



## Precigen Achieves Significant Clinical Progress for UltraCAR-T® and AdenoVerse™ Therapies

Nov 04, 2021

- **50% (3 out of 6) objective response rate (ORR) in relapsed or refractory (r/r) acute myeloid leukemia (AML) patients treated with PRGN-3006 at the two lowest dose levels (a single administration of 4 to 28 million UltraCAR-T cells) in the lymphodepletion cohort of the ongoing Phase 1 trial -**
- **40% ORR (2 out of 5) and 60% disease control rate (DCR) (3 out of 5) in recurrent or metastatic human papilloma virus (HPV)-associated cancer patients treated in the PRGN-2009 combination arm of the ongoing Phase 1 trial -**
- **Preliminary PRGN-2012 Phase 1 data show encouraging clinical activity, including ongoing reduction/elimination of the need for surgical intervention at the most recent follow-up, up to 12 weeks after PRGN-2012 treatment -**
  - **PRGN-3005 and PRGN-3006 UltraCAR-T demonstrate favorable safety profiles with no dose-limiting toxicities or neurotoxicity, dose-dependent in vivo expansion and durable persistence -**
  - **PRGN-2009 and PRGN-2012 AdenoVerse immunotherapies demonstrate favorable safety profiles with no dose-limiting toxicities, strong antigen-specific immune response and lack of significant neutralizing antibody response upon repeat administrations -**
- **PRGN-3006 clinical abstract (Abstract# 825) selected for oral presentation at the 63rd American Society of Hematology (ASH) Annual Meeting and Exposition -**
  - **Precigen to host 2021 R&D Day virtual event today at 11:00 AM ET -**

GERMANTOWN, Md., Nov. 4, 2021 /PRNewswire/ -- [Precigen, Inc.](#) (Nasdaq: PGEN), a biopharmaceutical company specializing in the development of innovative gene and cell therapies to improve the lives of patients, announced a topline summary of the presentations planned for today's 2021 R&D Day virtual event, which begins at 11:00 AM ET. Participants may register and access the live webcast through Precigen's investor relations website in the [Events & Presentations](#) section.



Today's event will showcase clinical progress for Precigen's UltraCAR-T platform, including PRGN-3005 UltraCAR-T, PRGN-3006 UltraCAR-T, PRGN-3007 UltraCAR-T and the AdenoVerse immunotherapy platform, including PRGN-2009 off-the-shelf (OTS) AdenoVerse Immunotherapy, and PRGN-2012 OTS AdenoVerse Immunotherapy. Presentations will be made by Precigen executives and clinical trial investigators, including:

- Helen Sabzevari, PhD, President and CEO of Precigen;
- Mary L. (Nora) Disis, MD, University of Washington (UW) Professor of Medicine, Director of UW Center for Translational Medicine, Professor in the Clinical Research Division at the Fred Hutchinson Cancer Research Center and a lead investigator for the PRGN-3005 clinical trial;
- David Sallman, MD, Assistant Member in the Department of Malignant Hematology at the H. Lee Moffitt Cancer Center & Research Institute and a lead investigator for the PRGN-3006 clinical trial;
- James L. Gulley, MD, PhD, FACP, Branch Chief and Director of the Medical Oncology Service at the National Institutes of Health (NIH) and a lead investigator for the PRGN-2009 clinical trial; and
- Clint T. Allen, MD, Principal Investigator with the Section on Translational Tumor Immunology at the NIH and a lead investigator for the PRGN-2012 clinical trial.

"Today's R&D Day highlights the most significant clinical data presented for the UltraCAR-T and AdenoVerse platforms to date," said Helen Sabzevari, PhD, President and CEO of Precigen, "and we are highly encouraged by the initial results we are seeing across assets in both platforms. With UltraCAR-T, initial data for PRGN-3005 and PRGN-3006 continue to demonstrate favorable safety profiles, dose-dependent expansion, and durable persistence. The very encouraging clinical responses in relapsed or refractory AML patients treated with PRGN-3006 at the two lowest dose levels in the lymphodepletion cohort, which are administered at significantly lower doses than competing approaches, highlight the potential of the UltraCAR-T platform. Our AdenoVerse immunotherapy platform is equally impressive with initial data for PRGN-2009 and PRGN-2012 showing antigen-specific immune responses, low neutralizing antibody responses, and favorable safety profiles highlighting the potential for repeat administrations. Preliminary data for PRGN-2009 show encouraging objective responses and suggest an attractive opportunity for potential combination of PRGN-2009 with checkpoint inhibitors in multiple HPV-associated cancers. Finally, preliminary data for PRGN-2012 show encouraging clinical responses in RRP patients, including a reduction in surgical interventions following PRGN-2012 treatment. We are on track to pursue potentially registrational trials for therapeutic candidates in both the UltraCAR-T and AdenoVerse platforms upon dose confirmation and expansion."

