Precigen Announces Further Advancement of UltraCAR-T® Platform with First Patient Dosed in Phase 1/1b Dose Escalation/Dose Expansion Study of PRGN-3007 in Advanced ROR1+ Hematological and Solid Tumors

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– Milestone represents the first patient dosed with the next generation UltraCAR-T, incorporating PD-1 checkpoint inhibition in addition to three effector genes –

– Proprietary technology for checkpoint blockade intrinsic to UltraCAR-T cells avoids the need for combination with a systemic checkpoint inhibitor, potentially limiting cost and systemic toxicity –

GERMANTOWN, Md., March 29, 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 announced that the first patient has been dosed in the Phase 1/1b dose escalation/dose expansion study (clinical trial identifier: NCT05694364) of PRGN-3007 in advanced ROR1-positive ($ROR1^+$) hematological and solid tumors. The target patient population for the study includes chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), acute lymphoblastic leukemia (ALL), and diffuse large B-cell lymphoma (DLBCL) and solid tumors, including breast adenocarcinomas encompassing triple negative breast cancer (TNBC). There are estimated to be more than 100,000 patients diagnosed in both the hematological and TNBC target populations in the United States, European Union and Japan in 2023.[a]

PRGN-3007 UltraCAR-T is a first-in-class investigational multigenic, autologous CAR-T cell therapy utilizing Precigen's clinically validated advanced non-viral gene delivery system and well-established overnight, decentralized manufacturing process. Precigen has further advanced the UltraCAR-T platform to address the inhibitory tumor microenvironment by incorporating intrinsic checkpoint blockade without the need for complex and costly gene editing techniques. PRGN-3007 is engineered using a single multicistronic transposon plasmid to simultaneously express a chimeric antigen receptor (CAR) targeting ROR1, membrane-bound interleukin–15 (mbIL15), a kill switch, and a novel mechanism for the intrinsic blockade of PD-1 gene expression. The innovative design of PRGN-3007, where the blockade of PD-1 expression is intrinsic and localized to UltraCAR-T cells, is aimed at avoiding systemic toxicity and the high cost of checkpoint inhibitors by eliminating the need for combination treatment.

The Phase 1/1b clinical trial is an open-label study designed to evaluate the safety and efficacy of PRGN-3007 in patients with advanced $ROR1^+$ hematological (Arm 1) and solid (Arm 2) tumors. The study is enrolling in two parts: an initial 3+3 dose escalation in each arm followed by a dose expansion at the maximum tolerated dose (MTD). Arm 1 and Arm 2 are enrolling in parallel. The investigator-initiated study is being conducted in collaboration with the H. Lee Moffitt Cancer Center & Research Institute (Moffitt).

"We are excited to work with Precigen and announce that the first patient, a CLL patient, has been dosed in the first-in-human study of PRGN-3007 UltraCAR-T," said Javier Pinilla-Ibarz, MD, PhD, Senior Member, Lymphoma Section Head and Director of Immunotherapy, Malignant Hematology Department, Moffitt, and Principal Investigator for the PRGN-3007 clinical study. "ROR1 is a promising target for addressing a wide variety of tumors and we are hopeful that the PRGN-3007 study will further the development of this novel CAR-T treatment, which combines intrinsic PD-1 inhibition and ease of administration from the validated overnight manufacturing of UltraCAR-T performed at our medical center bringing therapy to patients within one day."

"Dosing the first patient with PRGN-3007, the next generation of UltraCAR-T incorporating PD-1 inhibition, is a significant milestone for the UltraCAR-T platform," said Helen Sabzevari, PhD, President and CEO of Precigen. "The PRGN-3007 study targets a broad range of hematological and solid tumor indications and this milestone helps us move closer to our vision for UltraCAR-T, which aims to deliver a library of personalized autologous UltraCAR-T therapies using overnight manufacturing at the patient's medical center."

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.

