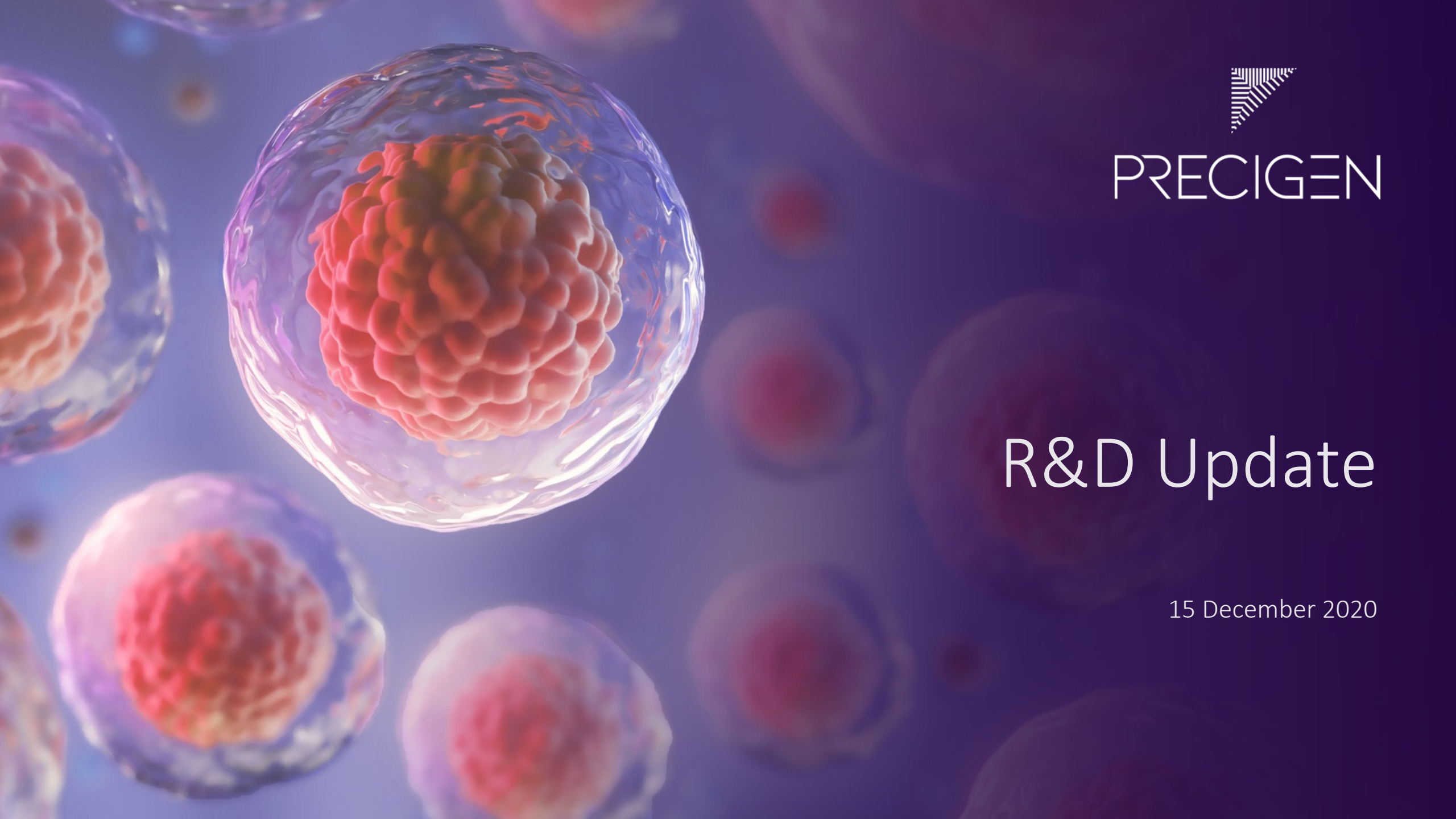

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R&D Update

15 December 2020

Forward-looking Statements

Some of the statements made in this presentation are forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based upon Precigen's current expectations and projections about future events and generally relate to plans, objectives and expectations for the development of Precigen's business and can be identified by forward-looking words such as “may,” “will,” “potential,” “seek,” “expect,” “believe,” “anticipate,” “intend,” “continue,” “opportunity,” “groundwork,” “poised,” “future,” “update” and similar expressions. Examples of forward-looking statements in his presentation, include statements about the timing, pace and progress of preclinical and clinical trials and discovery programs, and potential benefits of platforms and product candidates including in comparison to competitive platforms and products. Although management believes that the plans, objectives and results reflected in or suggested by these forward-looking statements are reasonable, all forward-looking statements involve risks and uncertainties and actual future results may be materially different from the plans, objectives and expectations expressed in this presentation. These risks and uncertainties include, but are not limited to, (i) the impact of the COVID-19 pandemic on Precigen’s businesses, operating results, cash flows and/or financial condition, (ii) Precigen’s strategy and overall approach to its business model; (iii) the uncertain timing and results of investigational studies and preclinical and clinical trials, including any delays or potential delays as a result of the COVID-19 pandemic; (iv) the fact that interim and preliminary results may change as more data becomes available and are subject to procedures that could result in changes to the final data; (v) the lengthy and expensive clinical development process and the potential difficulty in enrolling patients; (vi) the lengthy and unpredictable nature of the regulatory approval process; (vii) Precigen’s limited experience designing and implementing clinical trials; (viii) the ability to successfully enter into optimal strategic relationships with its subsidiaries and operating companies that it may form in the future; (**ix**) the ability to hold or generate significant operating capital, including through partnering, asset sales and operating cost reductions; (vii) actual or anticipated variations in operating results; (x) cash position; (xi) market conditions in the company’s industry; (xii) the volatility of Precigen’s stock price; (xiii) the ability, and the ability of collaborators, to protect Precigen’s intellectual property and other proprietary rights and technologies; (xiv) the ability, and the ability of collaborators, to adapt to changes in laws or regulations and policies, including federal, state, and local government responses to the COVID-19 pandemic; (xv) outcomes of pending and future litigation; (xvi) the ability to retain and recruit key personnel; and (xvii) expectations related to the use of proceeds from public offerings and other financing efforts. For a discussion of other risks and uncertainties, and other important factors, any of which could cause actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Precigen’s Annual Report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in Precigen's subsequent filings with the Securities and Exchange Commission. All information in this presentation is as of the date its cover page, and Precigen undertakes no duty to update this information unless required by law.

All of the pharmaceutical products described in this presentation are investigational new drugs, which are currently undergoing pre-clinical and/or human clinical trial testing. As a result, none of them have had their safety or efficacy established or are approved by the U.S. Food and Drug Administration or any other regulatory agency.

Today's Participants and Agenda

Agenda

- UltraCAR-T® Platform Discussion
- PRGN-3005 UltraCAR-T® in Ovarian Cancer
- PRGN-3006 UltraCAR-T® in AML and MDS
- AG019 ActoBiotics™ in Type 1 Diabetes
- Q&A

Participants

Helen Sabzevari, PhD
President and CEO of Precigen

Pieter Rottiers, PhD
CEO of Precigen ActoBio

Kevan Herold, MD
Professor of Immunobiology and of Medicine (Endocrinology)
Yale School of Medicine
One of the lead investigators for the AG019 clinical study

Mary L. (Nora) Disis, MD
Faculty member at the University of Washington and
Fred Hutchinson Cancer Research Center
One of the lead investigators for the PRGN-3005 clinical study

Precigen Clinical Pipeline

Immuno-oncology

PRODUCT	PLATFORM	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
PRGN-3005	UltraCAR-T	Ovarian Cancer					
PRGN-3006	UltraCAR-T	AML, MDS					
PRGN-2009	OTS AdenoVerse Immunotherapy	HPV+ Solid Tumors					

Autoimmune Disorders

PRODUCT	PLATFORM	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
AG019	ActoBiotics	Type 1 Diabetes					

Emerging Therapeutics

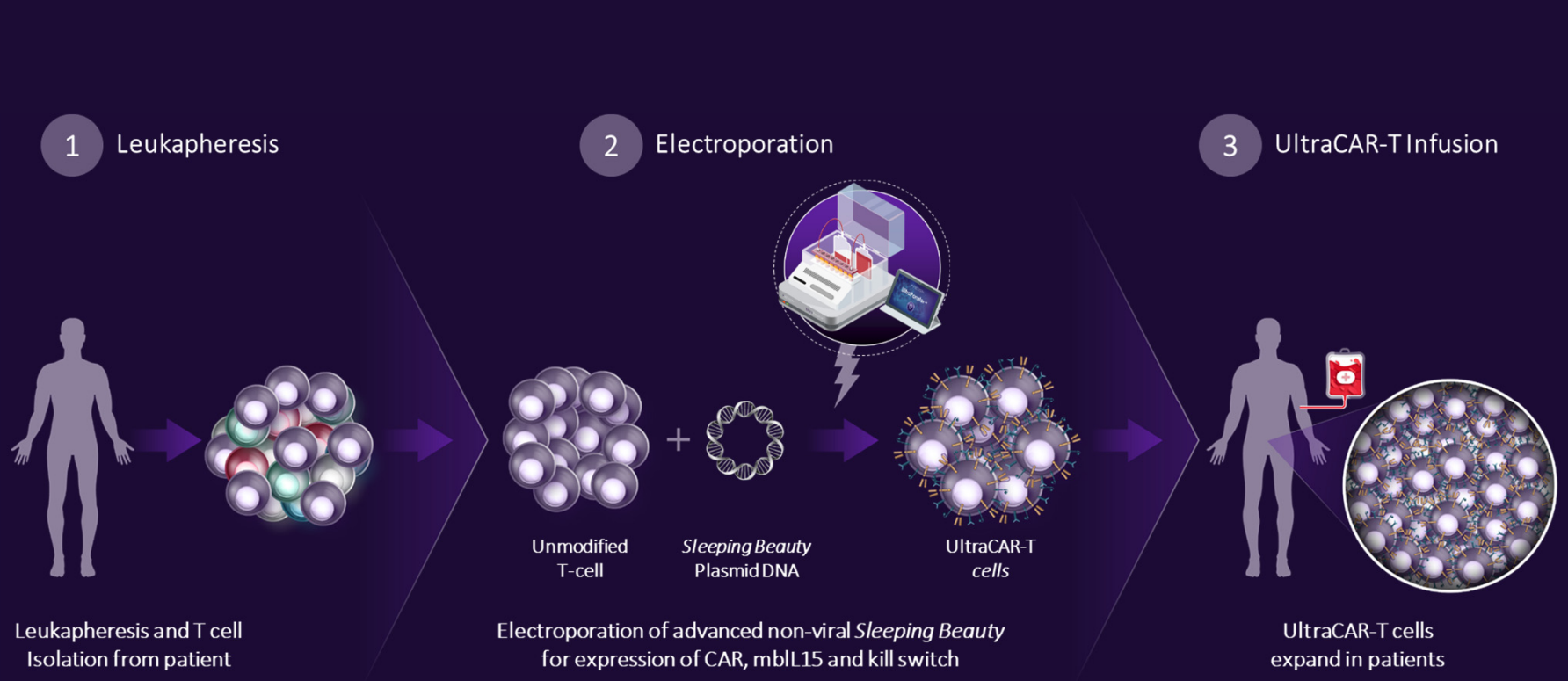
PRODUCT	PLATFORM	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
INXN-4001	Non-viral UltraVector	Heart Failure					

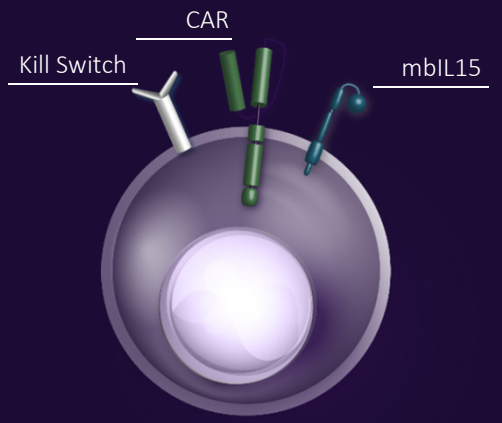
UltraCAR-T® Platform

Overcoming Limitations of Conventional and Allogeneic CAR-T

UltraCAR-T: Overnight, Decentralized Manufacturing Process Promises a More Effective Way to Treat Patients

