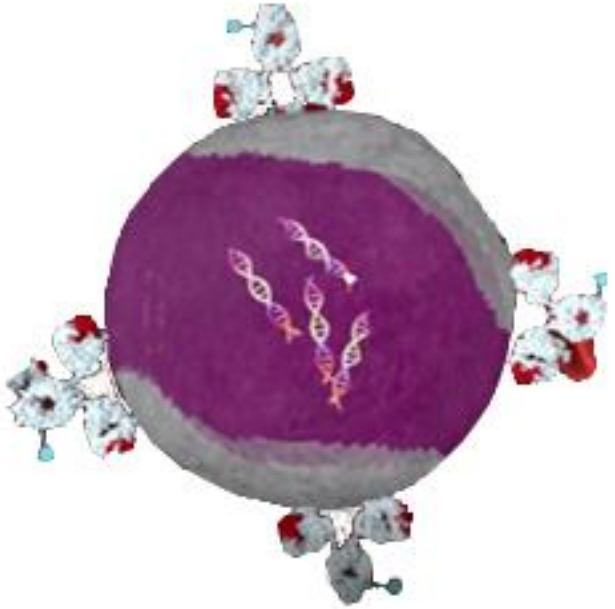
Actinium Pharmaceuticals, Inc.

Introducing Actimab-MDS: Bridge to Transplant for Patients with p53+ Myelodysplastic Syndrome



December 5, 2017

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Webinar Participants

Gail J. Roboz, M.D.

Director, Leukemia Program and Professor of Medicine

Weill Cornell Medicine

NewYork-Presbyterian

Sandesh Seth

Chairman & CEO

Mark Berger, M.D.

Chief Medical Officer

Actinium Pharmaceuticals, Inc.

Today's Agenda

Executive Overview

- Today's webinar unveils the latest clinical initiative from Actinium Pharmaceuticals, Inc.'s ("Actinium" or the "Company") CD33-Alpha Program
  - Program features an ARC – or Antibody Radio-Conjugate, namely actinium-225 linked to the monoclonal antibody lintuzumab
- Clinically driven insights into the ARC's efficacy, safety and ability to effectively target CD33 is enabling initiatives outside of the lead trial of Actimab-A in AML
  - In early 2017 we announced the Actimab-M trial in multiple myeloma
  - Today, announcing Actimab-MDS as a bridge to transplant for p53+ MDS patients shown to have poorer outcomes from bone marrow transplants
- Enabling this trial with Actimab-MDS is clinical evidence from the Actimab-A trial
  - ARC properties of minimal extramedullary toxicity and strong myelosuppression evidenced in our clinical trials can be strengths when used as a bone marrow conditioning agent to a stem cell transplant
- Actinium is grateful for the interest and support of a Key Opinion Leader, namely Dr. Gail Roboz who has and will be working with the Company on this latest clinical trial which has the potential as an important new tool for these MDS patients

Progressing and Expanding CD33 Program

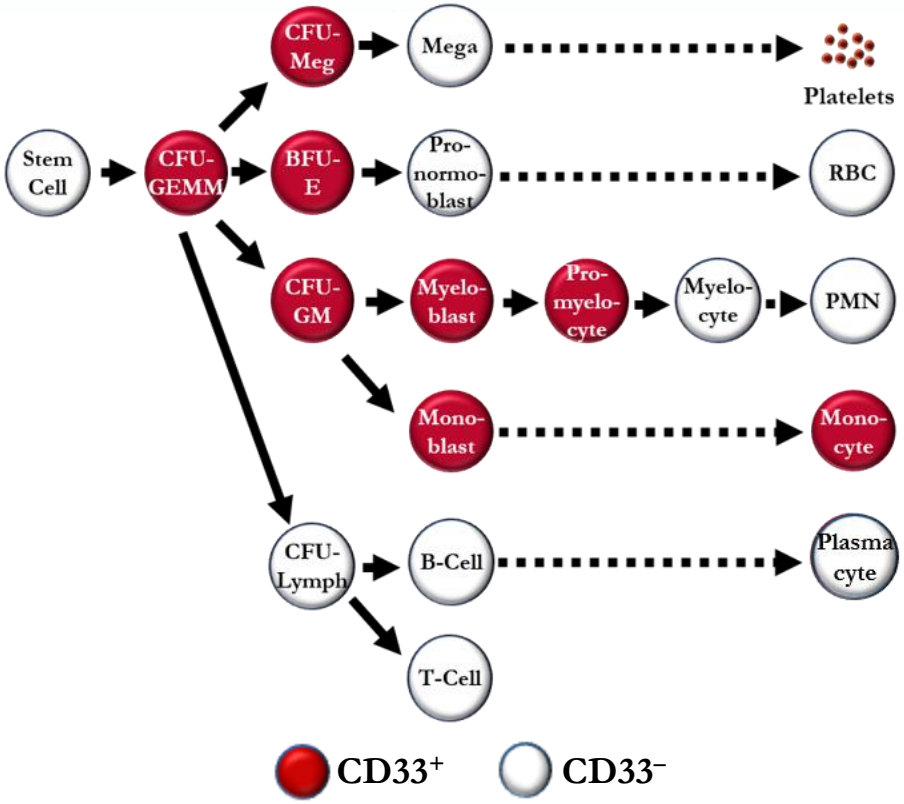
- CD33 program studied in over 100 patients to date
- Potentially best-in-class efficacy and safety in patients resistant to most forms of AML treatment

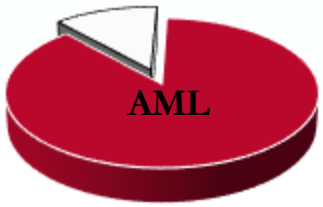
Drug Candidate	Status	Disease	Indication	Stage of Development
Bismab-A	First Generation	**AML**	Newly diagnosed with AML over age 60 Newly diagnosed ineligible for high-dose regimens AML in relapse AML refractory to 2 courses of induction therapy	Phase 1/2 **discontinued*
Actimab-A	Ongoing	**AML**	AML in relapse AML refractory to 2 courses of induction therapy	Phase 1
			Newly diagnosed with AML over age 60 ineligible for intense chemotherapy	Phase 2
Actimab-M	Ongoing	**Multiple Myeloma**	Patients with refractory multiple myeloma that have received at least 3 prior lines of treatment	Phase 1
Actimab-MDS	Planned	**Myelodysplastic Syndrome - MDS**	Myeloablative conditioning in high-risk p53+ MDS patients as a bridge to transplant	Phase 2 **planned*

