Precigen Provides Latest Clinical Developments at Virtual R&D Update Event

December 16, 2020

- 50% of advanced ovarian cancer patients treated with PRGN-3005 UltraCAR-T® at Dose Level 1 or Dose Level 2 in IP arm experienced regression of target tumor burden -

- Expanded preliminary data presented for PRGN-3006 UltraCAR-T® builds on recent presentation at the 62nd ASH Annual Meeting and Exposition -

- New AG019 ActoBiotics™ data for Phase 1b and Phase 2a indicate encouraging trends in C-peptide levels and ability to induce antigen-specific immune modulation following only one treatment cycle of oral AG019 as monotherapy or combination -

GERMANTOWN, Md., Dec. 15, 2020 /PRNewswire/ -- Precigen, Inc. (Nasdaq: PGEN), a biopharmaceutical company specializing in the development of innovative gene and cell therapies to improve the lives of patients, today held an R&D virtual event to provide an update on the latest progress for its clinical pipeline.

The event showcased data from several of Precigen's most advanced clinical programs—PRGN-3005 UltraCAR-T®, PRGN-3006 UltraCAR-T® and AG019 ActoBiotics™ with presentations and discussions from Precigen executives and key opinion leaders, including Dr. Helen Sabzevari, President and CEO of Precigen, Dr. Pieter Rottiers, CEO of Precigen ActoBio, Dr. Mary L. (Nora) Disis, faculty member at the University of Washington and Fred Hutchinson Cancer Research Center and one of the lead investigators for the PRGN-3005 clinical study, and Dr. Kevan Herold, Professor of Immunobiology and of Medicine (Endocrinology) at Yale School of Medicine and one of the lead investigators for the AG019 clinical study. An archive of the audio recording and presentation will be available in the Press & Events section of the investor relations website at investors.precigen.com/press-and-events.

"When we began the year, we set aggressive goals to deliver clinical data for our most advanced programs by the end of the year. Today's presentation delivers on several of these goals and represents numerous firsts with respect to new clinical data for Precigen," said Helen Sabzevari, PhD, President and CEO of Precigen. "We presented the first clinical data ever reported for our lead UltraCAR-T programs, including dosing and safety information. In addition, for PRGN-3005 UltraCAR-T in advanced ovarian cancer patients, we were pleased to report encouraging preliminary findings of expansion, persistence and clinical activity. Data presented on PRGN-3006 UltraCAR-T in acute myeloid leukemia showed encouraging expansion and persistence after low dose infusion and the ability for PRGN-3006 to traffic, expand and persist in bone marrow. Finally, we presented data indicating that a single eight-week treatment cycle of oral AG019 induces C-peptide stabilization and antigen-specific immune tolerance. We are incredibly encouraged by the results to date and look forward to providing future updates as these studies progress."

First Clinical Data Reported for PRGN-3005 UltraCAR-T® Demonstrating Encouraging Preliminary Results

The first clinical data for patients treated at Dose Level 1 (n=3) and Dose Level 2 (n=3) without prior lymphodepletion from the IP arm was reported, including case studies for three patients. PRGN-3005 UltraCAR-T is currently under clinical evaluation in a Phase 1 clinical study for the treatment of advanced, recurrent platinum resistant ovarian, fallopian tube or primary peritoneal cancer (clinical trial identifier: NCT03907527). Data were also provided for individual target lesion response and change in target tumor burden.

Summary of clinical trial status and key results from the first six patients treated with PRGN-3005 UltraCAR-T:

- **Enrollment:** The Phase 1 trial in the intraperitoneal (IP) arm is enrolling patients in the dose escalation phase.
- **Dosing:** The six patients received PRGN-3005 at one of the following dose levels without lymphodepletion:
  - Dose Level 1: $3x10^4$ - ≤ 1 x 10^5 UltraCAR-T cells/kg

- Dose Level 2: $1x10^5$ - ≤ 3 x 10^5 UltraCAR-T cells/kg
- **Prior Lines of Therapy:** Patients received between 6 to 9 prior therapies before enrolling in the PRGN-3005 study.
- **Safety:** PRGN-3005 treatment is safe and well-tolerated to date, with no dose-limiting toxicities (DLTs), neurotoxicity or cytokine release syndromes (CRS) reported.
- **Manufacturing:** 100% manufacturing success to date using decentralized, rapid manufacturing process.
- **Clinical Activity:** PRGN-3005 UltraCAR-T cells showed encouraging expansion and persistence after low dose IP infusion without lymphodepletion. Additionally:
  - PRGN-3005 treatment indicated clinical activity as evidenced by reduction in target lesions with 50% of patients treated (3 of 6) at either Dose Level 1 or Dose Level 2 experiencing regression in target tumor burden; and
  - 33% of patients (2 of 6) achieved Stable Disease (SD) according to RECIST v1.1 criteria at their restaging evaluation.

