

# Actinium Pharmaceuticals, Inc.



April 2015

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# Company Description

*A public biotechnology company using world class science to develop and commercialize antibody directed radioisotopes to target unmet medical needs in cancer.*



# Company Overview

- ✓ Two development stage targeted antibodies:
  - ✓ Iomab-B expected to enter its single pivotal Phase III study mid-2015 as a conditioning agent in elderly relapsed/refractory Acute Myeloid Leukemia (AML) patients prior to bone marrow transplant (BMT)
  - ✓ Actimab-A in ongoing Phase I/II study in elderly, untreated AML patients
- ✓ We believe as potential breakthrough therapies, Iomab-B and Actimab-A may achieve successful market penetration given the strong KOL support and significant unmet medical need
- ✓ Proprietary Alpha Particle Immunotherapy (APIT) platform poised to deliver multiple cancer drugs with blockbuster potential
- ✓ Expert team possessing the vision and desire to enhance shareholder value
- ✓ Positioned to benefit from increased market recognition of targeted payload therapies and an initial high-value, niche product model



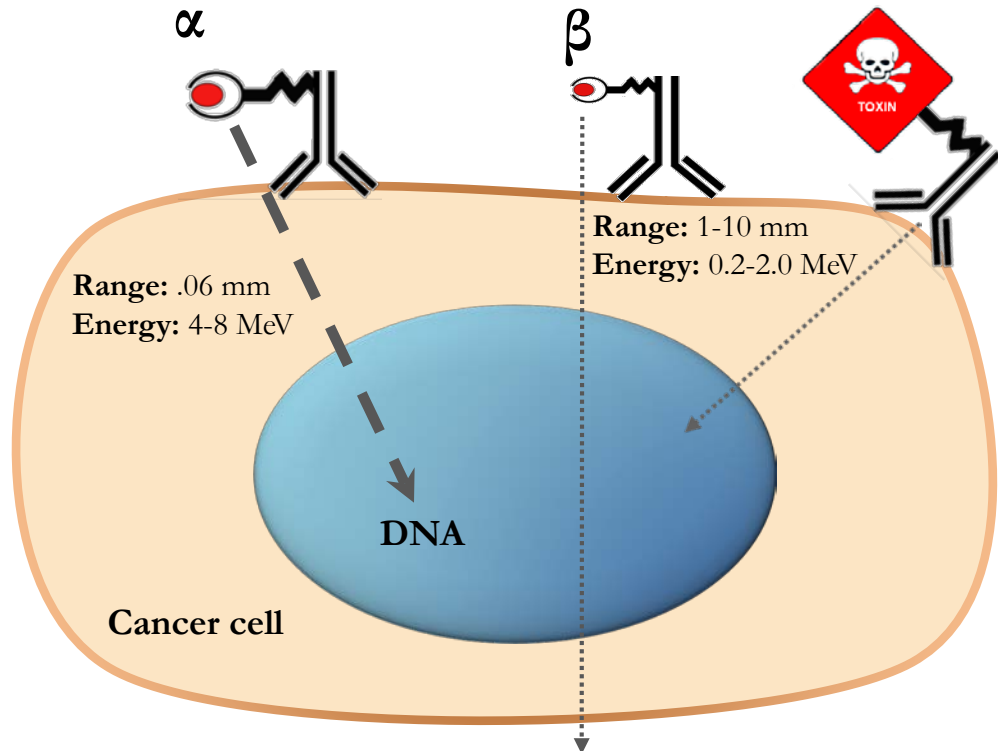
# Antibody Approaches Targeting Cancer Cells