Overview of Actinium's CD33 Program

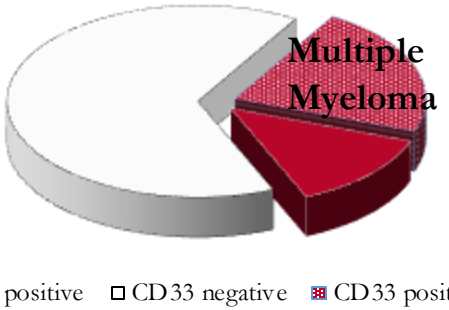
CD33 – A Viable Target in Multiple Diseases

AML Cells, MDS Cells and Multiple Myeloma Cells all have levels of CD33 expression

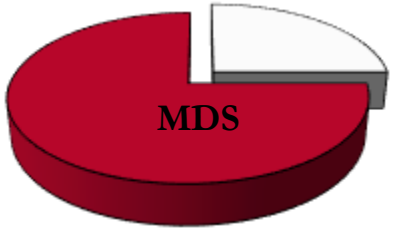




CD33 is expressed in virtually all AML patients[1]



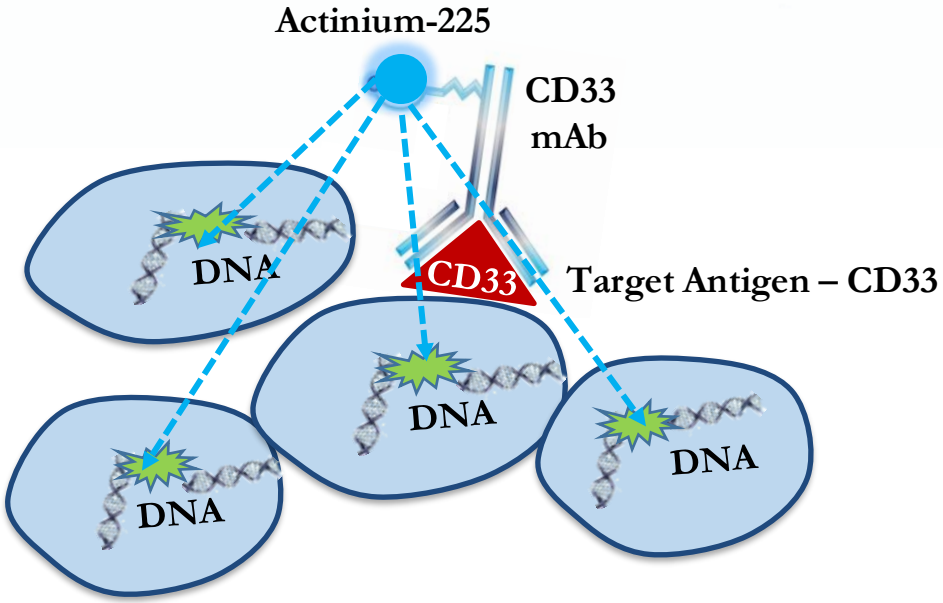
Up to 35% of MM patients express CD33, 22% of patients have >50% CD33 expression[2]



CD33 is expressed in up to 75% of MDS patients[3]

1) Blood Cancer J. 2014 Jun; 4(6): e218. Distribution and levels of surface expression of CD33 and CD123 in acute myeloid leukemia
2) H Avet-Loiseau, CD33 is expressed on plasma cells of a significant number of myeloma patients, and may represent a therapeutic target, Leukemia (2005) 19, 2021–2022.)
3) Leuk Lymphoma. 2016 August ; 57(8): 1965–1968. CD33 is frequently expressed in cases of myelodysplastic syndrome and chronic myelomonocytic leukemia with elevated blast count.

Benefits of Targeting CD33 with AWE Technology



Radiobiology of Actinium-225

- High Energy = High Potency
  - 5-8 MeV via emission of 4 α-particles[1]
  - Cell kill possible with 1 α-particle hit to DNA, also killing via crossfire effect[1]
- Short Pathlength = Safety Potential
  - 50-80 microns[1]
- Commercially Viable[1]
  - Ac-225 Half-life: 10 days
  - Biologic Half-life: 3 days

Benefits of AWE or Actinium Warhead Enabling Technology

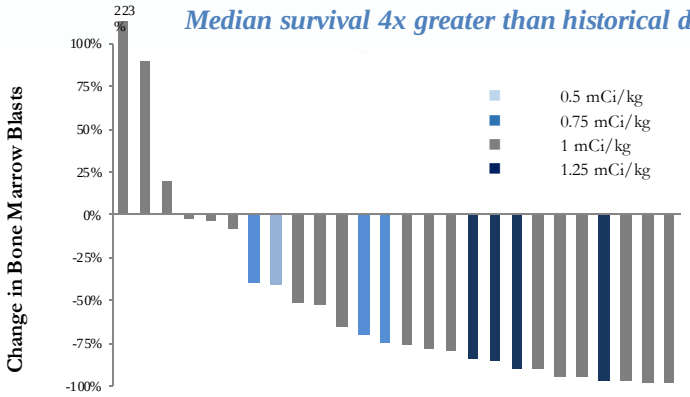
- Mechanism of action well suited for radiation sensitive hematologic indications
- Alpha particles (Ac-225) potentially capable of overcoming chemotherapy resistance
- Potential for combining with standard of care therapies due to safety/efficacy balance and adding a mechanistically different treatment modality
- Mechanism of killing impervious to genetic abnormalities which are common in the indications targeted

1) Sgouros et al. Radiobiology and Dosimetry of a-Particle Emitters for Targeted Radionuclide Therapy. The Journal of Nuclear Medicine 2010; 51:311–328

