PepGen Announces Positive Phase 2 FREEDOM2-DM1 10 mg/kg Results Demonstrating Highest Reported Splicing Correction and Improvements Across Multiple Functional Measures

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- Mean splicing correction of 46.5% following four monthly doses of PGN-EDODM1, five of six participants having more than 20% splicing correction and four participants exceeding 50% splicing correction –

- Video Hand Opening Time (vHOT), a measure of myotonia, improved by 3.9 seconds (52.7%) from baseline at Week 16 -

- Meaningful functional improvements observed across measures of strength, ambulation, and mobility, supporting the potential for broad clinical benefit in DM1 -

- PGN-EDODM1 was generally well tolerated, with no serious or severe adverse events or dose-limiting toxicities reported -

- Conference call scheduled today at 8:00 a.m. ET -

BOSTON--(BUSINESS WIRE)--Nov. 10, 2026-- PepGen Inc. (Nasdaq: PEPG), a clinical-stage biotechnology company pioneering oligonucleotide therapies with the potential to transform the treatment of rare genetic diseases, today announced positive topline results from the 10 mg/kg multiple ascending dose cohort of the ongoing Phase 2 FREEDOM2-DM1 trial (NCT06667453) evaluating PGN-EDODM1 in patients with myotonic dystrophy type 1 (DM1), a rare, progressive, and multisystemic genetic disease.

The results demonstrated the highest level of splicing correction ever reported in a multiple dose study for DM1, as well as notable improvements across multiple functional measures including myotonia, strength, ambulation, and mobility following four monthly doses of PGN-EDODM1. Mean splicing correction in muscle reached 46.5%, with five of six participants having more than 20% splicing correction and four participants showing more than 50% splicing correction, as measured by the 22-gene panel at Week 13[1]. These findings were accompanied by sustained improvements in video Hand Opening Time (vHOT), hand grip strength, 10-Meter Walk/Run Test (10MWRT), and Timed Up and Go (TUG) assessments, providing compelling evidence of PGN-EDODM1's potential to address multiple clinical manifestations of DM1 and supporting continued development.

"Our ambition is to fundamentally change how DM1 is treated through greater targeting of the underlying molecular mechanism of the disease," said James McArthur, Ph.D., President and Chief Executive Officer of PepGen. "The 10 mg/kg results mark an important milestone in that pursuit, with robust splicing correction accompanied by encouraging improvements across multiple measures of muscle function. Importantly, these findings strengthen our confidence not only in PGN-EDODM1's potential, but in our broader development strategy. With our 12.5 mg/kg cohort fully enrolled and the ongoing FREEDOM-OLE study exceeding 135 doses administered, we believe we are well positioned to continue building the evidence needed to advance toward pivotal studies."

"DM1 is a multisystemic disease, placing a major burden on patients and their families," said Hanns Lochmüller, M.D., Ph.D., FAAN, Professor of Neurology at the University of Ottawa, Senior Scientist at the CHEO Research Institute and Neurologist at The Ottawa Hospital, and a FREEDOM2 study investigator. "The improvements observed across myotonia, mobility and grip strength are encouraging because they reflect functions that affect patients' daily lives. The relationship between splicing correction and improvements in myotonia is particularly interesting, and longer-term follow-up will be important to better understand the durability and clinical relevance of these findings."

FREEDOM2-DM1 10 mg/kg Cohort Results

FREEDOM2-DM1 is an ongoing, randomized, double-blind, placebo-controlled Phase 2 multiple ascending dose study evaluating PGN-EDODM1 in patients with DM1. The 10 mg/kg cohort enrolled eight participants, randomized 3:1 to receive four doses of PGN-EDODM1 (n=6) or placebo (n=2) administered intravenously every four weeks. All eight participants completed the Week 16 assessment.

Splicing Correction and Functional Results:

- Mean splicing correction of 46.5% was observed at Week 13. Furthermore, five of six participants showed greater than 20% splicing correction and four having more than 50% splicing correction. Mean splicing correction in the pooled placebo group (n=4, combined from Cohorts 1 and 2) was 6.8% at Week 13.
- Video Hand Opening Time, an objective measure of myotonia, improved 4.3 seconds at Week 13 and 3.9 seconds at Week 16, representing an approximately 52.7% improvement at Week 16 (placebo improved 0.2 seconds at Week 16). A dose-dependent splicing correction of *CLCN1*, a muscle chloride channel believed to be a primary driver of myotonia in DM1, was also observed.
- Hand grip strength improved by approximately 16.2% at Week 16, corresponding to a 6.3-point improvement in maximum predicted percent normal (PPN) from baseline (placebo improved 0.9 PPN).
- At Week 16, the Timed Up and Go Assessment improved by 8.5%, or 0.6 seconds (placebo

worsened 0.5 seconds) and the 10-Meter Walk/Run Test improved by 6.8%, or 0.4 seconds (placebo improved 0.2 seconds). These findings suggest encouraging improvements in functional balance, ambulation, and mobility over the 16-week observation period.
- Patient Reported Outcome measures were inconclusive at Week 16. Patient Global Impression of Change (PGI-C) showed a favorable directional trend at 10 mg/kg versus placebo. Myotonic Dystrophy Health Index (MDHI) total scores showed mixed results at Week 16 due to improvements in all groups, including the placebo arm, and differences in baseline measurements.