UltraCAR-T® Platform is Engineered to Address Major Challenges of Current CAR-T Cell Approaches





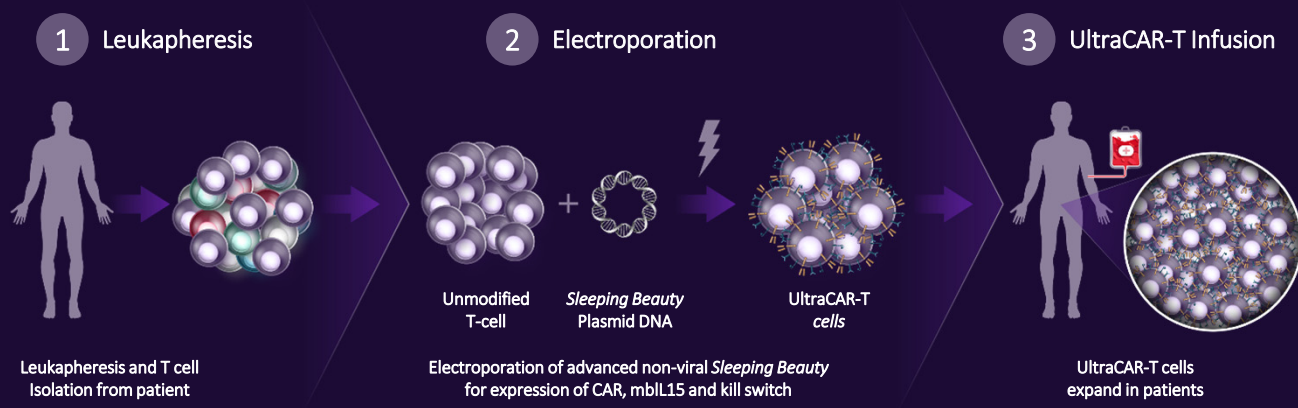
UltraCAR-T Advantages

- Non-viral multi-gene delivery
- Uniform, multigenic cell product
- Stem-like T cell memory phenotype
- Higher antigen-specific expansion
- Enhanced *in vivo* persistence
- Ability to deplete with kill switch
- Overnight manufacturing process

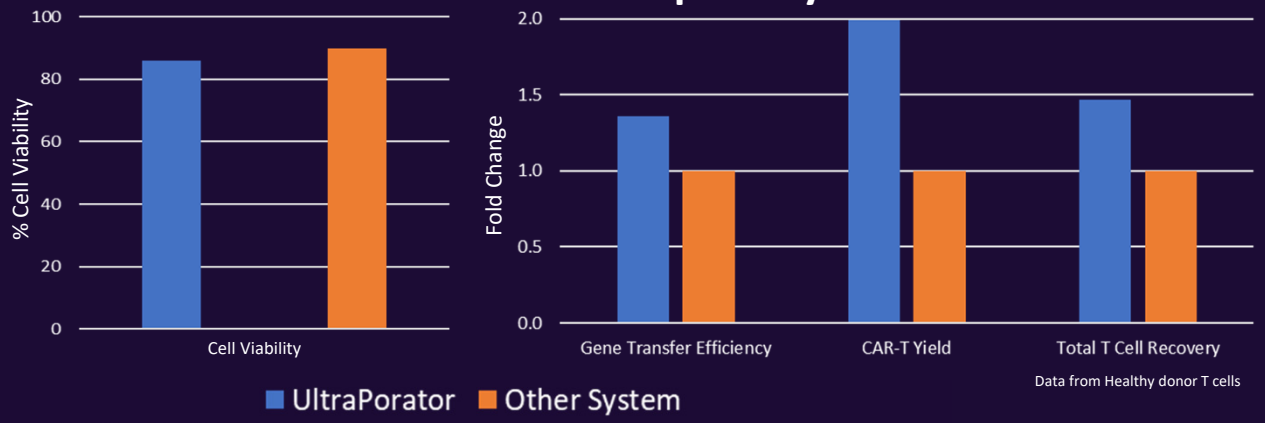
UltraCAR-T Platform Brings Benefits of Off-the-Shelf Allogeneic Therapy to Autologous CAR-T Treatment

UltraPorator™ is Designed to Commercially Scale-up UltraCAR-T Manufacturing

- **Precigen's proprietary system**
- **Electroporation optimized for UltraCAR-T**
- **Semi-closed system minimizes manual handling and reduces processing time**
- **Rapid, high efficiency gene transfer protocol**
- **High throughput system handles a large number of T cells per batch**
- **Streamlines tech transfer & implementation at medical centers**
- **Potential application in various gene and cell therapies**



UltraPorator demonstrates Improved Gene Transfer Capability in T cells



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PRGN-3005 UltraCAR-T®

PRGN-3005 UltraCAR-T: An Attractive Opportunity in Solid Tumors

Ovarian Cancer

- Ovarian cancer is the most lethal of the gynecologic malignancies[6]

High Unmet Need

Stage IV survival as low as 20%[3]

300K WW/22K US

Newly diagnosed patients per year[1, 2]

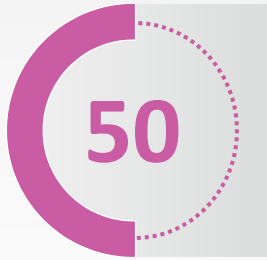
Current Treatment Paradigm

- The current standard of care for ovarian cancer is surgery, followed by chemotherapy with a combination of platinum agents and taxanes[4]
- Recurrence of the disease occurs in most patients after initial treatment, resulting in a cycle of repeated surgeries and additional rounds of chemotherapy
- Low overall response rate (< 10%) with anti-PD1 treatment[5]

Market Opportunity for Targeting MUC16

MUC16 expression (% patients)[8]

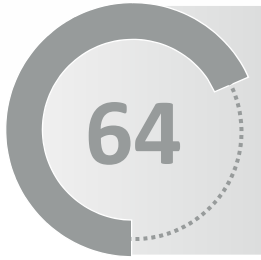
Ovarian Cancer
Addressable Patient Population:
24,000



Breast Cancer
Addressable Patient Population:
117,000

Pancreatic Cancer
Addressable Patient Population:
33,000

Endometrial Cancer
Addressable Patient Population:
42,000



Lung Cancer
Addressable Patient Population:
144,000

[1]World Health Organization, International Agency for Research on Cancer, Global Cancer Observatory. Cancer Today, Estimated number of new cases in 2018, worldwide, both sexes, all ages.
[2]American Cancer Society Ovarian Cancer Special Section.
[3]American Cancer Society. Survival Rates for Ovarian Cancer, by Stage.
[4]C. Della Pepa et al., Chin. J. Cancer 34, (2015).
[5]Bartl, T. et al. Current state and perspectives of checkpoint inhibitors in ovarian cancer treatment. memo 13 (2020).
[6]Giannone G. et al., AnnTransl Med (2019).
[7]WHO International Agency for Research on Cancer dataset
[8]Human Protein Atlas MUC16 Protein Expression Summary

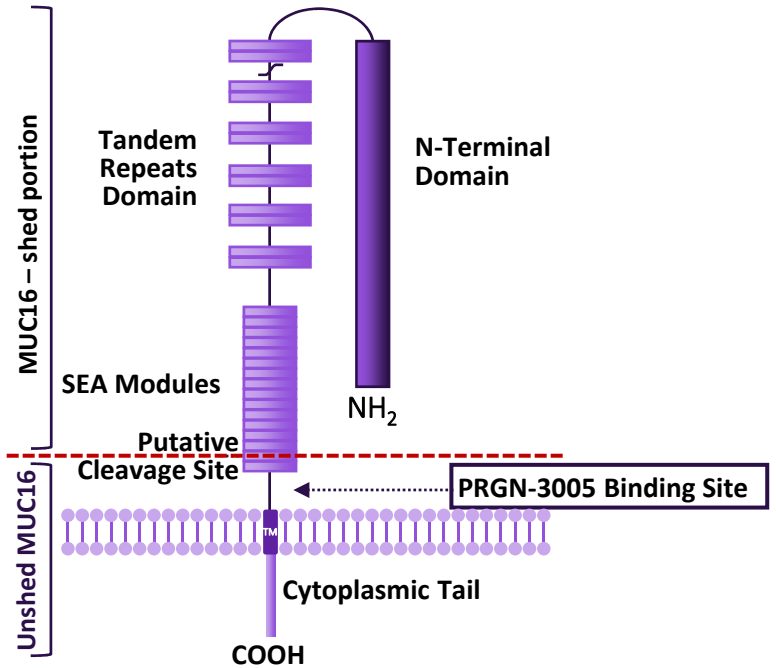
PRGN-3005 UltraCAR-T, A First-in-Class Therapy in Ovarian Cancer

MUC16 is an Attractive Target for Ovarian Cancer

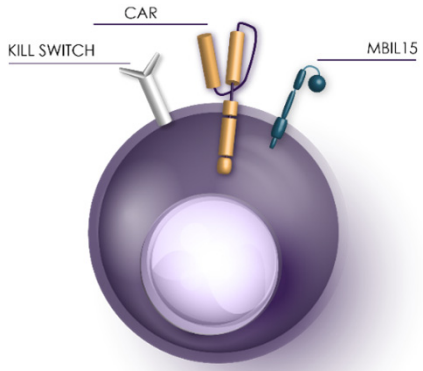
- MUC16 overexpressed on >80% of ovarian tumors[1]
- Limited expression found on healthy tissues

PRGN-3005 Targets Unshed Portion of MUC16

- Advanced non-viral system to simultaneously express MUC16 CAR, mbIL15 and kill switch
- Initial target is advanced stage platinum resistant ovarian cancer



Modified from Piché A. et al., World J Obstet Gynecol. 2016



PRGN-3005 UltraCAR-T

UltraCAR-T Advantages
Non-viral multi-gene delivery
Uniform, multigenic cell product
Stem-like T cell memory phenotype
Higher antigen-specific expansion
Enhanced *in vivo* persistence
Ability to deplete with kill switch
Overnight manufacturing process

[1]Suh H, et al., Chemo Open Access (2017)

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PRGN-3005 UltraCAR-T: Phase 1/1b Trial is Enrolling Patients

Eligibility:

- Advanced stage ovarian, fallopian or primary peritoneal cancer
- Measurable by RECIST
- CA125>ULN
- No stratification based on biomarker (MUC16) expression

Arm 1, IP infusion (No Lymphodepletion)

PRGN-3005

apheresis → In-patient observation → Follow-up (12m)

Arm 2, IV infusion (No Lymphodepletion)

PRGN-3005

apheresis → In-patient observation → Follow-up (12m)

Safety Monitoring:

- Standard battery for adverse events
- CRS, Neurotoxicity

Disease Response:

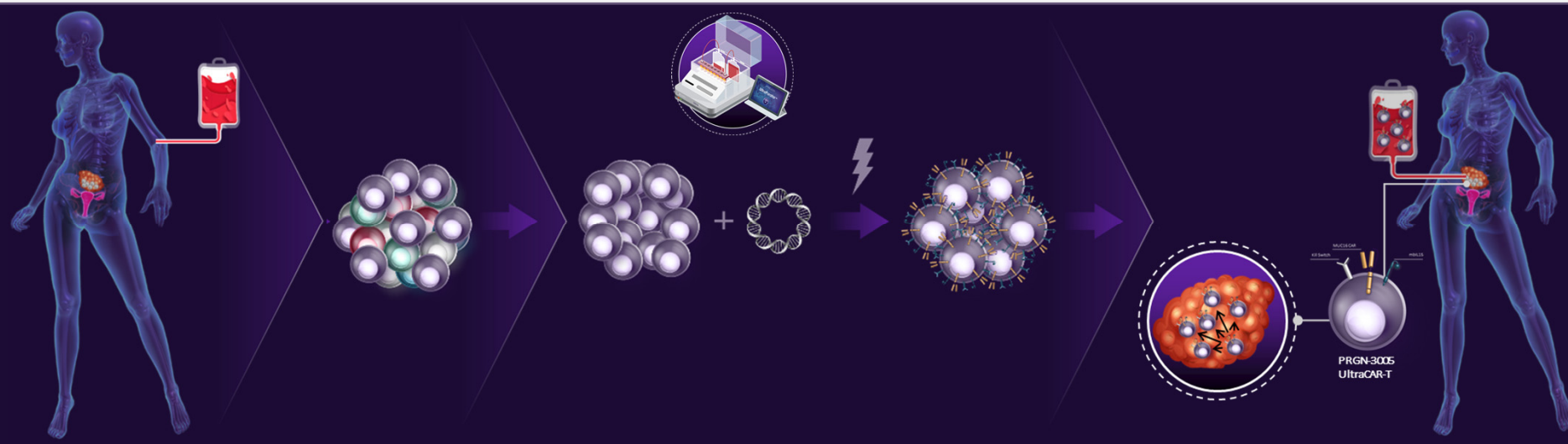
- RECIST and irRECIST

Correlatives:

