Precigen Announces Groundbreaking Pivotal Study Data for PRGN-2012 in Patients with Recurrent Respiratory Papillomatosis in Which More than Half of Patients Achieved Complete Response

Jun 03, 2024

– Phase 1/2 pivotal study met the primary safety and efficacy endpoints –

– 51% (18 out of 35) of patients achieved Complete Response, requiring no surgeries after treatment with PRGN-2012; complete responses have been durable beyond 12 months with median duration of follow up of 20 months as of data cutoff –

– 86% of patients (30 out of 35) had a decrease in surgical interventions in the year after PRGN-2012 treatment compared to the year prior to treatment; RRP surgeries reduced from a median of 4 pre-treatment to 0 post-treatment –

– PRGN-2012 was well-tolerated with no dose-limiting toxicities and no treatment-related adverse events greater than Grade 2 –

– PRGN-2012 treatment induced HPV 6/11-specific T cell responses in RRP patients with a significantly greater expansion of peripheral HPV-specific T cells in responders compared with non-responders –

– PRGN-2012 significantly ($p < 0.0001$) improved Derkay and quality of life scores in complete responders –

– RRP is a rare, devastating HPV-mediated chronic disease characterized by growth of benign tumors for which the current standard-of-care is repeated surgeries; if approved, PRGN-2012 has the potential to be the first FDA-approved therapeutic for the treatment of RRP –

– Clinical data associated with favorable safety, strong efficacy, ease of administration, and immunological responses, position PRGN-2012 to potentially be the preferred treatment-of-choice for RRP –

– PRGN-2012 rolling BLA submission, under an accelerated approval pathway, is anticipated in the second half of 2024 –

– Precigen to host webcast event today at 6:00 PM CT / 7:00 PM ET –

GERMANTOWN, Md., June 3, 2024 /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 released positive Phase 1/2 pivotal study results for the investigational PRGN-2012 off-the-shelf (OTS) AdenoVerse® gene therapy in patients with recurrent respiratory papillomatosis (RRP). Results were presented in a late-breaking oral presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting by Scott M. Norberg, DO, Associate Research Physician, Center for Immuno-Oncology, Center for Cancer Research, National Cancer Institute and a lead investigator for the PRGN-2012 clinical study. The Company will host a webcast event today at 6:00 PM CT / 7:00 PM ET to detail the results presented at ASCO.

"We are thrilled with the results of the Phase 1/2 pivotal study showing more than half of patients were surgery free–Complete Response–and 86% of patients had a significant reduction in the need for surgeries after PRGN-2012 treatment. Based on the efficacy, safety, and ease of administration, we believe PRGN-2012 is a game-changer for RRP patients and has the potential to be the preferred treatment-of-choice for RRP," said Helen Sabzevari, PhD, President and CEO of Precigen. "We look forward to sharing these results with the FDA as part of a rolling Biologics License Application submission under an accelerated approval pathway. We have ramped up our commercial readiness efforts in anticipation of a potential launch in 2025 and are excited by the potential to bring a long overdue new treatment option to the RRP community."

Pivotal Study Design and Endpoints

The Phase 1/2 clinical study (clinical trial identifier: NCT04724980) evaluated safety and efficacy of PRGN-2012. The study design included an initial 3+3 dose escalation cohort to identify the recommended Phase 2 dose (RP2D). Adult RRP patients who had three or more surgeries in the prior 12 months were eligible for the study. The Phase 1/2 study enrolled a total of 38 patients. Of these, 3 patients received four administrations of PRGN-2012 at 1x 10^{11} particle units (PU)/dose and 35 patients received four administrations of PRGN-2012 at RP2D (5 x 10^{11} PU/dose) over a 12 week treatment period via subcutaneous injection.

Primary endpoints included safety and Complete Response rate defined as the percentage of patients who require no RRP surgeries in the 12-month period after PRGN-2012 treatment completion. Key secondary endpoints included HPV-specific immune responses, extent of papilloma growth as measured by Derkay scoring, and quality of life measurement as measured by Vocal Handicap Index-10 (VHI-10).