Safety and Tolerability Results:

- PGN-EDODM1 was generally well tolerated at 10 mg/kg, supporting continued clinical development. All reported treatment-emergent adverse events (TEAEs) in the 10 mg/kg cohort were mild or moderate, with no severe adverse events, serious adverse events, adverse events of special interest, or dose-limiting toxicities. No treatment discontinuations were reported. The most commonly reported TEAE was nausea.
- Four renal TEAEs were reported, all were mild. Transient increases in protein in the urine (albuminuria) were observed after the first dose and decreased with later doses. No evidence of cumulative renal toxicity was observed over the 16-week study period.

“For people living with DM1, the impact extends far beyond any single symptom, underscoring the need for treatments that target the root cause of the disease,” said Paul Streck, M.D., MBA, Executive Vice President, Head of Research and Development of PepGen. “We are extremely encouraged by the magnitude of splicing correction observed at 10 mg/kg and the dose-dependent improvements across multiple measures of muscle function. Together, these findings strengthen our confidence in PGN-EDODM1’s potential to deliver meaningful benefit for patients. We are deeply grateful to the FREEDOM2 investigators, study teams, participants, and their families for their dedication and commitment to this study.”

The 12.5 mg/kg cohort of FREEDOM2 is fully enrolled, with participants having received up to three doses and clinical results expected in the first half of 2027. PepGen also expects to report interim clinical data at 5 mg/kg and safety data at 10 mg/kg from the open-label extension study in January 2027.

Conference Call Details

PepGen will host a conference call and webcast today at 8:00 a.m. ET to discuss the FREEDOM2-DM1 10 mg/kg results. To access the live webcast, please visit the Events & Presentations section of PepGen’s investor website here. An archived replay will be available following the event.

About Myotonic Dystrophy Type 1 (DM1)

Myotonic dystrophy type 1 (DM1) is a rare, progressive genetic disease that affects muscles and multiple systems throughout the body. DM1 is caused by an abnormal expansion of cytosine-thymine-guanine (CTG) repeats in the *dystrophia myotonica protein kinase* (*DMPK*) gene, resulting in pathogenic RNA that interferes with normal RNA splicing and drives the disease. Symptoms can begin in childhood or adulthood and vary widely in type, severity, and progression. DM1 has a world-wide distribution and is estimated to affect more than 110,000 people across the United States and the European Union, and average life expectancy for people with non-congenital DM1 is approximately 50 to 60 years. No approved therapies currently address the underlying cause of DM1.

About PGN-EDODM1

PGN-EDODM1 is an investigational Enhanced Delivery Oligonucleotide (EDO) designed to address the underlying molecular mechanism of DM1. Using PepGen’s proprietary EDO technology designed to enhance cellular uptake and nuclear delivery of a therapeutic oligonucleotide, PGN-EDODM1 selectively binds to expanded CUG repeats in pathogenic *dystrophia myotonica protein kinase* (*DMPK*) RNA. This binding releases MBNL1, a key regulator of RNA splicing, to restore correct splicing. Unlike approaches that degrade *DMPK* RNA, PGN-EDODM1 is designed to disrupt pathogenic *DMPK* hairpin structures while preserving normal *DMPK* function. The U.S. Food and Drug Administration has granted PGN-EDODM1 Orphan Drug and Fast Track designations, and the European Medicines Agency has granted it Orphan Designation.

About FREEDOM2-DM1

FREEDOM2-DM1 (NCT06667453) is a multinational, randomized, double-blind, placebo-controlled Phase 2 multiple ascending dose study evaluating PGN-EDODM1 in people living with DM1. The study enrolled three cohorts of eight participants each, randomized 3:1 to receive PGN-EDODM1 or placebo at doses of 5, 10, or 12.5 mg/kg. Participants receive four intravenous doses every four weeks over 12 weeks. Key endpoints include safety and tolerability, pharmacokinetics, correction of RNA mis-splicing in muscle tissue, and functional measures of myotonia, strength, and mobility. FREEDOM2 is being conducted in Canada, the United Kingdom, New Zealand, Australia, and South Korea and is subject to a partial clinical hold in the United States. Eligible participants may continue treatment in the FREEDOM-OLE study.

About PepGen

PepGen Inc. is a clinical-stage biotechnology company pioneering oligonucleotide therapies with the potential to transform the treatment of rare genetic diseases. Founded on more than a decade of research and development, PepGen’s Enhanced Delivery Oligonucleotide (EDO) technology leverages cell-penetrating peptides to improve the uptake and activity of conjugated oligonucleotide therapeutics. Using this EDO technology, PepGen is advancing PGN-EDODM1, a clinical candidate for the treatment of myotonic dystrophy type 1.

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 therapeutic potential and safety profile of PGN-EDODM1, statements regarding PGN-EDODM1’s potential to deliver meaningful benefit to the DM1 community, evidence of PGN-EDODM1’s potential to address multiple clinical manifestations of DM1 including PepGen’s ambition to change how DM1 is treated, the topline results from the 10 mg/kg multiple ascending dose cohort of the ongoing Phase 2 FREEDOM2-DM1 trial, expectations regarding the timing of data for the 12.5 mg/kg cohort of the FREEDOM2-DM1 trial, the FREEDOM-OLE 10mg/kg safety and 5 mg/kg clinical results, the potential for any functional improvements that may result from 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 or cross-trial comparisons, including for PGN-EDODM1 and cross-trial comparisons; 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

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