## Cancer Treatment Options

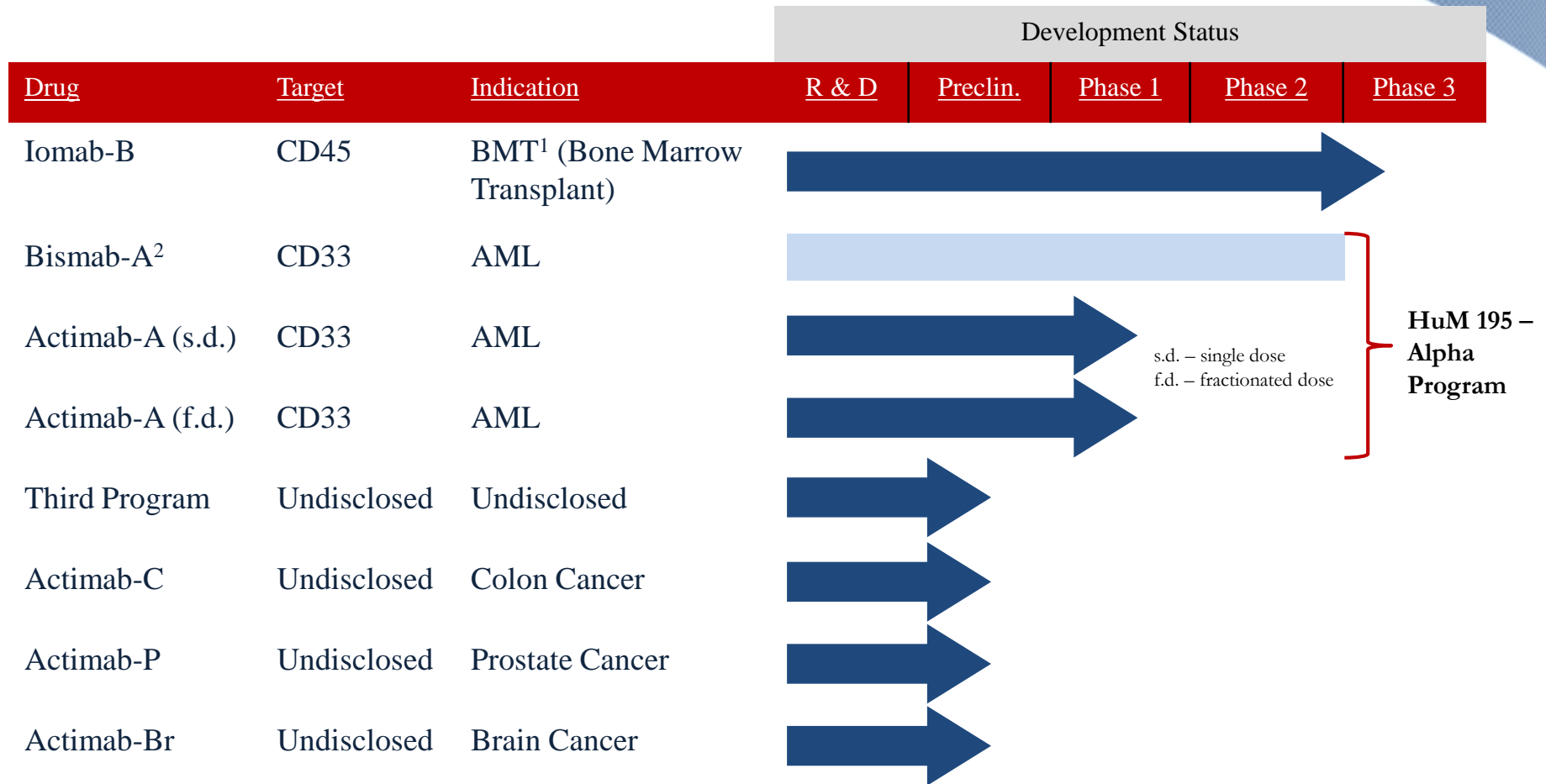
Opportunity	Radiation	Monoclonal Antibodies (mAbs)
<b>Treatment %</b>	<b>50%</b> ♦ External radiation majority treatment ♦ Internal radiation has mostly no IP	<b>&lt;10%</b> ♦ Always a pharmaceutical ♦ Strong IP protection
<b>Pharmaceutical Revenue %</b>	<b>&lt;3%</b> ♦ Commoditized	<b>~30%</b> ♦ Mostly proprietary

## Payload Approaches

	Company
$\alpha$	<b><math>\alpha</math> - emitters</b>
	Actinium Pharmaceuticals Algeta - Acquired by Bayer
$\beta$	<b><math>\beta</math> - emitters</b>
	GlaxoSmithKline Spectrum Pharmaceuticals Immunomedics Peregrine Pharmaceuticals
	<b>Toxins</b>
	Pfizer Seattle Genetics Immunogen Celldex Therapeutics Progenics



