Precigen Receives Breakthrough Therapy Designation for PRGN-2012 AdenoVerse™ Immunotherapy for the Treatment of Recurrent Respiratory Papillomatosis

June 20, 2023

– First FDA Breakthrough Therapy Designation granted for AdenoVerse immunotherapy platform; designation prioritizes PRGN-2012 as a potential treatment for RRP –

– Designation based on positive Phase 1 clinical data that showed 50% of patients were "surgery-free" (Complete Response) after PRGN-2012 treatment with a minimum follow up of 12 months post-treatment –

GERMANTOWN, Md. , June 20, 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 granted Breakthrough Therapy Designation for the first-in-class investigational PRGN-2012 AdenoVerse immunotherapy for the treatment of recurrent respiratory papillomatosis (RRP).

FDA's Breakthrough Therapy Designation expedites the development and review of medicines which are intended to treat serious or life-threatening diseases, and in which preliminary clinical evidence demonstrates substantial improvement on clinically significant endpoints over available therapies.

"This Breakthrough Therapy Designation is the first for Precigen's AdenoVerse platform and recognizes the immense potential of PRGN-2012 to change the lives of patients with RRP," said Helen Sabzevari, PhD, President and CEO of Precigen. "Standard-of-care for RRP consists of repeated surgical interventions, and there are currently no approved therapeutics. The potential of PRGN-2012 to reduce surgical interventions and improve outcomes for these patients makes us incredibly proud to receive the FDA's Breakthrough Therapy Designation. This designation will enable our direct engagement with senior leadership at the FDA regarding the most efficient product development pathway, including eligibility for rolling and priority review of a BLA to support a potential PRGN-2012 registration."

PRGN-2012 incorporates optimized antigen design that uses gorilla adenovector technology, part of Precigen's proprietary AdenoVerse platform, to elicit immune responses directed against cells infected with human papillomavirus type 6 (HPV 6) or HPV type 11 (HPV 11). Gorilla adenovectors have numerous advantages, including the ability for repeat administration, the inability to replicate *in vivo,* and the ability to deliver a large genetic payload. PRGN-2012 has previously been granted Orphan Drug Designation in patients with RRP by the FDA.

The Breakthrough Therapy Designation was informed by the clinical evidence for PRGN-2012 generated in the Phase 1 study (NCT04724980), which was presented at Precigen's most recent R&D day, and showed strong response at the recommended phase 2 dose (RP2D) in patients who had an average of 5.8 RRP surgeries (range 3 – 10) in the year prior to PRGN-2012 treatment. PRGN-2012 treatment resulted in 50% of patients (6 out of 12) in Complete Response, requiring no post-treatment surgeries with a minimum follow up of 12 months. PRGN-2012 treatment resulted in a reduction of surgeries in 83% (10 out of 12) patients in the 12 months following treatment. PRGN-2012 induced robust *de novo* HPV-specific T-cell immune response in RRP patients. PRGN-2012 was well-tolerated with no dose-limiting toxicities and no treatment-related adverse events greater than Grade 2. The Phase 1 clinical evidence demonstrating safety and efficacy of PRGN-2012 for the treatment of RRP patients, who have no approved therapeutic option, provides the foundation for this Breakthrough Therapy Designation.

PRGN-2012 is currently being evaluated in a Phase 2 study in adult patients with RRP. Precigen completed enrollment in the Phase 2 study with 23 patients dosed, bringing the total number of enrolled patients to 35 at the RP2D. Patient follow up is ongoing as are discussions with the FDA regarding potential rapid development paths to enable a future submission of a Biologics License Application (BLA).

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]

About PRGN-2012 AdenoVerse Immunotherapy
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. In preclinical models, PRGN-2012 has demonstrated strong and specific immune response against HPV 6 and HPV 11. Precigen's PRGN-2012 AdenoVerse immunotherapy is currently under clinical investigation in a Phase 2 study in adult patients with RRP (NCT04724980). PRGN-2012 has been granted Orphan Drug Designation and Breakthrough Therapy Designation in patients with RRP by the FDA.

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
Precigen, AdenoVerse, UltraVector 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 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

[1] Mounts, P *et al.* (1982). "Viral etiology of juvenile- and adult-onset squamous papilloma of the larynx." *Proc Natl Acad Sci* U S A 79(17): 5425-5429.

[2] Smith, E *et al.* (1993). "Human papillomavirus infection in papillomas and nondiseased respiratory sites of patients with recurrent respiratory papillomatosis using the polymerase chain reaction." *Arch Otolaryngol Head Neck Surg* 119(5): 554-557.

[3] Derkay, CS *et al.* (2008). "Recurrent respiratory papillomatosis: a review." *Laryngoscope* 118(7): 1236-1247.

[4] Derkay, CS *et al.* (2019). "Update on Recurrent Respiratory Papillomatosis." *Otolaryngol Clin North Am* 52(4): 669-679.

[5] Seedat, RY (2020). "Juvenile-Onset Recurrent Respiratory Papillomatosis Diagnosis and Management - A Developing Country Review." *Pediatric Health Med Ther* 11: 39-46.

[6] Dedo, HH *et al.* (2001). "CO(2) laser treatment in 244 patients with respiratory papillomas." *Laryngoscope* 111(9): 1639-1644.

[7] Silver, RD *et al.* (2003). "Diagnosis and management of pulmonary metastasis from recurrent respiratory papillomatosis." *Otolaryngol Head Neck Surg* 129(6): 622-629.

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

View original content to download multimedia:https://www.prnewswire.com/news-releases/precigen-receives-breakthrough-therapy-designation-for-prgn-2012-adenoverse-immunotherapy-for-the-treatment-of-recurrent-respiratory-papillomatosis-301854546.html

SOURCE Precigen, Inc.