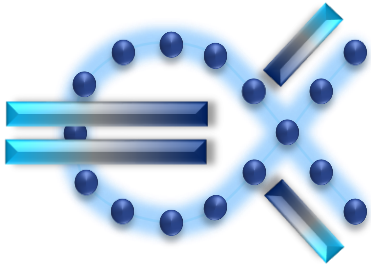

Actinium Pharmaceuticals, Inc.

Company Update

Next Generation Lymphodepletion for CAR-T

September 26th 2018

Disclaimer and Safe Harbor

Some of the information presented herein may contain projections or other forward-looking statements regarding future events or the future financial performance of the Company which the Company undertakes no obligation to update. These statements are based on management's current expectations and are subject to risks and uncertainties that may cause actual results to differ materially from the anticipated or estimated future results, including the risks and uncertainties associated with preliminary study results varying from final results, estimates of potential markets for drugs under development, clinical trials, actions by the FDA and other governmental agencies, regulatory clearances, responses to regulatory matters, the market demand for and acceptance of Actinium's products and services, performance of clinical research organizations and other risks detailed from time to time in Actinium's filings with the Securities and Exchange Commission (the "SEC"), including without limitation its most recent annual report on form 10-K, subsequent quarterly reports on Forms 10-Q and Forms 8-K, each as amended and supplemented from time to time.

Today's Speakers

Dr. Nirav Shah

Assistant Professor of Medicine,
Division of Hematology and Oncology

Sandesh Seth

Chairman & CEO

Dr. Dale Ludwig

Chief Scientific Officer

Actinium's Next Generation Lymphodepletion for CAR-T

Latest pipeline initiative is a universal tool addressing the unmet needs of the CAR-T space not addressed by current lymphodepletion regimens

Ideation 4Q17

- Identified new technology opportunity
- Idea conceptualized and evaluated
- Addresses CAR-T limitations
- Expands CAR-T access
- Improves CAR-T outcomes

Value Creating Activities YTD 2018

- Intellectual property filed
- Proof of concept data generated
- SAB members support concept
- KOL support secured
- Clinical strategy in place

Initiative Launched 3Q18

Actinium is focused on establishing our next generation lymphodepletion technology as an industry-wide tool that can positively impact CAR-T access and outcomes

Nirav Shah, MD, MSHP

- Assistant Professor of Medicine, Division of Hematology and Oncology
- Specializes in lymphoma and stem cell transplant at Froedtert Hospital
- MD, University of Illinois College of Medicine at Chicago – Alpha Omega Alpha
- Internal medicine residency, Massachusetts General Hospital
- Hematology/oncology fellowship, University of Pennsylvania
- Board certified in Hematology, Medical Oncology and Internal Medicine

- Commercial CAR-T site offering KITE's Yescarta® and Novartis' Kymriah
- One of the first centers accredited in the U.S. by the Foundation for the Accreditation of Cellular Therapy (FACT) for CAR-T
- Conducting trials for novel development stage CAR-T
- International leader in CAR-T, bone marrow transplant and cellular therapies

fact
Foundation for the Accreditation of Cellular Therapy

YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion

KYMRIAH® (tisagenlecleucel) Suspension for IV infusion

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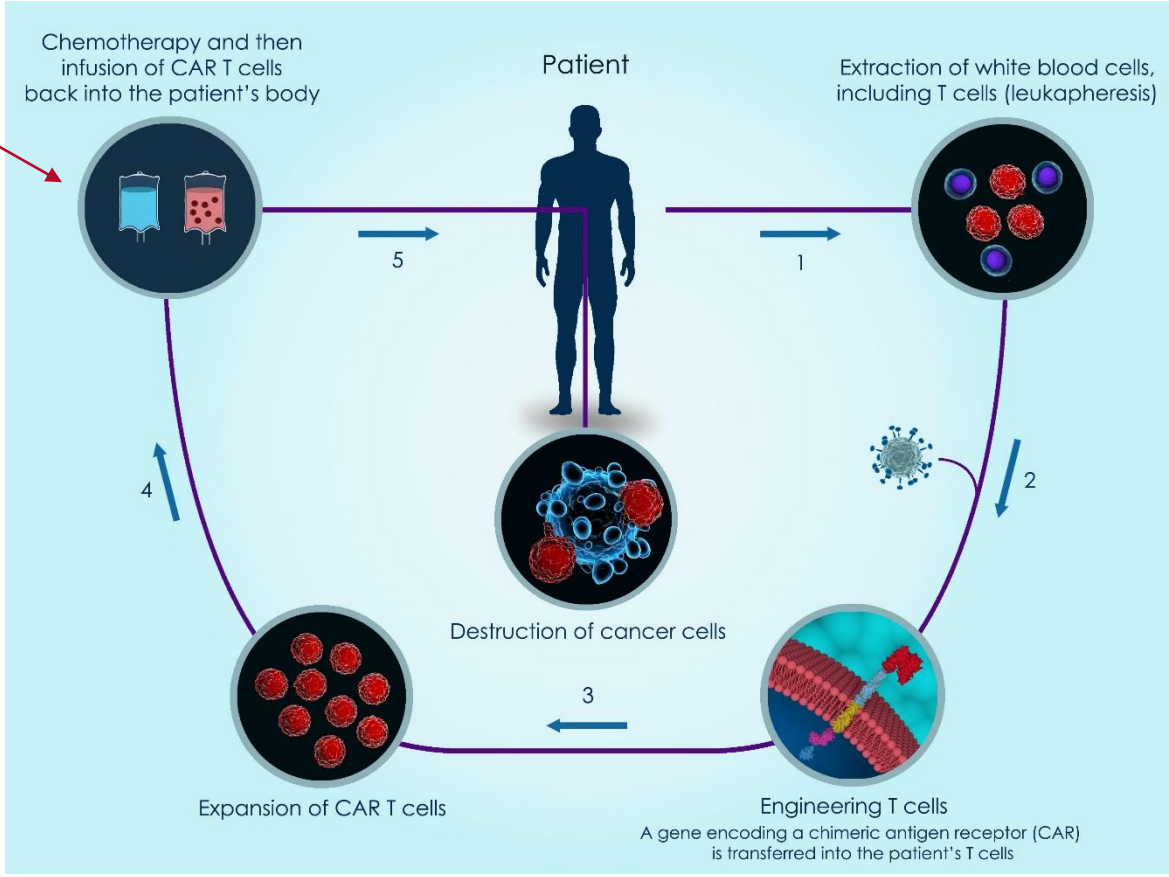
II. CAR-T and the Importance of Lymphodepletion

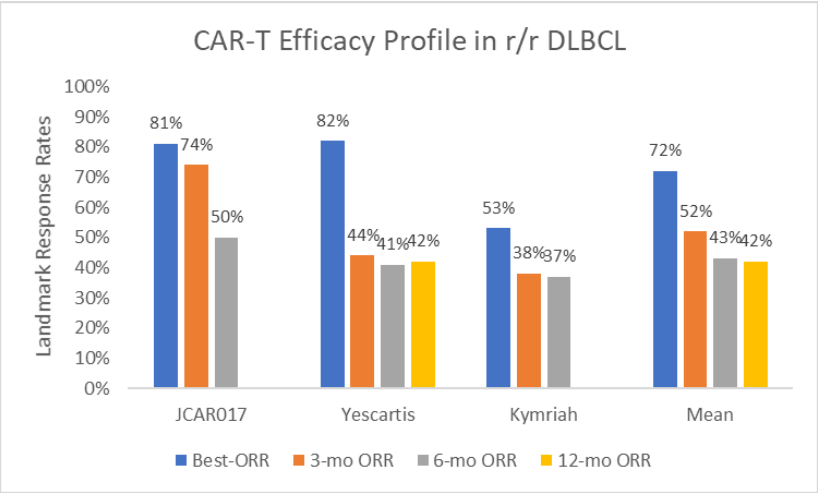
Introduction to the CAR-T Treatment Process

- Patient's own T-cells (autologous) are extracted through leukapheresis
- These T-cells are engineered outside of the body to express chimeric antigen receptor (CAR)
- Before CAR-T cells are infused, the patient receives chemotherapy referred to as conditioning
- Once inside the body, CAR-T cells target and kill cancer cells

Chemotherapy conditioning



Snapshot of the CAR-T Landscape



2 approved CAR-T Products

YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion

GILEAD Kite

KYMRIAH® (tisagenlecleucel) Suspension for IV infusion

NOVARTIS

Crowded Field

- 200+ CAR-T trials
- 60+ CAR-T developers
- 2nd & 3rd generation CAR-T's in development