- PRGN-3005 persistence/expansion
- Immune phenotype
- Expression of biomarkers, including MUC16

Study Objectives

- Primary: Evaluate the safety and determine the maximal tolerated dose of PRGN-3005 delivered either by intraperitoneal or intravenous infusion
- Secondary: To evaluate *in vivo* persistence and anti-tumor activity of PRGN-3005

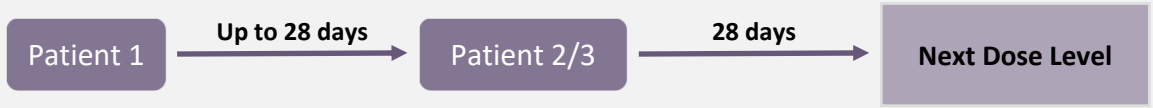


Overnight manufacturing and administration of UltraCAR-T

PRGN-3005 IP Arm: Dose Escalation

Dose Level	Dose Range	Total UltraCAR-T Cell dose	# Prior Treatments
1	$3x10^4$ - ≤ 1 x 10^5 cells/kg	6.1 to 7.6 x 10^6 CAR-T cells (N=3)	6-9 prior lines
2	1 x 10^5 - ≤ $3x10^5$ cells/kg	12 to 21 x 10^6 CAR-T cells (N=3)	6-9 prior lines
3+	> $3x10^5$ cells/kg	Planned enrollment 3-6 subjects/dose	
Expansion	MTD	Multicenter expansion Phase planned in 2021	

Study Design



- Dose escalation will proceed in IP and IV arms in parallel (IV arm will start enrolling after completion of dose escalation in IP arm)
- Expansion phase is planned at MTD for both arms
- Subjects receive **No lymphodepletion** prior to UltraCAR-T treatment

PRGN-3005 IP Arm: Safety

Summary of Grade ≥3 Treatment-Emergent Adverse Events (TEAEs)

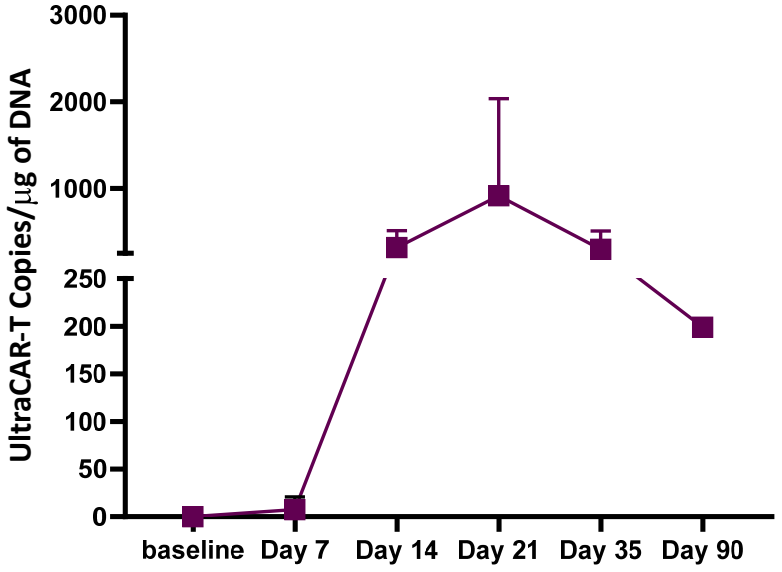
Adverse Event	N=6 (%)
Hematologic	
Decreased lymphocyte count	**2 (33%)**
Hypoalbuminemia	**1 (16.5%)**
Non-Hematologic	
Hypoxia	**1 (16.5%)**

- **No DLTs**
- **No incidence of neurotoxicity**
- **No incidence of Cytokine Release Syndrome (CRS)**

PRGN-3005 IP Arm: Expansion and Persistence in Peripheral Blood after Intraperitoneal (IP) Infusion of UltraCAR-T

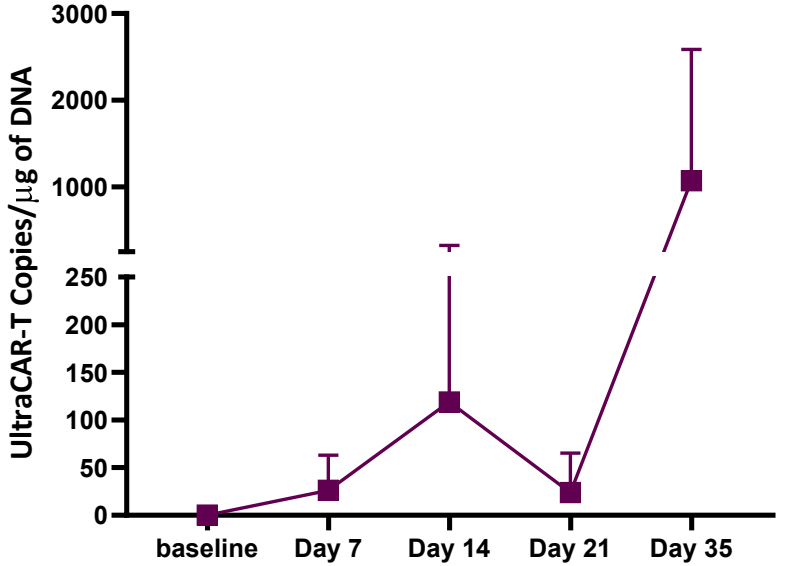
3 Patients Treated at each Dose Level without Lymphodepletion
UltraCAR-T cells Administered via Intraperitoneal (IP) Infusion

Dose Level 1 (N=3)



Limit of Quantification:50copies/μg
N= 1-3 patients at each time point
1/3 patients had ascites removal

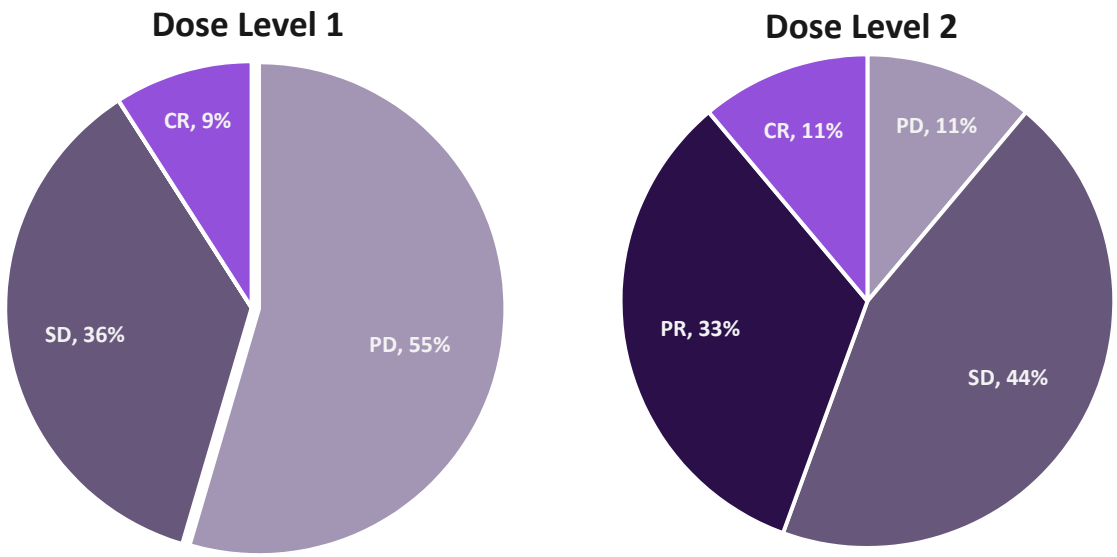
Dose Level 2 (N=3)



Limit of Quantification:50copies/μg
N= 1-3 patients at each time point
2/3 patients had ascites removal

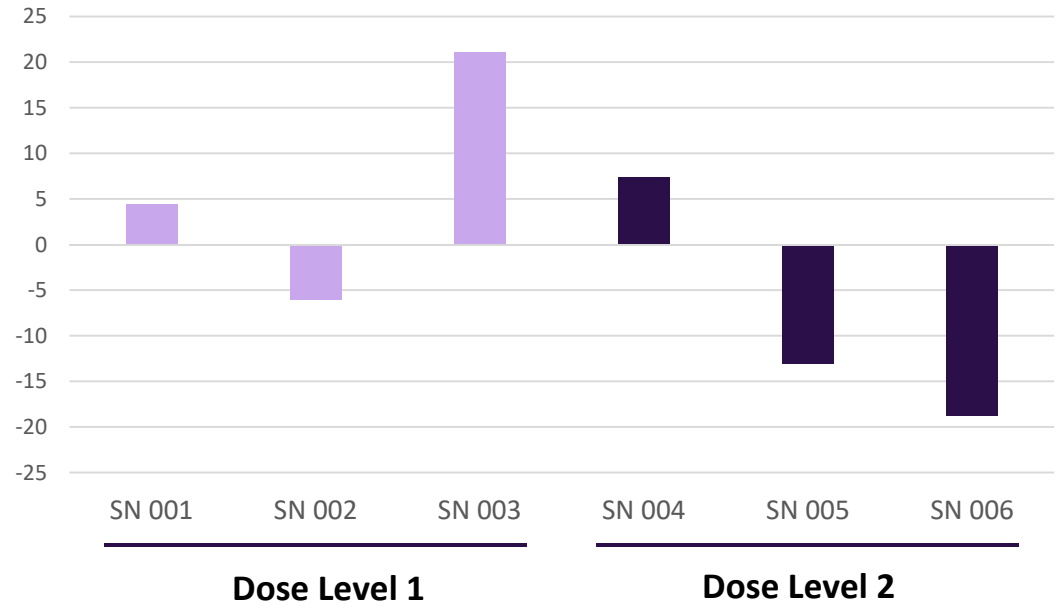
PRGN-3005 IP Arm: Individual Target Lesion Response and Change in Target Lesion Size in Patients Treated at Two Lowest Doses

Responses in Individual Target Lesions



Total number of target lesions:
Dose Level 1 = 11
Dose Level 2 = 9

Percent Change in Total Target Tumor Burden



Target Tumor Burden Regression in 3/6 (50%) Patients

Individual target lesion response:
CR: Complete Response
SD: Stable Disease
PR: Partial Response
PD: Progressive Disease