Expanded Preliminary Data for PRGN-3006 UltraCAR-T, Building on Recent Presentation at the 62nd ASH Annual Meeting And Exposition
Expanded preliminary data for patients treated at Dose Level 1 (n=3) and Dose Level 2 (n=3) without prior lymphodepletion and Dose Level 1 with lymphodepletion (n=3) were reported for PRGN-3006 UltraCAR-T, currently under clinical evaluation in a Phase 1/1b clinical study for the treatment of patients with relapsed or refractory (r/r) acute myeloid leukemia (AML) or higher-risk myelodysplastic syndromes (MDS) (clinical trial identifier: NCT03927261). These new data build on results presented at the 62nd ASH Annual Meeting and Exposition. A single patient case study provided additional clinical insights.

Summary of clinical trial status and key results from the first nine patients treated with PRGN-3006 UltraCAR-T:

- **Enrollment:** The Phase 1 trial is enrolling patients in the dose escalation phase of both the lymphodepletion and non-lymphodepletion cohorts.
- **Dosing:** The nine patients received PRGN-3006 at one of the following dose levels:
  - Dose Level 1: $3x10^4$ - ≤ 1 x 10^5 UltraCAR-T cells/kg
  - Dose Level 2: $1x10^5$ - ≤ 3 x 10^5 UltraCAR-T cells/kg
- **Safety:** PRGN-3006 treatment is safe and well-tolerated to date, with no DLTs or neurotoxicity. Transient grade 1-3 CRS were reported in two patients.
- **Manufacturing:** 100% manufacturing success to date using decentralized, rapid manufacturing process.
- **Clinical Activity:** PRGN-3006 cells showed encouraging expansion and persistence in peripheral blood after low dose infusion. Additionally:
  - PRGN-3006 cells showed the ability to traffic, expand and persist in bone marrow; and
  - PRGN-3006 treatment indicated clinical activity as evidenced by reduction in AML tumor blast levels.

New AG019 Actobiotics™ Data from Phase 1b Monotherapy (up to 12 months follow-up) and Phase 2a Combination Study (up to six months follow-up)
Precigen ActoBio, Inc., a wholly-owned subsidiary of Precigen, announced new data for the Phase 1b monotherapy and Phase 2a combination study of the ongoing Phase 1b/2a clinical study investigating AG019 ActoBiotics ™ for the treatment of early-onset type 1 diabetes (T1D) (clinical trial identifier: NCT03751007, EudraCT 2017-002871-24).

Key clinical results:

Phase 1b oral AG019 monotherapy:

- **Safety:** The AG019 monotherapy 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. There were no AG019 treatment discontinuations due to treatment emergent adverse events (TEAEs).
- **Clinical Activity:** Following a single 8-week treatment cycle of oral AG019, 58% of the adult patients (7 of 12) showed stabilization of C-peptide levels during the first 6 months and slower decline in C-peptide levels at 12 months compared to placebo. Results indicated the potential to preserve insulin production in early onset T1D through its capacity to induce antigen-specific immune modulation.
- **Potential Differentiation:** The ease of treatment due to oral dosing and disease modifying potential differentiates AG019 from competition.
- **Mechanistic Data:** In a mechanistic analysis performed by the Immune Tolerance Network, a leading independent research group, AG019 monotherapy showed the induction of antigen-specific tolerance in conjunction with the reduction of disease-specific T cell responses for adult patients three months after treatment initiation. Specific mechanistic data include:
  - An increase in antigen preproinsulin (PPI)-specific Type 1 regulatory (Tr1) cells;
  - An increase of islet-specific (memory) regulatory T-cells expressing inhibitory receptors, which may indicate induction of tissue-specific bystander suppression; and
  - A significant decrease in antigen (PPI)-specific CD8 T-cells.