Significant Unmet Needs

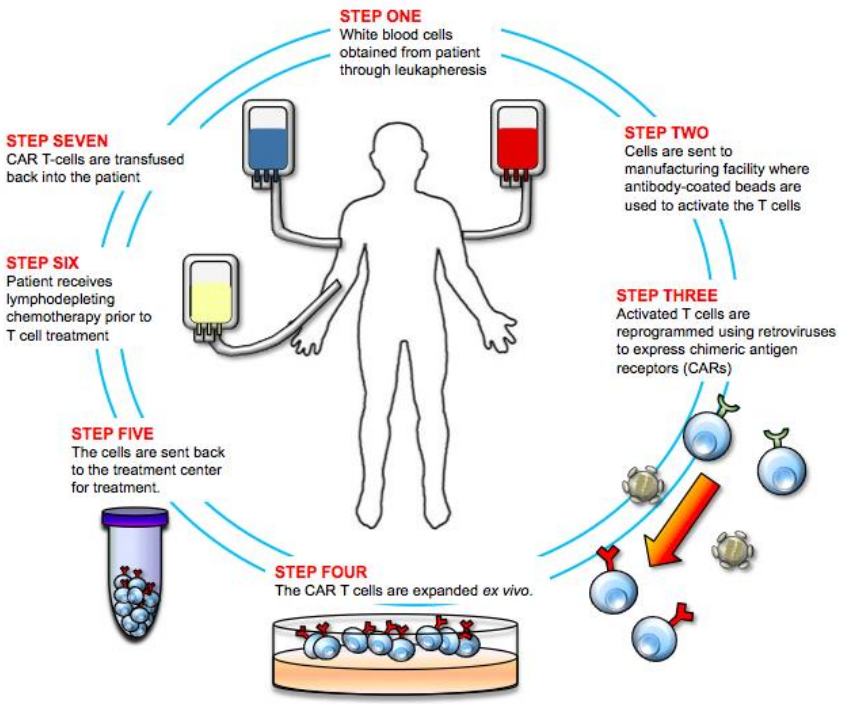
- Durability of Responses
- Cytokine Release Syndrome
- Neurotoxicity
- Patient Access

Source data: Abramson et al., Neelapu et al., Schuster et al. ASH 2017

Introduction to Lymphodepletion for CAR-T

- Lymphodepletion is being increasingly recognized by CAR-T developers as integral to the CAR-T process and critical to successful patient outcomes

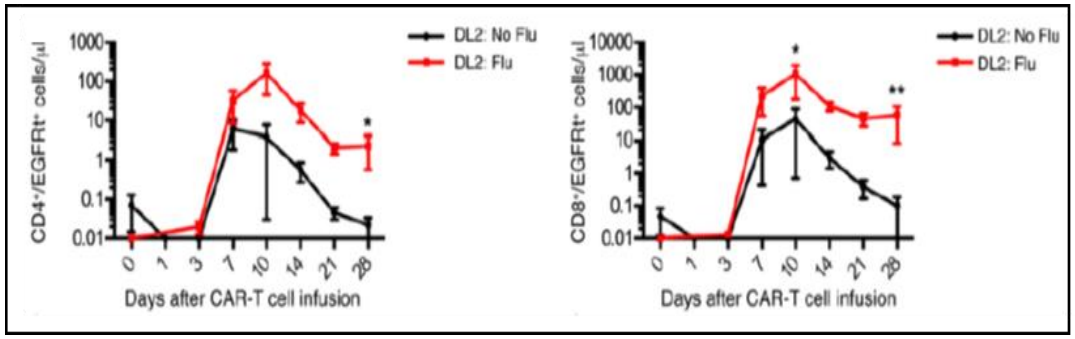
- Lymphodepletion is clinically necessary as it:
  - Depletes lymphocytes to create suitable environment for CAR-T cells to expand and persist
  - May reduce the patient's tumor burden



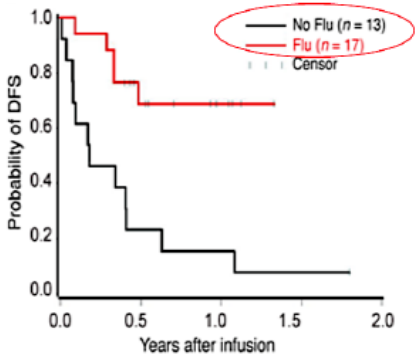
Lymphodepletion is a Critical Component of CAR-T Regimens

- Lymphodepletion is required for robust CAR-T cell expansion and persistance[1]
- Lymphodepletion typically consists of cyclophosphamide (Cy) and Fludarabine (Flu)
- More intense lymphodepletion with Fludarabine increased the peak of expansion and long-term persistence of infused CAR-T cells and improved disease free survival (DFS)[2].

Increased CAR-T expansion and persistence with more intense lymphodepletion



Lymphodepletion shown to play a role in patient outcomes



However, intense, non-targeted lymphodepletion can lead to increased toxicity and side effects

1) Turtle, et al, Sci. Tranl. Med (2016)
2) Turtle, et al, Journal Clin. Inbest.. 2016, 128:2123-2138

Implications of Intense Lymphodepletion with CAR-T

- The addition of Fludarabine to Cyclophosphamide led to significant increase in CAR-T expansion kinetics, which can result in a less optimal safety profile

Conditioning Regimen	Non-Flu/Cy	Flu/Cy		
Dose Level	All Doses	$2*10^5$/kg	$2*10^6$/kg	$2*10^7$/kg
Efficacy				
CR	1 (n=12)	1 (n=3)	3 (n=6)	1 (n=4)
CR/PR	6 (n=12)	1 (n=3)	4 (n=6)	3 (n=4)
Toxicity				
Severe Cytokine Release Syndrome	0 (n=12)	1 (n=3)	0 (n=6)	3 (n=6)
Severe Neurotoxicity*	2 (n=12)	1 (n=3)	1 (n=6)	4 (n=6)

JCAR014: demonstrates importance of conditioning regimen

Source: Juno Corporate Presentation

Standard Flu/Cy Lymphodepletion Chemotherapy is Not Ideal

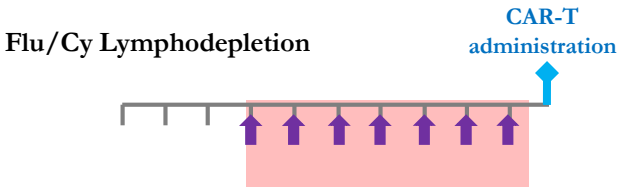
Effectiveness	Flu/Cy is toxic, and not fully optimized for CAR-T programs
Safety Concerns	Flu/Cy chemotherapy regimen contributes to Cytokine Release Syndrome (CRS) which remains a serious issue with CAR-T therapies Multi-variable analysis identified Flu/Cy lymphodepletion prior to CAR-T as a risk factor for CRS, a major adverse event related to CAR-T therapy.[1] The severity of CRS is related to the Flu/Cy administered and the dose of CAR-T cells.[1]
Pharmacoeconomics	Flu/Cy regimen may contribute to CRS-related treatment costs associated with CAR-T
Patient Convenience	Flu/Cy dosing regimen requires multiple administrations prior to CAR-T infusion
Improved Utilization	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[2]
Intellectual Property	Patent US9855298 covering use of Flu/Cy as lymphodepletion therapy in preparation for CAR-T administration can impair freedom to operate
Patient Access	Non-specific Flu/Cy chemotherapy lymphodepletion may restrict CAR-T access to a relatively robust patient population.

1) Hay et al., Blood. 2017; 130 (21):2295
2) Oncology Insights December 2017. Cardinal Health, Specialty Solutions

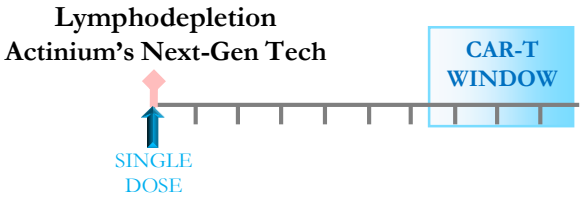
Significant Advantages of Actinium's Lymphodepletion Technology

Actinium's next generation lymphodepletion technology offers the potential for improved outcomes, patient convenience and pharmacoeconomic benefit

Multiple Doses



Single Dose



Flu/Cy Limitations

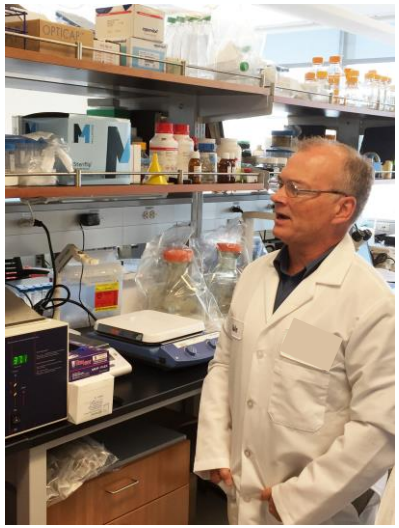
- Multiple administrations needed
- Non-targeted chemotherapy
  Off-target Toxicities
- Doses and scheduling for lymphodepletion not well optimized for CAR-T
- Identified as a risk factor for Cytokine Release Syndrome (CRS)
- Flu/Cy patents may limit optimization or use
- Limited patient access
  Not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