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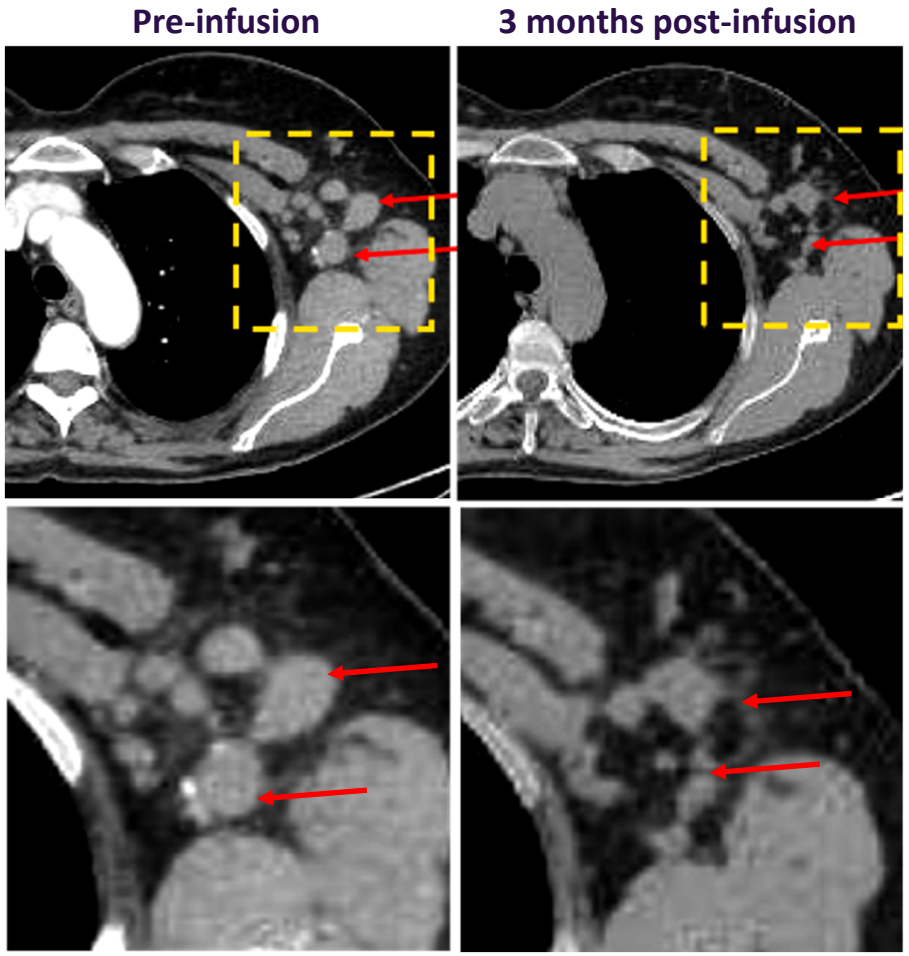
PRGN-3005 IP Arm: Case Study of Patient Dosed at Dose Level 1

Subject Characteristic and Treatment Outcome

- Platinum resistant with recurrent disease
- **Failed 7 prior lines of therapies**
- Disease status at enrollment: L axillary LN, liver lesions and abdominal lymph nodes
- PRGN-3005: Dose level 1 via IP infusion
  - 7.5 x 10^6 Total UltraCAR-T cells
  - No lymphodepletion
- No DLTs or neurotoxicity
- **Complete response in axillary lymph node target lesions after 3 months**
- Classified progressive disease (PD) due to new liver lesion

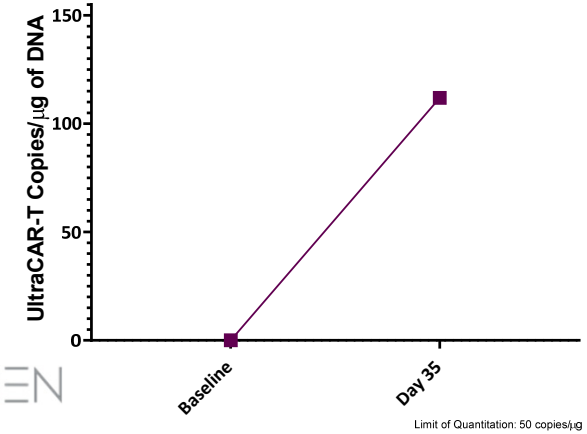
Complete Response in Axillary Lymph Node Target Lesions at 3 Months Post UltraCAR-T treatment



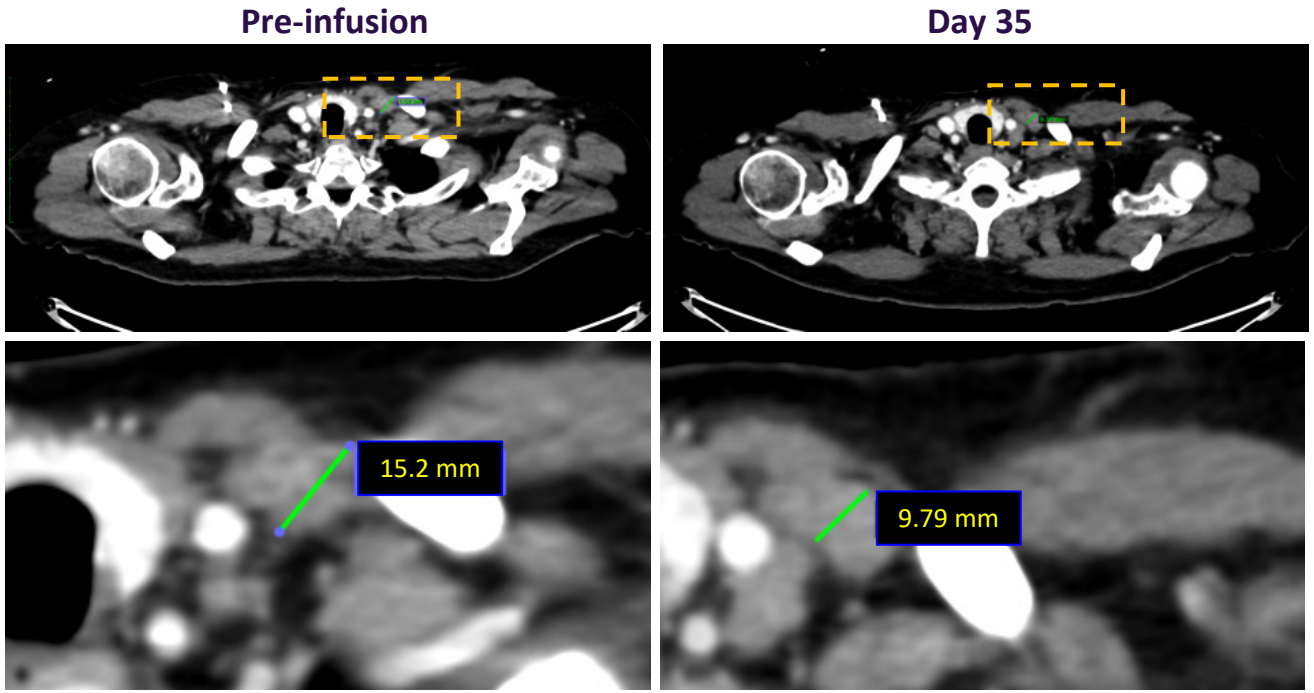
PRGN-3005 IP Arm: Case Study of Patient Dosed at Dose Level 2

Subject Characteristic and Treatment Outcome

- Platinum resistant with recurrent disease
- **Failed 6 prior lines of therapies**
- Disease status at enrollment: 10+ lesions in liver, lymph, abdominal wall, peritoneum
- PRGN-3005: Dose level 2 via IP infusion
  - 21 x 10^6 Total UltraCAR-T cells
  - No lymphodepletion
- No DLTs or neurotoxicity
- **UltraCAR-T expansion observed in ascites**



Complete Response in Supraclavicular Lymph Node Target Lesion at 35 Days Post UltraCAR-T treatment



- **Complete response in supraclavicular lymph node at Day 35**
- 13% reduction in sum of lesions at 5 weeks
- Classified progressive disease (PD) due to new liver and lung lesions

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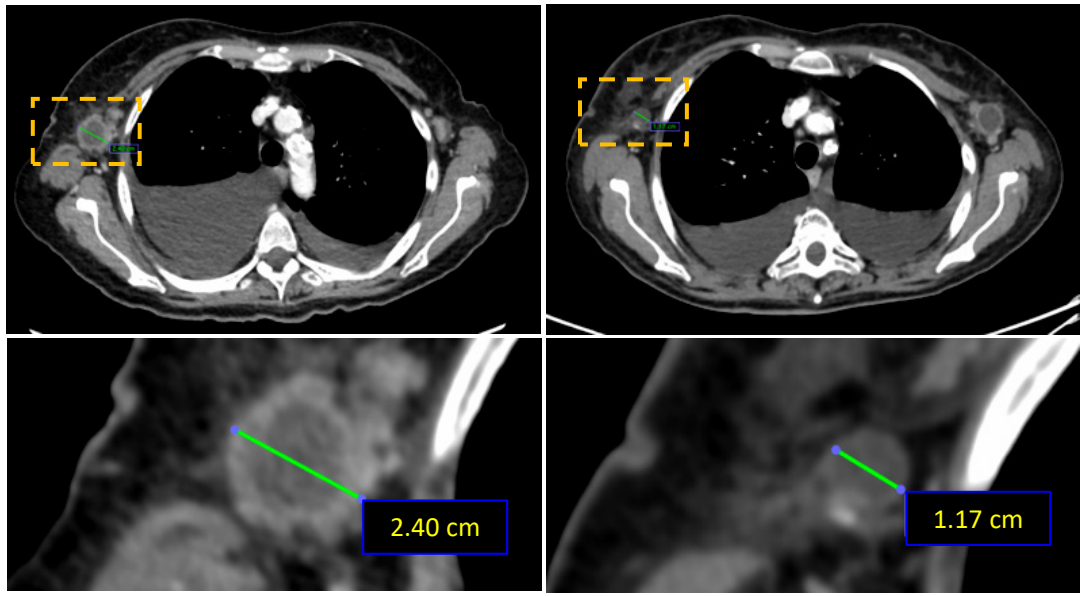
PRGN-3005 IP Arm: Case Study of Patient Dosed at Dose Level 2

Partial Response in Target Right Axillary Lymph Node

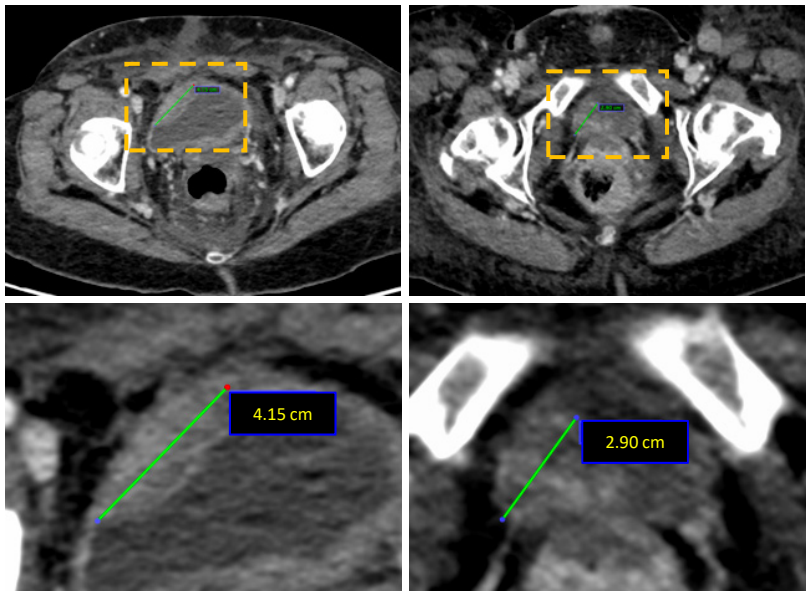
Pre-infusion **Day 22**



- Platinum resistant with recurrent disease
- Disease status at enrollment: 10+ lesions in liver, lymph, bladder, peritoneum
- **Failed 7 prior lines of chemotherapy**
- PRGN-3005: Dose level 2 via IP infusion
  - 19 x 10^6 Total UltraCAR-T cells
  - No lymphodepletion

Partial Response in Target Bladder Lesion

Pre-infusion **Day 22**



- No DLTs or neurotoxicity
- **Partial response (PR) in axillary and inguinal lymph nodes and bladder lesions**
- 19% reduction in sum of lesions at 3 weeks
- Overall Stable Disease (SD)

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PRGN-3005 UltraCAR-T: Summary

- **Phase 1 trial in intraperitoneal (IP) arm is enrolling patients in dose escalation phase**
- **PRGN-3005 treatment is safe and well tolerated to date; No DLTs or neurotoxicity**
- **100% manufacturing success to date using decentralized, rapid manufacturing process**
- **PRGN-3005 cells showed encouraging expansion and persistence after very low dose IP infusion**
- **PRGN-3005 treatment indicated clinical activity as evidenced by reduction in target lesions**

