PepGen Announces Update to Phase 2 CONNECT2-EDO51 Study in Patients with DMD

March 4, 2025

Company will temporarily pause CONNECT2 and focus efforts on ongoing CONNECT1-EDO51 study of PGN-EDO51 in DMD, with 10 mg/kg results expected in the third quarter of 2025

No new safety issues have been observed in PGN-EDO51 program

BOSTON--(BUSINESS WIRE)--Mar. 4, 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 announced its voluntary decision to temporarily pause the Phase 2 CONNECT2-EDO51 study of PGN-EDO51 in patients with Duchenne muscular dystrophy (DMD) until the Company can review results from the 10 mg/kg cohort in the ongoing Phase 2 CONNECT1-EDO51 study. The first two cohorts of the CONNECT1 study are fully enrolled and data from the 10 mg/kg cohort are expected during the third quarter of 2025. No new safety issues related to PGN-EDO51 have been observed since the Company's last safety update as of January 23, 2025.

"With our 10 mg/kg cohort of CONNECT1 study fully enrolled and data expected later this year, we decided to pause CONNECT2 until we are able to review results from the 10 mg/kg cohort in patients with DMD. This will allow us to gather additional safety data, assess the impact of this dose of PGN-EDO51 on dystrophin levels, and potentially improve the design of CONNECT2," said James McArthur, PhD, President and CEO of PepGen. "This decision enables us to focus resources on completing CONNECT1, as well as rapidly advancing our FREEDOM studies in myotonic dystrophy type 1 with PGN-EDODM1, in which we recently reported encouraging initial clinical data from the Phase 1 FREEDOM-DM1 study."

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 U.S. Food and Drug Administration (FDA) 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 the CONNECT Clinical Program

CONNECT1-EDO51 is an open-label, multiple ascending dose Phase 2 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 phase of the study. 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 is a double-blind, placebo-controlled, multiple ascending dose Phase 2 trial designed to evaluate PGN-EDO51 at dose levels administered intravenously once every four weeks for 24 weeks in patients with DMD amenable to an exon 51-skipping approach. 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 FDA regarding its Investigational New Drug application to initiate the CONNECT2 clinical trial in the U.S. The Company is working with the FDA to address its questions regarding supportive data for the dosing levels planned for the patient population.

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 voluntary pause of the CONNECT2-EDO51 study to enable review of additional results from the CONNECT1-EDO51 study expected in the third quarter of 2025, the advancement of our FREEDOM studies, the therapeutic potential and safety profile of our product candidates, PGN-EDO51 and PGN-EDODM1, including based on early clinical data, the expected timing for an additional data report from our CONNECT1 Phase 2 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 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-Kthat is 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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