Potential Advantages of Actinium's Targeted Technology

- **Single dose, outpatient administration**
- **Selectively targets immune cells, including those implicated in CRS**
- **Favorable pharmacokinetics**
  Flexibility to optimize lymphodepletion step
- **Potential for improved outcomes**
  Favorable immune environment; reduced tumor burden
- **Targeted technology available for collaboration/licensing**
- **Patient access expansion**
  Targeted
  Good safety profile

III. Introducing Actinium's Next Generation Lymphodepletion Technology

Dale Ludwig, PhD – Actinium's CSO



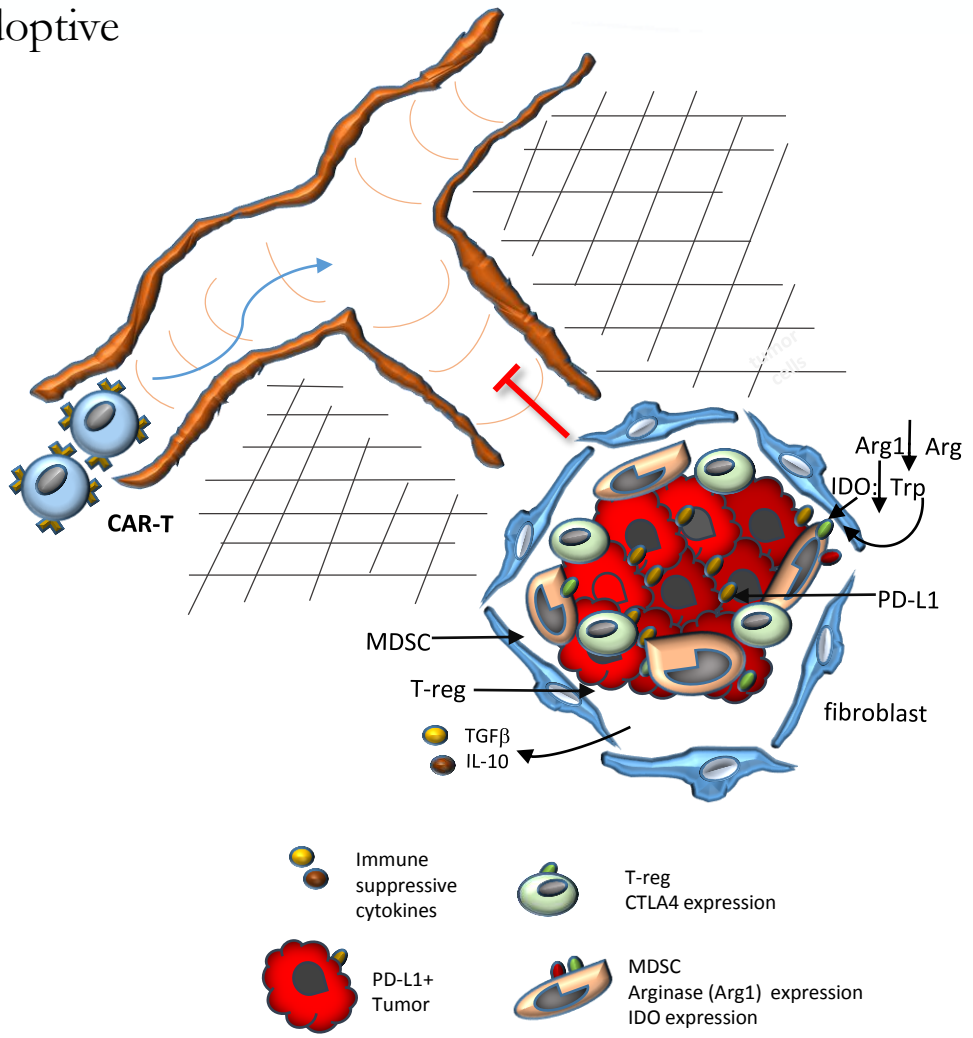
- Over 20 years of oncology biologics research and development experience at Eli Lilly and Company and ImClone Systems, Inc.
- Most recently, CSO, VP of Oncology Discovery Research – Biologics Technology at Eli Lilly and Company
- Supported development and launch of several approved biologic oncology drugs Erbitux®, Cyramza™, Portrazza®, and Lartruvo™
- Contributed to the development and clinical advancement of over 10 therapeutic antibodies
- Significant experience in alliance management centered around antibody drug based discovery programs

Tumor Microenvironment has Significant Impact on CAR-T Efficacy

Immune Suppressive Cells in the Tumor Microenvironment (TME): A reduction in immune suppressor cells can improve the response to adoptive cell therapy (ACT)[1]

- Both solid and liquid tumors exhibit a hostile tumor immune microenvironment
- Myeloid-derived suppressor cells (MDSC) secrete inhibitory cytokines including IL-10 and deplete essential amino acids (Trp and Arg) from the TME inhibiting T cell maintenance and proliferation
- Regulatory T cells (Tregs) secrete inhibitory cytokines and express the immune checkpoint receptor CTLA4, which can decrease the effectiveness of infused CAR-T cells
- Tumor cells express the immune checkpoint ligand PD-L1, suppressing T cell activation

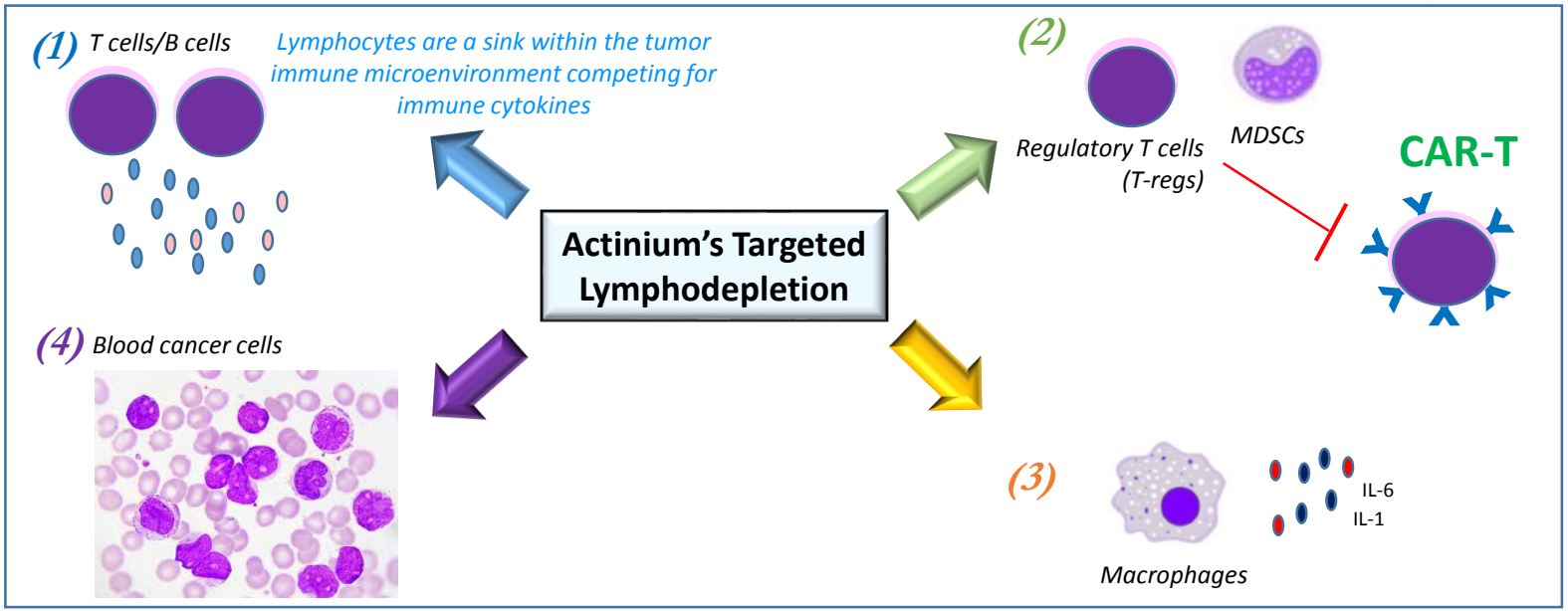
The Hostile Tumor Microenvironment[2]
(solid or liquid tumors)



1) Yao, *et al.*, (2012). *Blood.* **119**:5866.
2) Adapted from Newick, *et al*, (2016). *Mol Therapy*. 16006.