# Product Pipeline



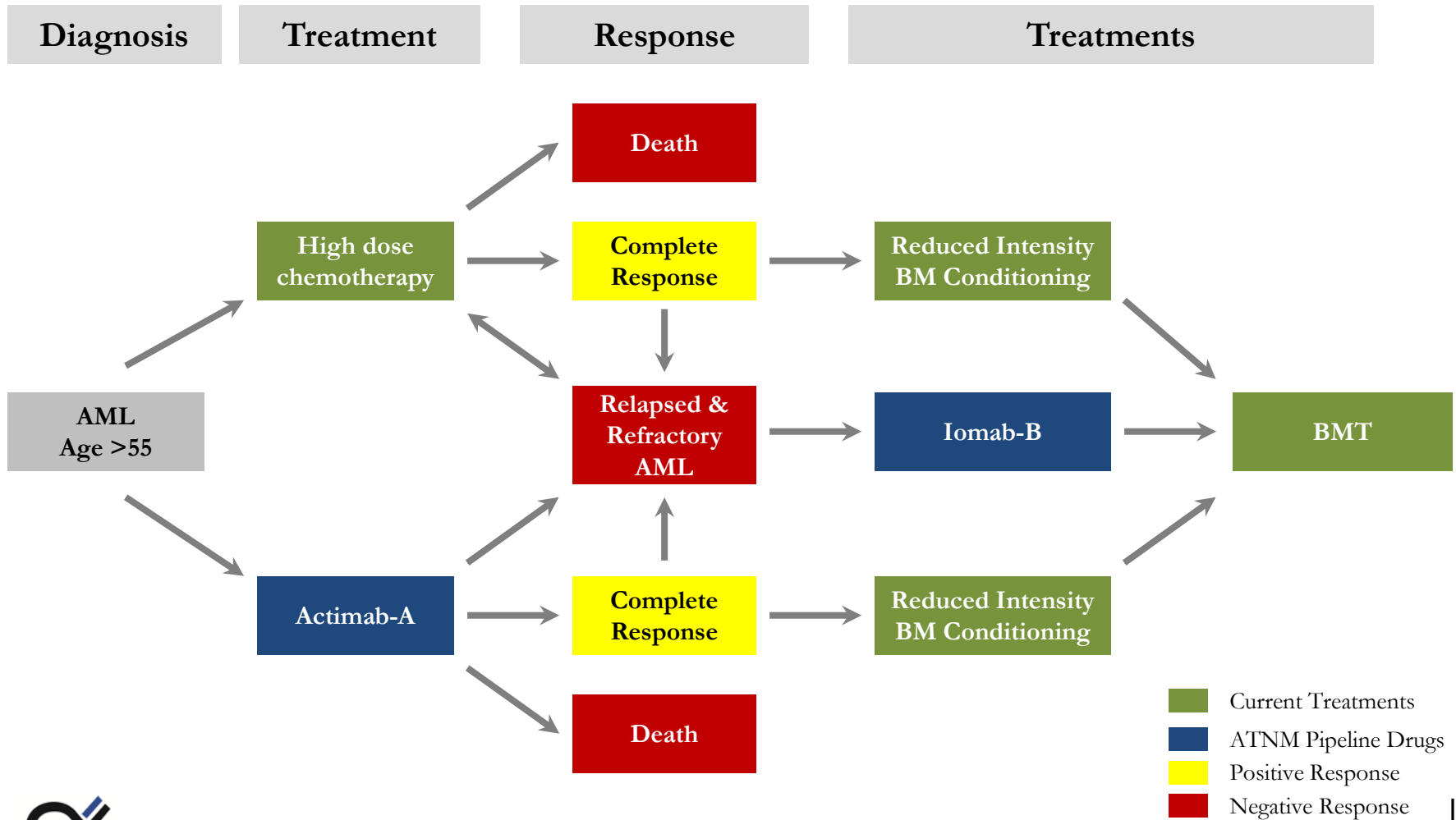
1. BMT or HSCT (Hematopoietic Stem Cell Transplantation) is a procedure in which cells capable of reconstituting normal bone marrow function are transplanted to a patient. Iomab-B is expected to enter a Phase III study in mid-2015 for hematopoietic stem cell transplantation in older subjects with active refractory AML.

2. ATNM has decided to discontinue development of Bismab-A at this time due to supply, logistics and cost reasons. Actimab-A is the second generation drug of Bismab-A.



# Market Positioning for Iomab-B and Actimab-A

*ATNM products target both treatment stages for AML patients over 55 years of age*



# Iomab-B Overview

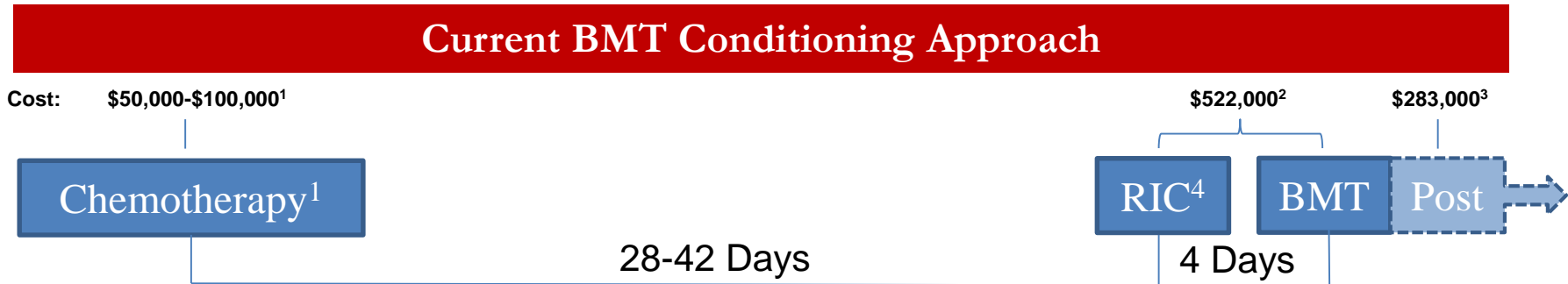
- ◆ Blockbuster therapy potential for BMT conditioning especially for elderly, very sick patients with few curative treatment options
  - Initial intended indication is relapsed, refractory AML patients over 55 years old
- ◆ Compelling clinical data from proof of concept trial in elderly refractory and relapsed Acute Myeloid Leukemia
  - Large safety database: experience with 300+ patients in 5 Phase I and II clinical trials
  - Antibody in-licensed from Fred Hutchinson Cancer Research Center
  - 7 ongoing physician trials with BC8 mAb, the antibody used in Iomab-B, for other indications
- ◆ Safety and efficacy data to date indicate that Iomab-B can potentially disrupt the field of BMT
- ◆ Trials results and implied medical benefits have attracted significant interest and involvement from leading physicians