PRGN-3006 UltraCAR-T

PRGN-3006 UltraCAR-T: An Attractive Opportunity in AML and MDS

Acute Myeloid Leukemia (AML)

- AML is a cancer that starts in the bone marrow, but most often moves into the blood
- AML is the most common acute leukemia in adults

Myelodysplastic Syndromes (MDS)

- MDS are cancerous conditions of the bone marrow generally found in adults in their 70s

Current Treatment Paradigm

- 60-80% AML patients achieve complete remission after induction chemotherapy[4,5]
- Approximately 50% of the AML patients relapse[4,5]
- Prognosis is very poor for relapsed or refractory (r/r) AML patients

Urgent Need for Effective Therapies to Improve Survival

Disease Snapshot

High Unmet Need

5-year survival as low as 5% for patients over 65[3]

20K US

Newly diagnosed r/r AML patients per year[2]

>10K US

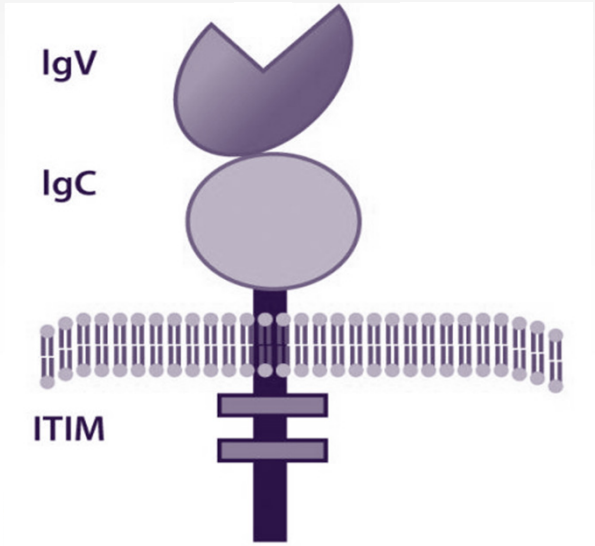
Newly diagnosed higher risk MDS patients per year[2]

[1]American Cancer Society. Key Statistics for Acute Myeloid Leukemia (AML).
[2]American Cancer Society. Key Statistics for Myelodysplastic Syndromes..
[3]Thein, M., et al., Outcome of older patients with acute myeloid leukemia: an analysis of SEER data over 3 decades. Cancer, 2013. 119(15): p.2720-7.
[4]Dohner H, et al., Blood (2010);115:453–474.
[5]Burnett A, et al., J Clin Oncol (2011);29:487–494

PRGN-3006 UltraCAR-T, A First-in-Class Therapy in AML and MDS

CD33 is an Attractive Target for AML

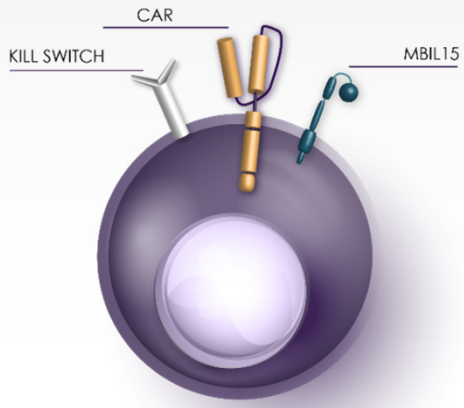
- CD33 is overexpressed on myeloid leukemia and leukemic stem cells
  - 85-90% of AML patients show expression of CD33 on blasts
  - Minimal expression outside of hematopoietic system



Modified from: https://www.openaccessgovernment.org/cd33-directed-therapy/47313/

PRGN-3006 Targets CD33

- Advanced non-viral system to simultaneously express CD33 CAR, mbIL15 and kill switch
- Orphan Drug Designation granted by the FDA



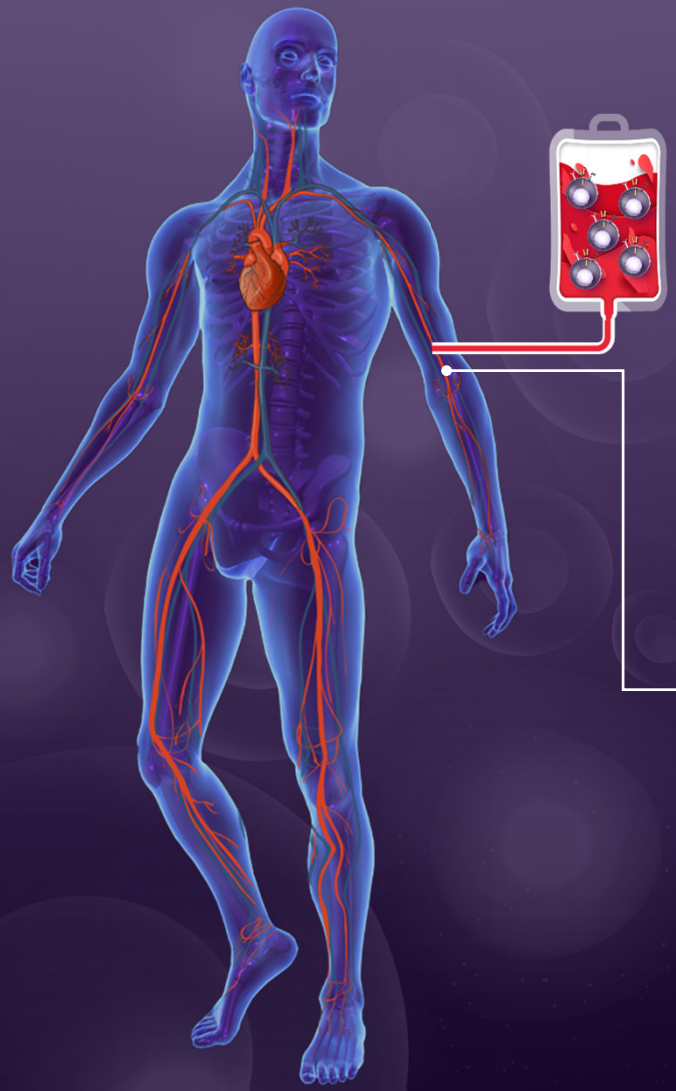
PRGN-3006 UltraCAR-T

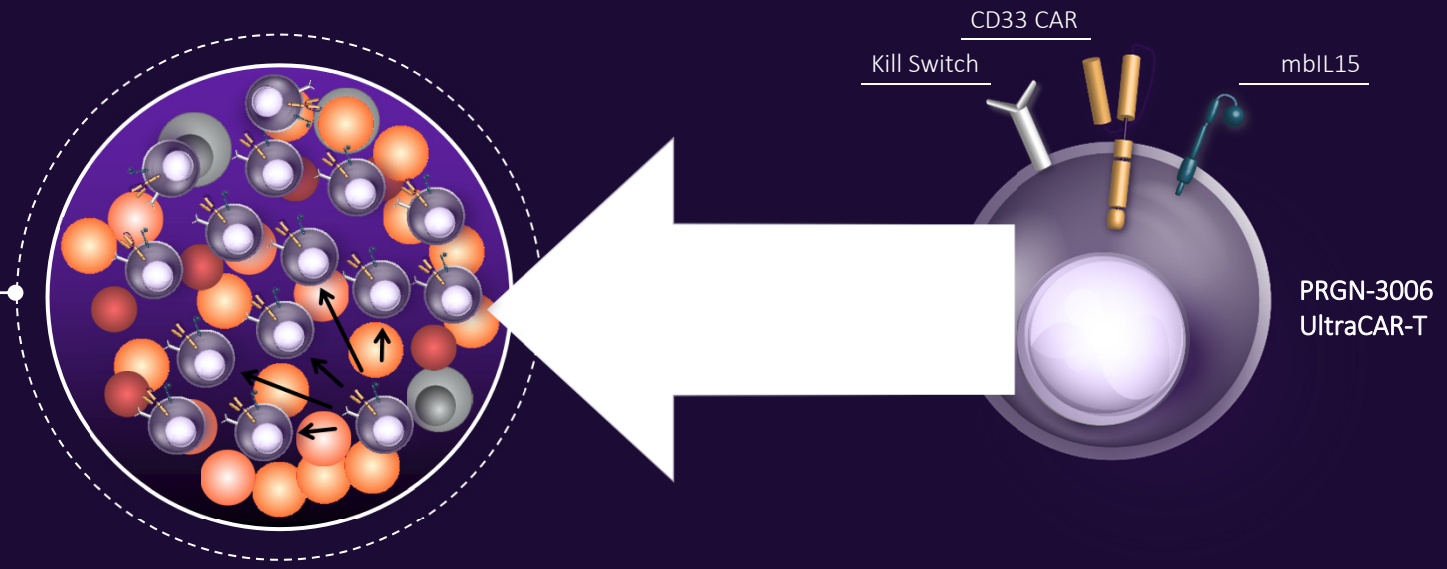
UltraCAR-T Advantages
Non-viral multi-gene delivery
Uniform, multigenic cell product
Stem-like T cell memory phenotype
Higher antigen-specific expansion
Enhanced *in vivo* persistence
Ability to deplete with kill switch
Overnight manufacturing process

PRGN-3006

A First-in-Class Therapy in AML, MDS

- Rapid, decentralized manufacturing process
- PRGN-3006 UltraCAR-T cells are administered one day after gene transfer
- 100% manufacturing success to-date
- Implemented proprietary UltraPorator high-throughput system for non-viral gene transfer





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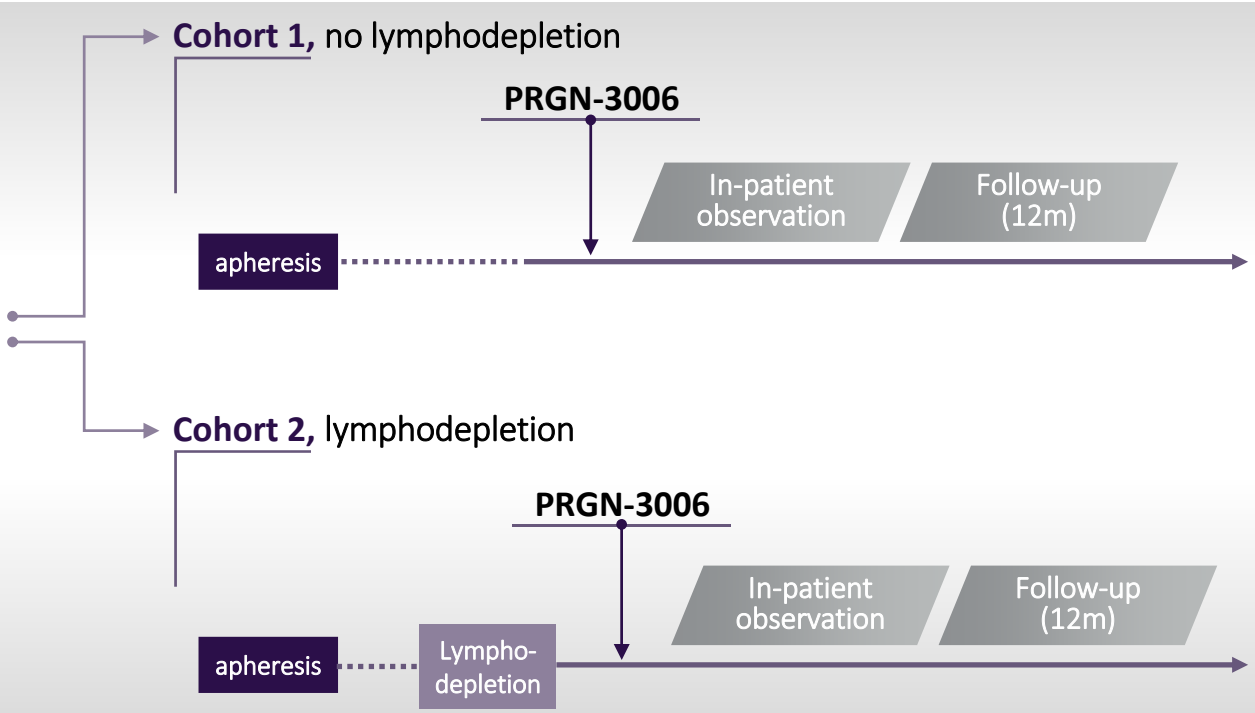
PRGN-3006 UltraCAR-T: Phase 1/1b Trial is Enrolling Patients