Actinium's Multi-Modal Targeted Lymphodepletion

Actinium's next generation lymphodepletion technology has the potential to create the ideal microenvironment enabling better CAR-T outcomes



(1) Lymphocytes – can reduce lymphocyte cytokine sinks creating a receptive immune microenvironment[1]

(2) Regulatory T cells **and** ***myeloid-derived suppressor cells (MDSCs)*** – can deplete immune suppressor cells that exert negative effects on CAR-T cells[3,4]

(3) Macrophages – can deplete cells that may contribute to cytokine release syndrome (CRS) through release of IL6 and IL1[2]

(4) Blood cancer cells – targets antigen found on most leukemia and lymphoma tumor cells and may effect a reduction in tumor burden

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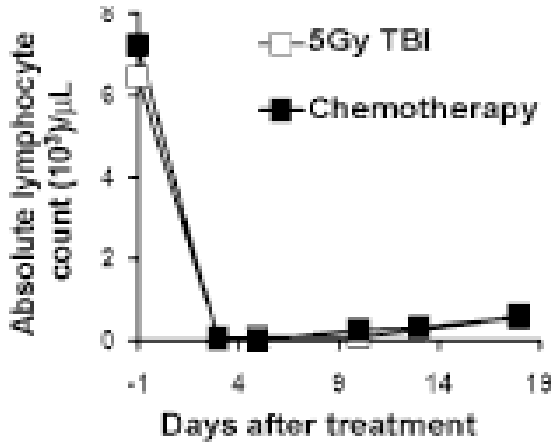
[1]Gattinoni, *et al.*, (2005). *JEM.* **202:**907
[2]Giavridis, *et al.*, (2018). *Nat. Med.* **24:**731.; Norelli, *et al.*, (2018). *Nat. Med.* **24:**739.
[3]Yao, *et al.*, (2012). *Blood.* **119**:5866.
[4]Pyzer, *et al.*, (2016). *Int. J. Cancer.* **139:**1915.

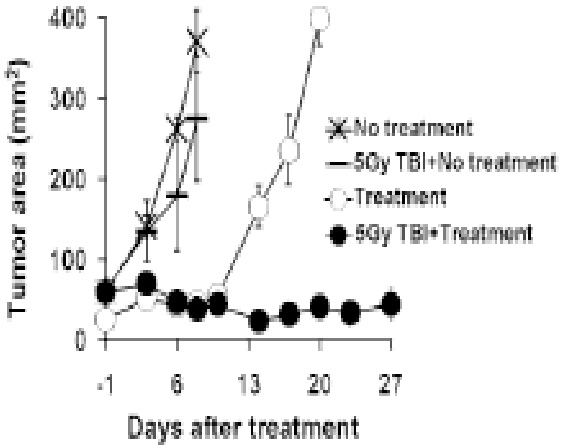
Strong Rationale for Targeted Lymphodepletion Supported by NCI Research

Research from the Rosenberg Lab at the NCI supports the use of radiation as an modality for achieving effective lymphodepletion

- 5 Gy of total body radiation delivered by external beam showed similar lymphodepletion to chemotherapy in NCI research study
- Radiation-mediated lymphodepletion shown to have positive impact on microenvironment amenable to cell therapy
- Actinium's next generation targeted technology enables safer and potentially more effective lymphodepletion

NIH NATIONAL CANCER INSTITUTE

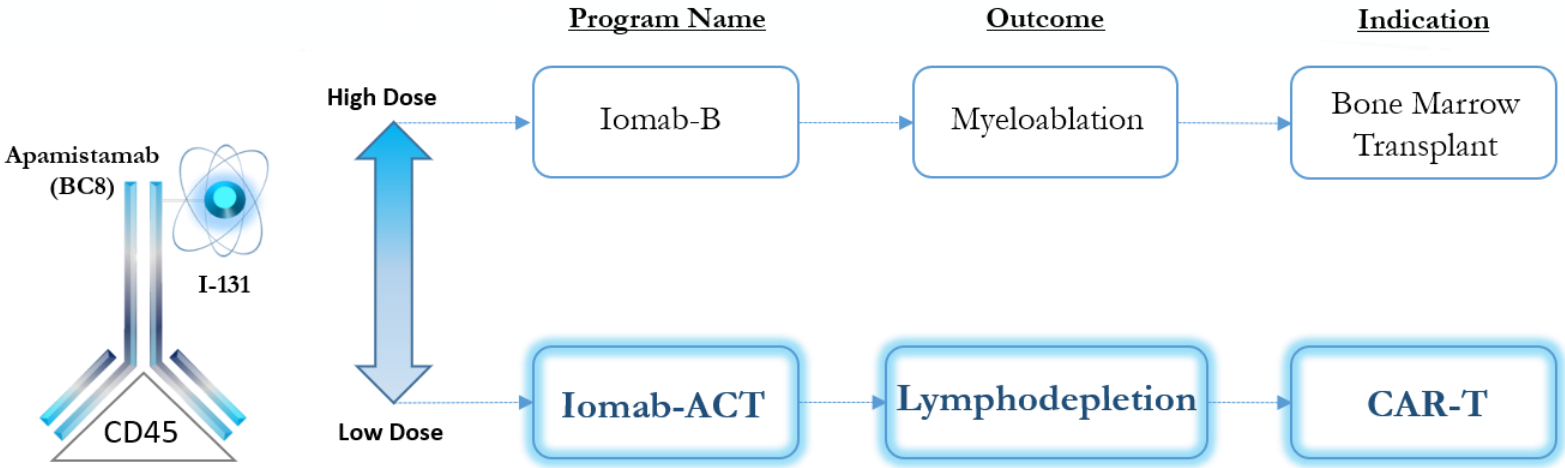




1) Gattinoni, *et al.*, JEM Vol. 202, No. 7, October 3, 2005 907–912

Introduction to the Iomab-ACT Program

Targeted lymphodepletion for CAR-T

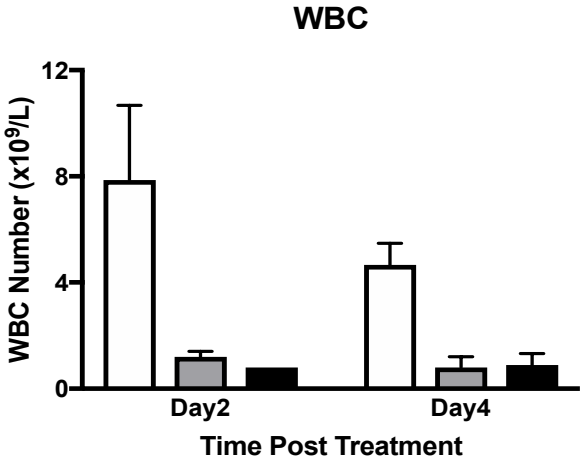


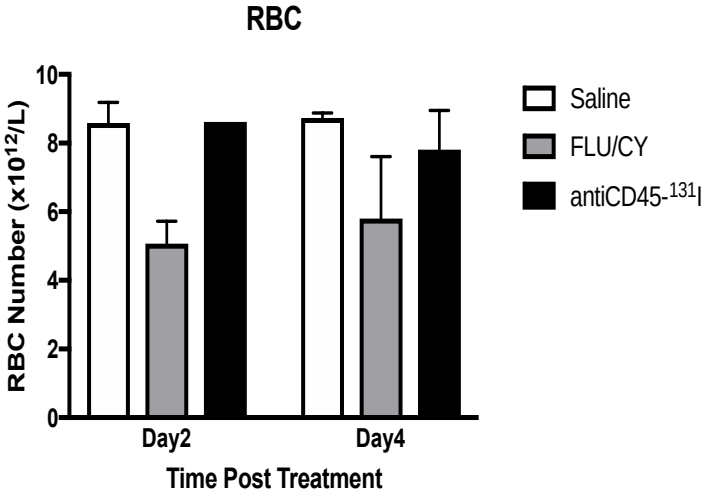
- Iomab-ACT program uses a low dose of apamistamab-I-131, as a single dose outpatient lymphodepleting regimen prior to CAR-T administration
- CD45 is expressed on leukemia and lymphoma cells and normal immune cells but not expressed on red blood cells or platelets
- Prior clinical experience with apamistamab-I-131 at low doses supports the validity of the Iomab-ACT lymphodepletion program
- Prior extensive clinical experience with apamistamab-I-131 at 5-20x higher doses (Iomab-B) in over 500 patients in 10 trials for targeted myeloablation strongly supports the safety potential of lymphodepleting doses