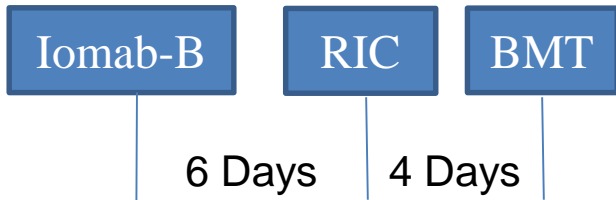


# Iomab-B Treatment

*Potentially faster pathway to a bone marrow transplant with fewer side effects*



## Iomab-B Regimen



1. Chemotherapy include MEC, FLAG-IDA, high-dose cytarabine, among others. Cost is for one or two rounds of inpatient chemotherapy treatment.
2. Transplant procedural costs include 30 day pre-procedure costs (RIC, donor cell procurement, fees, hospital costs, drug costs) and excludes chemotherapy.
3. Includes various associated costs during 180 days post-procedure, including immunosuppressive therapy.
4. RIC, reduced intensity conditioning, is a lower-dose (and therefore less toxic) treatment regimen which helps to facilitate BMT, particularly in older patients.



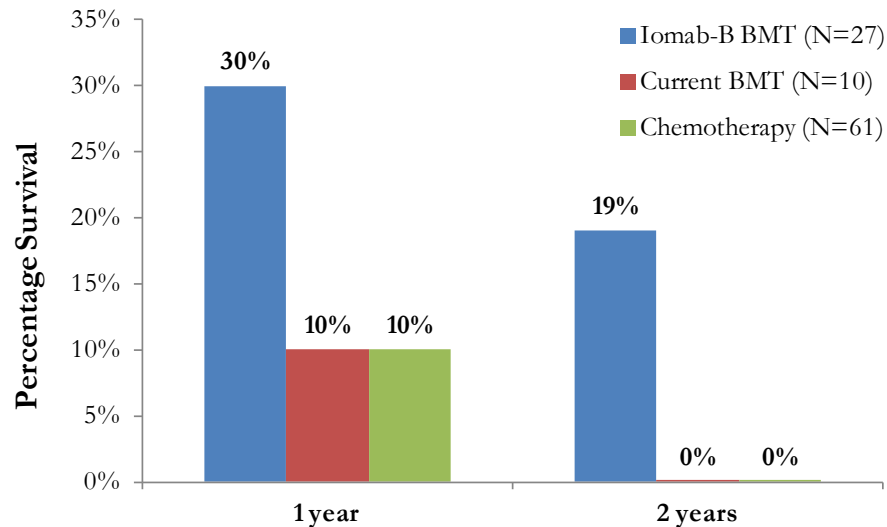
Sources: Milliman U.S. Organ and Tissue Transplant Cost Estimates and Discussion; Overall Economic Burden of Total Treatment Costs in AML throughout the Course of the Disease (Mahmoud); Company estimates.

# Iomab-B Phase I/II Results

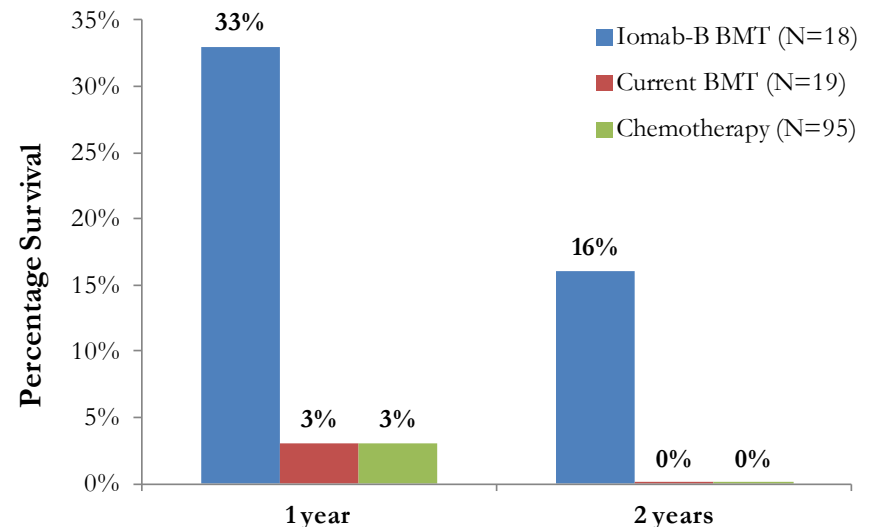
*Compelling clinical results enable pivotal Phase III trial*