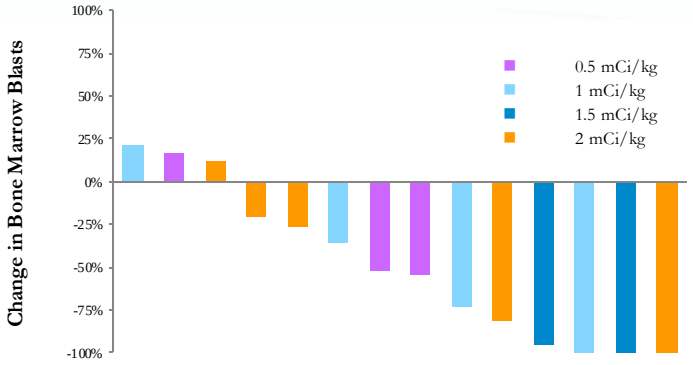
AML Program Overview – Bismab-A & Actimab-A

First Generation Bismab-A Results

Median survival 4x greater than historical data[1]



Second Generation Actimab-A Results[2]



Phase 1 Results (completed in 2016)

Dose Level (µCi/kg/ fraction)	Response Rate (CRc) Low Peripheral Blasts
2 x 0.5	0%
2 x 1.0	33%
2 x 1.5	67%
2 x 2.0	50%

Phase 2 Results (to date)[3]

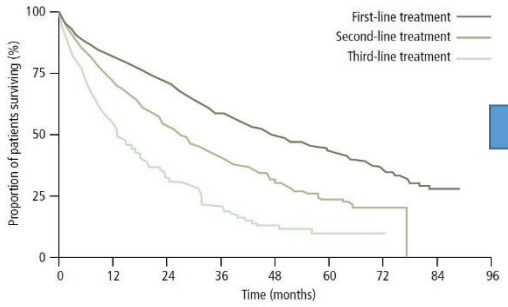
Dose Level (µCi/kg/ fraction)	Response Rate (CRc) Low Peripheral Blasts
2 x 1.5	Enrolling
2 x 2.0	56%

Updated data forthcoming via ASH Poster on 12/10/17

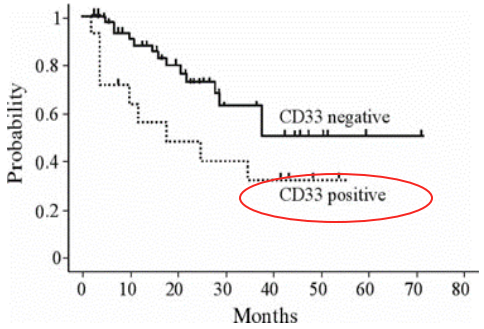
1) Median survival 7.6 mo. vs 1.7 mo. historically for untreated. Each bar equals an individual patient response.
2) Jurcic et al. 2016 ASH Abstract. Phase 1 Trial of Targeted Alpha-Partide Therapy with Actinium-225-Lintuzumab and LDAC in patients Age 60 or Older with Untreated AML.
3) 2017 ASH Abstract #2638. A Phase 2 Study of Actinium-225-Lintuzumab in Older Patients with Previously Untreated AML Unfit for Intensive Chemotherapy. Program: Oral and Poster Abstracts. Session: 616. Acute Myeloid Leukemia: Novel Therapy, excluding Transplantation: Poster II

Rationale for Targeting CD33 in Multiple Myeloma

Multiple myeloma remains incurable, limited treatment options for refractory patients



Poorer outcomes associated with CD33 expression



Large addressable market underserved by existing treatment options

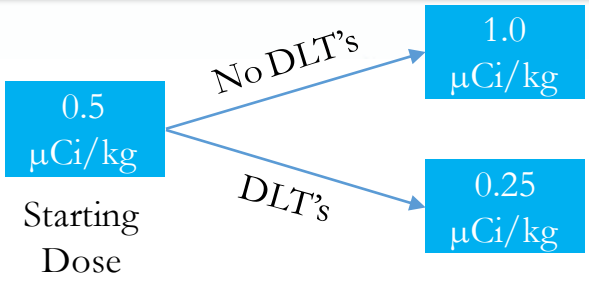
Multiple Myeloma Prevalence	Total # of Patients[1]	CD33 Positive[2]
US	89,600	22,400
Europe	100,000	25,000
Total	**189,600**	**47,400**

- CD33 is expressed on myeloma plasmocytes in ~25% - 35% of all patients[1]
- 22% of myeloma patients found to have CD33 expression above 50% with median expression of 85%[1]
- CD33 expression is associated with significantly poorer survival prognosis
- 3-year mortality 60% greater in CD33+ patients[3]

1) Onyx Pharmaceuticals, SEER, NCI, ACS, Celgene, Myeloma Euronet, GLOBOCAN, CIBMTR, Kyprolis insert, W Matsui JHI estimate, Ferlay et al *Eur J Cancer* 2013
2) Company estimates
3) H Avet-Loiseau, CD33 is expressed on plasma cells of a significant number of myeloma patients, and may represent a therapeutic target, Leukemia (2005) 19, 2021–2022.)

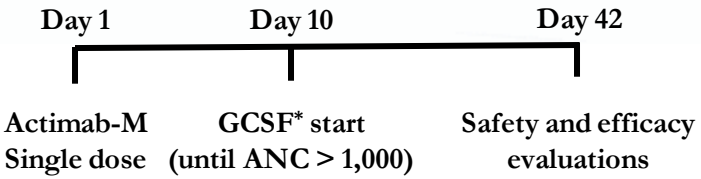
Potential for Actimab-M in Multiple Myeloma

Trial Design



- 3 + 3 trial design
- Up to 12 patients

Actimab-M Administration



- Single agent, single dose infusion
- Up to 8 cycles (up to max of 4.0 µCi/kg)

- Actimab-M has the potential to improve outcomes for refractory patients
  - Mechanism of action well suited for radiation-sensitive multiple myeloma
  - Alpha particles (Ac-225) potentially capable of overcoming chemotherapy resistance
  - Possibility to use in combination with standard of care (SoC) MM therapies
- Safety and Overall Response Rates (ORR) would be considered significant proof of concept
  - Daratumumab single agent had 2.8% sCR rate (no CR)[1]
  - Elotuzumab in combination with len-dex had CR +sCR rate of 4.4%[2]
- Actimab-M has the potential to be developed as both a single agent or in combination with approved therapeutics

1) Lancet. 2016 Apr 9;387(10027):1551-60
2) N Engl J Med 2015 Aug 13; 373:621-631

