Precigen ActoBio Announces Positive Topline Results from Phase 1b Study of AG019 ActoBiotics™, A Novel Therapy Designed to Address the Underlying Cause of Type 1 Diabetes

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- Primary endpoint met assessing safety and tolerability in the Phase 1b monotherapy portion of the study -

- Preliminary results demonstrate an encouraging trend in C-peptide levels, a biomarker for T1D disease progression -

- Preliminary data shows an increase in the frequency of islet-specific Tregs, a potential mechanistic indicator of therapeutic activity -

GERMANTOWN, Md., Aug. 10, 2020 /PRNewswire/ -- Precigen ActoBio, an innovative clinical-stage biotechnology company focused on a new class of microbe-based therapeutic agents and a wholly-owned subsidiary of Precigen, Inc. (Nasdaq: PGEN), today announced it has met the primary endpoint assessing safety and tolerability in the Phase 1b monotherapy portion 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).

T1D is an autoimmune disease in which the immune system destroys insulin-producing beta cells in the pancreas, resulting in a blood glucose imbalance. There is no approved disease-modifying treatment for T1D, which is currently managed through lifestyle modification and diet combined with exogenous insulin. Replacement insulin therapy is associated with a variety of near- and long-term adverse events, as is failure to properly control glucose levels within a narrow range.

AG019 is formulated as an oral capsule consisting of engineered *Lactococcus lactis* specifically modified to deliver autoantigen human proinsulin (hPINS) and the tolerance-enhancing cytokine human interleukin-10 (hIL-10) to the mucosal lining of the gastrointestinal tissues. Administration of AG019 is designed to induce specific regulatory T cells (Tregs) that could reduce or eliminate the destruction of insulin-producing cells, potentially stabilizing or improving insulin production.

The Phase 1b open-label portion of the study evaluates the safety and tolerability of AG019 administered as a single dose and repeated daily doses as a monotherapy in adult and adolescent patients. The primary endpoint for assessing safety and tolerability is treatment-emerging adverse events (TEAEs) reported up to six months after treatment initiation. Nineteen patients were treated in the Phase 1b monotherapy portion of the study and 17 patients were evaluated at six months. The Phase 2a portion of the study is currently ongoing and investigates the safety and tolerability of AG019 in combination with teplizumab (PRV-031), which is currently under investigation in the PROTECT Phase 3 study for the treatment of newly diagnosed T1D.

Key findings from the Phase 1b AG019 monotherapy portion study for patients six months after treatment initiation include:

- The study met its primary endpoint demonstrating safety and tolerability. No serious or severe TEAEs were reported in any of the patients treated with AG019 monotherapy, and no patient discontinued treatment.

- Eight-week treatment with AG019 monotherapy was safe and well-tolerated in daily dosages up to 6 x 10^{11} CFU (colony-forming units) in adult and adolescent patients with T1D.

- There was no evidence for systemic exposure of bacteria and proteins (hPINS/hIL-10) in the circulation, confirming the safety profile of AG019. The analysis of fecal samples confirmed gastrointestinal exposure of AG019 in most treated patients.

- C-peptide levels, a common biomarker used to measure pancreatic beta cell function, demonstrate slower decline in C-peptide levels in 67% of adult patients (6 out of 9) receiving AG019 monotherapy with 44% of these adult patients (4 out of 9) showing stabilization of mean four hours C-peptide area under the curve (AUC) levels at six months (within 9.7% of the baseline level).[1] This was based on the comparison of the median percent decline in mean four hours C-peptide AUC from baseline between patients receiving AG019 monotherapy and patients who received placebo from previous studies.[2]

Furthermore, in a preliminary analysis performed by the Immune Tolerance Network, a leading independent research group, AG019 monotherapy shows an increase in the frequency of islet-specific Tregs expressing inhibitory receptors, a potential mechanistic indicator of therapeutic activity, for

patients three months after treatment initiation.

"Though preliminary, C-peptide data for the Phase 1b AG019 monotherapy is encouraging in this limited data set," said Kevan Herold, MD, Professor of Immunobiology and of Medicine at Yale University and Principal Investigator for the AG019 Phase 1b/2a clinical study. "The positive topline data from the Phase 1b monotherapy portion of study provides compelling rationale for continued clinical development of this promising investigational therapeutic candidate."

"These preliminary data for the Phase 1b monotherapy portion of the study are very promising," said Pieter Rottiers, PhD, CEO of Precigen ActoBio. "In particular, the encouraging trend we are seeing in C-peptide levels indicates potential treatment-related disease modification over time. We look forward to providing expanded data in the coming months for both the AG019 Phase 1b monotherapy and the Phase 2a combination with teplizumab."

About Type 1 Diabetes (T1D)
T1D is an autoimmune disease in which the immune system destroys insulin-producing beta cells in the pancreas, resulting in a blood glucose imbalance. There is no approved disease-modifying treatment for T1D, which is currently managed through lifestyle modification and diet combined with exogenous insulin. As of 2019, more than 463 million adults (20-79 years, diagnosed and undiagnosed) globally are living with diabetes with T1D estimated to account for 23 million to 46 million (5 to 10%) of all diabetes cases. Over 1.1 million below 20 years of age have T1D with an estimated 128,900 under the age of 20 expected to develop T1D worldwide annually.[3]

About AG019 ActoBiotics ™
AG019 ActoBiotics 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 ActoBiotics as a monotherapy and in combination with teplizumab, a Phase 3 anti-CD3 monoclonal antibody in development for the interception and prevention of clinical T1D. Both the Phase 1b portion of the study, testing AG019 monotherapy in patients 12 to 17 years of age and adults, and the first cohort of the Phase 2a portion, testing the combination dosing of AG019 plus teplizumab (PRV-031) in adults, are fully enrolled.

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/.

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 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 and clinical trials and discovery programs, the promise of the Company's portfolio of therapies, the Company's refocus to a healthcare-oriented business, and its continuing evaluation of options for the Company's non-healthcare businesses. 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:	**Corporate Contact:**
Steven Harasym	Marie Rossi, PhD
Vice President, Investor Relations	Vice President, Communications
Tel: +1 (301) 556-9850	Tel: +1 (301) 556-9850
investors@precigen.com	press@precigen.com

References

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[2]Herold et al., *Diabetes* 2013; Gitelman et al., *Lancet Diabetes Endocrinol* 2013; Rigby et al., *Lancet Diabetes Endocrinol* 2013

[3]International Diabetes Foundation, Diabetes Atlas Ninth Edition 2019. IDF website.

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