- ◆ Non-relapse mortality (NRM):
  - Day 100: 10%
  - Overall: 20% (NRM = 46% in comparable patients with myeloablative conditioning)
- ◆ Transplant related mortality: 14% (same as reduced intensity conditioning)
- ◆ Complete response rate: 100%
- ◆ Engraftment by day 28: 100%

## All relapsed/refractory AML patients over 50



## Rel/ref AML patients over 50 w/ poor cytogenetics



N = Number of patients treated

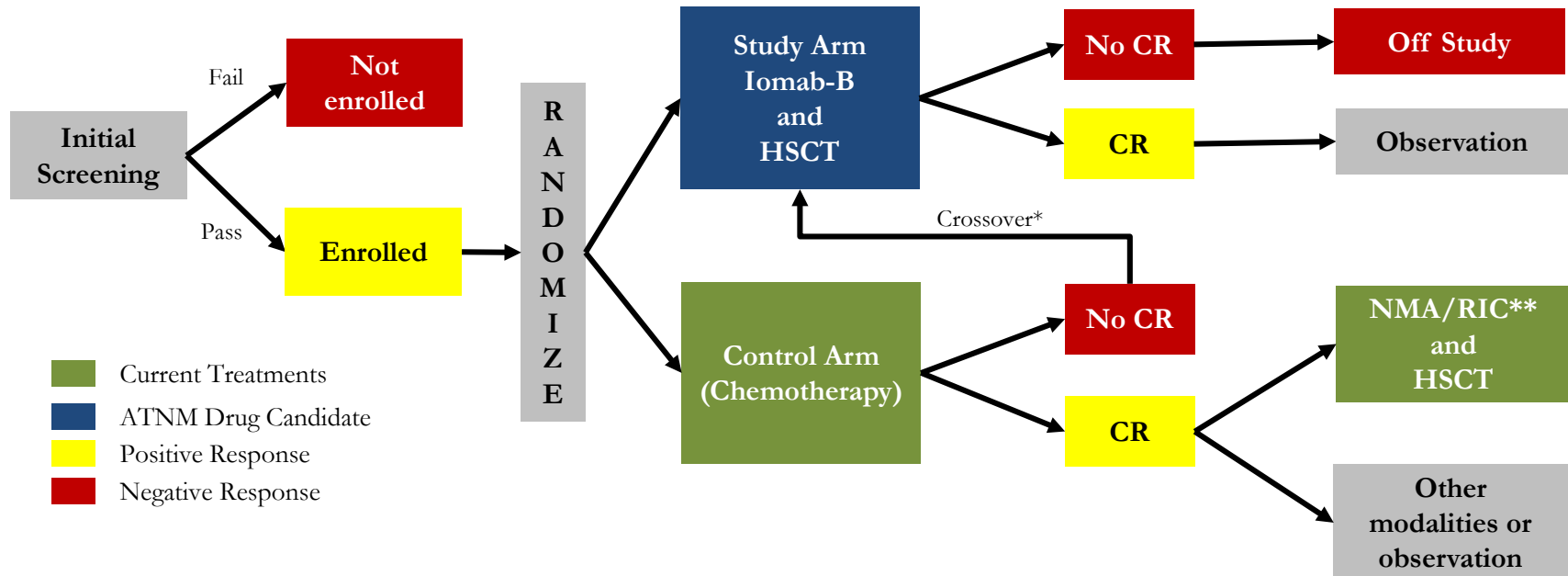
Iomab-B results from FHCRC clinical trials; Current BMT and Chemotherapy results from MD Anderson outcomes analysis

Sources: Blood 2009 114:5444-5453; unpublished FHCRC data



# Iomab-B Pivotal Phase III Trial Design

- ◆ FDA has identified the following design features of the Phase III clinical trial as generally acceptable with approval dependent on trial results<sup>1</sup>:
  - Single pivotal study, pending trial results
  - Patient population: refractory AML patients over the age of 55<sup>2</sup>
  - Trial arms: study arm and control arm with physician's choice of conventional care with curative intent
  - Trial size: 150 patients total, 75 patients per arm



\*Control arm subjects with no CR are offered crossover to Iomab-B for ethical reasons.

