



## Precigen Presents New Data Supporting the Safety, Clinical Activity, Expansion and Persistence of PRGN-3006 UltraCAR-T® at the 62nd ASH Annual Meeting and Exposition

Dec 07, 2020

**- PRGN-3006 has been safe and well-tolerated to date -**

**- Case study demonstrated persistence of PRGN-3006 administered without prior lymphodepletion in blood at seven months post-infusion and reduction in blood and bone marrow blasts -**

**- Milestone marks a global first report of direct infusion of non-expanded CAR-T cells leading to in vivo expansion and long-term persistence in patients -**

GERMANTOWN, Md., Dec. 7, 2020 /PRNewswire/ -- [Precigen, Inc.](#), a biopharmaceutical company specializing in the development of innovative gene and cell therapies to improve the lives of patients, today announced at the 62nd ASH Annual Meeting and Exposition ([Abstract 2864](#)) clinical progress and new data from the ongoing Phase 1/1b clinical study of PRGN-3006 UltraCAR-T® in patients with relapsed or refractory (r/r) acute myeloid leukemia (AML) and higher risk myelodysplastic syndrome (MDS) (clinical trial identifier: [NCT03927261](#)).

AML is a rapidly progressing disease with poor prognosis and high unmet need. Precigen's UltraCAR-T platform is designed to overcome limitations of currently available chimeric antigen receptor (CAR)-T therapies by utilizing an advanced overnight non-viral gene delivery manufacturing process at a medical center's cGMP facility without the need for *ex vivo* expansion. Current CAR-T cell therapies are limited due to, *inter alia*, the prolonged interval between apheresis to product infusion and an exhausted phenotype of T cells resulting from lengthy *ex vivo* expansion. As announced in November 2020, [UltraCAR-T cells for the PRGN-3006 study are now manufactured](#) overnight using Precigen's proprietary UltraPorator™ device. PRGN-3006 UltraCAR-T is a multigenic autologous CAR-T simultaneously expressing a CAR specifically targeting CD33; membrane bound IL-15 (mbIL15) for enhanced *in vivo* expansion and persistence; and a kill switch to conditionally eliminate CAR-T cells for an improved safety profile. CD33 is over-expressed on AML blasts with lesser expression on normal hematopoietic stem cells.

An investigator-initiated, non-randomized Phase 1/1b dose-escalation study to evaluate the safety and maximal tolerated dose of PRGN-3006 UltraCAR-T is currently ongoing in collaboration with the H. Lee Moffitt Cancer Center & Research Institute (Moffitt). The study population includes adult patients (≥ 18 years) with r/r AML and hypomethylating agent (HMA) failure, higher risk MDS or chronic myelomonocytic leukemia (CMML) patients with ≥ 5% blasts. To test the hypothesis that expression of mbIL15 on PRGN-3006 can promote UltraCAR-T cell expansion and persistence without the need for lymphodepletion and improve the overall safety profile, study subjects receive the PRGN-3006 infusion either without prior lymphodepletion (Cohort 1) or following lymphodepleting chemotherapy (Cohort 2). A multicenter expansion of the trial is planned.

Key findings:

- At the data cutoff (November 10):
  - Six patients have been treated across the two lowest dose levels in Cohort 1 (no lymphodepletion):
    - N=3 at Dose Level 1 ( $3 \times 10^4$  -  $\leq 1 \times 10^5$  UltraCAR-T cells/kg); Total 1.8 to  $7 \times 10^6$  UltraCAR-T cells
    - N=3 at Dose Level 2 ( $1 \times 10^5$  -  $\leq 3 \times 10^5$  UltraCAR-T cells/kg); Total 24 to  $29 \times 10^6$  UltraCAR-T cells
  - Three patients have been treated at the lowest dose level in Cohort 2 (with lymphodepletion):
    - N=3 at Dose Level 1 ( $3 \times 10^4$  -  $\leq 1 \times 10^5$  UltraCAR-T cells/kg); Total  $4.9 \times 10^6$  to  $1 \times 10^7$  UltraCAR-T cells
- Encouraging expansion and persistence of PRGN-3006 UltraCAR-T was observed in both lymphodepletion and non-lymphodepletion cohorts and across all dose levels.
- PRGN-3006 has been safe and well-tolerated with no dose limiting toxicities (DLTs), no neurotoxicity, and a low incidence of treatment-related adverse events (TRAEs) and serious adverse events (SAEs). A few treatment-related SAEs have been observed, including transient grade 1-3 cytokine release syndrome (CRS), which is more indicative of the biologic activity of the cells.
- There has been a 100% manufacturing success rate using the UltraCAR-T manufacturing process.

