Precigen Announces Positive Phase 1 Data for Off-the-Shelf PRGN-2009 AdenoVerse™ Immunotherapy Alone and in Combination with an Investigational Checkpoint Inhibitor in Patients with Recurrent/Metastatic HPV-associated Cancers

Jun 03, 2023

– PRGN-2009 combined with an investigational checkpoint inhibitor resulted in a 30% ORR in patients with heavily pre-treated HPV-associated cancers that were naïve or resistant to checkpoint blockade with prolonged duration of responses –

– Recurrent/metastatic HPV-associated cancers (cervical, anal, oropharyngeal, etc.) are incurable by current therapies –

– PRGN-2009 was safe and well-tolerated with only Grade 1 or 2 treatment related adverse events –

– PRGN-2009 treatment induced HPV-specific T-cell immune responses and subsequently enhanced T-cell responses with repeat administrations without the development of neutralizing antibodies in the majority of patients –

GERMANTOWN, Md., June 3, 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 presented positive clinical data from the Phase 1 study of the off-the-shelf (OTS) PRGN-2009 AdenoVerse ™immunotherapy alone and in combination with an investigational anti-PDL1/TGF-Beta Trap checkpoint inhibitor (bintrafusp alfa) in patients with recurrent/metastatic (R/M) HPV-associated cancers (clinical trial identifier: NCT04432597) at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract# 2628).

"Recurrent/metastatic HPV-associated cancers such as cervical, anal, and oropharyngeal are incurable by current therapies and there remains significant unmet need for new safe and effective treatments. Checkpoint inhibitors alone have shown some promise, but have not produced durable responses and many patients relapse or become resistant," said Helen Sabzevari, PhD, President and CEO of Precigen. "In our Phase 1 study, combining PRGN-2009 with checkpoint inhibition demonstrated a favorable safety profile and resulted in a 30% ORR with prolonged duration of responses in patients with heavily pre-treated HPV-associated cancers, including those who were checkpoint blockade resistant. We are highly encouraged by these Phase 1 data and, as we announced on May 31, we are moving rapidly to initiate a Phase 2 study to combine PRGN-2009 with a checkpoint inhibitor to further investigate safety and efficacy in recurrent or metastatic cervical cancer. This new trial is the second Phase 2 for PRGN-2009 AdenoVerse, adding to the ongoing Phase 2 in oropharyngeal squamous cell carcinoma."

PRGN-2009 is an OTS investigational immunotherapy utilizing the AdenoVerse platform designed to activate the immune system to recognize and target HPV-positive (HPV^+) solid tumors. PRGN-2009 is a novel, replication-incompetent gorilla adenovirus targeting HPV 16/18. PRGN-2009 can be administered repeatedly leading to enhancement of T-cells without increasing neutralizing antibodies. PRGN-2009 is under development through a Cooperative Research and Development Agreement, or CRADA, within the Center for Immuno-Oncology (CIO), Center for Cancer Research (CCR), National Cancer Institute (NCI), part of the National Institutes of Health (NIH).

The Phase 1 trial is an open label, single-center study evaluating safety and response of PRGN-2009 as a monotherapy (Arm A) and in combination with bintrafusp alfa (Arm B) in previously treated adult patients with R/M HPV-associated cancers. In the monotherapy arm, patients (N = 6) enrolled in two sequential PRGN-2009 dose level cohorts, Dose Level 1 ($1x10^{11}$ particle units (PU)) and Dose Level 2 ($5x10^{11}$ PU) delivered via subcutaneous injection. In the combination arm, PRGN-2009 was administered at the recommended phase 2 dose (RP2D) in combination with bintrafusp alfa.

The primary objective of the study was to evaluate safety and RP2D of PRGN-2009 and safety of PRGN-2009 in combination with a checkpoint inhibitor. Secondary objectives included Objective Response Rate (ORR) (per RECIST 1.1), and progression free survival (PFS).

Patient Characteristics
Seventeen adult patients were enrolled in the Phase 1 study (Table 1). Patients received up to 20 doses of PRGN-2009 for a duration of 1.8 to 17.9 months in the monotherapy arm and 0.5 to 23.0 months in the combination arm. The median age in both arms was 61. The median number of prior lines of therapies in the metastatic setting was 2.5 for the monotherapy arm and 2 for the combination arm. All patients in the monotherapy arm (N=6) and 10 of 11 patients in the combination arm received prior immune checkpoint blockade (ICB) therapy.