Strengths Uncovered from our CD33 Program

- CD33 targeting construct (lintuzumab + actinium-225) has high single agent response rates in older AML patients unfit for cytotoxic chemotherapy and who had prior MDS
  - Remissions independent of prior MDS
- Safety profile made-to-order for Stem Cell Transplant or SCT preparation
  - Minimal extramedullary toxicity
  - Most significant side effect is myelosuppression
  - Not an issue if patient is quickly having allogeneic stem cell transplant
- Administration is uncomplicated
  - Given in the outpatient setting and patients can go wherever they want after infusions with the construct
- Emphasizing importance of safer myeloablation with no extramedullary toxicities in the setting of myelodysplastic syndrome

Today's Featured Speaker

Weill Cornell Medicine

NewYork-Presbyterian

MDS Overview

Myelodysplastic Syndrome

- MDS occurs when the bone marrow produces stem cells that fail to mature to red blood cells, white blood cells or platelets
- Low blood cell counts or cytopenias are hallmarks of MDS

- Prevalence of MDS in the US and EU estimated at 100,000 cases [1, 2]
- 86% of patients diagnosed with MDS are over the age of 60[3]
- Approximately 1/3 of MDS cases progress to AML[3]
- Patients are assessed using the Revised International Prognostic Scoring System (IPSS-R)

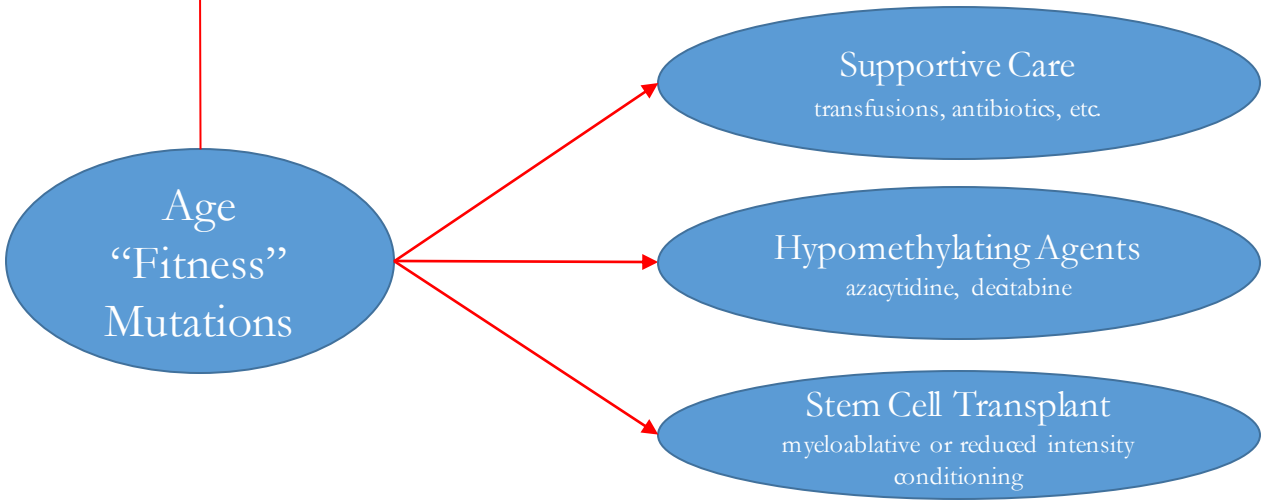
1) Xiaomei MA, Ph.D. Am J Med. 2012 Jul; 125(7 Suppl): S2-S5
2) http://eco.iarc.fr/eucan/Country.aspx?ISOCountryCd=930
3) American Cancer Society. https://www.cancer.org/cancer/myelodysplastic-syndrome.html

Stratifying MDS Patients to Determine Treatment

Revised – International Prognostic Scoring System (IPSS-R)[1]

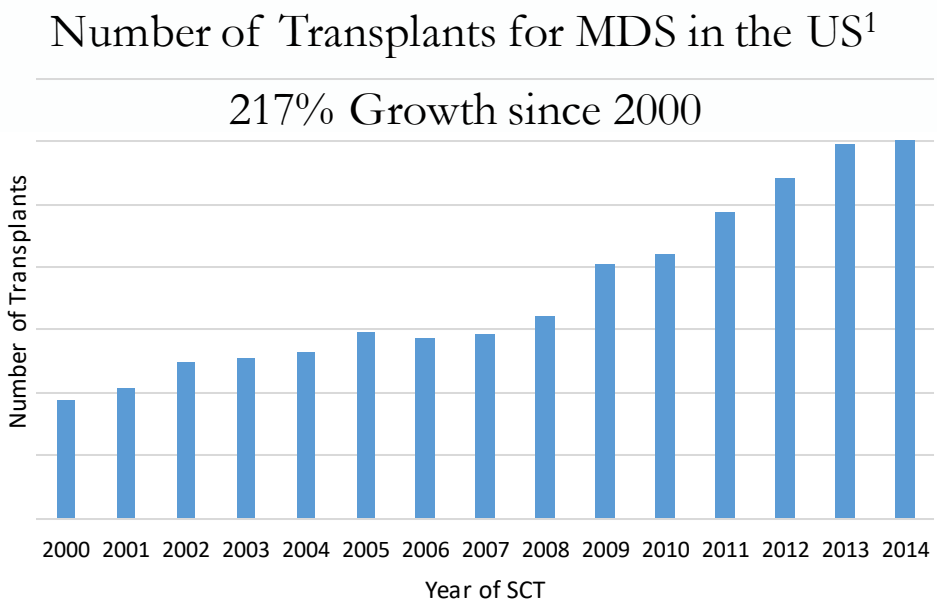
Prognostic Variables[1]
Cytogenetics
BM Blast %
Hemoglobin
Platelets
ANC[2]

Risk Category	Risk Score	Median Survival (years)	Time to AML Evolution (years)
Very Low	<=1.5	8.8	NR
Low	>1.5 – 3	5.3	10.8
Intermediate	3- 4.5	3.0	3.2
High	>4.5 – 6	1.6	1.4
Very High	>6	0.8	0.7



1) Greenberg, Tuechler, Schanz et al, Revised International Prognostic Scoring System (IPSS-R) for Myelodysplastic Syndrome, Blood 120: 2454, 2012
2) ANC – Absolute Neutrophil Count

