# Precigen ActoBio Announces Additional Positive Interim Data from Phase 1b/2a Study of AG019 ActoBiotics™, A Novel Therapy Designed to Address the Underlying Cause of Type 1 Diabetes

Oct 01, 2021

**- Latest results presented at the EASD 57th Annual Meeting -**
**- AG019 monotherapy and AG019 combination therapy resulted in stabilization of HbA1c and IDAA1c levels, important indicators of long-term glycemic control associated with reduced risk of microvascular complications in T1D patients -**
**- Mechanistic analysis showed AG019 treatment resulted in reduction of conventional T-cells with an inflammatory phenotype -**
**- New metabolic results strengthen previously reported data on C-peptide and antigen-specific immune modulation for the AG019 monotherapy and AG019 combination therapy -**
**- Monotherapy results suggest the potential for AG019 as a standalone therapeutic agent for T1D -**

GERMANTOWN, Md., Oct. 1, 2021 /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 additional positive interim data from the ongoing Phase 1b/2a clinical study investigating AG019 ActoBiotics™ for the treatment of recent-onset type 1 diabetes (T1D) (clinical trial identifier: NCT03751007, EudraCT 2017-002871-24). Results were presented in an oral presentation entitled, *"AG019 ActoBiotics as monotherapy or in association with teplizumab in recent-onset type 1 diabetes was safe and demonstrated encouraging metabolic and immunological effects"* at the European Association for the Study of Diabetes (EASD) 57th Annual Meeting by Chantal Mathieu, MD, PhD, Professor of Medicine at the Katholieke Universiteit Leuven, Belgium.

The Phase 1b open-label portion of the study evaluates the safety and tolerability of AG019 as a monotherapy in adult (age 18-42) and adolescent (age 12-17) patients. The Phase 2a double-blind portion of the study investigates the safety and tolerability of AG019 in combination with an investigational anti-CD3 monoclonal antibody, teplizumab (PRV-031).

Previously reported Phase 1b/2a topline data showed the potential of oral AG019 treatment to preserve insulin production in recent-onset T1D through its capacity to induce antigen-specific immune modulation:

- The primary endpoint of both the Phase 1b AG019 monotherapy study and the Phase 2a AG019 combination therapy study was met.
- AG019 was well tolerated as a monotherapy and in combination with teplizumab with no serious adverse events (SAEs) reported.
- A single 8-week treatment cycle of oral AG019 as a monotherapy and in combination with teplizumab showed stabilization or increase of C-peptide levels during the first 6 months post treatment initiation in recent-onset T1D.
- In an independent analysis performed by the Immune Tolerance Network (ITN), a leading independent research group sponsored by the US National Institutes of Health, oral AG019 treatment induced antigen-specific tolerance in conjunction with the reduction of disease-specific T-cell responses 6 months post treatment initiation. The extent of the antigen-specific tolerance was similar in both the AG019 monotherapy and combination therapy indicating that this effect may be attributed to the oral AG019 treatment.

New clinical results presented at EASD include:

**Phase 1b oral AG019 monotherapy:**

***Dosing****:* Patients received a daily dose of oral AG019 monotherapy for 8 weeks and were evaluated for pharmacodynamic and metabolic markers. The average time of T1D diagnosis was 104 days at dosing initiation.

***Clinical Activity****:* New AG019 monotherapy data show that glycated hemoglobin (HbA1c) was below the 7% target for 100% of adult patients (9 of 9) and 92% of the patients aged 17 years and above (11 of 12) up to 12 months after dosing initiation. An HbA1c level below 7% is an important indicator of long-term glycemic control as defined by the American Diabetes Association (ADA). Moreover, insulin-dose adjusted HbA1c (IDAA1c) is a model

that uses both weight-adjusted insulin dose and HbA1c in the same formula to reduce the influence of the insulin treatment regimen. A stabilization of IDAA1c below 9 was demonstrated in 78% of adult patients (7 of 9) and in 75% of patients aged 17 years and above (9 of 12) up to 12 months after dosing initiation. Stable glycemia, measured as a reduction of HbA1c/IDAA1c, is known to reduce the long-term risk of developing microvascular complications, including diabetic retinopathy, nephropathy, and other vascular complications.

***Mechanistic Data**:* In an independent analysis performed by the ITN, the AG019 monotherapy showed a decrease of conventional T-cells with an inflammatory phenotype (% TNFα+) in 100% of adult patients (4 of 4) analyzed up to 6 months after dosing initiation, whereas the mean expression of the inhibitory receptor PD-1 remained overall stable.