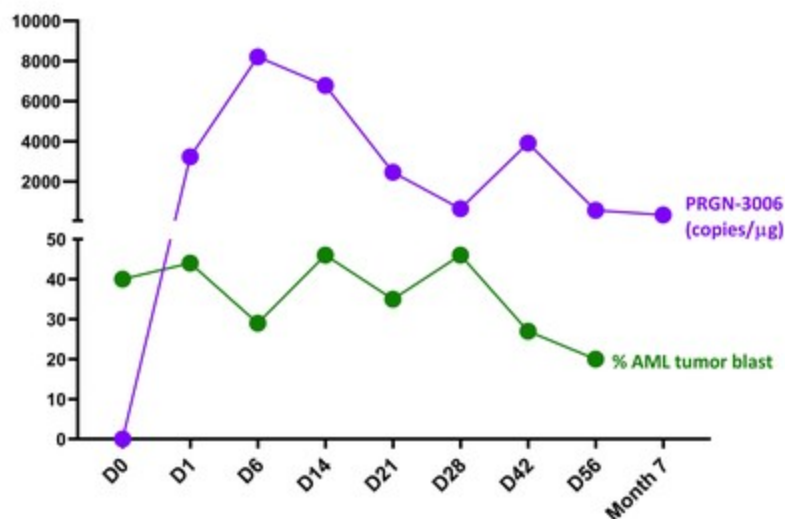
A case study of the patient with the longest follow-up as of the data cutoff was also presented. This patient received, one day after gene transfer and without prior lymphodepletion, a very low dose, approximately three hundred thousand UltraCAR-T per kilogram ( $3 \times 10^5$  UltraCAR-T/kg) for a total of only 24 million UltraCAR-T. She is a 69 year old female with secondary AML (sAML) and four prior lines of therapy, including induction chemotherapy (IC), allogeneic hematopoietic stem cell transplantation (allo-HSCT), HMA plus venetoclax (HMA+VEN), refractory to all therapy post allo-HSCT. The patient had approximately 40% peripheral blasts and 47% bone marrow blasts at baseline.

Case study findings:

- After a very low dose infusion without prior lymphodepletion, PRGN-3006 UltraCAR-T cells demonstrated robust expansion and persistence in blood at seven months post-infusion at the time of the most recent sample collection (see FIGURE 1).
- UltraCAR-T cells demonstrated trafficking to bone marrow and the ability to expand and persist in bone marrow.

- The patient showed a decline in blast levels in blood and bone marrow concomitant with UltraCAR-T expansion and persistence (see FIGURE 1) and had stable disease. Patient follow-up is ongoing.

**FIGURE 1:** Expansion and persistence of PRGN-3006 UltraCAR-T cells and level of AML blasts in patient's blood after UltraCAR-T infusion without prior lymphodepletion.



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

"There is an urgent need for novel therapies for relapsed or refractory AML patients as the median overall survival for this patient population is less than six months. Current CAR-T approaches for AML have faced challenges due to long manufacturing durations resulting in subsequent delays in treatment," said David A. Sallman, MD, of Moffitt and lead investigator for the PRGN-3006 clinical study. "We are encouraged by the initial data, including safety and manufacturing success from patients treated with autologous UltraCAR-T cells, which were manufactured on-site with almost instant turnaround. We are excited by the expansion and continued persistence of PRGN-3006 UltraCAR-T cells in the patient case study for over seven months post-infusion without prior lymphodepletion and are looking forward to higher doses in the lymphodepleted and non-lymphodepletion cohorts."

"Currently commercialized CAR-T therapies have not demonstrated the persistence needed to drive sustained, durable responses," said Helen Sabzevari, PhD, President and CEO of Precigen. "The results from Dr. Sallman's patient case study are particularly encouraging as the patient received a very low dose of cells without any *ex vivo* expansion or activation and no lymphodepletion, which highlights the importance of membrane bound IL-15 in expansion and persistence of these cells and, we believe, differentiates the UltraCAR-T platform from other CAR-T's. In particular, expansion and persistence of UltraCAR-T cells in the patient's blood through seven months post-infusion show promise for the durability of PRGN-3006. We look forward to providing additional details for the PRGN-3006 study at our upcoming clinical update call this month."