#### PRGN-3006 UltraCAR-T

- Overview:** PRGN-3006 is an investigational multigenic, autologous chimeric antigen receptor T cell (CAR-T) therapy engineered to simultaneously express a chimeric antigen receptor (CAR) specifically targeting CD33, membrane bound IL-15 (mbIL15), and a kill switch. PRGN-3006 UltraCAR-T is under evaluation in a Phase 1/1b clinical trial for the treatment of patients with r/r AML or higher-risk myelodysplastic syndromes (MDS). Trial subjects receive the PRGN-3006 infusion either without prior lymphodepletion (Cohort 1) or following lymphodepleting chemotherapy (Cohort 2). PRGN-3006 UltraCAR-T has been granted [Orphan Drug Designation](#) in patients with AML by the US Food and Drug Administration (US FDA).
- Enrollment:** Enrollment in Dose Level 4 of the non-lymphodepletion cohort and Dose Level 3 of the lymphodepletion cohort of the Phase 1 dose escalation trial is ongoing concurrently.
- Dosing:** As of the July 25, 2021 data cut-off, 15 r/r AML patients were treated in the non-lymphodepletion cohort (N=9) and the lymphodepletion cohort (N=6). Patients were heavily pre-treated with a median of 4 (range: 1 to 6) and 3 (range: 1 to 7) prior regimens in the non-lymphodepletion and the lymphodepletion cohorts, respectively. Additionally, 33% and 50% of the patients had failed prior allogeneic hematopoietic stem cell transplant (allo-HSCT) in the non-lymphodepletion and the lymphodepletion cohorts, respectively. Patients received a single PRGN-3006 administration at one of the following dose levels:

#### Non-lymphodepletion Cohort (Cohort 1)

Dose Level (DL)	Subjects	Dose Range (UltraCAR-T Cells/kg)	Total UltraCAR-T Dose Administered
DL1	N=3	$>3 \times 10^4$ to $\leq 1 \times 10^5$	1.8 to 7.1 $\times 10^6$ cells
DL2	N=3	$>1 \times 10^5$ to $\leq 3 \times 10^5$	24 to 29 $\times 10^6$ cells
DL3	N=3	$>3 \times 10^5$ to $\leq 1 \times 10^6$	34 to 50 $\times 10^6$ cells

#### Lymphodepletion Cohort (Cohort 2)

Dose Level (DL)	Subjects	Dose Range (UltraCAR-T Cells/kg)	Total UltraCAR-T Dose Administered
DL1	N=3	$>3 \times 10^4$ to $\leq 1 \times 10^5$	4.4 to 10 $\times 10^6$ cells
DL2	N=3	$>1 \times 10^5$ to $\leq 3 \times 10^5$	18 to 28 $\times 10^6$ cells

- Safety data:** Data from the first three dose levels in Cohort 1 (non-lymphodepletion) and the first two dose levels in Cohort 2 (lymphodepletion) show that PRGN-3006 was well-tolerated with no dose-limiting toxicities (DLTs) and no neurotoxicity. Only one transient Grade 3 cytokine release syndrome (CRS) was reported (DL1, Cohort 1), which resolved in less than 24 hours with tocilizumab and dexamethasone. Remaining cases of CRS were Grade 1 or 2 that either required no specific intervention or resolved following standard CRS management.
- Clinical activity:** Dose-dependent expansion and persistence in both the non-lymphodepletion and the lymphodepletion cohorts was observed.
  - An ORR of 50% (3 out of 6) was reported in the lymphodepletion cohort (Cohort 2) in patients treated at the two lowest dose levels. This included an ORR of 33% (1 out of 3) at Dose Level 1 and 67% (2 out of 3) at Dose Level 2.
  - Objective responses included one partial response (PR) in a patient with extramedullary AML, one complete response with incomplete hematologic recovery (CRi) which was bridged to allo-HSCT, and one complete response with hematologic recovery (CRh).
- Upcoming presentation:** An abstract for the PRGN-3006 Phase 1 trial (Abstract# 825) titled, "Phase 1/1b Safety Study of PRGN-3006 UltraCAR-T in Patients with Relapsed or Refractory CD33-Positive Acute Myeloid Leukemia and Higher Risk

