG-M ⁸	Actimab-A + CLAG-M ⁷
MRD- Rate	39%	70%

- 100% remission rate (1 CR, 2 CRp) in cohort 3 compares favorably to 54% remission rate with CLAG-M alone
 - 85% increase in CR rate compared to CLAG-M alone**
- Proof of concept data supports mechanistic synergy of the combination
- MRD negativity in 70% of all patients with remissions (7/10)
- CR/CRi and MRD- observed in all dose cohorts
- First two dose cohorts included subtherapeutic doses of Actimab-A

Trial expansion includes additional dose cohort of 1.0 uCi/kg to evaluate efficacy criteria—including MRD- rate, duration of response, overall response—and establish MTD

1) Itzykson et al. Azacitidine for the treatment of relapsed and refractory AML in older patients. *Leuk Res.* 2015 Feb;39(2):124-30. 2) Konopleva et al. Efficacy and Biological Correlates of Response in a Phase II Study of Venetoclax Monotherapy in Patients with Acute Myelogenous Leukemia. *Cancer Discov.* 2016 Oct;6(10):1106-1117. 3) Stein et al. Enasidenib in mutant IDH2 relapsed or refractory acute myeloid leukemia. *Blood.* 2017 Aug 10;130(6):722-731. 4) Aldoss et al. Efficacy of the combination of venetoclax and hypomethylating agents in relapsed/refractory acute myeloid leukemia. *Haematologica.* 2018 Sep;103(9):e404-e407. 5) Perl et al. Gilteritinib or Chemotherapy for Relapsed or Refractory FLT3-Mutated AML. *N Engl J Med.* 2019 Oct 31;381(18):1728-1740. 6) Mushtaq et al. Comparison of Salvage Chemotherapy Regimens in Relapsed/Refractory Acute Myeloid Leukemia. *ASH Annual Meeting 2018* 7) Jurcic et al. Phase 1 trial of targeted alpha-particle therapy with LDAC in patients age 60 or older with untreated AML. *ASH 2016* 7) Abedin, S., et al. A Phase 1 Study of Lintuzumab Ac225 in Combination with CLAG-M Chemotherapy in Relapsed/Refractory AML. *Blood*, 2020 ASH 2020 Abstract #165; 8) Mushtaq et al. Comparison of salvage chemotherapy regimens and prognostic significance of minimal residual disease in relapsed/refractory acute myeloid leukemia. *Leukemia & Lymphoma* 2020;

Actimab-A + Venetoclax Combination Trial

Venetoclax is used widely across AML segments, however, most patients ultimately relapse - preclinical and clinical data support mechanistic synergy of Actimab-A with Venetoclax

- Venetoclax is a Bcl-2 inhibitor approved in 3 hematologic indications and is recommended for fit and unfit patients with AML with HMA or LDAC per NCCN guidelines. **Venetoclax showed a 19% ORR in R/R AML as single agent¹**

Actimab-A + Venetoclax First in Human Results

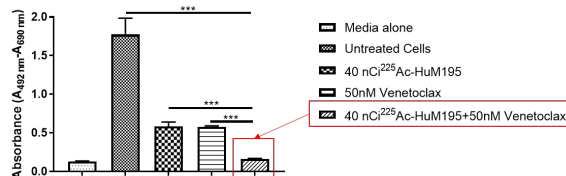
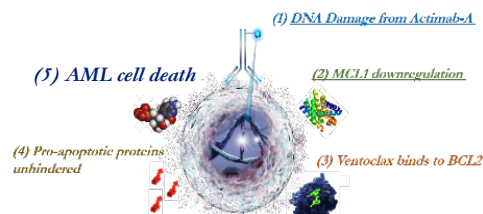
- 67% ORR in cohort 1:** 1 Complete Response and 1 Partial Response with a subtherapeutic dose of 0.5 μ Ci/kg of Actimab-A and one cycle of venetoclax
- All 3 patients were poor risk with adverse cytogenetics, and each patient has an additional high-risk marker (FLT3-ITD+, antecedent JAK2+ myelofibrosis, or TP53 mutation)
- No DLTs in dose cohort 1, trial has advanced to dose cohort 2 of 1.0 μ Ci/kg of Actimab-A
- Phase 1 trial completion and Phase 1 POC data in 2021

Actimab-A restores sensitivity to venetoclax and has single agent anti-leukemic activity supporting the rationale for ongoing Phase 1/2 combination trial