\*\*Nonmyeloablative Conditioning/Reduced Intensity Conditioning.



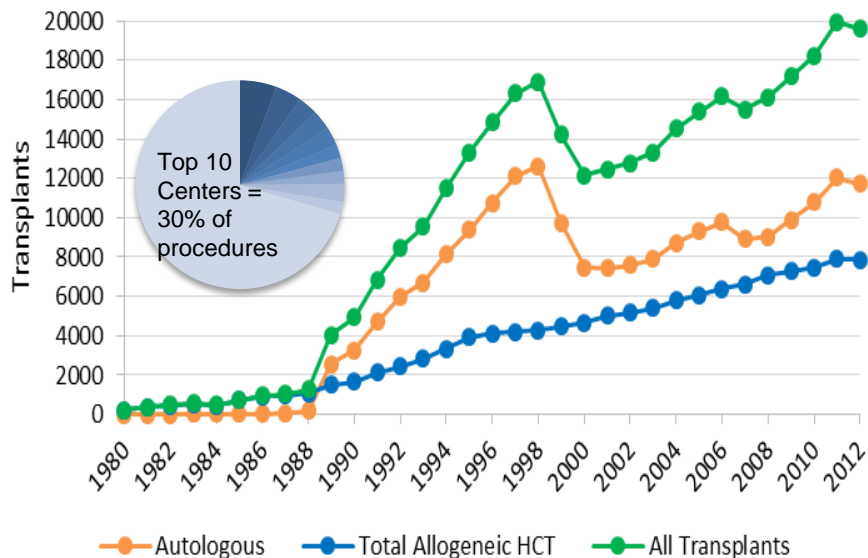
1. Based on the End of Phase II meeting and subsequent communications with the FDA.
2. Refractory is defined as either primary failure to achieve a complete remission after 2 cycles of induction therapy; relapsed after <6 months in complete remission; second or higher relapse; or relapsed disease not responding to intensive salvage therapy

# Bone Marrow Transplant Market Opportunity

*Currently no approved treatments for Iomab-B targeted patients implies blockbuster potential*

## HSCT Fastest Growing Hospital Procedure

Transplant Activity in the US



Indication*	2014	2015E	2016E	2017E	2018E	Market Potential
AML		III		Anticipated Approval	Anticipated Launch	\$750
MDS	II				III	\$300
ALL	II				III	\$250
NHL/HL	I		II		III	\$1,500
MM	I		II		III	\$1,300
<b>Total</b>						<b>\$4,100</b>

Sources: Healthcare Cost and Utilization Project, AHRQ; US Dept. of HHS; CIBMTR (Preliminary review of information submitted to the CIBMTR)

Phase I and Phase II represent physician trials at Fred Hutchinson Cancer Research Center. Phase III trials represent ATNM sponsorship. Timelines are projections and the Company makes no representation as to their ability to meet these timelines.

Sources: "Current Uses and Outcomes of Hematopoietic Stem Cell Transplantation 2010", CIBMTR Summary Slides; "Trade, foreign policy, diplomacy and health: Pharmaceutical Industry", WHO website, <http://www.who.int/trade/glossary/story073/en/>; "Hematopoietic stem cell transplantation A Global Perspective", NIH Public Access, JAMA 2010; Company Estimates



# HuM 195-Alpha Platform

*Second generation Actimab-A 500x more potent than Bismab-A*

## 1<sup>st</sup> Generation

### Bismab-A Profile

- Target:** ♦ AML
- Effectiveness:** ♦ Proof of concept in humans
- Clinical Stage:** ♦ Promising results in Phase II
- Supply Chain:** ♦ Complex, high COGS
- Ease of Use:** ♦ Complex on site preparation

