PepGen Announces Highest Mean Splicing Correction Reported in DM1 Patients

September 24, 2025

– 53.7% mean splicing correction observed following a single 15 mg/kg dose of PGN-EDODM1, with all patients showing an improvement in splicing –

– PGN-EDODM1 was generally well-tolerated at 15 mg/kg, with drug-related adverse events mild or moderate in severity –

BOSTON--(BUSINESS WIRE)--Sep. 24, 2025-- PepGen Inc. (Nasdaq: PEPG), a clinical-stage biotechnology company developing the next generation of oligonucleotide therapies with the goal of transforming the treatment of severe neuromuscular and neurological diseases, announced positive clinical data today from the 15 mg/kg dose cohort of its ongoing FREEDOM-DM1 Phase 1 single ascending dose (SAD) study in patients with myotonic dystrophy type 1 (DM1). These latest results demonstrated a mean splicing correction of 53.7% following a single 15 mg/kg dose of PGN-EDODM1, substantially higher than any previously reported splicing correction in DM1 patients.

“We are delighted to report that the FREEDOM clinical study achieved all of its key objectives, including unprecedented splicing correction following a single dose of PGN-EDODM1 at 15 mg/kg,” said Paul Streck, MD, MBA, Executive Vice President of Research and Development at PepGen. “Since mis-splicing is the underlying cause of DM1, we believe high levels of splicing correction have the potential to reverse the underlying molecular defects, and produce functional improvements in multiple outcome measures, including myotonia and muscle weakness, in repeat dose studies.”

James McArthur, PhD, PepGen’s President and Chief Executive Officer, added, “These data build upon and reinforce our previously reported splicing correction levels seen in the FREEDOM single dose cohorts of 5 and 10 mg/kg of PGN-EDODM1. Additionally, we are excited to report that 100% of patients in the 15 mg/kg cohort of our FREEDOM trial showed improved splicing correction following treatment. We look forward to reporting data from the first cohort of FREEDOM2, our multiple ascending dose (MAD) study currently underway, in the first quarter of 2026.”

FREEDOM Results for the 15 mg/kg (n=8) Dose Cohort

Splicing and Muscle Concentration Data:

- Mean splicing correction of 53.7% in patients receiving 15 mg/kg of PGN-EDODM1 (n=6), as measured by the 22-gene panel[1] at 28 days post-dosing. The Company previously reported mean splicing correction at 5 mg/kg (n=6) and at 10 mg/kg (n=4)[2, 3] of 12.3% and 29.1%, respectively, demonstrating greater than dose-proportional increases in splicing correction.
- All six patients (100%) receiving a 15 mg/kg dose of PGN-EDODM1 responded to treatment by showing improved splicing correction.
- In addition, greater than dose-proportional increases in muscle tissue concentrations of PGN-EDODM1 were observed across 5 mg/kg (n=6), 10 mg/kg (n=5)[2] and 15 mg/kg (n=6) at Day 28.

Safety Data:

- PGN-EDODM1 was generally well-tolerated at 15 mg/kg, with no serious treatment-related adverse events (AEs). All treatment-related AEs at 15 mg/kg were mild or moderate, transient, and with the exception of one patient (who received oral OTC antihistamines), did not require intervention.
- There were no electrolyte-related AEs, including an absence of hypomagnesemia AEs.
- All renal biomarker-related AEs were asymptomatic, transient (~48hrs) and resolved without intervention. A transient and reversible kidney biomarker elevation in one patient qualified as a dose-limiting toxicity, as defined by the study protocol, and was classified as a mild AE, which resolved without intervention. The patient remained in study.

PepGen anticipates reporting results from the FREEDOM2-DM1 MAD study 5 mg/kg cohort in the first quarter of 2026, and also expects to begin dosing its 10 mg/kg cohort in the first quarter of 2026.

A copy of our corporate presentation including these results will be posted on the Events & Presentations section of the PepGen investor website, investors.pepgen.com.

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 Enhanced Delivery Oligonucleotide (EDO) technology to deliver a therapeutic oligonucleotide that is designed to restore the normal

splicing function of MBNL1, a key RNA splicing protein. PGN-EDODM1 addresses the deleterious effects of cytosine-uracil-guanine (CUG) repeat expansion in the dystrophia myotonic protein kinase (*DMPK)* transcripts which sequester MBNL1, by binding to the pathogenic CUG trinucleotide repeat expansion present in the *DMPK* transcripts, and disrupting the binding between the CUG repeat expansion and MBNL1. PepGen believes this innovative therapeutic approach may have considerable advantages over oligonucleotide modalities that rely on knockdown or degradation of the *DMPK* transcripts as it will allow the *DMPK* transcripts to continue to perform their normal function within the cell, while also liberating MBNL1 to correct downstream mis-splicing events. The U.S. Food and Drug Administration has granted PGN-EDODM1 both Orphan Drug and Fast Track Designations for the treatment of patients with DM1.