Phase 2a AG019 combination therapy:

- **Safety:** The combination of AG019 and teplizumab is safe and well-tolerated to date.
- **Clinical Activity:** Following the treatment with the combination of AG019 and teplizumab, 70% of the adult patients (7 of 10) showed stabilization of C-peptide levels at 6 months post treatment initiation with a trend towards higher C-peptide levels as compared to baseline levels.
- **Mechanistic Data:** Similar to the immunological effects seen in AG019 monotherapy patients, the combination of AG019 and teplizumab showed the induction of antigen-specific tolerance in conjunction with reduction of disease-specific T cell responses for adult patients three months after treatment initiation. The extent of these antigen-specific immune modulatory effects in the combination therapy patients is similar to what was seen in AG019 monotherapy patients indicating that this effect may be attributed to the single 8-week treatment cycle of oral AG019. Specific mechanistic data include:
    - An increase in PPI- and islet-specific specific Type 1 regulatory (Tr1) cells; and
    - A significant decrease in antigen (PPI)-specific CD8 T-cells.

"The Phase 1b monotherapy data for AG019 up to six months after treatment and the interim Phase 2a combination data in adult patients show the treatment is safe and well-tolerated and continue to showcase the potential of the ActoBiotics therapeutic platform," said Pieter Rottiers, PhD, CEO of Precigen ActoBio. "The Phase 1b study continues to show higher C-peptide levels at 12 months compared to placebo following only one treatment cycle of oral AG019. The Phase 2a study shows the potential to boost or prolong teplizumab-induced metabolic effects through induction of antigen-specific immune modulation and the opportunity to explore combinations with other systemic inducers in addition to teplizumab."

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 or follow us on Twitter @Precigen and LinkedIn.

About Precigen ActoBio ™
Precigen ActoBio is a clinical stage biotechnology company and a wholly-owned subsidiary of Precigen (Nasdaq: PGEN) pioneering a new class of therapeutic agents created on the ActoBiotics™ platform. The ActoBiotics™ platform provides a new class of therapeutic agent, a unique delivery platform precisely tailored for specific disease modification, with the potential for superior efficacy and safety via local delivery directly to the relevant tissue. ActoBiotics are targeted, microbe-based, specifically designed agents that express and locally deliver potential disease-modifying therapeutics at disease sites including the intestine, the mouth and the nasopharynx, to treat a range of disorders. Precigen ActoBio has a strong R&D pipeline and an extensive portfolio of candidates advancing toward clinical development across a number of potential indications. Learn more about Precigen ActoBio at www.precigen.com/actobio.

About PRGN-3005 UltraCAR-T
PRGN-3005 UltraCAR-T is a multigenic autologous CAR-T cell treatment utilizing Precigen's *Sleeping Beauty* system to simultaneously express a CAR specifically targeting the unshed portion of MUC16, which is highly expressed on ovarian tumors with limited normal tissue 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-3005 is being evaluated in collaboration with the University of Washington and Fred Hutchinson Cancer Research Center in an investigator-initiated open-label, dose escalation Phase 1 study to evaluate the safety and maximal tolerated dose of PRGN-3005 delivered by intraperitoneal infusion (IP) or intravenous infusion (IV) (clinical trial identifier: NCT03907527). The study population includes patients with advanced stage (III/IV) recurrent ovarian, fallopian tube, and primary peritoneal cancer who are platinum-resistant and have progressed after receiving standard-of-care therapies or are not eligible to receive available therapies with known clinical benefit.

About PRGN-3006 UltraCAR-T
PRGN-3006 UltraCAR-T is a multigenic autologous CAR-T cell treatment utilizing Precigen's *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 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). The study population includes patients with relapsed or refractory acute myeloid leukemia or higher risk myelodysplastic syndrome.

About AG019
AG019 is an investigational therapy designed to induce oral immune tolerance to reverse T1D and currently under clinical evaluation for the treatment of early-onset type 1 diabetes (T1D) (clinical trial identifier: NCT03751007, EudraCT 2017-002871-24). The Phase 1b/2a clinical trial is evaluating AG019 as a monotherapy and in combination with teplizumab (PRV-031), which is currently under investigation in the PROTECT Phase 3 study for the treatment of newly diagnosed T1D. Both the Phase 1b portion of the study, testing AG019 monotherapy in patients 12 to 17 years of age and adults 18-40 years of age, and the first cohort of the Phase 2a portion, testing the combination dosing of AG019 plus teplizumab in adults 18-40 years of age, are fully enrolled.

Trademarks

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.

For more information, contact:

Investor Contact:	**Media Contact:**
Steven Harasym Vice President, Investor Relations Tel: +1 (301) 556-9850 investors@precigen.com	Glenn Silver Lazar-FINN Partners glenn.silver@finnpartners.com

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