Myelodysplastic Syndromes," was selected for oral presentation at the [63rd ASH Annual Meeting and Exposition](#) on December 13, 2021 at 5:00 PM ET.

#### PRGN-3005 UltraCAR-T

- **Overview:** PRGN-3005 UltraCAR-T is an investigational multigenic, autologous CAR-T cell therapy engineered to express a CAR specifically targeting the unshed portion of MUC16, which is highly expressed on ovarian tumors with limited normal tissue expression, mbIL15, and a kill switch. PRGN-3005 UltraCAR-T is under evaluation in a Phase 1/1b clinical trial for the treatment of patients with advanced, recurrent platinum resistant ovarian cancer. Trial subjects receive PRGN-3005 either via intraperitoneal (IP) (Arm A) or intravenous (IV) (Arm B) infusion.
- **Enrollment:** Doses are currently being administered without lymphodepletion. Dose escalation in the IP arm and IV arm is ongoing concurrently.
- **Dosing:** Ten heavily pretreated, advanced, platinum resistant ovarian cancer patients with aggressive disease were treated with a single IP infusion of PRGN-3005 without prior lymphodepletion at one of the following dose levels:

Dose Level (DL)	Subjects	Dose Range (UltraCAR-T Cells/kg)	Total UltraCAR-T Dose Administered
DL1	N=3	$>3 \times 10^4$ to $\leq 1 \times 10^5$	6 to 7.6 $\times 10^6$ cells
DL2	N=3	$>1 \times 10^5$ to $\leq 3 \times 10^5$	12 to 21 $\times 10^6$ cells
DL3	N=4	$>3 \times 10^5$ to $\leq 5 \times 10^6$	33 to 321 $\times 10^6$ cells

- **Manufacturing:** Precigen's UltraPorator™ system has enabled escalation to higher doses, as evidenced by the successful infusion of greater than 320 million UltraCAR-T cells, through the decentralized UltraCAR-T manufacturing process.
- **Safety data:** New data continue to show a favorable safety profile with no DLTs, no neurotoxicity, and no CRS reported.
- **Clinical activity:** Data show dose-dependent expansion and persistence in the peripheral blood for more than 3 months after PRGN-3005 treatment without lymphodepletion, and clinical activity as evidenced by a decrease or stabilization of total target tumor burden at the first restaging in a majority of patients.
- **Next steps:** Complete dose escalation in the IP and IV arms and, subsequently, incorporate lymphodepletion prior to PRGN-3005 infusion, which was cleared by the US FDA. Additionally, based on the favorable safety profile, the potential for repeat dosing is being evaluated.

#### PRGN-3007 Next Generation UltraCAR-T with Intrinsic PD-1 Inhibition

- **Overview:** PRGN-3007, based on the next generation of UltraCAR-T platform, is an investigational multigenic, autologous CAR-T cell therapy engineered to simultaneously express a CAR targeting receptor tyrosine kinase-like orphan receptor 1 (ROR1), mbIL15, a kill switch, and a novel mechanism for the intrinsic blockade of PD-1 gene expression. ROR1 is aberrantly expressed in multiple hematological and solid tumors with minimal expression in healthy adult tissues.
- **Trial design:** As [recently announced](#), the US FDA cleared the investigational new drug (IND) application to initiate a Phase 1/1b open-label trial designed to evaluate the safety and efficacy of PRGN-3007 in patients with advanced ROR1+ hematological (Arm 1) and solid (Arm 2) tumors. The target patient population for Arm 1 includes r/r chronic lymphocytic leukemia (CLL), r/r mantle cell leukemia (MCL), r/r acute lymphoblastic leukemia (ALL), and r/r diffuse large B-cell lymphoma (DLBCL). The target patient population for Arm 2 includes locally advanced unresectable or metastatic histologically confirmed triple negative breast cancer (TNBC). The trial will enroll in two parts: an initial 3+3 dose escalation in each arm followed by a dose expansion at the maximum tolerated dose. Arm 1 and Arm 2 will enroll in parallel.
- **Preclinical data:** An abstract highlighting PRGN-3007 preclinical data (Abstract# 1694) titled, "Preclinical evaluation of PRGN-3007, a non-viral, multigenic, autologous ROR1 UltraCAR-T® cell therapy with novel mechanism of intrinsic PD-1 blockade for treatment of hematological and solid cancers," will be presented as a poster presentation at the [63rd ASH Annual Meeting and Exposition](#).

