PepGen Announces CONNECT Program Updates

January 29, 2025

BOSTON--(BUSINESS WIRE)--Jan. 29, 2025-- PepGen Inc. (Nasdaq: PEPG), a clinical-stage biotechnology company advancing the next generation of oligonucleotide therapies with the goal of transforming the treatment of severe neuromuscular and neurological diseases, today provided recent updates on its CONNECT clinical program investigating PGN-EDO51 in Duchenne muscular dystrophy (DMD) for patients amenable to an exon-51 skipping approach.

CONNECT1-EDO51: Phase 2, open-label, multiple ascending dose (MAD) clinical trial being conducted in Canada.

CONNECT1 has enrolled two cohorts of boys and young men living with DMD amenable to exon 51 skipping and its endpoints include safety and tolerability, dystrophin production, exon skipping, and muscle tissue concentration. The 10 mg/kg cohort is fully enrolled (n=4) and participants in the 5 mg/kg cohort (n=3) are continuing to dose at that level in the long-term extension portion of the study. The Company remains on track to report clinical data from the 10 mg/kg cohort by year-end 2025.

Magnesium levels in two of the participants in the 10 mg/kg cohort, who were previously reported as having asymptomatic hypomagnesemia, have returned to baseline levels with administration of ongoing oral magnesium supplementation. Dosing of one of these two participants was paused due to a reduction of his estimated glomerular filtration rate (eGFR). This event did not meet the pre-specified criteria for a dose limiting toxicity. A subsequent nuclear scan indicated measured glomerular filtration rate was in the normal range. The participant's eGFR is improving and the investigator is evaluating for the resumption of dosing as this value normalizes. The Company is continuing to review the event and associated potential confounding factors to better understand its manifestation.

The Company has received communication from Health Canada that dosing of patients in the 5 and 10 mg/kg cohorts may continue at their current dose levels and has requested additional information from the Company to address Health Canada's safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels. The Company is working with Health Canada to address its questions.

CONNECT2-EDO51: Phase 2, multinational, double-blind, placebo-controlled, MAD clinical trial currently open in the United Kingdom.

CONNECT2 will enroll boys and young men amenable to exon 51 skipping and its endpoints include safety and tolerability, dystrophin production, exon skipping, and functional outcome measures. In December, the Company announced that it had received a clinical hold notice from the US Food and Drug Administration (FDA) regarding its Investigational New Drug application to initiate the CONNECT2 clinical trial in the US, which was previously authorized to proceed by the UK's Medicines and Healthcare products Regulatory Agency (MHRA). The Company is working with the FDA to address its questions regarding supportive data for the dosing levels planned for the patient population.

Paul Streck, MD, Head of R&D, commented, "As of January 23, 2025, all treatment related adverse events in CONNECT1 have been mild, and we believe that the emerging safety profile of PGN-EDO51 remains favorable. We are encouraged that the decreased eGFR reported for one of our CONNECT1 10 mg/kg cohort patients has improved during his brief pause in dosing. We are evaluating the etiology, and we will continue to closely monitor safety in our PGN-EDO51 clinical program. We look forward to providing clinical data updates from both CONNECT1 and our FREEDOM-DM1 study in myotonic dystrophy type 1 during 2025, including initial data from FREEDOM during the first quarter, as well as an update on the status of CONNECT2, as we continue to advance our platform with a focus on addressing patients in need."

About PGN-EDO51

PGN-EDO51, PepGen's investigational candidate in development for the treatment of DMD, utilizes the Company's proprietary Enhanced Delivery Oligonucleotide (EDO) technology to deliver a therapeutic oligonucleotide that is designed to target the root cause of this devastating disease. PGN-EDO51 is designed to skip exon 51 of the dystrophin transcript, an established therapeutic target for approximately 13% of DMD patients, thereby aiming to restore the open reading frame and enabling the production of a truncated, yet functional dystrophin protein. The US Food and Drug Administration has granted PGN-EDO51 both Orphan Drug and Rare Pediatric Disease Designations for the treatment of patients with DMD amenable to an exon-51 skipping approach.

About PGN-EDODM1

PGN-EDODM1, PepGen's investigational candidate in development for the treatment of myotonic dystrophy type 1 (DM1), utilizes the Company's proprietary EDO technology to deliver a therapeutic oligonucleotide that is designed to restore the normal splicing function of MBNL1, a key RNA splicing protein. DM1 is a progressively disabling, life-shortening genetic disorder. DM1 is estimated to affect 40,000 people in the United States, and over 74,000 people in Europe. The US Food and Drug Administration has granted PGN-EDODM1 both Orphan Drug and Fast Track Designations for the treatment of patients with DM1.

About PepGen

PepGen is a clinical-stage biotechnology company advancing the next generation of oligonucleotide therapies with the goal of transforming the treatment of severe neuromuscular and neurological diseases. PepGen's EDO platform is founded on over a decade of research and development and leverages cell-penetrating peptides to improve the uptake and activity of conjugated oligonucleotide therapeutics. Using these EDO peptides, we are generating a pipeline of oligonucleotide therapeutic candidates designed to target the root cause of serious diseases.

For more information, please visit PepGen.com. Follow PepGen on LinkedIn and X.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will," and variations of these words or similar expressions that are intended to identify forward-looking

statements. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include, without limitation, statements regarding the ongoing status of our CONNECT1 and CONNECT2 Phase 2 trials of PGN-EDO51, including recent safety and dosing updates, the expected timing for additional data reports from our CONNECT1 Phase 2 trial, and our data from our FREEDOM Phase 1 trial, and ongoing and planned regulatory interactions.

Any forward-looking statements in this press release are based on current expectations, estimates and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to risks related to: delays or failure to successfully initiate or complete our ongoing and planned development activities for our product candidates, including PGN-EDO51 and PGN-EDODM1; our ability to enroll patients in our clinical trials, including CONNECT1, CONNECT2, FREEDOM and FREEDOM2; that our interpretation of clinical and preclinical study results may be incorrect, or that we may not observe the levels of therapeutic activity in clinical testing that we anticipate based on prior clinical or preclinical results, including for PGN-EDO51 and PGN-EDODM1; our product candidates, including PGN-EDO51 and PGN-EDODM1, may not be safe and effective or otherwise demonstrate safety and efficacy in our clinical trials; adverse outcomes from our regulatory interactions, including delays in regulatory review, clearance to proceed or approval by regulatory authorities with respect to our programs, including clearance to commence planned clinical studies of our product candidates, or other regulatory feedback requiring modifications to our development programs, including in each case with respect to our CONNECT1, CONNECT2, FREEDOM and FREEDOM2 clinical trials; changes in regulatory framework that are out of our control; unexpected increases in the expenses associated with our development activities or other events that adversely impact our financial resources and cash runway; and our dependence on third parties for some or all aspects of our product manufacturing, research and preclinical and clinical testing. Additional risks concerning PepGen's programs and operations are described in our most recent annual report on Form 10-K and quarterly report on Form 10-Q that are filed with the SEC. PepGen explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

This release discusses PGN-EDO51 and PGN-EDODM1, investigational therapies that have not been approved for use in any country and is not intended to convey conclusions about their efficacy or safety. There is no guarantee that PGN-EDO51, PGN-EDODM1 or any other investigational therapy will successfully complete clinical development or gain regulatory authority approval.

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