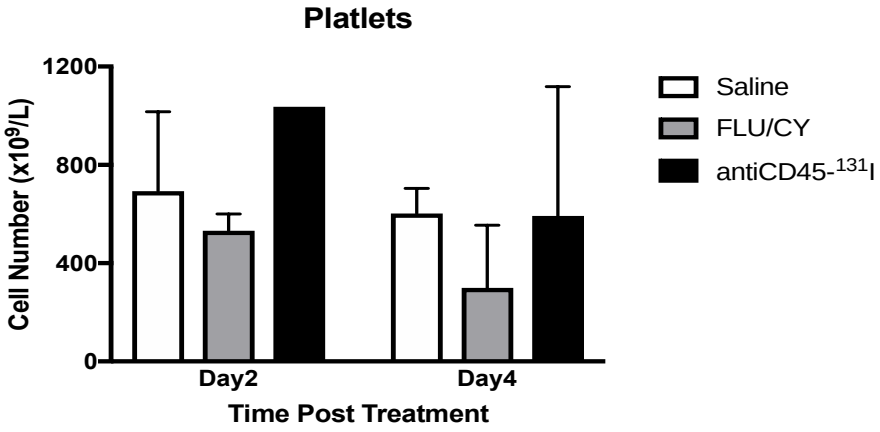
Effective Lymphodepletion Demonstrated in Pre-clinical Studies

Targeted lymphodepletion directed at CD45 depletes immune cells with the potency of Flu/Cy and is sparing of red blood cells and platelets

Peripheral Blood[1]

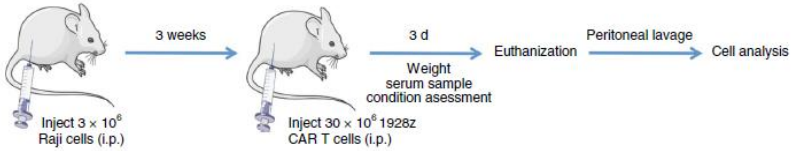




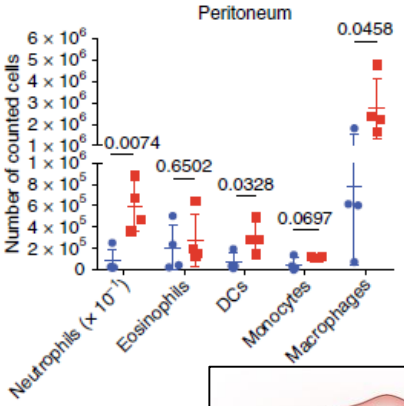


1) Company generated data

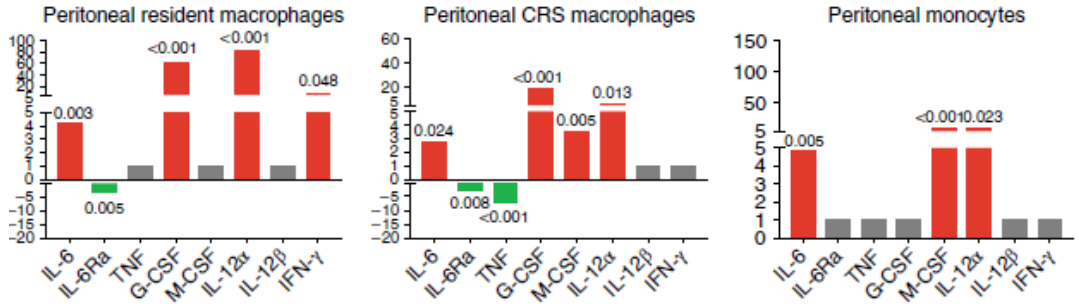
Macrophages are Implicated in CAR-T Toxicities



CAR-T macrophage recruitment

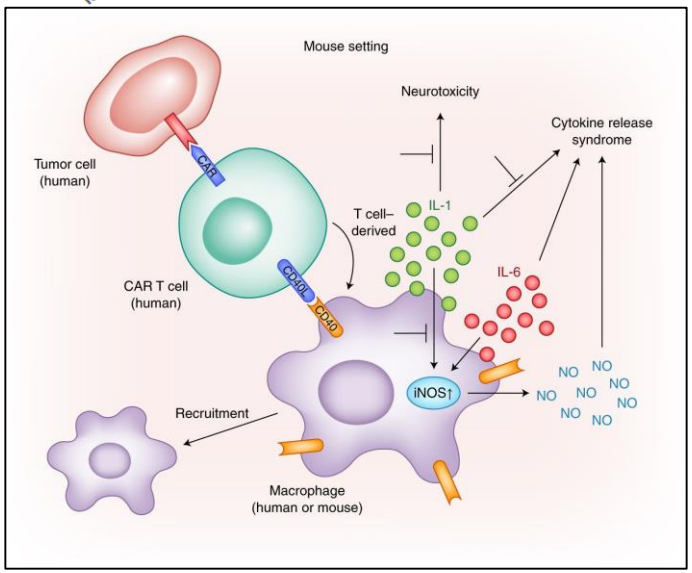


Activated macrophages release proinflammatory cytokines



Giavidris, et al., NATURE MEDICINE | VOL 24 | JUNE 2018 | 731-738

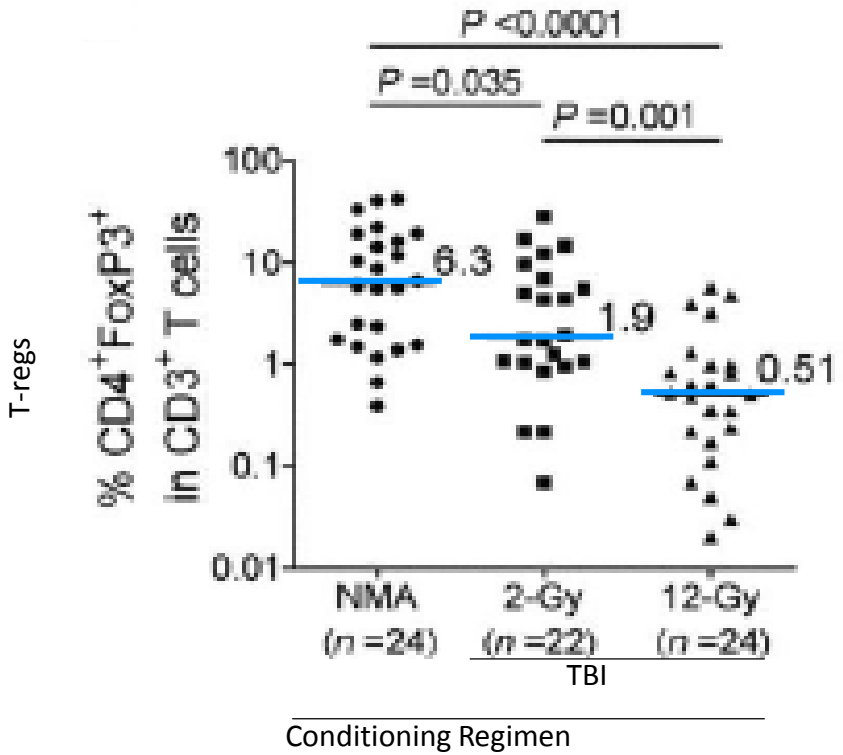
Norelli, *et al.*, NATURE MEDICINE | VOL 24 | JUNE 2018 | 739-748 |

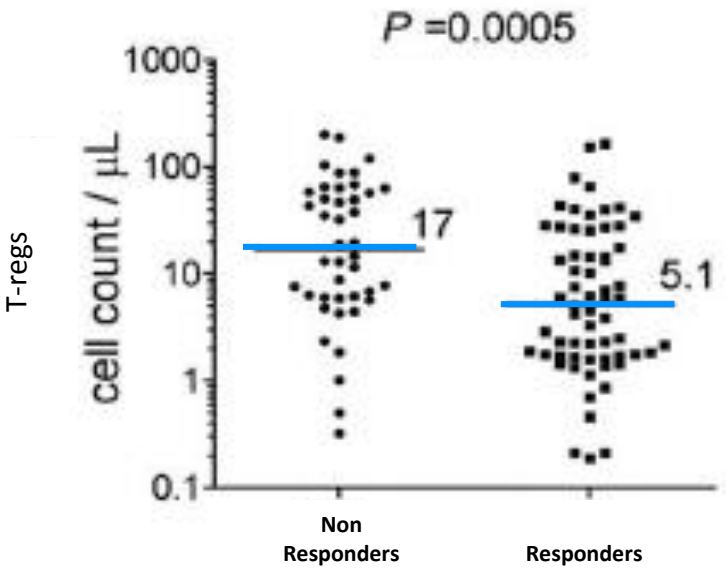


CRS and neurotoxicity are associated with release of proinflammatory cytokines following macrophage activation