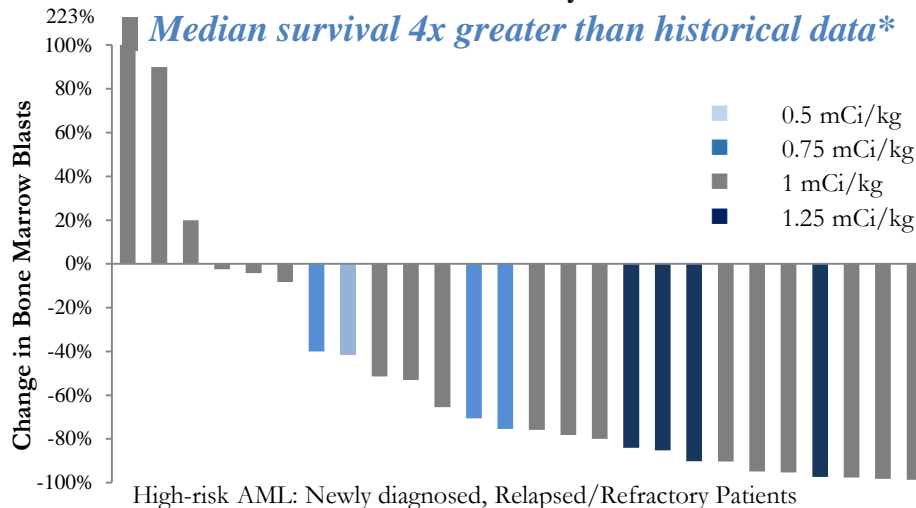
## 2<sup>nd</sup> Generation

### Actimab-A Advantages

- ♦ AML
- + 500x more potent than Bismab-A
- ♦ Currently in a Phase I/II Trial
- + Simple, 10x lower COGS
- + Central manufacturing

### Bismab-A + Cyto-reduction

*Median survival 4x greater than historical data\**



### Bismab-A vs. Actimab-A Monotherapy

*Actimab-A efficacy superior to Bismab-A*

Parameter	Bismab-A	Actimab-A
Peripheral blast elimination	27%	67%
Bone marrow blasts decrease $\geq 50\%$	28%	53%
Bone marrow blasts $\leq 5\%$ post treatment	0%	20%

Relapsed/Refractory Patients only



\* Median survival 7.6 mo. vs 1.7 mo. historically for untreated. Each bar equals an individual patient response.

Sources: Clin Cancer Res. 2010, 16(21):5303-5311; Jurcic JG et al. Blood (ASH Meeting Abstracts) 2012, 118:768; Company documents

# Actimab-A Multicenter Phase I/II Study

- ◆ Phase I/II clinical trial ongoing at world-class treatment centers
  - Memorial Sloan Kettering, MD Anderson, Johns Hopkins, Columbia University, University of Pennsylvania, Fred Hutchinson, Baylor Sammons Cancer Center
- ◆ New protocol sets lower standard than first Phase I trial
  - Treating newly diagnosed patients;
  - Introducing cytoreduction which reduces the number of cancer cells
  - Fractionated dosing at day one and seven
  - New patient population likely to respond better to treatment based on medically accepted criteria
  - No toxicity has been observed to date outside of blood cells at doses expected to be clinically effective



# Why Actimab-A Should Play Critical Role in Elderly AML

## ◆ “Low-Intensity Hypothesis”

- In patients 65+ intensive chemotherapy is associated with high mortality rate; 2 month mortality ~ 22%<sup>1</sup>
- Low intensity treatments are better at extending overall survival in elderly patients even without high CR rates<sup>1</sup>
- Postulates that AML in elderly patients is closer to MDS which informs this line of reasoning<sup>2</sup>
- FDA guiding toward overall survival endpoints for frontline treatment of older AML<sup>3</sup>

## ◆ Actimab-A is a low intensity product candidate for older AML patients

- Favorable safety profile in clinical trials to date may allow for use in most patients, unlike high-dose chemotherapy
- Results to date are supportive of the “Low-Intensity Hypothesis”

**Based on the favorable safety profile in clinical trials to date, Actimab-A has the potential to be a low intensity therapy for older AML patients**

1. Report from 'Great Debates & Updates in Hematology' Conference, Oncology Times 25 January 2009, Volume 31 Issue 2 pp 22-24; Hagop Kantarjian, MD
2. Medscape Oncology CME: Current Treatment of Myelodysplastic Syndrome, 26 June 2008
3. FDA Guidance for Industry: Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics, 2007





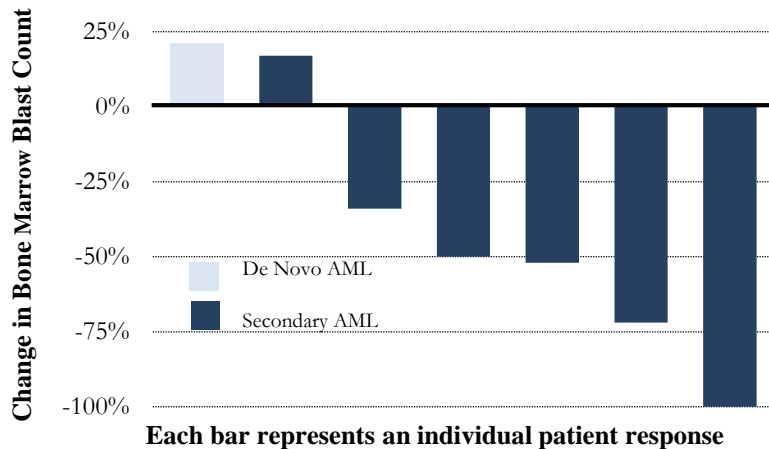
# Actimab-A Phase I/II Interim Data Highlights

