Precigen Announces FDA Confirmation that the Ongoing Phase 1/2 Study of PRGN-2012 AdenoVerse Immunotherapy Will Serve as the Pivotal Study to Support Accelerated Approval

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– *FDA confirmed that the ongoing Phase 1/2 single arm study will serve as pivotal and no additional randomized, placebo-controlled trial will be required to support submission of a BLA* –

– *FDA agreed on the required efficacy and safety endpoints that will support filing an accelerated approval BLA for licensure* –

– *Enrollment and dosing in the ongoing Phase 2 portion of the study is completed* –

– *If approved, PRGN-2012 would potentially be the first therapeutic for the treatment of RRP, a serious and difficult-to-treat orphan indication for which the current standard-of-care is repeated surgeries* –

GERMANTOWN, Md., Aug. 9, 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 US Food and Drug Administration (FDA) has agreed that the ongoing Phase 1/2 single arm study (NCT04724980) of the first-in-class investigational PRGN-2012 AdenoVerse ™ immunotherapy for the treatment of recurrent respiratory papillomatosis (RRP) will serve as pivotal for the purpose of filing an accelerated approval request for licensure. The FDA also confirmed no additional randomized, placebo-controlled trial will be required to support submission of a biologics license application (BLA). Based on the FDA guidance, the Company plans to initiate a confirmatory study prior to submission of the BLA.

The FDA has confirmed that the current primary endpoint for the ongoing Phase 1/2 study, which is Complete Response rate (percentage of patients with no surgical interventions during the 12 months following treatment with PRGN-2012), along with an immunological surrogate marker demonstrating an induction of HPV-specific T cell responses following PRGN-2012 treatment, is acceptable for the accelerated approval request.

PRGN-2012 is an innovative therapeutic vaccine with optimized antigen design that uses Precigen's gorilla adenovector technology, part of Precigen's proprietary AdenoVerse platform, to elicit immune responses directed against cells infected with HPV 6 or HPV 11. Gorilla adenovectors have numerous advantages, including the ability for repeat administration, the inability to replicate *in vivo*, which may improve safety, and the ability to deliver a large genetic payload. The FDA granted PRGN-2012 Breakthrough Therapy Designation and Orphan Drug Designation for the treatment of RRP.

Data from the Phase 1 portion of the study showed that 50% of adult RRP patients (who had ≥3 surgeries to treat the disease in the year prior to treatment) were "surgery-free" (Complete Response) after PRGN-2012 treatment during the 12 month follow-up. All complete responders continue to be surgery-free with a minimum follow-up of 18 months post-treatment. Precigen has completed enrollment and dosing in the Phase 2 portion of the study (N=23) bringing the total number of enrolled patients to 35 at the recommended Phase 2 dose. Patient follow up is currently ongoing and data collection is anticipated to be completed by the second quarter of 2024.

"The eligibility of the Phase 1/2 study, which has already been fully enrolled and dosed, as the pivotal study to support accelerated approval has the potential to significantly reduce the product development time for PRGN-2012. We are thankful for the FDA's decision, which underscores the importance of bringing innovative approaches for the treatment of this serious and rare disease," said Helen Sabzevari, PhD, President and CEO of Precigen. "I also want to thank the patients who participated in the study and our investigators, Dr. Clint T. Allen and Dr. Scott Norberg from the National Institutes of Health, as well as the Precigen team."

"The potential of this treatment is tremendously exciting for RRP patients. The RRP community has only ever had one treatment option—surgery," said Kim McClellan, President of Recurrent Respiratory Papillomatosis Foundation. "The potential to eliminate even one surgery and improve the quality of our lives would have a profound impact on those living with RRP."

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 Recurrent Respiratory Papillomatosis (RRP)

Recurrent respiratory papillomatosis (RRP) is a rare, difficult-to-treat and sometimes fatal neoplastic disease of the upper and lower respiratory tracts that is caused by infection with HPV 6 or HPV 11.[1-4] RRP is classified based on age of onset as juvenile or adult. Juvenile-onset disease has an incidence of 4 per 100,000 and adult-onset RRP has an incidence of 2 to 3 per 100,000. Currently there is no cure for RRP and the current standard-of-care is repeated endoscopic debulking with ablation or excision of papillomatous lesions.[3,4] Recurrence of papilloma after surgical removal is very common and repeated procedures are required to debulk and monitor the disease, which exposes patients to anesthetic and surgical risks, and emotional distress. RRP morbidity and mortality results from the effects of papilloma mass on the vocal cords, trachea, and lungs, which may cause voice changes, stridor, airway occlusion, loss of lung volume, and/or post-obstructive pneumonia.[5] Although rare, one to three percent of RRP cases can transform into invasive squamous cell carcinoma.[6,7]

AdenoVerse ™ Immunotherapy Clinical Program

Precigen's AdenoVerse immunotherapy platform is currently under clinical investigation in a Phase 1/2 study of PRGN-2009 AdenoVerse immunotherapy alone or in combination with anti-PDL1/TGF-Beta Trap (bintrafusp alfa) in patients with HPV-associated cancers (NCT04432597), including oropharyngeal squamous cell carcinoma (OPSCC), and a Phase 1/2 study of PRGN-2012 AdenoVerse immunotherapy in patients with recurrent respiratory papillomatosis (RRP) (NCT04724980). PRGN-2012 has been granted Orphan Drug Designation and Breakthrough Therapy Designation in patients with RRP by the FDA. Additionally, the FDA has cleared the IND to initiate a Phase 2 study of PRGN-2009 AdenoVerse immunotherapy in combination with pembrolizumab in patients with recurrent or metastatic cervical cancer.

For patients interested in enrolling in NCI-led clinical studies, please call NCI's toll-free number 1-800-4-Cancer (1-800-422-6237) (TTY: 1-800-332-8615), email NCIMO_Referrals@mail.nih.gov, and/or visit the website: https://trials.cancer.gov.

AdenoVerse ™ Immunotherapy

Precigen's AdenoVerse immunotherapy platform utilizes a library of proprietary adenovectors for the efficient gene delivery of therapeutic effectors, immunomodulators, and vaccine antigens designed to modulate the immune system. Precigen's gorilla adenovectors, part of the AdenoVerse library, have potentially superior performance characteristics as compared to current competition. AdenoVerse immunotherapies have been shown to generate high-level and durable antigen-specific T-cell immune responses as well as an ability to boost these responses via repeat administration. Superior performance characteristics and high yield manufacturing of AdenoVerse vectors leveraging UltraVector® technology allows Precigen to engineer cutting-edge investigational gene therapies to treat complex diseases.

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 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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