Precigen Presents Preclinical Data for the Next Generation Mesothelin UltraCAR-T® with Intrinsic PD-1 Blockade at the AACR Annual Meeting 2023

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– First preclinical data presented for the next generation of the UltraCAR-T platform utilizing a mesothelin (MSLN) chimeric antigen receptor (CAR) –

– MSLN is overexpressed on multiple solid tumors such as mesothelioma, ovarian cancer and pancreatic cancer –

– Proprietary technology for checkpoint blockade intrinsic to UltraCAR-T cells has the potential for an improved safety profile and reduced cost by eliminating the need for checkpoint inhibitor combination –

– Single administration of next generation MSLN UltraCAR-T incorporating intrinsic PD-1 blockade resulted in robust UltraCAR-T cell expansion and durable persistence leading to strong antitumor efficacy, even upon tumor rechallenge after three months –

GERMANTOWN, Md., April 17, 2023 /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 presents preclinical data for the next generation UltraCAR-T platform utilizing MSLN CAR from Precigen's library of non-viral plasmids at the American Association for Cancer Research (AACR) Annual Meeting 2023. The abstract titled, "Next Generation UltraCAR-T® Cells with Intrinsic Checkpoint Inhibition and Overnight Manufacturing Overcome Suppressive Tumor Microenvironment Leading to Sustained Antitumor Activity" will be presented as a poster presentation on Monday, April 17, 2023 from 9:00 AM to 12:30 PM ET (Abstract #1791).

Next Generation MSLN UltraCAR-T
UltraCAR-T cells are engineered to co-express a CAR, membrane bound IL-15 (mbIL15), and kill switch genes using non-viral gene transfer via the high-throughput UltraPorator® system. UltraCAR-T cells offer the potential for enhanced potency, safety and scalability. Next generation MSLN UltraCAR-T cells also incorporate a novel mechanism for blockade of PD-1, to potentially supersede the need for combination therapy with checkpoint inhibitors and mitigating classic T cell exhaustion that occurs from chronic stimulation, thereby expanding the therapeutic window for efficacy. MSLN has limited expression in normal healthy tissue but is commonly overexpressed on multiple solid tumors such as mesothelioma, ovarian cancer and pancreatic cancer and is associated with poor prognosis making it an attractive anti-tumor target.

Preclinical Summary Results
Next generation MSLN UltraCAR-T cells were successfully engineered using a single multicistronic non-viral transposon and overnight manufacturing process to simultaneously express a CAR, mbIL15, a kill switch, and a novel mechanism for intrinsic PD-1 blockade. Next generation MSLN UltraCAR-T cells showed specific and significant downregulation of PD-1 leading to significant increase in cytotoxicity of $MSLN^+$ $PD\text{-}L1^+$ tumor cells *in vitro* at low effector to target cell ratios compared to control MSLN CAR-T cells lacking PD-1 blockade. Next generation MSLN UltraCAR-T cells exhibited markedly enhanced polyfunctionality as well as enhanced inflammatory cytokine production in the presence of $MSLN^+$ $PD\text{-}L1^+$ tumor cells.

In two different *in vivo* xenograft models, $MSLN^+$ $PD\text{-}L1^+$ ovarian cancer and $MSLN^+$ $PD\text{-}L1^+$ mesothelioma, a single administration of next generation MSLN UltraCAR-T cells to tumor bearing mice resulted in robust UltraCAR-T cell expansion and durable persistence leading to significant antitumor efficacy. Moreover, rechallenging the previously treated mice who became tumor-free for a second time with mesothelioma tumors to simulate tumor relapse led to the significant reduction in tumor burden without additional MSLN UltraCAR-T treatment demonstrating the durable persistence and functionality of UltraCAR-T cells *in vivo*.

In mice, the next generation MSLN UltraCAR-T cells demonstrated significant downregulation of PD-1 and preferred CAR-T phenotype that was most

similar to T central memory (T_{CM}) and stem cell memory (T_{SCM}). These data demonstrate the potential of UltraCAR-T cells to persist long-term *in vivo*, prevent CAR-T cell exhaustion, and mount a durable anti-tumor response with the ability for continued response upon tumor rechallenge.

"Precigen has built one of the most comprehensive clinical and preclinical CAR-T portfolios with antigen-specific targets spanning both hematological and solid tumors, including CD33, MUC16, ROR1, CD19, BCMA and MSLN," said Helen Sabzevari, PhD, President and CEO of Precigen. "MSLN is the second target for the next generation UltraCAR-T incorporating intrinsic checkpoint inhibition, following our recently initiated Phase 1/1b study for PRGN-3007. With every milestone, we move closer to our ultimate vision to transform the personalized cell therapy landscape using Precigen's library approach to target tumor-associated antigens to address unmet medical needs for cancer patients."

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 therapies toward clinical proof-of-concept and commercialization. For more information about Precigen, visit www.precigen.com or follow us on Twitter @Precigen, LinkedIn or YouTube.

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, mbIL15 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.

UltraCAR-T® Clinical Program
The UltraCAR-T platform has shifted the autologous CAR-T manufacturing paradigm using an advanced non-viral multigene delivery system and an overnight, decentralized manufacturing process for administration of autologous CAR-T cells one day after gene transfer to reduce vein-to-vein time. Precigen's UltraCAR-T platform is currently under clinical investigation for hematological and solid tumors, including a Phase 1/1b study of PRGN-3005 UltraCAR-T in patients with advanced, recurrent platinum resistant ovarian, fallopian tube or primary peritoneal cancer (NCT03907527), a Phase 1/1b study of PRGN-3006 UltraCAR-T in patients with relapsed or refractory acute myeloid leukemia (AML) or higher risk myelodysplastic syndrome (MDS) (NCT03927261) and a Phase 1/1b study of PRGN-3007 UltraCAR-T incorporating PD-1 checkpoint inhibition in patients with ROR1-positive ($ROR1^+$) hematologic chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), acute lymphoblastic leukemia (ALL), diffuse large B-cell lymphoma (DLBCL) and solid tumor triple negative breast cancer (TNBC) malignancies (NCT05694364).

UltraCAR-T® Library Approach
Precigen's UltraCAR-T library approach is designed to transform the personalized cell therapy landscape for cancer patients. Precigen's goal is to develop and validate a library of non-viral plasmids to target tumor-associated antigens. Enabled by design and manufacturing advantages of UltraCAR-T, coupled with the capabilities of the UltraPorator® system, Precigen is working to empower cancer centers to deliver personalized, autologous UltraCAR-T treatment with overnight manufacturing to any cancer patient. Based on the patient's cancer indication and biomarker profile, one or more non-viral plasmids would be selected from the library to build a personalized UltraCAR-T treatment. After initial treatment, this approach has the potential to allow for redosing of UltraCAR-T targeting the same or new tumor-associated antigen(s) based on the treatment response and the changes in antigen expression of the patient's tumor. Precigen believes that the combination of the advanced UltraVector® DNA construction platform and the ease of overnight manufacturing gives this library approach a proprietary advantage over traditional T-cell therapies.

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.

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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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