Eligibility:

- r/r AML, high risk MDS or CMML with >5% blasts
- ALC > 0.2 k/µL
- Prior HSCT allowed



Safety Monitoring:

- CRS
- Neurotoxicity (ICANS)
- Management via ASTCT guidelines

Disease Response:

- ELN Criteria (AML)
- IWG 2006 criteria (MDS)

Correlatives:

PRGN-3006 persistence/expansion immune phenotype/biomarkers

Study Population	• Relapsed or refractory acute myeloid leukemia (AML), higher risk myelodysplastic syndromes (MDS) or chronic myelomonocytic leukemia (CMML)

Study Design	• Open label, single center study with 3x3 dose escalation
	  • Cohort 1: Subjects receive **No Lymphodepletion**
	  • Cohort 2: Subjects receive **Lymphodepletion** (Cyclophosphamide/Fludarabine)
	  • Cohort 1 & Cohort 2 are enrolling simultaneously
	• Expansion phase is planned at MTD for both Cohorts

Study Objectives	• Primary objective is to evaluate the safety and to identify the maximal tolerated dose of PRGN-3006 delivered via IV infusion with or without lymphodepletion • Secondary objectives are to evaluate *in vivo* persistence and anti-tumor activity
Collaborators	• H. Lee Moffitt Cancer Center & Research Institute

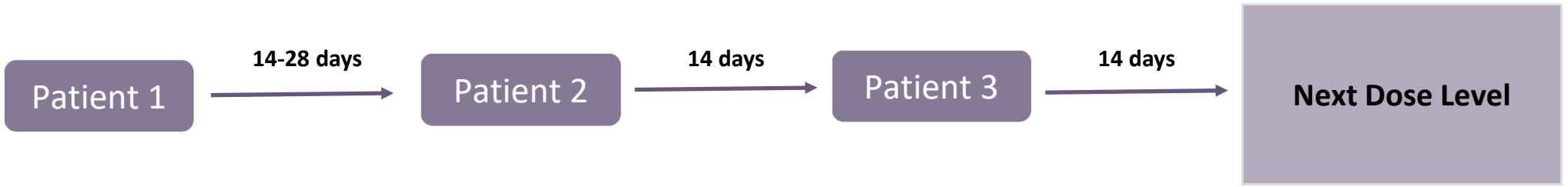
PRGN-3006 Phase 1: Dose Escalation

Non-lymphodepletion (Cohort 1)		
Dose Level	**Dose Range**	**Total Cell dose**
1	$3x10^4$ - $\leq 10^5$ cells/kg	1.8 to 7 x 10^6 CAR-T cells (n=3)
2	10^5 - $\leq 3x10^5$ cells/kg	24 to 29 x 10^6 CAR-T cells (n=3)
3+	> $3x10^5$ cells/kg	Planned enrollment 3-6 subjects/dose
Expansion	MTD	Planned enrollment 20 subject total

Lymphodepletion (Cohort 2)		
Dose Level	**Dose Range**	**Total Cell dose**
1	$3x10^4$ - $\leq 10^5$ cells/kg	4.9 x 10^6 to $1x10^7$ CAR-T cells (n=3)
2	10^5 - $\leq 3x10^5$ cells/kg	Planned enrollment 3-6 subjects
3+	> $3x10^5$ cells/kg	Planned enrollment 3-6 subjects/dose
Expansion	MTD	Planned enrollment 20 subject total

3+3 Dose escalation in Cohort 1 and Cohort 2

- Cohorts are dosing in parallel: Dose level cleared in Cohort 1 prior to enrolling to Cohort 2



PRGN-3006: Safety

Summary of Grade ≥3 PRGN-3006 Treatment-Emergent Adverse Events (TEAEs)

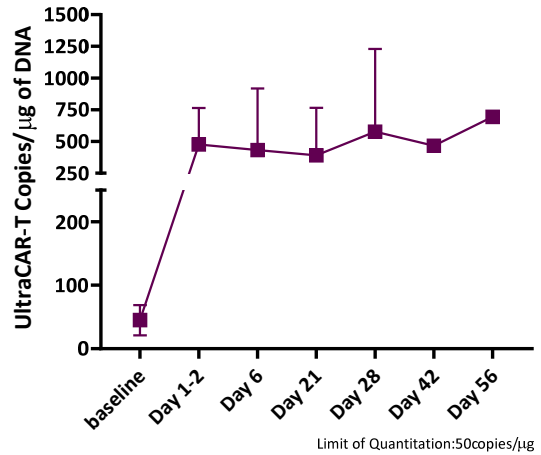
Adverse Event	N=9 (%)
Hematologic	
Anemia	**7 (78%)**
Decreased lymphocyte count	**6 (67%)**
Decreased neutrophil count	**2 (25%)**
Decreased Platelet Count	**3 (33%)**
Decreased white blood cell count	**4 (44%)**
Adverse Events of Interest	
Cytokine Release Syndrome	**1 (11%)**
Decreased electrolytes (hypokalemia, hypophosphatemia, hyponatremia)	**3 (33%)**
Infections	**3 (33%)**
Mucositis, oral	**1 (11%)**

- **No DLTs or neurotoxicity**
- **Low incidence of treatment-related adverse events and serious adverse events**
- **Transient grade 1-3 CRS in two patients**

PRGN-3006: Expansion and Persistence in Peripheral Blood after Intravenous (IV) Infusion of UltraCAR-T

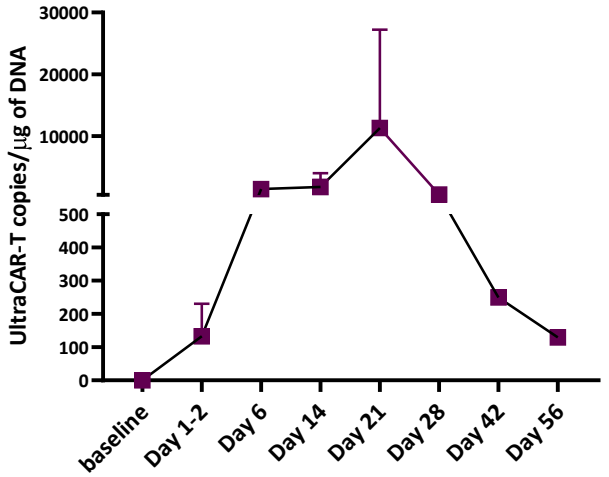
3 Patients Treated at Each Dose Level
UltraCAR-T Cells Administered via Intravenous (IV) Infusion

Dose Level 1 – No Lymphodepletion (N=3)



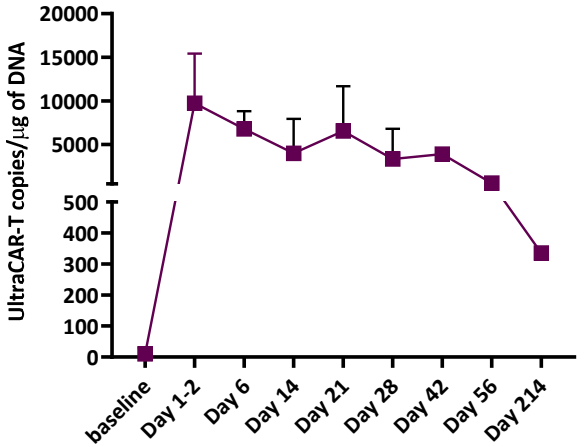
Limit of Quantitation:50copies/μg

Dose Level 1 – Lymphodepletion (N=3)



Limit of Quantitation:50copies/μg

Dose Level 2 - No Lymphodepletion (N=3)



Limit of Quantitation:50copies/μg

N= 1-3 patients at each time point

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PRGN-3006 Case Study: Subject Treated at Low Dose (Dose Level 2) **Without** Lymphodepletion

Subject Characteristic and Treatment Outcome

- 69 year old female with sAML s/p IC, allo-HSCT, HMA+ven (4 prior lines of therapy)
- Refractory to all therapy post allo-HSCT
- ~40% peripheral blasts, 47% bone marrow (BM) blasts
- PRGN-3006: Dose level 2 via IV infusion
  - 24 x 10^6 Total UltraCAR-T cells
  - No lymphodepletion (Cohort 1)

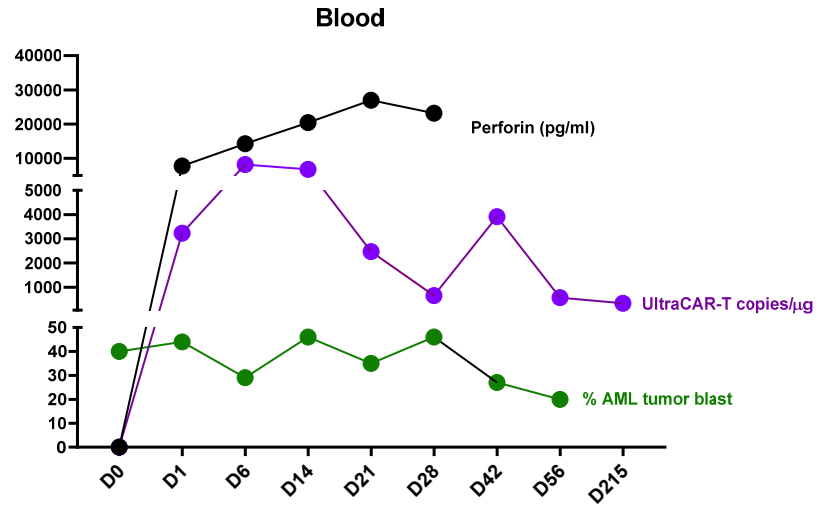
28-day DLT observation interval:

- No DLTs, SAEs or treatment related adverse events
- No incidence of CRS, ICANS or any other CAR-T related toxicity

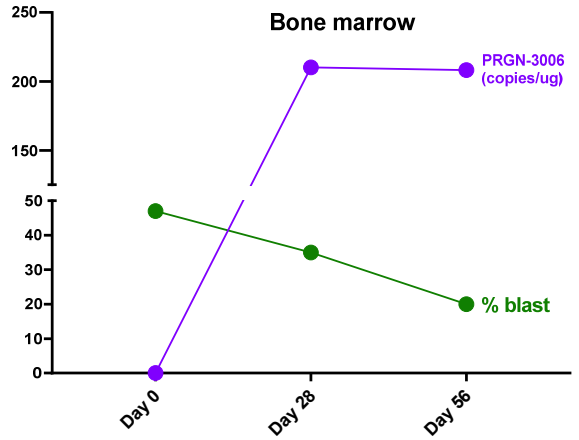
Day 56 bone marrow biopsy:

- Steady BM blast reduction over 2 assessments, durable SD

PRGN-3006 Expansion & Persistence in Peripheral Blood & Bone Marrow



Perforin: values above background (Day 0)



SOURCE: Sallman DA et al., 62nd American Society of Hematology (ASH) Annual Meeting and Exposition, 2020

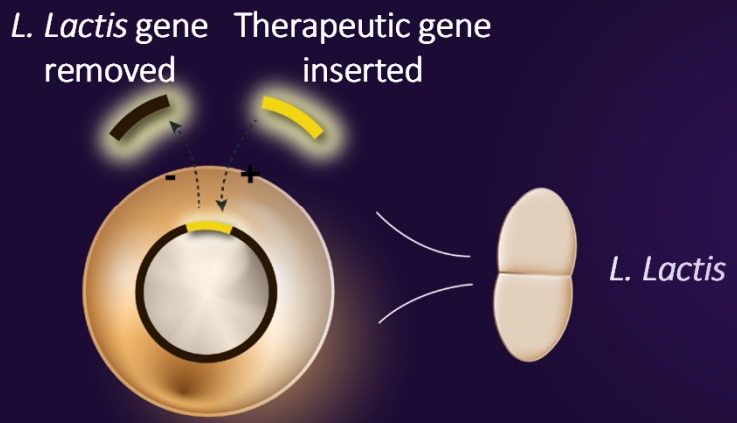
PRGN-3006 UltraCAR-T: Summary

- **Phase 1 trial in is enrolling patients in dose escalation phase of both lymphodepletion and non-lymphodepletion cohorts**
- **PRGN-3006 treatment is safe and well tolerated to date; No DLTs or neurotoxicity**
- **100% manufacturing success to date using decentralized, rapid manufacturing process**
- **PRGN-3006 cells showed encouraging expansion and persistence after low dose infusion**
- **PRGN-3006 cells showed ability to traffic, expand and persist in bone marrow**
- **PRGN-3006 treatment indicated clinical activity as evidenced by reduction in tumor blast levels**