Patient Characteristics

Baseline patient characteristics of the 35 adult patients included a median age of 49 years (range: 20-88); 20 of the patients were male and 15 were female. Patients had a median of 4 surgeries (range: 3-10) in the 12 months before PRGN-2012 treatment initiation. Average years since RRP diagnosis was 20 (range: 1-65) with 12 and 23 patients with juvenile and adult onset RRP, respectively.

Clinical Efficacy

Primary efficacy endpoint analysis demonstrated that 51% (18 out of 35) (95% CI: 34-69) patients achieved Complete Response, defined as no need for RRP surgeries in the 12-month period following completion of PRGN-2012 treatment. The Complete Response rate was 50% (6 out of 12) and 52% (12 out of 23) in the Phase 1 and Phase 2 portions of the study, respectively (TABLE 1). Complete Responses were durable. Median durability of response has not yet been reached with median follow up of 20 months as of the data cutoff date of May 20, 2024. PRGN-2012 treatment significantly

($p < 0.0001$) reduced the need for surgeries in RRP patients compared to pre-treatment history (FIGURE 1). PRGN-2012 treatment reduced the need for RRP surgeries in 86% (30 out of 35) of patients compared to their pre-treatment history. RRP surgeries were reduced from a median of 4 (range: 3-10) in the 12 months pre-treatment to 0 (range: 0-7) in the 12 months post PRGN-2012 treatment completion.

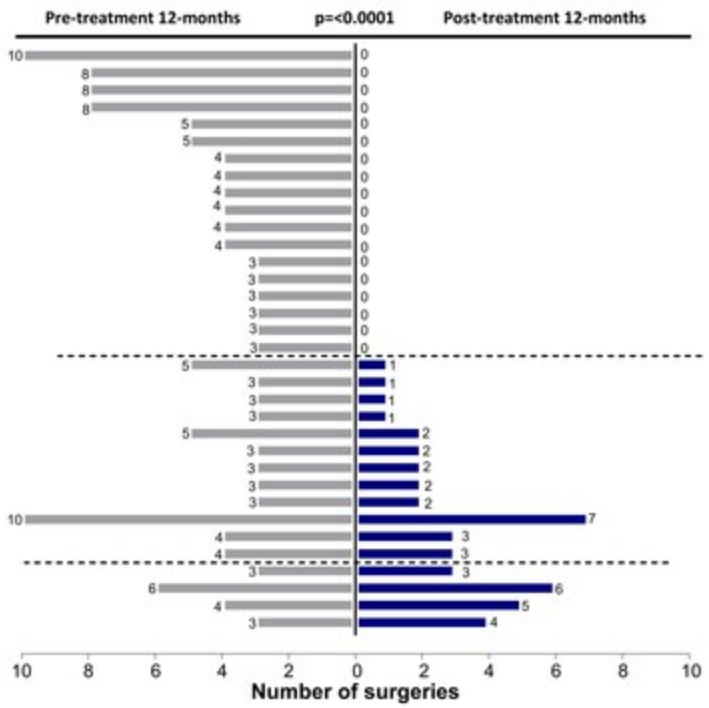
PRGN-2012 treatment showed significant ($p < 0.0001$) improvement in anatomical Derkay scores, a tool used for research purposes to quantify RRP severity based on involvement of laryngeal structures, with mean Derkay scores reducing from 9 (range: 5-19) at baseline to 1 (range: 0-5) at 24 weeks post-treatment in patients with Complete Response. Quality of life, as evaluated using the validated VHI-10, significantly ($p < 0.0001$) improved from a mean of 25 (range: 12-38) at baseline to 7 (range: 0-30) at 24 weeks post PRGN-2012 treatment in patients with Complete Response. PRGN-2012 treatment induced HPV 6/11-specific T cell responses in RRP patients with a significantly greater expansion of peripheral HPV-specific T cells observed in responders compared with non-responders.