Stem Cell Transplant for MDS

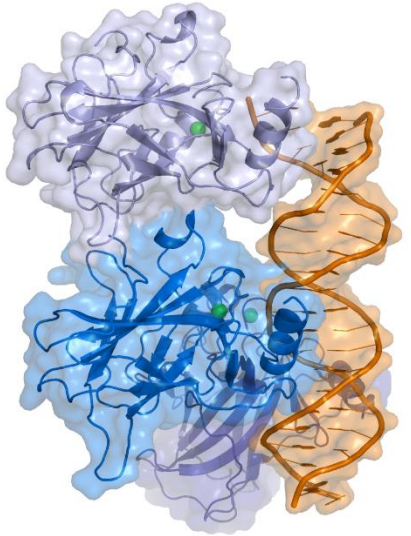


- SCT is considered the only curative treatment option for MDS
- SCT for MDS has been growing rapidly
- Current approaches to SCT
  - Myeloablative Conditioning
  - Reduced Intensity Conditioning

1) Wael Saber and Mary M. Horowitz. Transplantation for myelodysplastic syndromes: who, when, and which conditioning regimens. Department of Medicine, Center for International Blood and Marrow Transplant Research, Medical College of Wisconsin, Milwaukee, WI. ASH Hematology 2016. 478 - 484

TP53s Role in MDS

- TP53 (tumor protein 53) is a tumor suppression gene
- Its activity is to stop the formation of tumors
- p53 mutations in patients with MDS have been found to be correlated with worse overall survival[1]
- In an analysis of 963 patients, patients with a p53 mutation had significantly poorer survival outcomes[1]



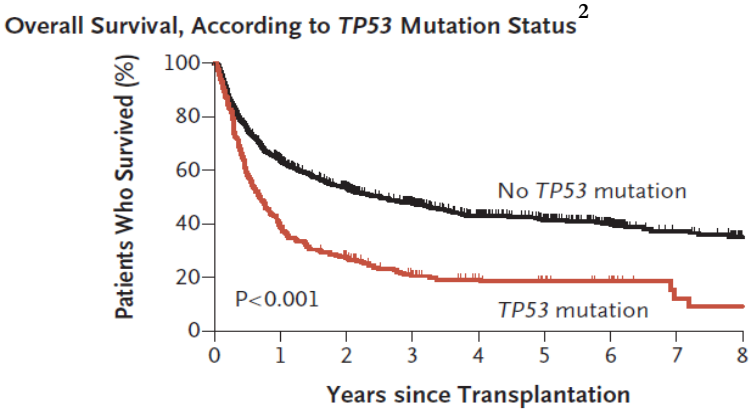
crystal structure of p53 DNA binding domains

Gene	N	Hazard Ratio for OS	P-value
P53 moderate impact	125 (17%)	2.35	< 0.001
P53 high impact	18 (2%)	2.63	< 0.001

1) Lee, Roboz et al. Prediction of Clinically Relevant Mutations in (MDS): A Report on Behalf of the MDS Clinical Research Consortium (CRC). ASH 2017 Annual Meeting Abstract #2965. Program: Oral and Poster Abstracts Session: 637. Myelodysplastic Syndromes—Clinical Studies: Poster II

Must Consider TP53 in SCT for MDS Patients

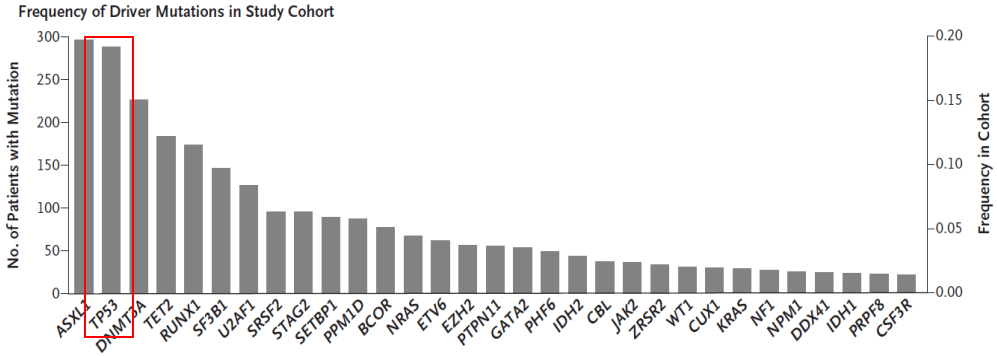
- p53 shown to be a predictor of poor outcomes for transplant and the most powerful predictor of survival[1]



Overall Survival Percentages

N	Year	1	2	3	4	5	6	7	8
1224	No p53 Mutation	61.8%	43.2%	30.2%	21.3%	15.0%	8.9%	4.3%	2.6%
289	p53 Mutation	37.7%	22.8%	13.5%	9.0%	6.9%	4.8%	2.1%	1.7%

- p53 is a highly occurring mutation found in ~ 20% of MDS patients[1]