Table 1. Patient Demographics and Clinical Characteristics

	Monotherapy Arm (N=6)	**Combination Arm (N=11)**
Age, years (median, range)	61 (43-70)	61 (54-80)
Female, n (%)	6 (100)	3 (27)
Tumor types (n,%)		
Oropharyngeal	-	7 (63.6)
Cervical	3 (50.0)	3 (27.3)
Anal	2 (33.3)	1 (9.1)
Vaginal	1 (16.7)	-

HPV status (n, %)		
HPV16	3 (50)	9 (81.8)
HPV18	-	1 (9.1)
Other	2 (33.3)	1 (9.1)
N/A	1 (16.7)	-
Previous lines of therapy in metastatic setting, median (range)	2.5 (2-3)	2 (1-4)
ICB exposure, n (%)	6 (100)	10 (90.9)
Primary resistance	4 (66.7)	5 (50)
Secondary resistance	2 (33.3)	5 (50)

Safety Data

PRGN-2009 treatment in both monotherapy and combination arms was safe and well-tolerated (Table 2). In both study arms, there was a low incidence of treatment-related adverse events (TRAEs) with only Grade 1 or 2 TRAEs in the monotherapy arm. The most common TRAEs in the monotherapy arm were injection site reactions, flu-like symptoms, fatigue and rash. In addition to these in the combination arm, patients also experienced Grade 1 or 2 epistaxis, headache, keratoacanthoma, fever, decreased lymphocyte count, anemia and oral hemorrhage. TRAEs reported in the combination arm were in line with the safety profile reported for bintrafusp alfa and only Grade 1 or 2 TRAEs were attributable to PRGN-2009 in the combination arm.

Table 2: Safety Data

	Monotherapy Arm (N=6)		**Combination Arm (N=11)**	
Treatment-related adverse events, n (%)	Grade 1-2 (all)	Grade 3-4 (all)	Grade 1-2 (≥10%)	Grade 3-4 (all)
Injection site reactions	4 (66.7)	0	9 (81.8)	0
Flu-like symptoms,	3 (50.0)	0	6 (54.5)	0
Fatigue	2 (33.3)	0	3 (27.3)	0
Rash, maculopapular	1 (16.7)	0	3 (27.3)	0
Epistaxis	0	0	3 (27.3) *	0
Headache	0	0	3 (27.3)	0
Keratoacanthoma	0	0	3 (27.3)*	0
Fever	0	0	2 (18.2)	0
Lymphocyte count, decreased	0	0	2 (18.2)*	0
Anemia	0	0	2 (18.2)*	0
Oral hemorrhage	0	0	2 (18.2)*	0
Duodenal Hemorrhage	0	0	0	2 (18.2)*†‡
Pharyngeal mucositis	0	0	0	1 (9.1) *

*Attributed to bintrafusp alfa; † both patients concurrently receiving NSAIDs; ‡ 1 patient died following refusal of standard supportive medical management measures (blood transfusion).

Clinical Activity

Tumor responses were observed in patients after treatment with PRGN-2009 in combination with bintrafusp alfa (Arm 1B), including in ICB-resistant patients (Table 3). PRGN-2009 combined with bintrafusp alfa resulted in a 30% ORR in patients with pretreated R/M HPV-associated cancers with prolonged duration of responses (Table 3, Figure 1). The majority of patients developed HPV-16 and/or HPV-18 specific immune responses after treatment with PRGN-2009 in both monotherapy and combination arms (Table 4) without the development of neutralizing antibodies (Figure 2).

Table 3: Best Response by Arm

	Monotherapy Arm	**Combination Arm**
Evaluable patients, n	6	10
Best response, n		
CR	-	1[a]
PR	-	2[c,d]
SD	4[b]	1
PD	2	6
ORR, % (95% CI)	-	**30 (6.7-65.3)**

[a] immune checkpoint blockade (ICB)-resistant; [b] 1 SD confirmed; [c] 1 PR confirmed; [d] 1 ICB-resistant, 1 TCR treatment-resistant; 2 patients treated beyond progression without delayed response; CI: confidence interval