About the FREEDOM Clinical Program

FREEDOM-DM1 is a multinational, randomized, double-blind, placebo-controlled Phase 1 single ascending dose (SAD) study, enrolling 24 adult participants with DM1 in multiple geographies including the United States, the United Kingdom (UK) and Canada, to evaluate the safety and tolerability of PGN-EDODM1. Per the protocol, PGN-EDODM1 was administered at starting doses of 5 mg/kg and 10 mg/kg with subsequent dose escalation to 15 mg/kg, based upon evaluation by a data safety monitoring board of safety data from the prior dose cohort(s). Muscle biopsies are being conducted at baseline, at Day 28 and at Week 16. In addition to safety and tolerability, oligonucleotide muscle concentrations, splicing correction and functional outcome measures are being assessed at Day 28 and at Week 16 following a single dose of PGN-EDODM1.

FREEDOM2-DM1 is a Phase 2 randomized, double-blind, placebo-controlled, multiple ascending dose clinical trial evaluating PGN-EDODM1 in approximately 24 adult participants with DM1 in Canada, the United Kingdom, and potentially other geographies, including the United States, subject to regulatory clearances. An Open Label Extension study (PGN-EDODM1-OLE) is cleared by the UK Medicines and Healthcare products Regulatory Agency and Health Canada. FREEDOM and FREEDOM2 patients will have the opportunity to participate in that study.

About Myotonic Dystrophy Type 1

Myotonic dystrophy type 1 (DM1) is a monogenic, autosomal dominant, progressive disorder that primarily affects skeletal, cardiac and smooth muscle, with central nervous system symptoms also being evident. Globally, the prevalence of DM1 is estimated to be 1 in 8,000 people, with approximately 40,000 patients in the United States, 75,000 patients in Europe and 15,000 patients in Japan.

DM1 patients can suffer from various manifestations of disease including myotonia, or a temporary rigidity due to the inability to relax muscles, muscle weakness, cardiac abnormalities, respiratory problems, fatigue, gastrointestinal complications, early cataracts, and cognitive and behavioral impairments. For patients with more severe forms of DM1, life expectancy is reduced due to increased mortality rates resulting from pulmonary and cardiac complications.

About PepGen

PepGen Inc. is a clinical-stage biotechnology company developing the next generation of oligonucleotide therapies with the goal of transforming the treatment of severe neuromuscular and neurological diseases. PepGen's Enhanced Delivery Oligonucleotide (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, the Company is generating a pipeline of oligonucleotide therapeutic candidates designed to target the root cause of serious diseases.

For more information, please visit www.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 potential of our EDO platform to deliver high levels of oligonucleotide to the nuclei, the therapeutic potential and safety profile of PGN-EDODM1 based on data from the 5, 10 and 15 mg/kg cohorts of the FREEDOM-DM1 study, our expectations regarding the potential for significant correction of mis-splicing with more doses of PGN-EDODM1 over a longer treatment period to potentially provide improved functional benefit for patients with DM1, the design and conduct of clinical trials with our candidates, including expected timelines for additional data reports from our FREEDOM trial and the initial data report from our FREEDOM2-DM1 trial, the potential for any functional improvements that may result from robust splicing correction with PGN-EDODM1, dose-dependent increases in splicing suggesting that PGN-EDODM1 is getting into the muscle and effectively binding to the target, 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-EDODM1; our ability to enroll patients in our clinical trials, including 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-EDODM1; our product candidates, including 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 FREEDOM2 program; 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 reports 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-EDODM1, an investigational therapy that has not been approved for use in any country, and is not intended to convey conclusions about its efficacy or safety. There is no guarantee that PGN-EDODM1 or any other investigational therapy will successfully complete clinical development or gain regulatory authority approval.

1. Provenzano et al., The Splice Index as a prognostic biomarker of strength and function in myotonic dystrophy type 1, *J Clin. Invest*. 2025
2. One patient's biopsy was not collected at day 28 due to pseudoaneurysm in connection with

the biopsy procedure.

3. One patient’s sample showed a splicing index outside the pre-specified assay range at both baseline and day 28 (no detectable mis-splicing) and was excluded from the analysis.

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