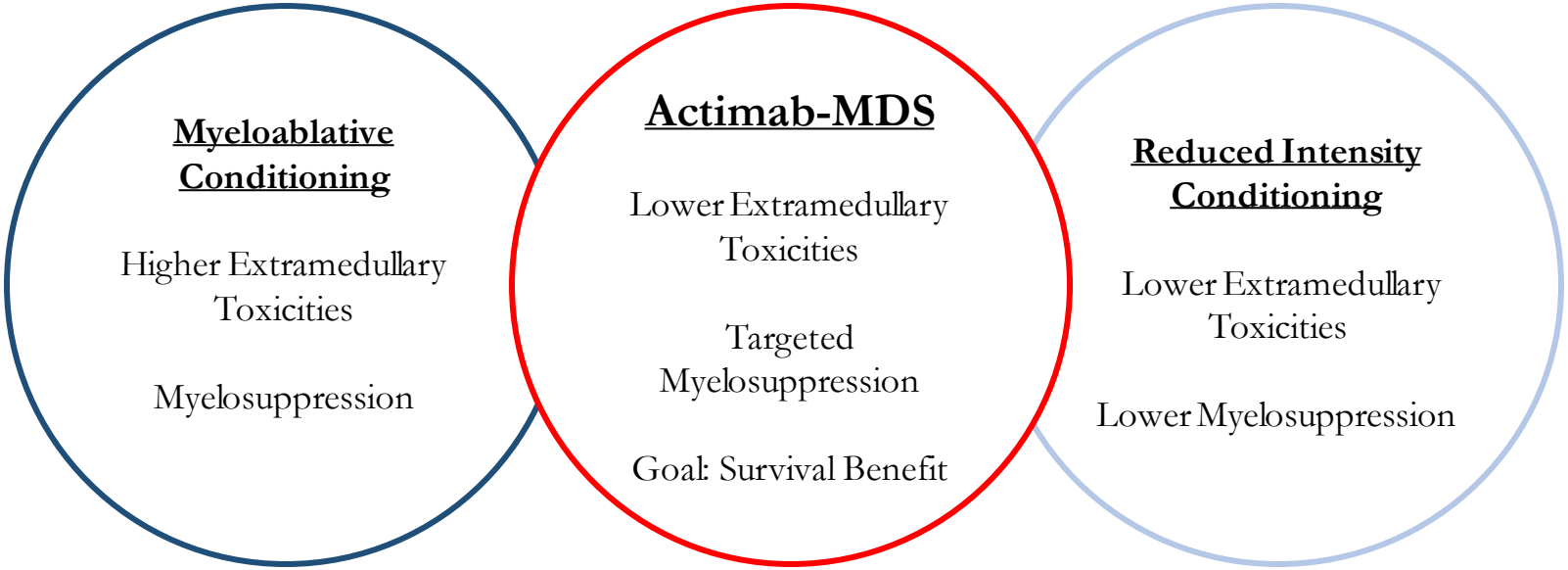


1) Lindsley, Saveer, Mar, et al, Prognostic Mutations in Myelodysplastic Syndrome after Stem-Cell Transplantation, The New England Journal of Medicine 376:536-47, 2017

2) P53 is also referred to as TP53

Actimab-MDS For SCT Conditioning

Myeloablative Conditioning		Reduced Intensity Conditioning
↑	Treatment Related Mortality	↓
↓	Relapse	↑
↑	Myelosuppression	↓
↑	Extramedullary toxicities	↓



SCT Preparation for p53+ MDS Patients via Actimab-MDS

Rationale

- Median survival for higher risk MDS patients is < 2 years
- Especially high unmet medical need in p53 patients, poor survival even with SCT
- Hypothesis: Actimab-MDS can be used to destroy MDS cells prior to allogeneic SCT
  - CD33 well expressed in MDS
  - High degrees of cytoreductive myelosuppression combined with decreased extramedullary toxicities attributable to Actimab-MDS may present an alternative to standard conditioning
- Trial initiated by Roboz/Weill Cornell, with plan to include members of the MDS Clinical Research Consortium (CRC)
  - MDACC, DFCI, Moffitt, Cleveland Clinic, Johns Hopkins

Study Details

Gail J. Roboz, M.D

Principal Investigator

Weill Cornell Medicine

NewYork-Presbyterian

Phase 2 Trial Consortium

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

DANA-FARBER CANCER INSTITUTE

MOFFITT CANCER CENTER

Cleveland Clinic

JOHNS HOPKINS MEDICINE

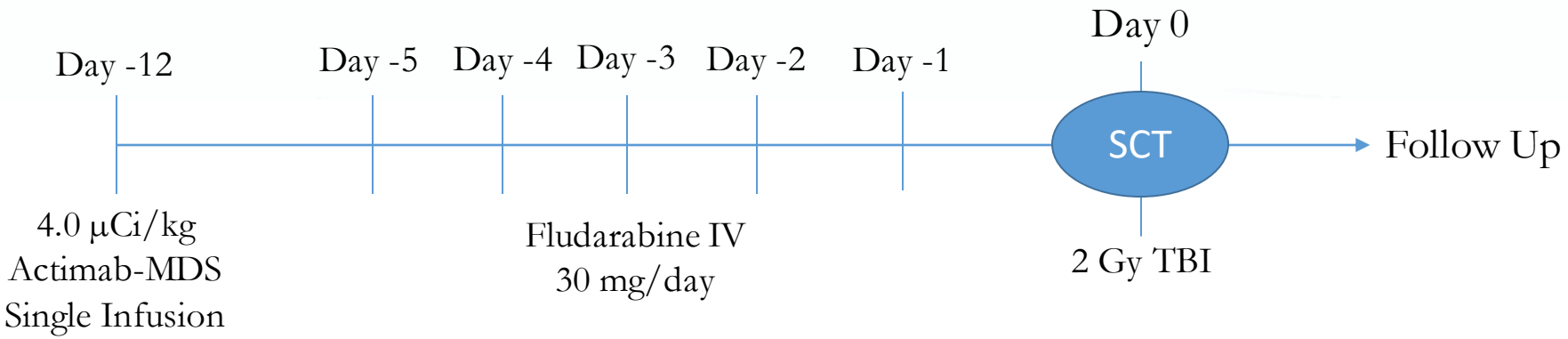
Trial Details:

- Phase 2
- Open-label
- Manageable Size – (60-80 Patients)

Patient Population:

- Diagnosis of MDS, prior treatment with HMAs is allowed
- 53 mutated
- Age 18 and above
- Greater than 25% of MDS bone marrow cells must be CD33 positive

Actimab-MDS Phase 2 Study Design



Primary Endpoint:

- TBD following discussions with FDA – tentatively Overall Survival (OS) at 1-2 years

Secondary Objectives:

- Relapse-free survival (RFS) and time to relapse among subjects who achieve CR or CRp
- Disease status among subjects who survive 1-2 years
- Time to engraftment of neutrophils and platelets
- Characterize the association between cytogenetics and molecular genetics and disease response
- Median OS after SCT

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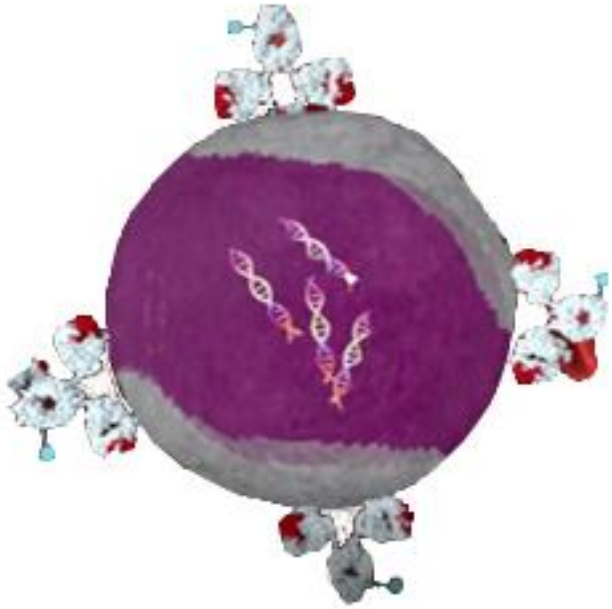
Next Steps for Actimab-MDS & Closing Remarks