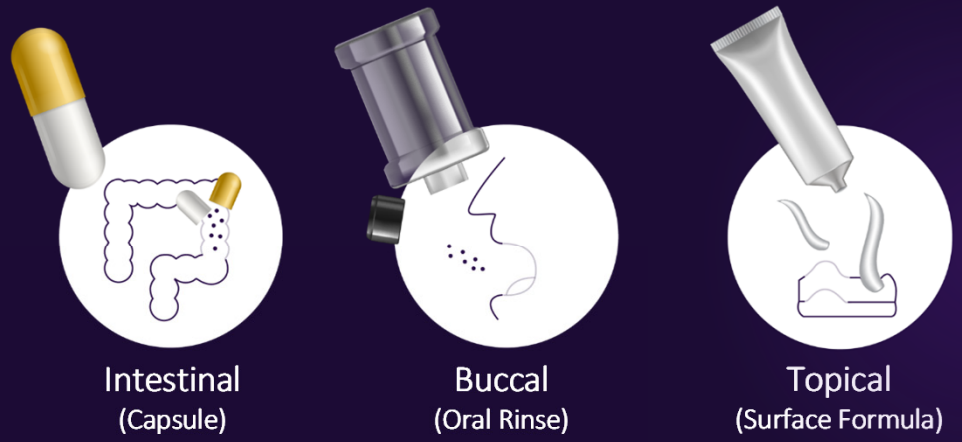
AG019 ActoBiotics®

ActoBiotics™, Microbe-based Therapeutics Platform

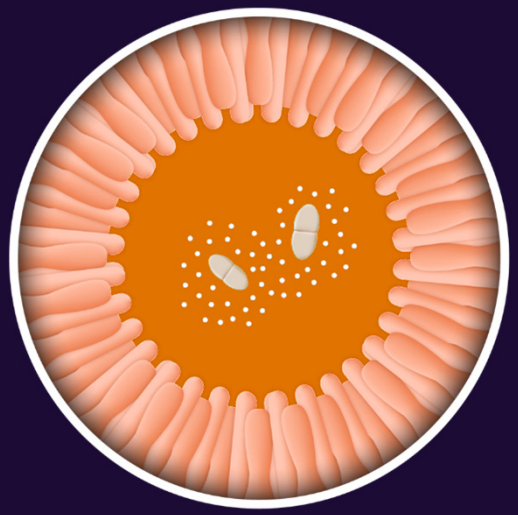
1 Genetic Engineering



2 Multiple Modes of Delivery



3 Direct Delivery to Mucosal Sites



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Type 1 Diabetes, Unmet Need for Disease-modifying Treatment with Ease of Delivery

Type 1 Diabetes

- Chronic autoimmune disease in which the immune system destroys insulin-producing beta cells in the pancreas, resulting in a blood glucose imbalance
- Most common form of diabetes in children

Current Treatment Paradigm

- Exogenous insulin shots combined with diet and lifestyle modification
- Lifelong treatment with insulin injections required for survival
- Enormous impact on quality of life due to fear of hypoglycemia and complexity of day-to-day management

Disease-modifying Treatment to Prevent β-cell Loss and Ease of Delivery to Improve the Quality of Life is Highly Desirable for T1D Patient Population

Disease Snapshot

High Unmet Need

No curative or disease-modifying treatment available

132K*

Newly diagnosed patients per year

*Total for US, EU, Japan.

Katsarou, A. et al.. Nat. Rev. Dis. Primers 3, 17016 (2017).

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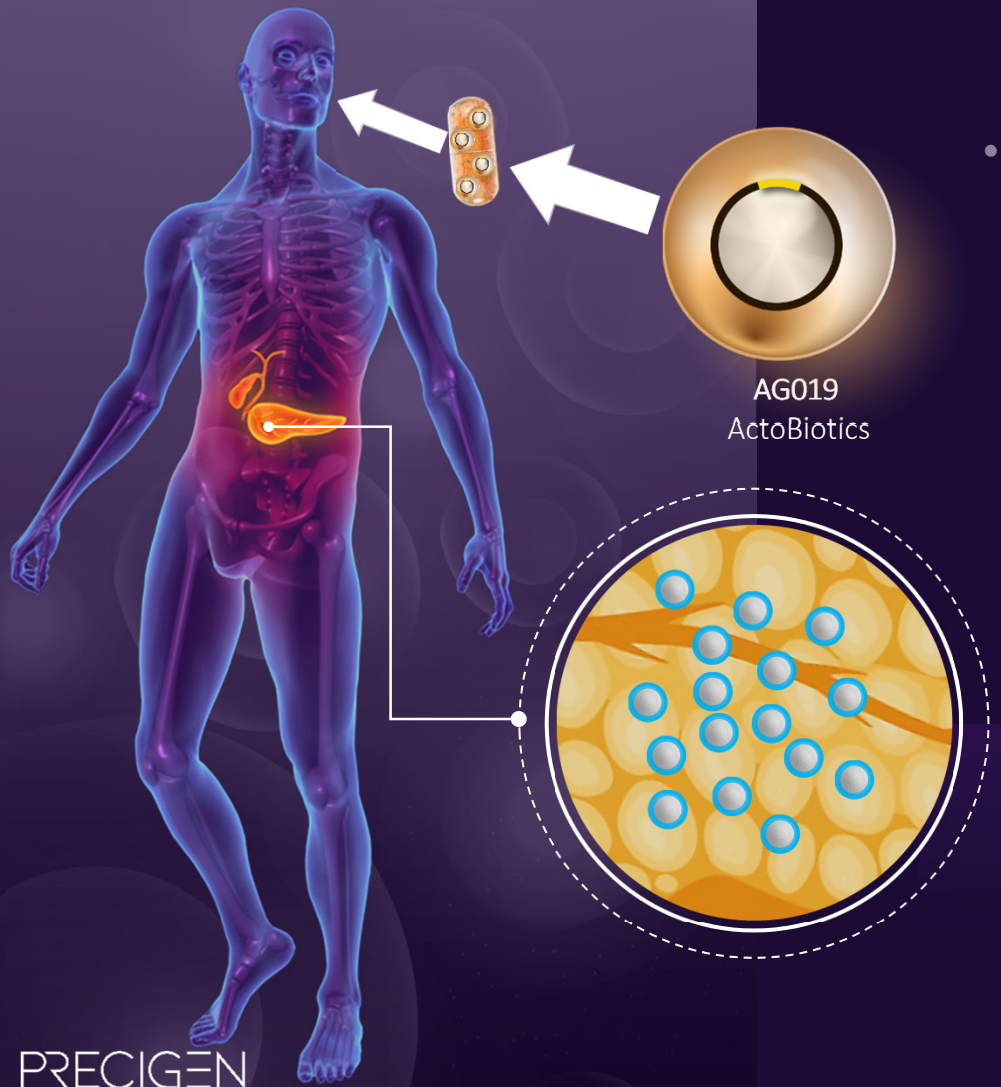
AG019 ActoBiotics

A First-in-Class Oral Therapy in Type 1 Diabetes



- **AG019 is a capsule formulation to deliver human Proinsulin (hPINS) and human Interleukin-10 (hIL-10)**
  - Targeting gut immune system (GALT) to induce antigen-specific regulatory cells that migrate to inflamed pancreatic tissue to re-establish tolerance in order to maintain/restore functional beta-cell mass
- **Phase 1b/2a trial ongoing in recent-onset T1D patients**
  - Phase 1b: AG019 monotherapy; Phase 2a: AG019 in combination with teplizumab (anti-CD3 mAb)

Oral AG019 targets the GALT

induce hPINS-specific regulatory T cells which migrate to inflamed tissue to block tissue destruction

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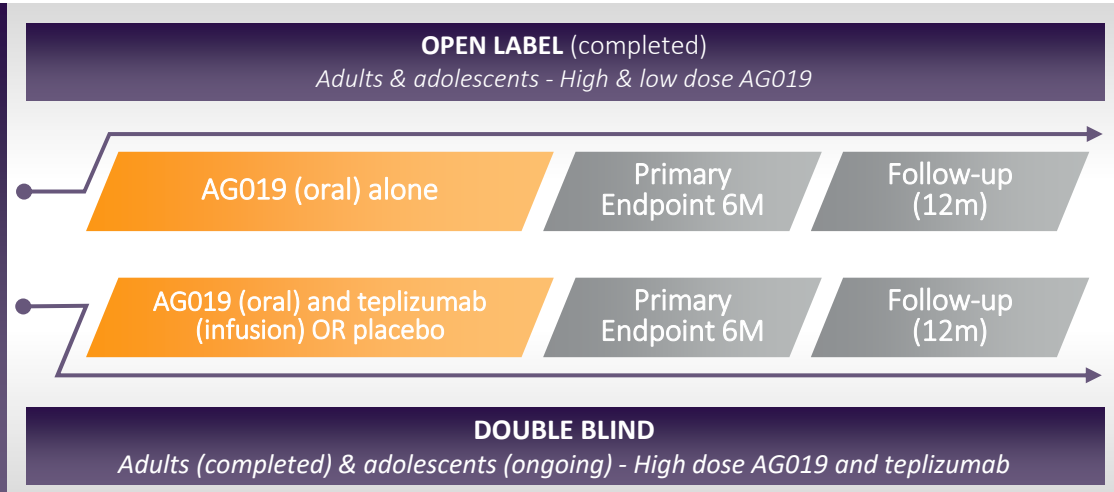
AG019 – Phase 1b/2a Ongoing - Clinical Study Design

Eligibility:
- 12-42 years of age
- Diagnosis of diabetes according to ADA (*)
- Stimulated C-peptide >0.2 nmol/L
- Treatment start within 150 days of diagnosis (**)
- Autoantibody positivity to at least 1 (Insulin, IA-2, GAD65, ZnT8)
- No active infections



Safety Monitoring:
- Incidence of SAE
- Incidence of TEAE

Pharmacokinetics:
- Absence of *L. lactis* in blood
- Absence of hPINS/hIL-10 in blood
- Presence of *L. lactis* in feces

Pharmacodynamics/metabolic:
- C-peptide preservation
- Mechanistic assessments & biomarkers for immunological changes

Study Objectives

- The primary objective of this study is to assess the safety and tolerability of AG019 alone (monotherapy) as well as AG019 in association with teplizumab (co-administration therapy)
- The secondary objectives of this study are to obtain pharmacodynamic (PD) data of AG019 alone as well as AG019 in association with teplizumab; and to determine the potential presence of AG019 in systemic circulation and the presence of *L. lactis* bacteria in fecal excretion (pharmacokinetic [PK] profile)

(*) https://www.diabetes.org/a1c/diagnosis

(**) Recent-onset in this study defined as within 150 days of diagnosis. Other studies (e.g. teplizumab studies PROTECT and Protégé) use other definitions, e.g. 42 days.