#### About Acute Myeloid Leukemia (AML)

AML is a cancer that starts in the bone marrow, but most often moves into the blood.<sup>1</sup> Though considered rare, AML is among the most common types of leukemia in adults.<sup>2</sup> In 2019, it was estimated that 21,450 new cases of AML would be diagnosed in the US.<sup>2</sup> AML is uncommon before the age of 45 and the average age of diagnosis is about 68.<sup>2</sup> The prognosis for patients with AML is poor with an average 5-year survival rate of approximately 25 percent overall, and less than a 5 percent 5-year survival rate for patients older than 65.<sup>3</sup> Amongst elderly AML patients (≥ 65 years of age), median survival is short, ranging from 3.5 months for patients 65 to 74 years of age to 1.4 months for patients ≥ 85 years of age.<sup>3</sup>

#### About Myelodysplastic Syndrome (MDS)

MDS are diseases of the bone marrow generally found in adults in their 70s.<sup>4</sup> Incidence in the US is not known for sure, but estimates range from 10,000 each year and higher.<sup>4</sup> Using International Prognostic Scoring System (IPSS-R), median survival for MDS patients can vary from less than one year for the "very high" IPSS-R risk group to more than eight years for the "very low" IPSS-R group.<sup>4</sup>

#### About PRGN-3006 UltraCAR-T

PRGN-3006 UltraCAR-T is a multigenic autologous CAR-T cell treatment utilizing Precigen's non-viral *Sleeping Beauty* system to simultaneously express a CAR specifically targeting CD33, which is over expressed on acute myeloid leukemia blasts with lesser expression on normal hematopoietic stem cell populations and minimal non-hematopoietic expression; membrane bound IL-15 for enhanced *in vivo* expansion and persistence; and a kill switch to conditionally eliminate CAR-T cells for an improved safety profile. PRGN-3006 is being evaluated in collaboration with the Moffitt Cancer Center in a nonrandomized, investigator-initiated Phase 1/1b dose escalation study to evaluate the safety and maximal tolerated dose of PRGN-3006 UltraCAR-T (clinical trial identifier: [NCT03927261](https://clinicaltrials.gov/ct2/show/study/NCT03927261)). The study population includes patients with relapsed or refractory acute myeloid leukemia or higher risk myelodysplastic syndrome. The US Food and Drug Administration (FDA) has granted [orphan drug designation \(ODD\) for PRGN-3006 UltraCAR-T](#) in patients with AML.

#### Precigen: Advancing Medicine with Precision™

Precigen (Nasdaq: PGEN) is a dedicated discovery and clinical stage biopharmaceutical company advancing the next generation of gene and cell therapies using precision technology to target urgent and intractable diseases in our core therapeutic areas of immuno-oncology, autoimmune disorders, and infectious diseases. Our technologies enable us to find innovative solutions for affordable biotherapeutics in a controlled manner. Precigen operates as an innovation engine progressing a preclinical and clinical pipeline of well-differentiated unique therapies toward clinical proof-of-concept and commercialization. For more information about Precigen, visit [www.precigen.com](http://www.precigen.com) or follow us on Twitter [@Precigen](#) and [LinkedIn](#).

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## Cautionary Statement Regarding Forward-Looking Statements

Some of the statements made in this press release are forward-looking statements. These forward-looking statements are based upon the Company's current expectations and projections about future events and generally relate to plans, objectives, and expectations for the development of the Company's business, including the timing and progress of preclinical studies, clinical trials, discovery programs and related milestones, the promise of the Company's portfolio of therapies, and in particular its CAR-T therapies, and the Company's refocus to a healthcare-oriented business. Although management believes that the plans and objectives reflected in or suggested by these forward-looking statements are reasonable, all forward-looking statements involve risks and uncertainties, including the possibility that the timeline for the Company's clinical trials might be impacted by the COVID-19 pandemic, and actual future results may be materially different from the plans, objectives and expectations expressed in this press release. The Company has no obligation to provide any updates to these forward-looking statements even if its expectations change. All forward-looking statements are expressly qualified in their entirety by this cautionary statement. For further information on potential risks and uncertainties, and other important factors, any of which could cause the Company's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in the Company's most recent Annual Report on Form 10-K and subsequent reports filed with the Securities and Exchange Commission.

## References

<sup>1</sup> American Cancer Society. [What is Acute Myeloid Leukemia \(AML\)?](#)

<sup>2</sup> American Cancer Society. [Key Statistics for Acute Myeloid Leukemia \(AML\)](#)

<sup>3</sup> 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

<sup>4</sup> American Cancer Society. [Key Statistics for Myelodysplastic Syndromes](#)

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