#### PRGN-2012 OTS AdenoVerse Immunotherapy

- **Overview:** PRGN-2012 is an investigational OTS AdenoVerse immunotherapy designed to elicit immune responses directed against cells infected with HPV 6 or HPV 11 for treatment of recurrent respiratory papillomatosis (RRP). PRGN-2012 is currently under evaluation in a Phase 1 clinical trial under a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI). The Phase 1 trial is designed to follow 3+3 dose escalation of PRGN-2012 as an adjuvant immunotherapy following standard-of-care surgical removal of visible papillomas in adult patients with RRP. PRGN-2012 has been granted [Orphan Drug Designation](#) in patients with RRP by the US FDA.
- **Enrollment:** Enrollment in the Phase 1 dose escalation portion of the trial is complete and enrollment in the expansion cohort is ongoing.

- **Dosing:** Six patients have been enrolled in the Phase 1 dose escalation arm at one of the following dose levels with patients receiving four PRGN-2012 administrations (on days 1, 15, 43 and 85) via subcutaneous injection:
  - Dose Level 1:  $1 \times 10^{11}$  viral particles (vp)/dose; N=3
  - Dose Level 2:  $5 \times 10^{11}$  vp/dose; N=3
- Additionally, 8 patients have been enrolled in the Phase 1 dose expansion arm to receive four PRGN-2012 administrations (on days 1, 15, 43 and 85) at  $5 \times 10^{11}$  vp/dose via subcutaneous injection.
- Baseline patient characteristics (N=14) included an average of 51 lifetime surgeries (range: 9 to > 800), and an average of 5.5 surgeries (range: 2 to 9) in the last 2 months before enrolling in the trial.
- **Safety data:** Repeated administrations of PRGN-2012 were well-tolerated with no DLTs and no treatment-related adverse events greater than Grade 2. The lack of a significant neutralizing antibody response over time with subsequent additional vaccinations highlights the ability to deliver repeated administrations of PRGN-2012, a differentiating feature of the AdenoVerse platform.
- **Clinical activity:** Preliminary data from three RRP patient case studies demonstrate very encouraging clinical activity of PRGN-2012 with reduction or elimination in the need for surgical interventions at the most recent follow-up, up to 12 weeks after PRGN-2012 treatment, compared to the recent history of surgical interventions for these patients before enrolling in the trial.