Rationale: Actimab-A depletes Mcl-1, a mediator of venetoclax resistance

Demonstrable Mechanistic Synergy⁽²⁾

First in Human Clinical Proof of Concept⁽³⁾

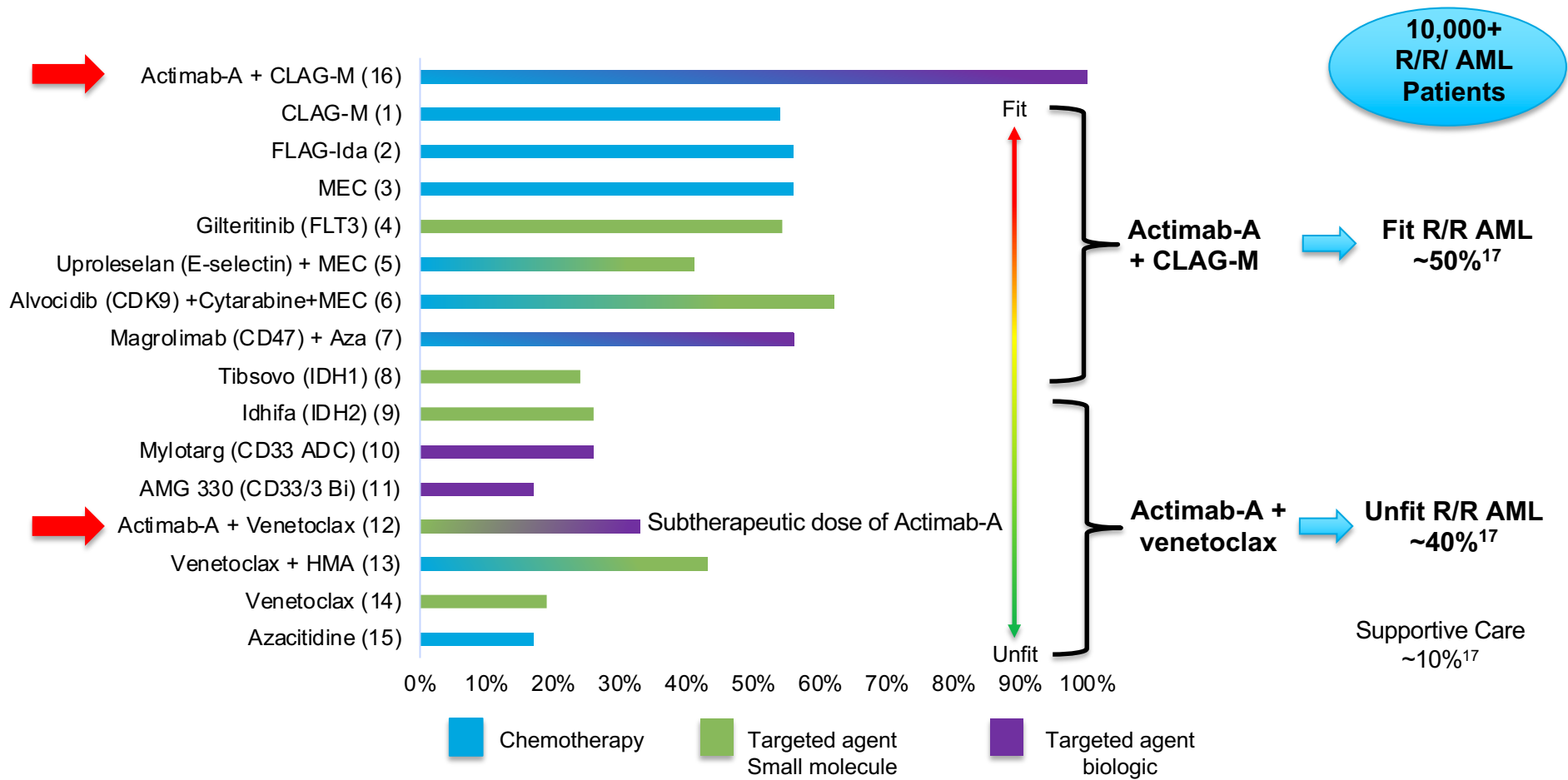


Patient Characteristics	Patient Outcome
2 nd Relapse, 20-25% BM blasts ASXL1, BRAF, IDH2, RUNX1, SRSF2, TP53 mutations	CRi after 1 cycle of Actimab-A + ven, proceeded to 2 nd cycle
Refractory, > 60% BM blasts, FLT3-ITD mutation	Partial Response, BM blasts decreased to 30%
Relapsed, 30% BM blasts, prior myelofibrosis with JAK2, SRSF2 mutations	Disease progression, discontinued study

1) Aldosset al. Efficacy of the combination of venetoclax and hypomethylating agents in relapsed/refractory acute myeloid leukemia. Haematologica2018.1888094.; 2) Garg et al. 225-Ac-CD33 radioimmunotherapy potentially increases the sensitivity of resistant acute myeloid leukemia lines to the Bcl-2 inhibitor venetoclax by mediating a reduction in cellular Mcl-1 levels. Poster 3808. AACR Annual Meeting 2019. 3) Hegazi, et. al. Lintuzumab-225Ac in Combination with Venetoclax in Relapsed/Refractory AML: Early Results of a Phase I/II Study Poster 2875. 62nd ASH Annual Meeting 2020.