**Phase 2a AG019 combination therapy:**

***Dosing**:* Patients received a daily dose of oral AG019 monotherapy for 8 weeks in combination with daily intravenous infusions of teplizumab for 12 days and were evaluated for pharmacodynamic and metabolic markers. The average time of T1D diagnosis was 103 days at dosing initiation.

***Clinical Activity***:* New AG019 combination therapy data show stabilization of HbA1c below the ADA target (7%) was demonstrated in 70% of adult patients (7 of 10) up to 12 months after dosing initiation. HbA1c levels were below target in 75% of the adolescent patients (3 of 4) up to 6 months after dosing initiation and remained below target for whom 12-month data is available (n=2). In addition, a stabilization of IDAA1c was demonstrated in 100% of adult patients (10 of 10) up to 12 months after dosing initiation. Stabilization of IDAA1c was demonstrated in 75% of adolescent patients (3 of 4) up to 6 months after dosing initiation and remained below target for whom 12-month data is available (n=2). HbA1c and IDAA1c levels were below the target in 33% of placebo-treated patients (1 of 3) up to 6 months after dosing initiation.

***Mechanistic Data***: In an independent analysis performed by the ITN, the combination of AG019 and teplizumab showed a decrease of conventional T-cells with an inflammatory phenotype (% TNFα+) in 67% of adult patients (2 of 3) analyzed up to 6 months after dosing initiation, while an increase was shown in 100% of placebo-treated adult patients (2 of 2). Moreover, an increase in the expression of inhibitory receptor PD-1 in PPI and islet-reactive conventional T-cells was demonstrated in 67% of adult patients (2 of 3) analyzed up to 6 months after dosing initiation. This effect was not shown for placebo-treated adult patients (n=2) at 6 months after dosing initiation.

In the AG019 combination therapy study, the expansion of the exhausted phenotype in total CD8+ T-cells in adult and adolescent patients (n=12) was in line with previously reported anti-CD3 specific effects indicating an attenuation of the effector function. This effect was not shown for placebo-treated adult patients (n=2).

"AG019 showed stabilization of the long-term glycemic control markers, HbA1c and IDAA1c, for the majority of patients treated with the AG019 monotherapy and AG019 combination therapy," said Chantal Mathieu, MD, PhD, Professor of Medicine at the Katholieke Universiteit Leuven, Belgium, and principal investigator for the AG019 Phase 1b/2a clinical study. "Antigen-specific immune modulation, which is the keystone for the mechanism of action of AG019 as demonstrated in preclinical studies, is now translated into the immunological clinical data in the Phase 1b/2a clinical study."

"The new data presented at EASD strengthens previously reported findings on C-peptide and antigen-specific immune modulation, and the exciting data for the AG019 monotherapy reinforces our belief that AG019 is promising as a standalone therapy. We look forward to further investigating the potential of AG019 in type 1 diabetes." Said Pieter Rottiers, PhD, CEO of Precigen ActoBio.

*Per Protocol Analysis Set: All data from patients who received at least 75% of the scheduled doses of AG019 and at least one dose of teplizumab in the combination cohorts and had no major protocol deviations affecting the main pharmacodynamic endpoints at the time point of data collection.

**About AG019 ActoBiotics™**
AG019 is formulated as an oral capsule 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 endogenous insulin production.

**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. 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. 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 age 20 years, expected to develop T1D worldwide annually.[2]

**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 http://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.

**Trademarks**

Precigen, Precigen ActoBio, ActoBiotics, and Advancing Medicine with Precision are trademarks of Precigen and/or its affiliates. Other names may be trademarks of their respective owners.

**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 Precigen's current expectations and projections about future events and generally relate to plans, objectives, and expectations for the development of Precigen's business and the business of Precigen ActoBio, including the timing and progress of preclinical and clinical trials and discovery programs, and the promise of their portfolio of 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 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. Precigen 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 Precigen's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Precigen'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:**
Steven 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

**References**

[1] Greenbaum et al., *Diabetes* 2012

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

View original content to download multimedia:https://www.prnewswire.com/news-releases/precigen-actobio-announces-additional-positive-interim-data-from-phase-1b2a-study-of-ag019-actobiotics-a-novel-therapy-designed-to-address-the-underlying-cause-of-type-1-diabetes-301389445.html

SOURCE Precigen ActoBio