Depletion of T-reg Cells Can Improve Clinical Response

Radiation based mechanism of action has been shown to enhance the depletion of immune suppressive T-reg cells, which has a statistically significant improvement in outcomes



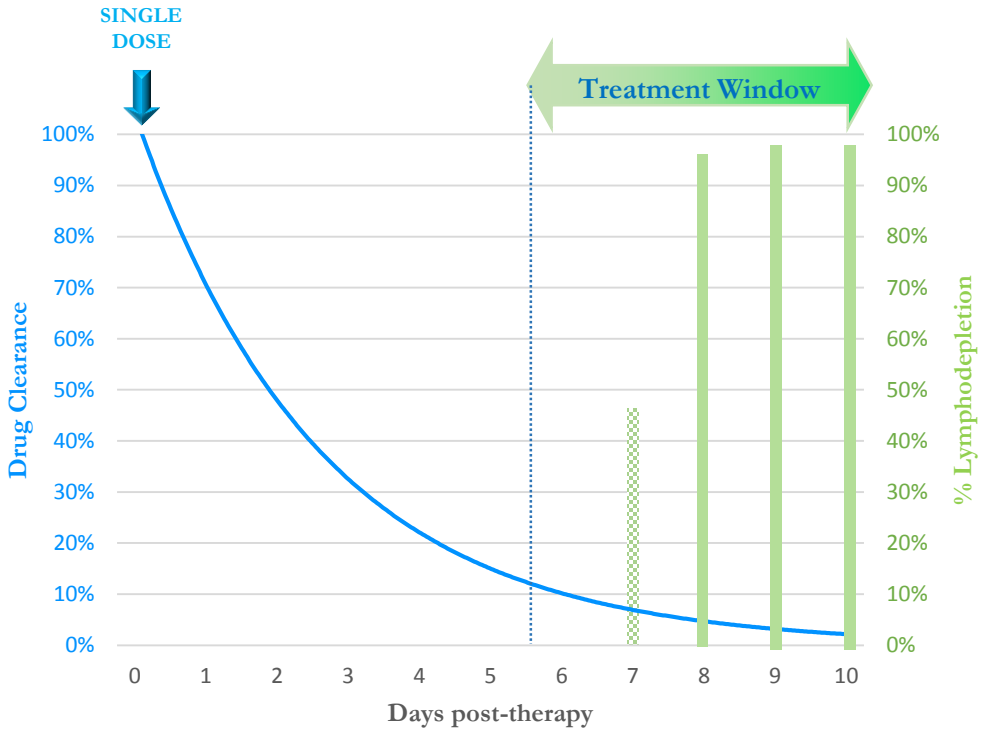


Yao, *et al., Blood.* (2012). 119:5688 - Melanoma patients

Single Dose 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's technology fits seamlessly with CAR-T process
  - **Potential for patient to be in optimal state before CAR-T therapy**
  - **Potential for optimal environment for CAR-T cells**
  - **Provide flexibility for CAR-T logistics**



Demonstrable safety and dose-dependent lymphodepletion observed across a wide dose range around the proposed targeted lymphodepletion dose

% Lymphodepletion

3x Proposed Dose Targeted Lymphodepletion

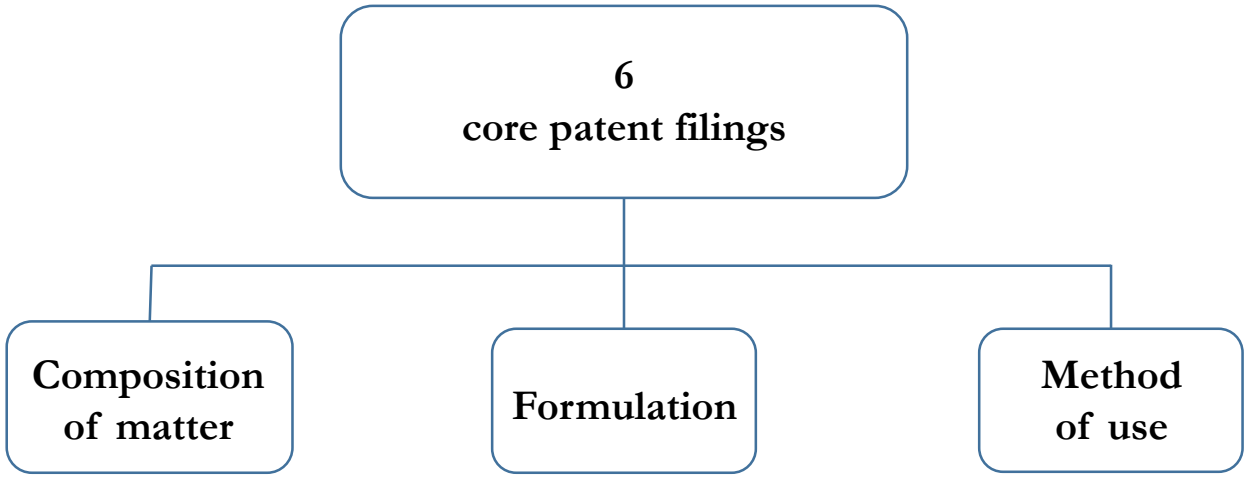
0.1x Proposed Dose Targeted Lymphodepletion

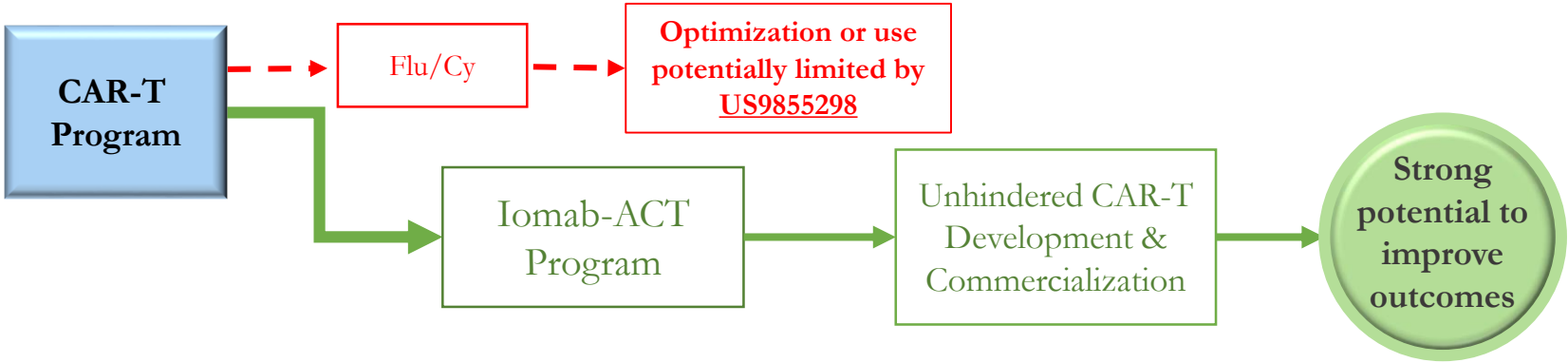
Drug clearance

Source: company data

Iomab-ACT Program Strong IP Portfolio and Know How

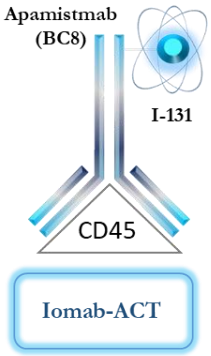
Bolstered R&D efforts have allowed us to architect an intellectual property portfolio related to the Iomab-ACT Program

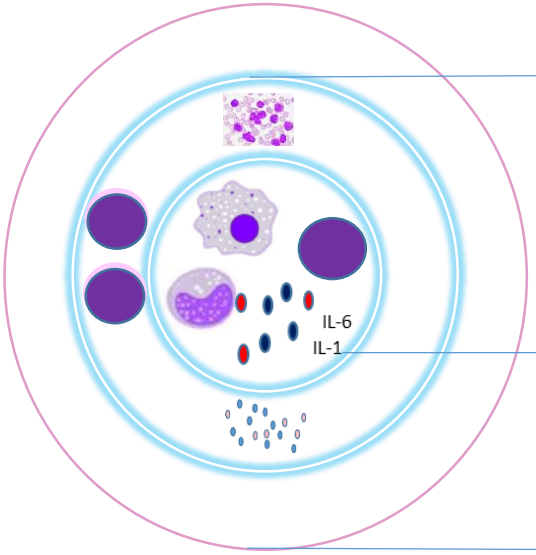




Iomab-ACT's Value Proposition to the CAR-T Paradigm

Using a proven modality in a novel targeted manner 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/NT
- 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-T