Actimab-A Combinations Showing Impressive Results in R/R AML

Potential best in class profiles for both fit and unfit patients with R/R AML



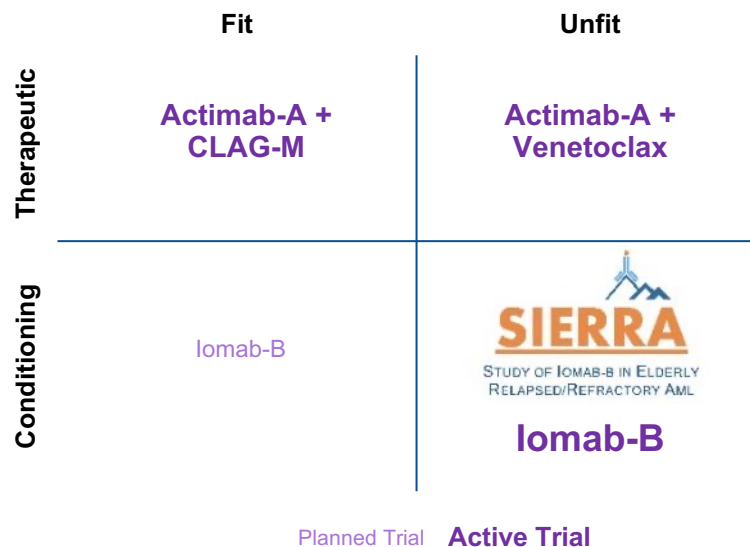
1) Mushtaq, et al. Leukemia & Lymphoma 2020, September (9)] ; 2) Westhus, et. al., Leuk Lymphoma. 2019 Apr ; 60(4) :1014-1022; 3) Scheckel, et. al., Leuk Res. 2020 Mar ;90 :106300; 4) Perl, et. al, N Engl J Med 2019; 381:1728-1740; 5) DeAngelo, et. al., Blood (2018) 132 (Supplement 1): 331; 6) Zeidner, et. al., Blood (2018) 132 (Supplement 1): 30 7) Sallman, et. al., J Clin Oncol 38 : 2020 (suppl ; abstr 7507); 8) Pollyea, et. al., J Clin Oncol 36 : 2018 (suppl 15); 9) Stein, et. al., Blood 2017 Aug 10 ; 130(6) : 722-731; 10) FDA Label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761060s003lbl.pdf; 11) Ravandi, et. al., J Clin Oncol 38 (suppl 15; abstr 7508); 12) Ram, et. al., Ann Hematol. 2019 Aug; 98(8):1927-1932; 13) Konopleva, et. al., Cancer Discov. 2016 Oct; 6(10):1106-1117; 14) Itzykson, et. al., Leuk Res. 2015 Feb ;39(2) :124-30; 15) Abedin, S., et. al, A Phase 1 Study of Lintuzumab Ac225 in Combination with CLAG-M Chemotherapy in Relapsed/Refractory AML, Blood, 2020; 17) Borlenghi, et. al., Validating the Patient's "Fitness" Criteria Proposed to Guide Treatment Decisions in Elderly AML: a Multicenter Study on a Population-Based Series of 362 Patients by the Network "Rete Ematologica Lombarda" (REL), Blood (2014) 124(21):279

Attractive Market Opportunity in R/R AML Led By Iomab-B

Iomab-B and Actimab-A programs address both fit and unfit patients as a conditioning agent and therapeutic

Actinium's ARCs may offer novel treatment options for key R/R AML patient segments

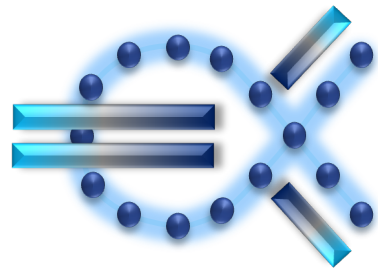
Potential to build a specialty oncology business capturing a majority of the R/R AML patient population who are treated at the top 100 cancer hospitals



Expected Value Creating Milestones

Multiple clinical and corporate milestones expected throughout 2021 enabled by strong balance sheet and enhanced clinical development and R&D capabilities

	Milestone	Status
Targeted Conditioning		
Iomab-B Pivotal Phase 3 SIERRA Trial	Present feasibility, engraftment and detailed safety data from 75% of patient enrollment at ASH	✓
	Interim ad hoc analysis	✓
	Complete enrollment/BLA filing	2021/2022
Iomab-ACT Program	Secure GeneTx development partner	✓
	GeneTx proof of concept data	2021
	CAR-T clinical collaboration with MSK; NIH grant funding	✓
	CAR-T proof of concept data	2021
CD33 ARC Combinations and AWE Technology Platform		
Actimab-A + CLAG-M	Complete 3 rd and planned final cohort and present PoC data	✓
	Complete expanded 4 th cohort and present full Phase 1 data	2021
Actimab-A + Venetoclax	Phase 1 POC data from Actimab-A venetoclax combination trial	2021
Actimab-MDS Pivotal Program	Regulatory Update/Initiate pivotal program	2021
AWE Technology Platform	Secured collaboration with Astellas utilizing AWE for solid tumor theranostics	✓



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Thank You
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