About Receptor Tyrosine Kinase-like Orphan Receptor 1 (ROR1)

ROR1 is a type I orphan-receptor that is expressed during embryogenesis and by certain hematological and solid tumors but is undetectable on normal adult tissues.[1-3] ROR1 plays an important role in oncogenesis by activating cell survival signaling events, particularly the non-canonical WNT signaling pathway.[4] Aberrant expression of ROR1 is detected in multiple hematological malignancies including CLL[5], MCL[6], ALL[7], and DLBCL.[8] Elevated ROR1 expression is detected in various solid tumors, including breast adenocarcinoma encompassing TNBC, pancreatic cancer, ovarian cancer, Ewing's sarcoma and lung adenocarcinoma.[9-14] Many human breast adenocarcinomas express high levels of ROR1, which is not expressed by normal breast tissue.[15]

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.

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

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.

References

[a] GlobalData Epidemiology Market Size Research.

[1] Balakrishnan, A., *et al.*, Analysis of ROR1 Protein Expression in Human Cancer and Normal Tissues. *Clin Cancer Res*, 2017. 23(12): p. 3061-3071.

[2] Green, J.L., *et al*., ROR receptor tyrosine kinases: orphans no more. *Trends in Cell Biology*, 2008. 18(11): p. 536-544.

[3] Rebagay, G., *et al.*, ROR1 and ROR2 in Human Malignancies: Potentials for Targeted Therapy. *Front Oncol*, 2012. 2(34).

[4] Zhao Y, *et al*., Tyrosine Kinase ROR1 as a Target for Anti-Cancer Therapies. *Front. Oncol,* 2021.

[5] Baskar, S., *et al.*, Unique Cell Surface Expression of Receptor Tyrosine Kinase ROR1 in Human B-Cell Chronic Lymphocytic Leukemia. *Clin Cancer Res,* 2008. 14(2): p. 396-404.

[6] Hudecek, M., *et al.*, The B-cell tumor–associated antigen ROR1 can be targeted with T cells modified to express a ROR1-specific chimeric antigen receptor. *Blood*, 2010. 116(22): p. 4532-4541.

[7] Enayati H, *et al*., Expression of ROR1 Gene in Patients with Acute Lymphoblastic Leukemia. *IJBC* 2019; 11(2): 57-62.

[8] Ghaderi, A., *et al.*, ROR1 Is Expressed in Diffuse Large B-Cell Lymphoma (DLBCL) and a Small Molecule Inhibitor of ROR1 (KAN0441571C) Induced Apoptosis of Lymphoma Cells. *Biomedicines*, 2020. 8(6).

[9] Zhang, S., *et al.*, The onco-embryonic antigen ROR1 is expressed by a variety of human cancers. *Am J Pathol*, 2012. 181(6): p. 1903-10.

[10] Zhang, S., *et al.*, ROR1 is expressed in human breast cancer and associated with enhanced tumor-cell growth. *PLoS One*, 2012.7(3): p. e31127.

[11] Potratz, J., *et al.*, Receptor tyrosine kinase gene expression profiles of Ewing sarcomas reveal ROR1 as a potential therapeutic target in metastatic disease. *Mol Oncol*, 2016. 10(5): p. 677-92.

[12] Zheng, Y.Z., *et al.*, ROR1 is a novel prognostic biomarker in patients with lung adenocarcinoma. *Sci Rep*, 2016. 6: p. 36447.

[13] Choi, M.Y., *et al.*, Pre-clinical Specificity and Safety of UC-961, a First-In-Class Monoclonal Antibody Targeting ROR1. *Clin Lymphoma Myeloma Leuk*, 2015. 15 Suppl: p. S167-9.

[14] Balakrishnan, A., *et al.*, Analysis of ROR1 Protein Expression in Human Cancer and Normal Tissues. *Clin Cancer Res*, 2017. 23(12): p. 3061-3071.

[15] Zhang S. *et al.,* ROR1 is expressed in human breast cancer and associated with enhanced tumor-cell growth. *PLoS One,* 2012, 7:e31127.

Investor Contact:
Steven M. Harasym
Vice President, Investor Relations
Tel: +1 (301) 556-9850
investors@precigen.com

Media Contacts:
Donelle M. Gregory
press@precigen.com

Glenn Silver
Lazar-FINN Partners
glenn.silver@finnpartners.com

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