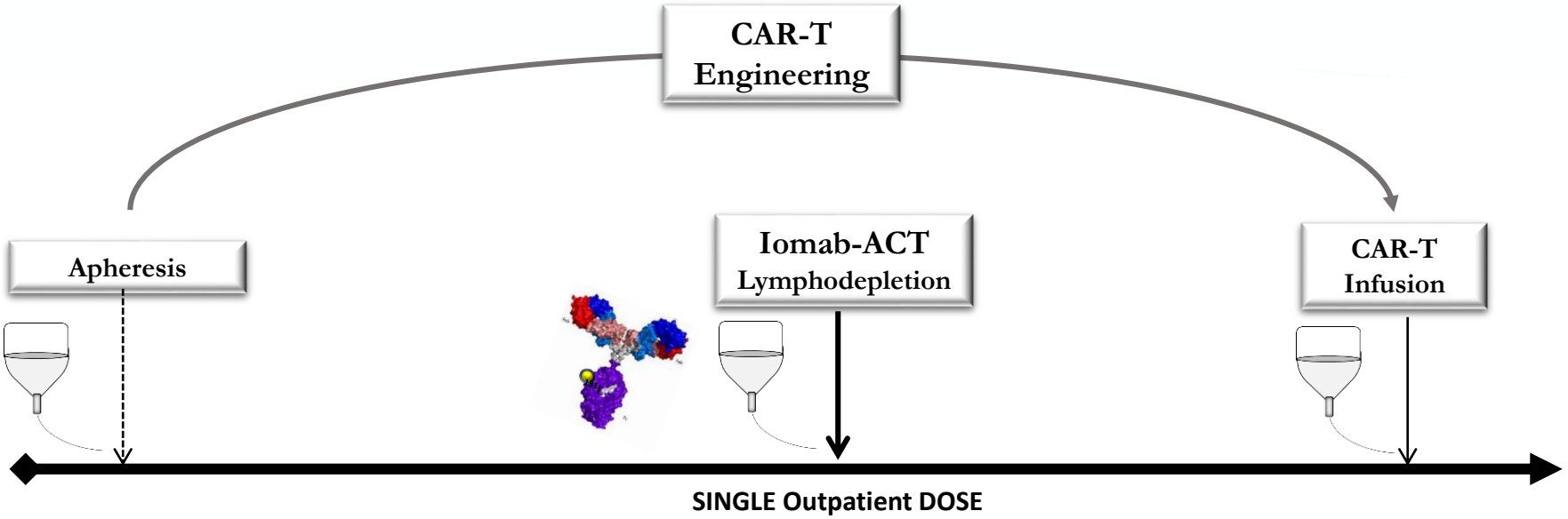
Targeted	Single Dose	Out Patient	Improved Outcomes	Expanded Access

III. Iomab-ACT Clinical Trial and Development

Iomab-ACT Program at MCW

- MCW intends to initiate a trial that will study Iomab-ACT as a targeted lymphodepletion in conjunction with CAR-T
- Together with Actinium, MCW physicians are working to finalize an Investigational New Drug (IND) application for this trial
- Teams are finalizing protocols and preparing materials to submit to the FDA
- IND will reference Iomab-B's IND that is supported by extensive clinical data
- CAR-T construct expected to be studied in this trial will be for a validated CAR-T target that is supported by clinical data

Proposed Iomab-ACT Clinical Study Design



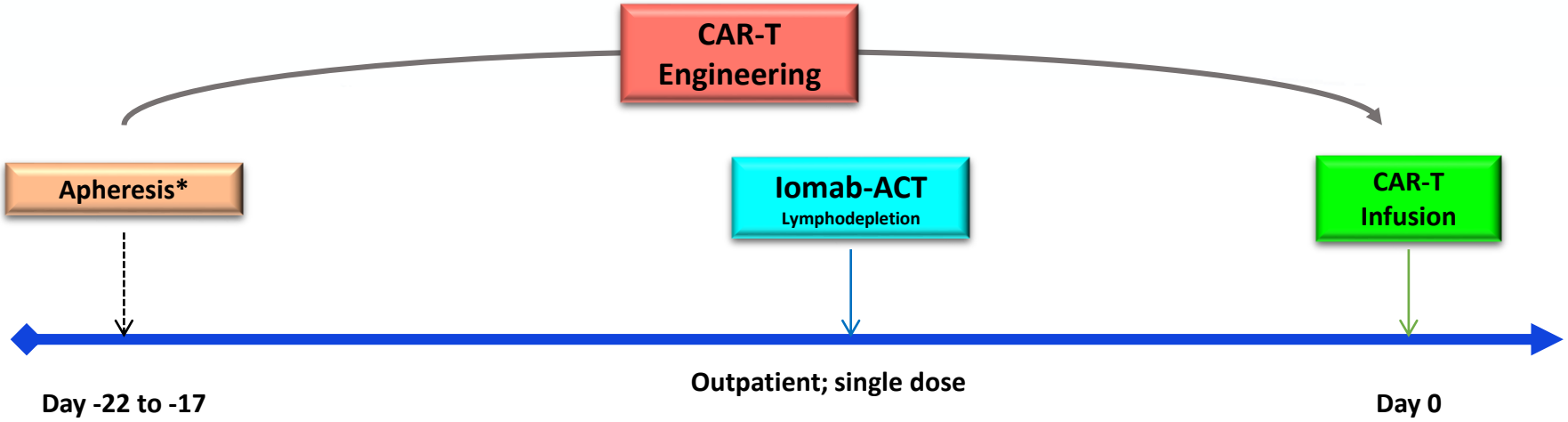
Starting dose →

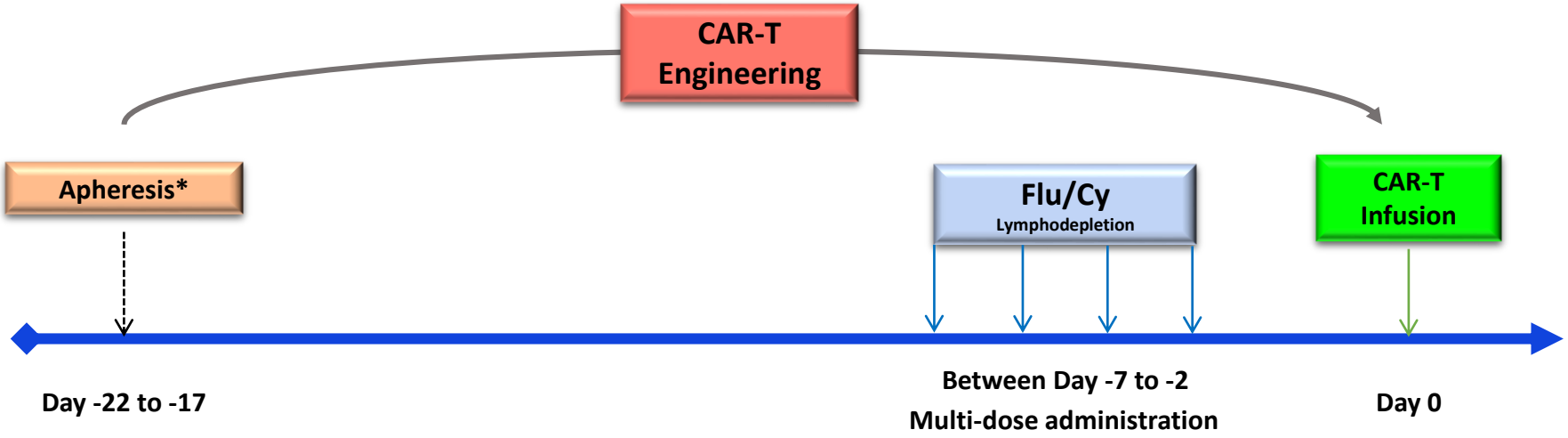
Dose 1a (if DLT)
Lymphodepletion Dose Level 1
Lymphodepletion Dose Level 2
Lymphodepletion Dose Level 3

Follow-up post-CAR-T

Phase I, 3+3 dose-escalation trial

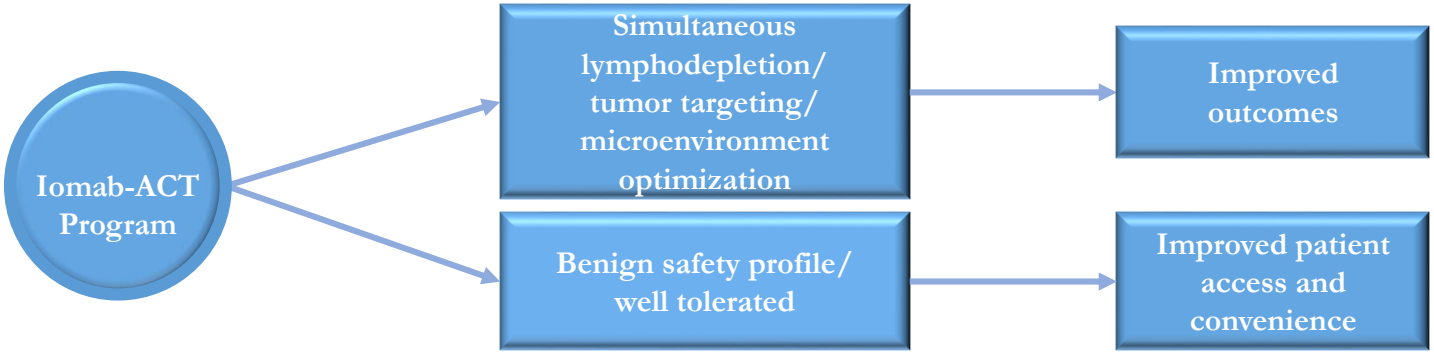
Iomab-ACT Lymphodepletion Optimized for CAR-T





Iomab-ACT Program's Potential Clinical Benefits

Iomab-ACT is a targeted and predictable lymphodepletion alternative to nonspecific chemotherapy regimens that can offer enhanced CAR-T expansion and persistence.