*Meaningful overall survival benefit, no treatment mortality, lowered blast count*

- ◆ Patients evaluated thus far were high-risk, elderly
  - All nine were greater than 70 years of age (mean: 76, range: 73-81)
  - All but two had secondary AML (antecedent MDS); five had prior treatment with HMA or allogeneic hematopoietic cell transplantation
  - All had intermediate or poor cytogenetics
- ◆ No significant drug related safety issues thus far; MTD yet to be established

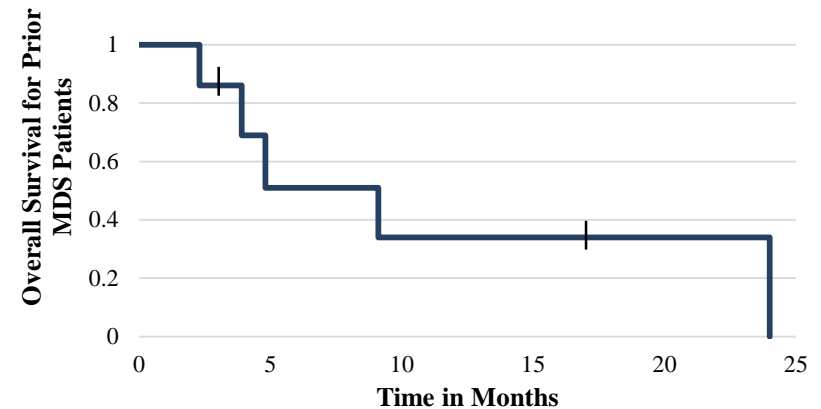
## *Clear antileukemic effect in most patients*

- ◆ 5 of 7 (71%) evaluable patients had bone marrow blast reductions
- ◆ 61% mean reduction in blast count (range 34%-100%)



## *Improved median survival greatest for secondary AML*

- ◆ 9.1 month median overall survival in 7 secondary AML patients (range 2.3-24 months)
- ◆ Compares favorably to 2-5 month expected survival in secondary AML



Sources: Phase I Trial of Targeted Alpha-Particle Therapy Using Actinium-225 (<sup>225</sup>Ac)-Lintuzumab (Anti-CD33) in Combination with Low-Dose Cytarabine (LDAC) for Older Patients with Untreated Acute Myeloid Leukemia (AML), 56<sup>th</sup> ASH Annual Meeting and Exposition. Abstract #5293; Oran B, and Weisdorf DJ, Survival for older patients with acute myeloid leukemia: a population-based study. *Haematologica* 2012; 97(12):1916-1924. N Okuyama et al, Prognosis of acute myeloid leukemia transformed from myelodysplastic syndromes: A multicenter retrospective study, *Leukemia Research* 37 (2013) 862–867.





# Market Potential of Product Pipeline

#	Cancer Indication	Cases/Yr. in Target Market <sup>1</sup>	Target Population	Worldwide Market Potential (\$mm) <sup>2</sup>
1 <sup>st</sup>	Bone Marrow Transplant (BMT)	48,000	48,000	\$4,100
2 <sup>nd</sup>	Acute Myeloid Leukemia (AML)	41,600	24,000	\$920
3 <sup>rd</sup>	Glioblastoma Multiforme (GBM)	26,500	26,500	\$1,100
4 <sup>th</sup>	Prostate Cancer (metastatic)	591,000	298,455	\$5,959
5 <sup>th</sup>	Metastatic Colorectal Cancer	536,000	241,200	\$4,824

1. Target market includes USA, EU and Japan

2. Market Potential calculated based on assumption that Actinium products for solid cancer indications will be priced at \$20,000 per treatment; BMT preparation product will be priced at \$85,000 per treatment; AML product will be priced at \$60,000 per treatment; and GBM product will be priced at \$60,000 per treatment. Estimates based on independent third party research and adjusted for lower pricing in non-US markets.

## BMT (Iomab-B)

- ◆ The \$1.3 billion Bone Marrow Transplant (BMT) market in the US is largely unaddressed by novel pharmaceutical drug companies
- ◆ BMT is the fastest growing hospital procedure in the US
  - ~20,000 of the ~60,000 BMTs in 2010 were performed in the US
- ◆ Sustained growth in patients treated over 55 yrs old
  - 8% in 2000 to 21% in 2005 and 27% in 2007

## AML (Actimab-A)

- ◆ Acute Myeloid Leukemia is the deadliest form of leukemia
  - 55% of AML patients are over 65 years old
  - Disease is worse in older people
  - Insufficient treatment options are available in the marketplace
  - Treatment kills as many patients as it helps due to toxicity



Source: “Current Uses and Outcomes of Hematopoietic Stem Cell Transplantation 2010”, CIBMTR Summary Slides; Company estimates

# Company Overview

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