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Oral AG019: Safety

Primary Endpoint Met Assessing Safety and Tolerability in the Phase 1b Monotherapy (up to 12 Months) and Phase 2a (Adult; up to 6 Months) Combination Portion of the Study

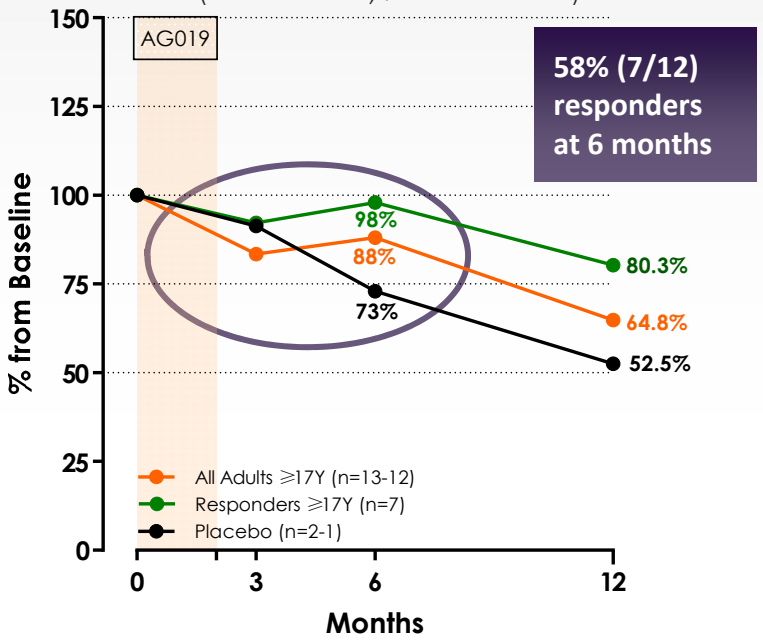
- **AG019 treatment was well tolerated and safe** when administered as a single low or high dose and as a repeated low or high daily dose for 8 weeks, be it **as monotherapy or in combination with teplizumab infusions**
- **No AG019 treatment discontinuation** due to TEAEs
- There was **no evidence of dose-related adverse events**
- **No serious adverse events** were reported and the TEAEs reported were mostly of mild, sometimes of moderate severity. In absence of a placebo comparison and with the limited number of patients included in this study, no evidence exists as to whether any TEAE reported represents a true side-effect of AG019
- **Combination of AG019 and teplizumab was safe and well tolerated**
- **Pharmacokinetic analysis** demonstrated **localized intestinal delivery of AG019 with no systemic exposure,** confirming safety profile of AG019

PRECIGEN ACTOBIO

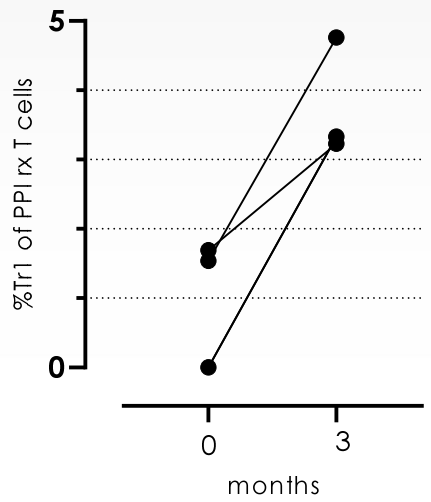
AG019 Monotherapy Shows Encouraging Immunomodulating Effect in Adults*

One 8 Weeks' Treatment Cycle of Oral AG019 Induces C-peptide Stabilization and Antigen-specific Immune Tolerance

C-peptide median values*
(mean 2h AUC; % from baseline)

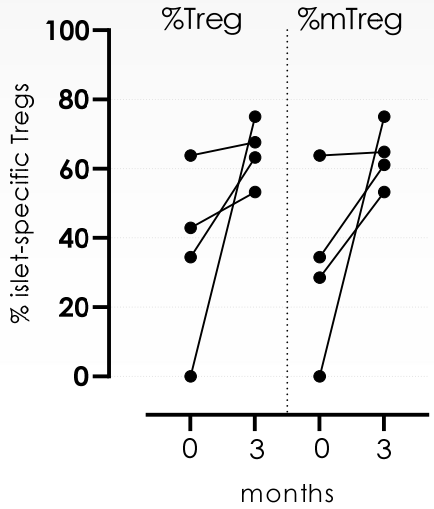


PPI-reactive Type1 regulatory T-cells#
(frequency)



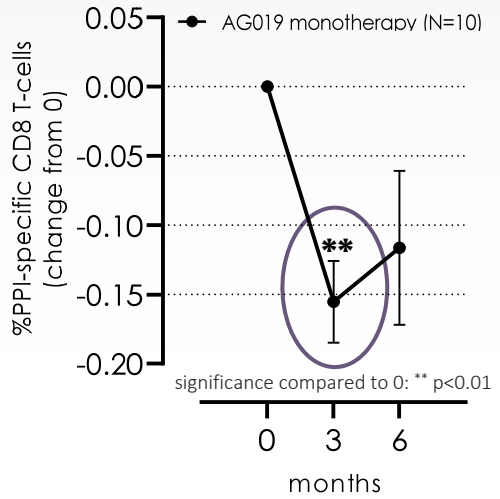
Analysis by flow cytometry at baseline (0) & 3M; n=4

Islet-specific regulatory T-cells$
(frequency)



Analysis by flow cytometry at baseline (0) & 3M; n=4

% PPI-specific CD8 T-cells#
(change from baseline)



- **Stabilization of C-peptide during the first 6 months in 58% (7/12)** of the T1D patients (Responders) - similar to teplizumab (historical control)
- **Slower decline in C-peptide levels during the first 12 months,** compared to placebo
- **Additional treatment cycle(s) may prolong C-peptide stabilization**

- **Induction of antigen-specific tolerance in conjunction with reduction of disease-specific T cell responses at 3 months:**
  - ⇨ **Increase in antigen (PPI)-specific Type 1 regulatory (Tr1) cells**
  - ⇨ **Increase of islet-specific (memory) regulatory T-cells expressing inhibitory receptors**
    – may indicate induction of tissue-specific bystander suppression
  - ⇨ **Significant decrease in antigen (PPI)-specific CD8 T-cells**

*Adult patients between 17 - 42 years were used for this analysis
#Representing T-cells stimulated with a pool of peptides from pre-proinsulin (PPI)
$Representing T-cells stimulated with a pool of islet peptides from GAD65 and IGRP

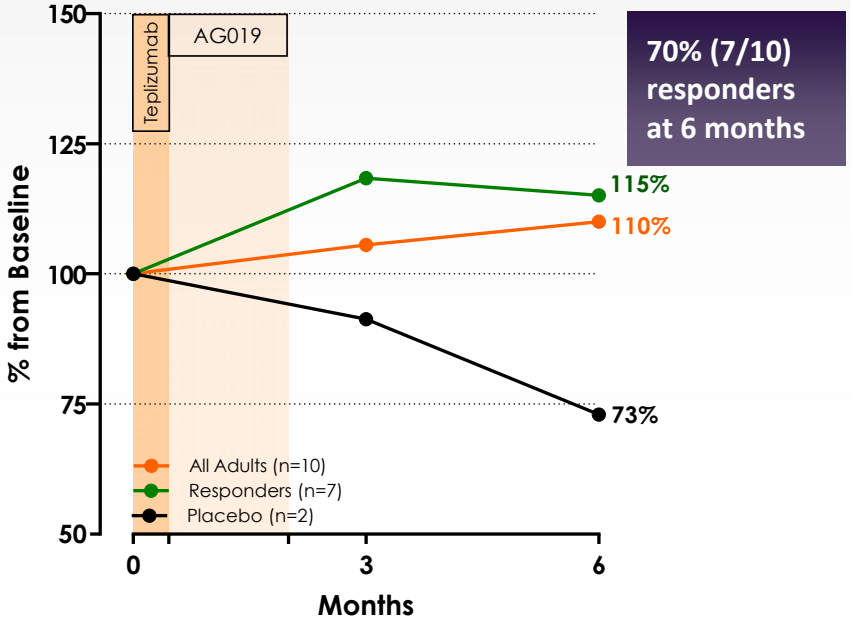
PRECIGEN ACTOBIO

AG019 Combination Therapy Shows Encouraging Treatment Effect in Adults*

Combination with Teplizumab Results in Higher C-peptide and Confirms Induction of Antigen-specific Tolerance

C-peptide median values*

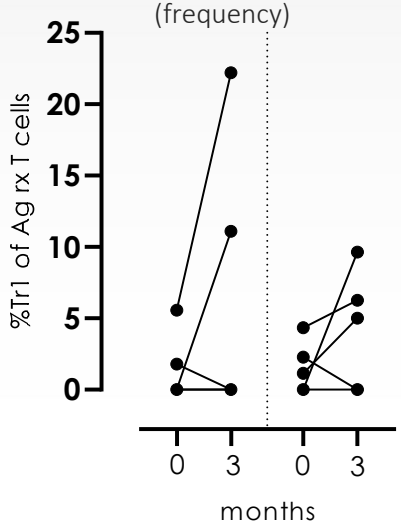
(mean 2h AUC; % from baseline)



70% (7/10) responders at 6 months

Disease-reactive Type1 regulatory T-cells#

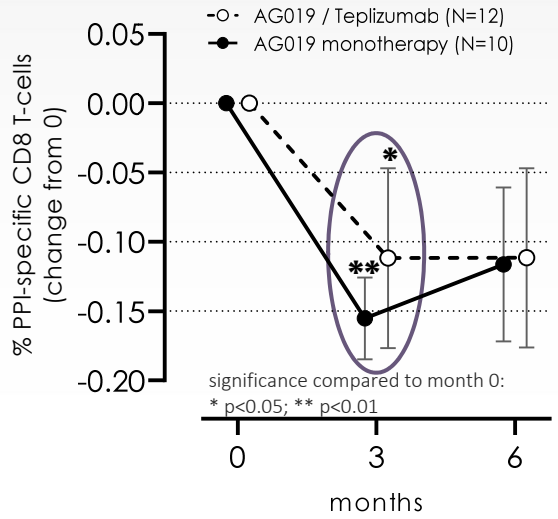
(frequency)



Analysis by flow cytometry at baseline (0) & 3M; n=4

% PPI-specific CD8 T-cells#

(change from baseline)



- **C-peptide stabilization in 70% (7/10) of adult patients (Responders) at 6 months**
- **Trend towards higher C-peptide levels in AG019 combination therapy-treated patients as compared placebo at 6 months**

- **Induction of antigen-specific tolerance in conjunction with reduction of disease-specific T cell responses at 3 months:**
  - ⇨ **Increase in PPI- and islet-specific specific Type 1 regulatory (Tr1) cells**
  - ⇨ **Significant decrease in antigen (PPI)-specific CD8 T-cells -** comparable between AG019 mono- and combination therapy - suggesting that the **reduction of PPI-specific effector CD8 is mediated by AG019**

PRECIGEN ACTOBIO

*Adult patients between 18 - 40 years were used for this analysis

#Representing T cells stimulated with a pool of peptides from pre-proinsulin (PPI) and/or a pool of islet peptides from GAD65 and IGRP

Overall Conclusions

Oral AG019 monotherapy:

- Safe and well tolerated
  - Opportunity for chronic treatment
- Stabilizes C-peptide at 6 months following only one treatment cycle of oral AG019
  - Opportunity for repeat dosing to prolong treatment
- Potential to preserve insulin production in early onset T1D through its capacity to inducing antigen-specific immune modulation
- Ease of treatment due to oral dosing and disease modifying potential differentiates AG019 from competition

AG019 combination therapy

- Safe and well tolerated
- Potential to boost/prolong teplizumab induced metabolic effects through induction of antigen-specific immune modulation
- Opportunity to explore combinations with other systemic inducers in addition to teplizumab

Validates ActoBiotics platform for antigen-specific immunotherapy:

- Ease of administration and high safety profile encompasses treating a wide range of chronic immune-mediated diseases
- Ability to establish antigen-specific immune modulation by inducing disease-specific immune tolerance and reducing disease specific effector T cell responses may broaden therapeutic application towards other autoimmune diseases in humans

Summary

Precigen in 2020: Multiple Clinical Milestones

- Initial data released from IP arm of PRGN-3005 UltraCAR-T Phase 1 trial in Ovarian Cancer
- Initial data released from PRGN-3006 UltraCAR-T Phase 1 trial in AML and MDS
- Interim data released from Phase 2 trial of AG013 ActoBiotics in Oral Mucositis
- Interim data released from Phase 1b/2a trial of AG019 ActoBiotics in Type 1 Diabetes
- Phase 1 study of INXN-4001 completed in Heart Failure patients with LVAD
- Initiated Phase 1 trial of PRGN-2009 off-the-shelf AdenoVerse immunotherapy in HPV^{+} cancers

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