- **Potential Advantages**:
  - Efficacy: Targeted lymphodepletion enables potential for improved outcomes with cellular therapy
  - Safety: Drug tolerability demonstrated in several hundred patients in conjunction with cell therapy
  - Patient Convenience: Single dose administration in an outpatient setting
  - Improved Patient Access: Targeted technology is patient-sparing and may expand the eligible population for cellular therapy

III. Iomab-ACT Program – Opportunity for Actinium and the CAR-T Industry

Latest Pipeline Initiative in CAR-T

Only multi-disease, multi-target pipeline for targeted conditioning and lymphodepletion

Only company with a clinical stage CD45 drug candidate

Target	Program	Indication	Focus	Development Stage			
				Pre	1	2	3
CD45	Iomab-B	R/R AML 55+	Targeted Conditioning -BMT				Pivotal Phase 3
	Iomab-B	AML, MM, ALL	Targeted Conditioning -BMT			Phase 1/2	
	Iomab-ACT	CAR-T Programs	Targeted Lymphodepletion –CAR-T		Planned Phase 1		
CD33	Actimab-MDS	MDS	Targeted Conditioning -BMT			Phase 1/2	
	Actimab-A CLAG-M	R/R AML	Targeted Conditioning/Therapeutic		Phase 1		
	Actimab-A	AML	Therapeutic				Phase 2
	Actimab-M	MM	Therapeutic		Phase 1		
	Actimab-A MRD	AML	Therapeutic		Phase 1		
CD38	Daratumumab + Ac-225	MM	Therapeutic	Preclinical			
AWE Platform	Ac-225 + Undisclosed	Undisclosed	Undisclosed	Preclinical			
	Ac-225 + Undisclosed	Colon, Prostate & Brain	Therapeutic	Preclinical			

MEDICAL COLLEGE OF WISCONSIN

astellas

Memorial Sloan Kettering Cancer Center

AML = Acute Myeloid Leukemia, MDS = Myelodysplastic Syndrome, MM = Multiple Myeloma
** Investigator initiated trials using Actinium technology*

Iomab-ACT Program - Universal Potential in CAR-T

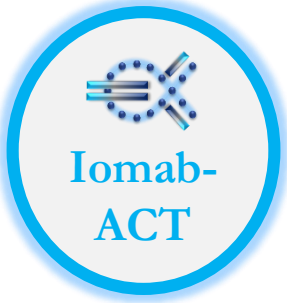
Iomab-ACT Program presents significant value potential along the CAR-T paradigm

Rapidly Growing CAR-T Opportunity

Landscape	Targets	Indications
2 approved therapies 4 pivotal stage programs 200+ development programs 60+ Companies	CD19 CD20 CD38 BCMA Others	B-Cell cancers Multiple Myeloma Leukemias Solid Tumors

CAR-T Developers

- Optimizes tumor microenvironment
- Potential to address CRS & NT
- Simplifies patient experience – single dose, outpatient
- Allows for program optimization
- Expands addressable patient populations
- Addresses Flu/Cy patent issues



Healthcare System

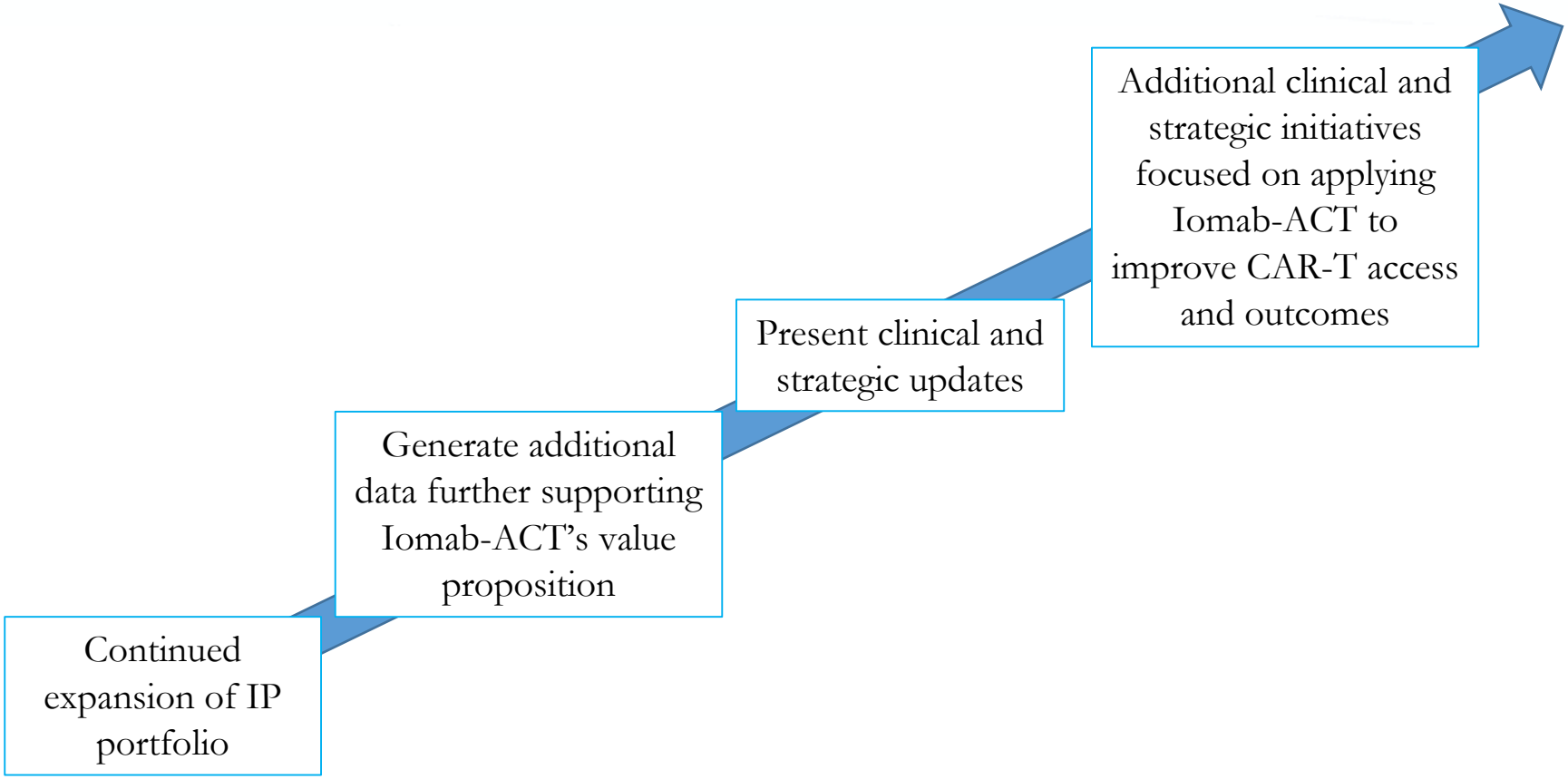
- Reduced hospitalization costs
- Improved CAR-T outcomes

Patients

- Potentially stronger patient receiving CAR-T
- Potentially reduces toxicities
- More convenient single infusion, outpatient
- Expand access to CAR-T

Expected Value Creating Events

Iomab-ACT program planned progression and expected milestones



American Society of Hematology
Helping hematologists conquer blood diseases worldwide

TCT | TRANSPLANTATION & CELLULAR THERAPY MEETINGS of ASBMT AND CIBMTR

AACR American Association for Cancer Research ANNUAL MEETING 2019 ATLANTA

2019 ASCO ANNUAL MEETING

Thank You

Actinium Pharmaceuticals, Inc.

Questions & Answer Session