Figure 1: Time to Response and Duration of Response to Treatment

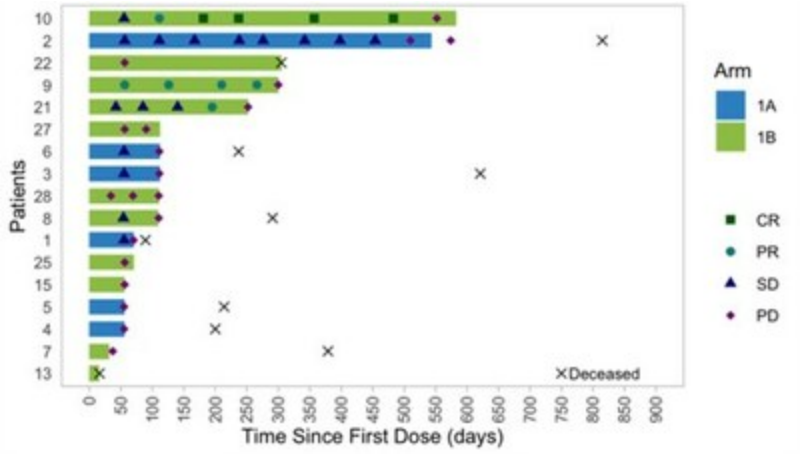
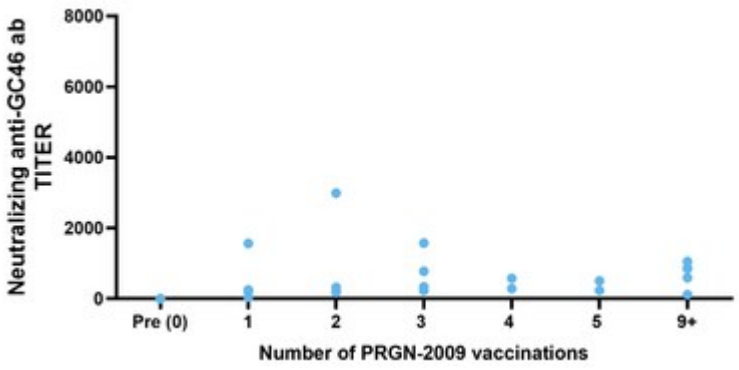


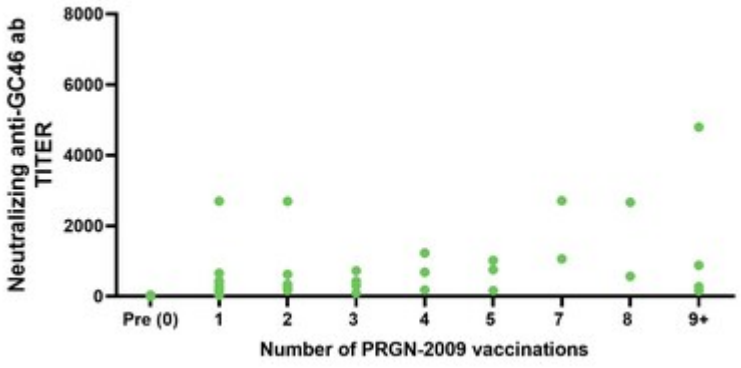
Table 4: HPV-specific T-cell Immune Responses

	Monotherapy Arm	Combination Arm
HPV-16, n/N (%)	5/6 (83)	7/10 (70)
HPV-18, n/N (%)	5/6 (83)	7/8 (88)
HPV-16 and/or HPV-18 n/N (%)	6/6 (100)	8/10 (80)

N: number of patients tested

Figure 2: Neutralizing Antibodies





Phase 2 Clinical Study in Newly Diagnosed Oropharyngeal Squamous Cell Carcinoma

The Phase 2 portion of the study is ongoing at the RP2D and enrollment was completed in the monotherapy arm with 20 evaluable patients with newly diagnosed oropharyngeal squamous cell carcinoma (OPSCC). An interim clinical data presentation from the Phase 2 monotherapy arm is expected in the second half of 2023.

Phase 2 Randomized Control Study in Recurrent or Metastatic Cervical Cancer

The Company recently announced that the US Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application to initiate a Phase 2 study of the first-in-class PRGN-2009 OTS AdenoVerse ™ immunotherapy in combination with pembrolizumab in patients with recurrent or metastatic cervical cancer. The Phase 2 randomized, open-label, two-arm, multicenter study will evaluate the efficacy and safety of PRGN-2009 in combination with pembrolizumab versus pembrolizumab monotherapy in patients with recurrent or metastatic cervical cancer who are pembrolizumab resistant.

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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.

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.

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), a Phase 2 study of PRGN-2009 AdenoVerse immunotherapy in combination with pembrolizumab in patients with recurrent or metastatic cervical cancer, and a Phase 2 study of PRGN-2012 AdenoVerse immunotherapy in patients with recurrent respiratory papillomatosis (RRP) (NCT04724980). PRGN-2012 has been granted Orphan Drug Designation in patients with RRP by the FDA.

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.

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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 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.

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