TABLE 1: Clinical Efficacy Summary

Total Patients (N=35)

	Phase 1 (N=12)	**Phase 2 (N=23)**	**Phase 1/2 Total (N=35)**
Complete Response No surgeries needed during 12 months post-treatment	**50% (6/12)**	**52% (12/23)**	**51% (18/35)**
Decrease in Rate of Surgery 12 months post-treatment compared to 12 months pre-treatment	**83% (10/12)**	**87% (20/23)**	**86% (30/35)**

FIGURE 1: PRGN-2012 Demonstrated Significant Clinical Efficacy (51% Complete Response Rate; 86% Patients had a Reduction in Surgeries)



Safety

PRGN-2012 treatment was well-tolerated with no dose-limiting toxicities and no treatment-related adverse events (TRAEs) greater than Grade 2 (TABLE 2). All patients received four administrations of PRGN-2012 at the intended dose levels. TRAEs were mostly mild with no treatment-related serious adverse events reported. The most common TRAE was injection site reaction. Other common TRAEs occurring in more than one subject were fatigue, chills, and fever. There was no meaningful anti-drug antibody response with repeat administrations of PRGN-2012.

TABLE 2: Treatment-related Adverse Events Occurring in More Than 1 Patient

Total Patients (N=38)

	1×10^{11} PU (N = 3)		**5×10^{11} PU (N=35)**	
	Grade 1	**Grade 2**	**Grade 1**	**Grade 2**
Event	**(N, %)**	**(N, %)**	**(N, %)**	**(N, %)**
Chills	-	-	25 (71 %)	-
Fatigue	-	-	28 (80 %)	2 (6 %)
Fever	-	-	24 (69 %)	-
Headache			2 (6 %)	

Hyperhidrosis	-	-	2 (6 %)	-
Injection site reaction	3 (100 %)	-	34 (97 %)	-
Myalgia	-	-	9 (26 %)	2 (6 %)
Nausea	-	-	8 (23 %)	-
Vomiting	-	-	2 (6 %)	-

About RRP
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. 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®
Precigen's AdenoVerse 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 gene therapies 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.

About PRGN-2012 AdenoVerse® Gene Therapy
PRGN-2012 is an investigational off-the-shelf AdenoVerse gene therapy designed to elicit immune responses directed against cells infected with human papillomavirus (HPV) 6 or HPV 11 for the treatment of RRP. PRGN-2012 was the first to receive Breakthrough Therapy Designation and an accelerated approval pathway for RRP from the US Food and Drug Administration (FDA). PRGN-2012 received Orphan Drug Designation from the FDA and from the European Commission. Results from the Phase 1 portion of the Phase 1/2 study were published in the peer-reviewed journal, *Science Translational Medicine*, a leading publication from the American Association for the Advancement of Science (AAAS).

AdenoVerse® Clinical Programs
Precigen's AdenoVerse platform is currently under clinical investigation in a Phase 1/2 study of PRGN-2009 alone or in combination with an anti-PDL1/TGF-Beta Trap in patients with HPV-associated cancers (NCT04432597), a Phase 2 study of PRGN-2009 in combination with pembrolizumab in newly diagnosed patients with HPV-associated oropharyngeal squamous cell carcinoma (OPSCC) (NCT05996523), a Phase 2 study of PRGN-2009 in combination with pembrolizumab in patients with recurrent or metastatic cervical cancer (NCT06157151), and a Phase 1/2 study of PRGN-2012 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 and Orphan Drug Designation by the European Commission.

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 X @Precigen, LinkedIn or YouTube.

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.

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

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.

PRECIGEN

ADVANCING MEDICINE WITH PRECISION™

View original content to download multimedia:https://www.prnewswire.com/news-releases/precigen-announces-groundbreaking-pivotal-study-data-for-prgn-2012-in-patients-with-recurrent-respiratory-papillomatosis-in-which-more-than-half-of-patients-achieved-complete-response-302161493.html

SOURCE Precigen, Inc.