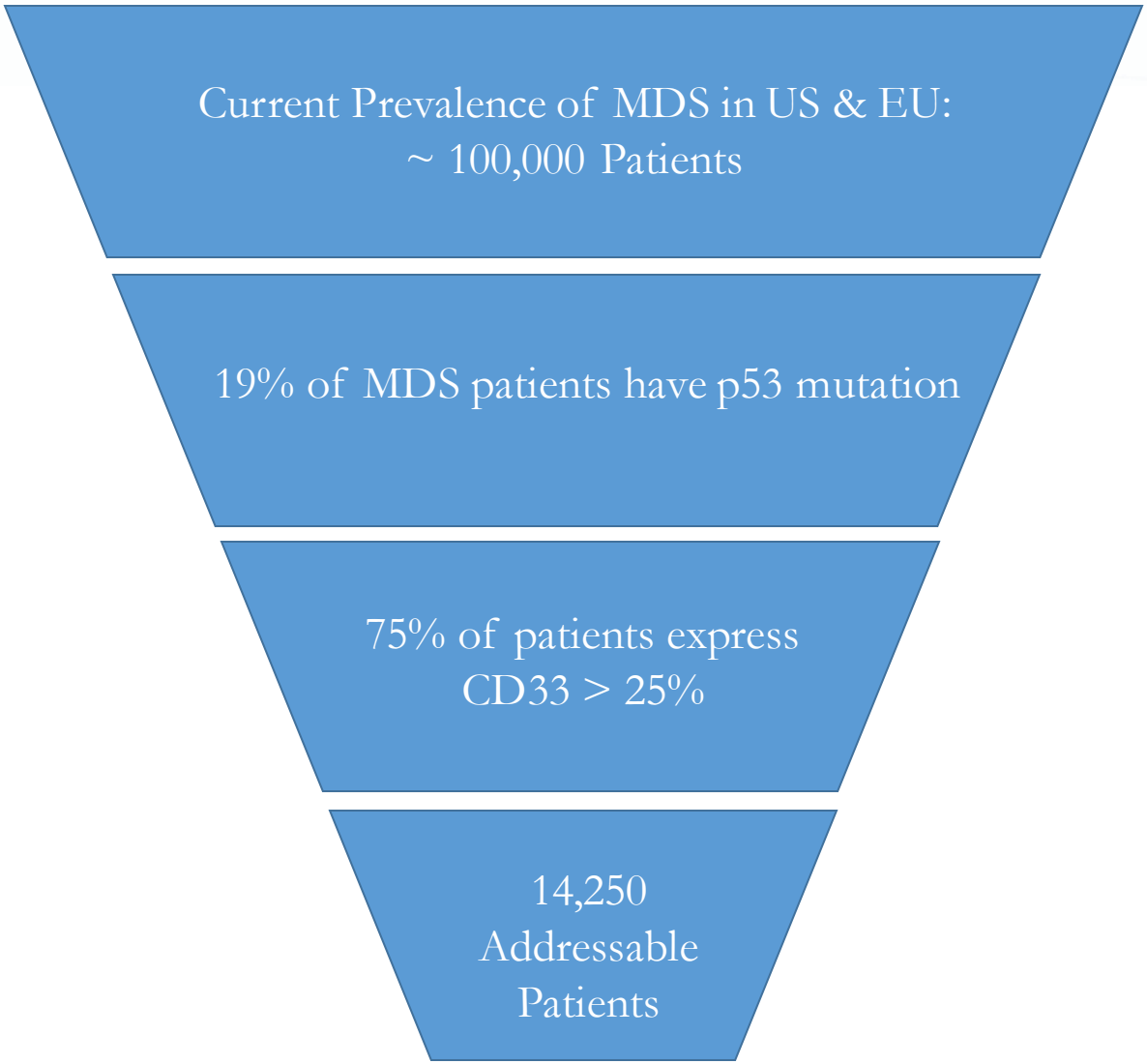


Sandesh Seth
Chairman & CEO
Actinium Pharmaceuticals, Inc.

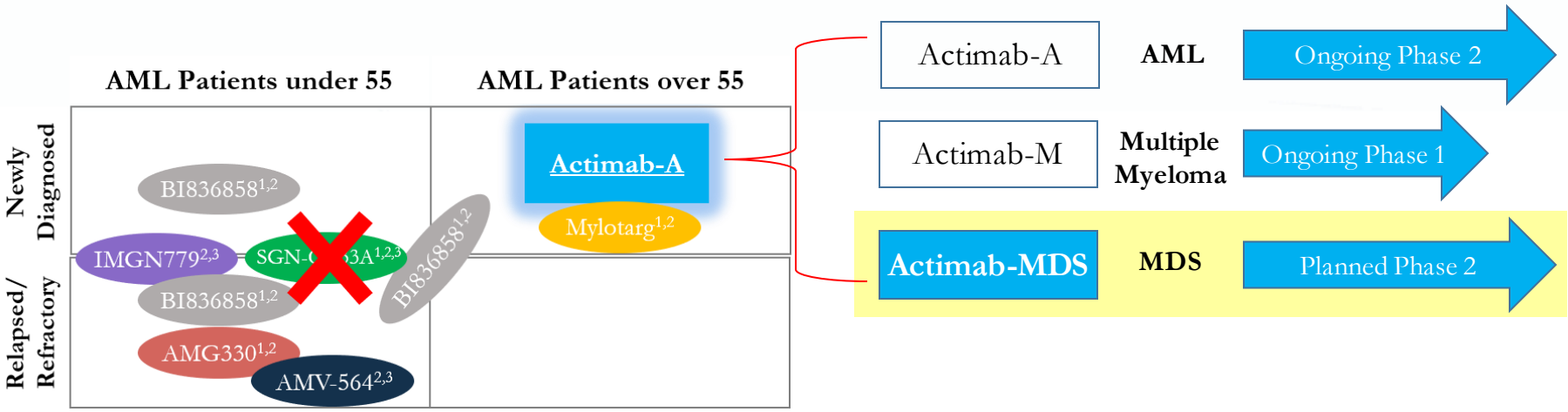
Next Steps

- IND package under preparation
- Working with Dr. Roboz led consortium on protocol, trial logistics, timing
- Optimal regulatory pathway to pivotal trial being strategized
- Cost-effective initiative due to support of the consortium with trial costs estimated in low single digit millions spread over life of the trial; drug supply on hand
- FDA Pre-IND Meeting 1H:2018
- Update on development path and trial timing to follow FDA Meeting
- Targeting trial initiation with Dr. Roboz led MDS Clinical Research Consortium in mid-2018