#### PRGN-2009 OTS AdenoVerse Immunotherapy

- **Overview:** PRGN-2009 is an OTS investigational immunotherapy utilizing the AdenoVerse platform that has been designed to activate the immune system to recognize and target HPV-positive solid tumors. PRGN-2009 is currently under evaluation in a Phase 1/2 clinical trial under a CRADA with the NCI. The Phase 1 trial is evaluating safety and response of PRGN-2009 as monotherapy (Arm A) and in combination with bintrafusp alfa (Arm B) in previously treated patients with recurrent or metastatic HPV-associated cancers.
- **Enrollment:** Enrollment in the Phase 1 monotherapy dose escalation arm is complete and enrollment in the Phase 1 combination arm is ongoing. In addition, enrollment in the monotherapy arm of the Phase 2 trial, which evaluates PRGN-2009 as a neoadjuvant therapy for newly diagnosed oropharyngeal or sinonasal squamous cell cancer patients (OPSCC) is ongoing.
- **Dosing:** Six patients (all with prior anti-PD-1/PD-L1 treatment) have been treated in the Phase 1 monotherapy dose escalation arm at one of the following dose levels with patients receiving three PRGN-2009 administrations (on days 1, 15 and 29), followed by PRGN-2009 administration once every 4 weeks for up to 1 year:
  - Dose Level 1:  $1 \times 10^{11}$  vp/dose; N=3
  - Dose Level 2:  $5 \times 10^{11}$  vp/dose; N=3
- Additionally, 6 patients (all with prior anti-PD-1/PD-L1 treatment) were treated in the Phase 1 combination arm with patients receiving three PRGN-2009 administrations ( $5 \times 10^{11}$  vp/dose on days 1, 15 and 29) in combination with bintrafusp alfa (1200 mg) once every 2 weeks, followed by PRGN-2009 administration once every 4 weeks in combination with bintrafusp alfa administrations once every 2 weeks for up to 1 year. Five patients with at least one post-treatment scan were evaluable for disease response.
- **Safety data:** Phase 1 data show that repeated administrations of PRGN-2009 demonstrated a favorable safety profile as monotherapy and in combination therapy with no DLTs. The lack of a significant neutralizing antibody response over time with subsequent additional vaccinations highlights the ability to deliver repeated administrations of PRGN-2009.
- **Clinical activity:** Patient case studies show encouraging increases in the HPV16 and/or HPV18-specific immune response with repeated administrations of PRGN-2009.
  - In the Phase 1 monotherapy arm, a DCR of 50% (3 out of 6 with stable disease (SD)) at the first restaging was observed. This includes a patient with durable (>1 year) SD who has received 16 PRGN-2009 monotherapy administrations.
  - In the Phase 1 combination therapy arm, an ORR of 40% (2 out of 5) per RECIST v1.1 was observed. Objective responses included one ongoing CR at approximately 6 months after treatment initiation and one ongoing PR at approximately 7 months after treatment initiation. Additionally, a DCR of 60% (3 out of 5) at first restaging was observed.

#### 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 the most 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](https://twitter.com/Precigen) and [LinkedIn](https://www.linkedin.com/company/precigen).

#### UltraCAR-T

UltraCAR-T is a multigenic autologous CAR-T platform that utilizes Precigen's advanced non-viral *Sleeping Beauty* system to simultaneously express an antigen-specific CAR to specifically target tumor cells, mBLL15 for enhanced *in vivo* expansion and persistence, and a kill switch to conditionally

eliminate CAR-T cells for a potentially improved safety profile. Precigen has advanced the UltraCAR-T platform to address the inhibitory tumor microenvironment by incorporating a novel mechanism for intrinsic checkpoint blockade without the need for complex and expensive gene editing techniques. UltraCAR-T investigational therapies are manufactured via Precigen's overnight manufacturing process using the proprietary UltraPorator electroporation system at the medical center and administered to patients only one day following gene transfer. The overnight UltraCAR-T manufacturing process does not use viral vectors and does not require *ex vivo* activation and expansion of T cells, potentially addressing major limitations of current T cell therapies.

#### **AdenoVerse Immunotherapy**

Precigen's AdenoVerse immunotherapy platform utilizes a library of proprietary adenovectors for the efficient gene delivery of therapeutic effectors, immunomodulators, and vaccine antigens designed to modulate the immune system. Precigen's gorilla adenovectors, part of the AdenoVerse library, have potentially superior performance characteristics as compared to current competition. AdenoVerse immunotherapies have been shown to generate high-level and durable antigen-specific neutralizing antibodies and effector T cell immune responses as well as an ability to boost these antibody and T cell responses via repeat administration. Superior performance characteristics and high yield manufacturing of AdenoVerse vectors combined with UltraVector<sup>®</sup> technology allows Precigen to engineer cutting-edge investigational gene therapies to treat complex diseases.

#### **UltraPorator**

The UltraPorator system is an exclusive device and proprietary software solution for the scale-up of rapid and cost-effective manufacturing of UltraCAR-T therapies and potentially represents a major advancement over current electroporation devices by significantly reducing the processing time and contamination risk. The UltraPorator device is a high-throughput, semi-closed electroporation system for modifying T cells using Precigen's proprietary non-viral gene transfer technology. UltraPorator is being utilized for clinical manufacturing of Precigen's investigational UltraCAR-T therapies in compliance with current good manufacturing practices.

#### **Trademarks**

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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 and AdenoVerse therapies. 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.

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