Actimab-MDS Patient Population & Addressable Market



CD33 Program Continuing to Evolve Beyond AML



Advantages of our ARC approach in CD33

- ARC – Antibody Radio-Conjugate
- No internalization required
- No known resistance mechanism
- Short infusion, one or two doses
- Monotherapy
- Very high potency
- Safety/Tolerability allows focus on "unfit" patients

CD33 Program Disease Prevalence

Drug	Disease	Addressable US, EU Market[4]
Actimab-A	AML	69,800
Actimab-M	CD33 Positive Multiple Myeloma	47,400
Actimab-MDS	MDS – SCT Prep	14,250
Addressable Patient Population:		**131,450**

Actinium Pharmaceuticals

Sources: 1. Clinicaltrials.gov 2. Company Materials 3. Conference Abstracts (ASH, AACR, ASCO) 4. Company estimates

Impact of Actimab-MDS for Actinium

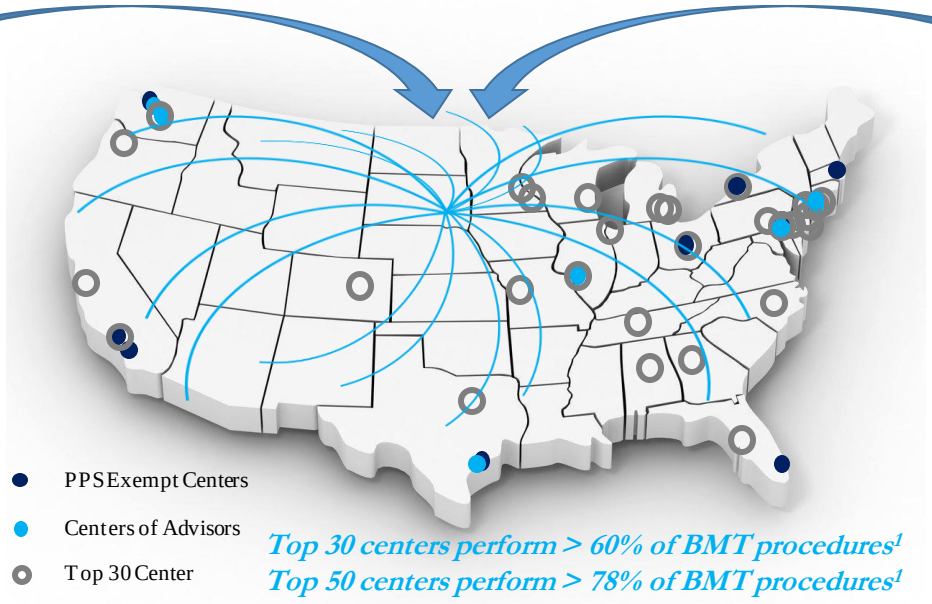
Potential for 2 Drug Approvals in the 2020 – 2021 timeframe

Compelling revenue opportunity providing Safer Myeloablative therapies with potential for increasing Curative Outcomes from Bone Marrow Transplant

Focused on the top 50 – 100 transplant centers in the United States extending our current presence in centers representing > 33% of the market

Iomab-B

10,000+ Addressable Patients[1]



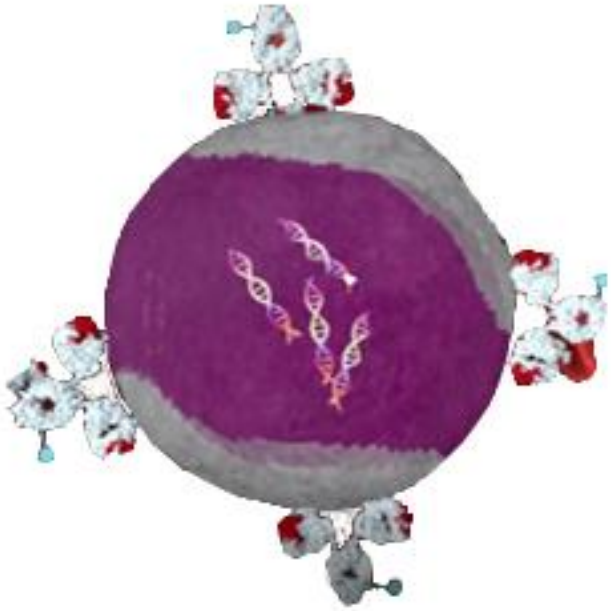
Actimab-MDS

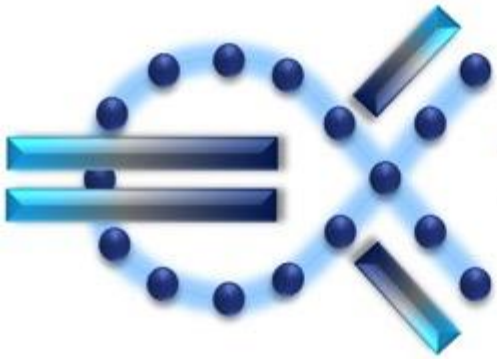
8,500+ Addressable Patients[1]

1) SEER Database, Company Estimates
2) CIBMTR Volumes Dataset 2015. National Marrow Donor Program® (NMDP)/Be The Match® and the Medical College of Wisconsin

Actinium Pharmaceuticals, Inc.

Actimab-MDS: Bridge to Transplant for Patients with p53+ Myelodysplastic Syndrome





Actinium Pharmaceuticals, Inc.

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