PepGen Inc. Announces FDA has Lifted the Clinical Hold on its Investigational New Drug Application for FREEDOM-DM1 Phase 1 Study of PGN-EDODM1 for Myotonic Dystrophy Type 1 (DM1)

– Lifting of FDA hold allows FREEDOM-DM1 study to launch in the U.S. with target dose levels of 5 mg/kg, 10 mg/kg and 20 mg/kg –

– Safety, transcript splicing and clinical outcome measures data at 5 mg/kg PGN-EDODM1 dose level in patients from FREEDOM-DM1 clinical study expected in 2024 –

– Continue to expect safety, muscle exon skipping and dystrophin data at 5 mg/kg PGN-EDO51 dose level in patients from CONNECT1-EDO51 clinical study in mid-2024 –

– Cash runway expected to fund operations into 2025 –

BOSTON, October 12, 2023 (GLOBE NEWSWIRE) -- 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 that the U.S. Food and Drug Administration (FDA) has lifted the full clinical hold and cleared the Company's Investigational New Drug Application (IND) to initiate the FREEDOM-DM1 Phase 1 study of PGN-EDODM1 in patients with myotonic dystrophy type 1 (DM1) in the U.S.

"We have worked closely with the FDA to resolve their questions expeditiously and are pleased that the clinical hold on our DM1 program in the United States has been lifted. Our novel PGN-EDODM1 approach targets the toxic RNA species responsible for the disease, and the strength of our Enhanced Delivery Oligonucleotide (EDO) safety preclinical package has enabled us to launch this study in both the U.S. and internationally at doses that we believe could provide a clinically meaningful benefit to patients. We are very pleased after review of our existing safety data that the FDA agreed with our proposed starting dose of 5 mg/kg, moving up to 10 mg/kg and 20 mg/kg," said James McArthur, Ph.D., President and CEO of PepGen.

As previously communicated, the Company opened FREEDOM-DM1 in Canada in September of this year. FREEDOM-DM1 is a randomized, double-blind, placebo-controlled, single ascending dose (SAD) study, designed to assess PGN-EDODM1 safety and tolerability, correction of mis-splicing of transcripts, and clinical functional outcome measures. Sites in both the U.S. and Canada will evaluate PGN-EDODM1 in 3 cohorts of 5 mg/kg, 10 mg/kg, and 20 mg/kg dose levels. The decision to advance to the next dose level will be contingent upon the evaluation of safety data derived from previous dose cohorts.

Dr. McArthur added, "In a preclinical DM1 mouse model, where EDO technology achieved oligonucleotide muscle concentrations of 6 nM of PGN-EDODM1, we observed 76% reversal of myotonia and 68% correction of mis-splicing. This was increased to 99% correction of both

measures following multiple doses. Based on these preclinical results, we anticipate proof-of-concept data in patients in 2024, including transcript splicing and clinical outcome measures, at the 5 mg/kg PGN-EDODM1 dose level in DM1 patients. With clearance of our IND from the FDA, we are eager to open study sites in the U.S. to accelerate the development of PGN-EDODM1 for individuals worldwide living with DM1."

The Company expects to obtain proof-of-concept data, including transcript splicing and clinical outcome measures, as well as safety data, for DM1 patients in the FREEDOM-DM1 clinical study in 2024. The Company also anticipates proof-of-concept data, including exon skipping and dystrophin data, as well as safety data, at the 5 mg/kg PGN-EDO51 dose level for exon 51 amenable DMD patients in the CONNECT1-EDO51 clinical study in mid-2024. The Company continues to expect its cash and cash equivalents to be sufficient to fund currently planned operations into 2025.

About PGN-EDODM1

PGN-EDODM1 is an investigational candidate designed to deliver a peptide-conjugated antisense oligonucleotide (ASO) to restore cellular function. DM1 is caused by an expansion of CUG repeats that form hairpin loops in the *DMPK* RNA, resulting in sequestration of the MBNL1 protein, a key RNA processing factor. The sequestration of MBNL1 results in downstream mis-splicing events and aberrant expression of many proteins that play a critical role in muscle and other systemic functions (e.g. endocrine, gastrointestinal, central nervous system). By specifically blocking the toxic CUG repeats, the goal of PGN-EDODM1 is to liberate MBNL1 protein and to restore functional downstream splicing and muscle and other systemic functions.

About Myotonic Dystrophy Type 1 (DM1)

Myotonic dystrophy type 1, or DM1 (also known as Steinert's disease), is a progressively disabling, life-shortening genetic disorder. DM1 is the most prevalent form of the disease and generally the most severe. DM1 affects an estimated 40,000 people in the U.S., and 70,000 in the EU. The average life expectancy for people living with DM1 is 45-60 years old. People living with DM1 typically present with myotonia (stiff or contracted muscles), muscle weakness, and cardiac and respiratory abnormalities. Many people living with DM1 also experience excessive daytime sleepiness, fatigue, and issues with gastrointestinal or cognitive dysfunction that significantly affect their quality of life.

About PGN-EDO51

PGN-EDO51, PepGen's lead clinical candidate for the treatment of Duchenne muscular dystrophy (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. In preclinical studies, PepGen observed that treatment of non-human primates with PGN-EDO51 resulted in greater levels of exon-skipping when compared in head-to-head studies against a molecule that we believe is structurally equivalent to the most clinically-advanced peptide-conjugated oligonucleotide therapeutic candidate, which could translate to higher levels of dystrophin production in patients. PGN-EDO51 also exhibited the highest level of exon 51 skipping in primate skeletal muscles, including the diaphragm, reported for any approved therapeutic or known development candidate, based on cross-trial comparisons of publicly available data with preclinical PGN-EDO51 data. In humans, in a single ascending dose study, PGN-EDO51 also exhibited the 20-fold higher exon 51 skipping than naked oligo following a single dose, based on cross-trial comparisons of publicly available data with clinical PGN-EDO51 data.

About Duchenne Muscular Dystrophy (DMD)

Duchenne muscular dystrophy (DMD) is an X-linked recessive muscle-wasting disease that predominantly affects males. This debilitating disease is caused by genetic mutations in the gene encoding dystrophin, a protein critical for healthy muscle function, and is one of the most prevalent rare genetic diseases, with an incidence rate of approximately one in every 3,500 to 5,000 male births. DMD is characterized by progressive muscle weakness, which leads to patients losing the ability to walk, a loss of upper body function, cardiac issues and difficulties breathing. DMD is invariably fatal by young adulthood. Despite significant advances in treatments for this devastating disease, current therapies are limited by poor delivery to muscle tissue and have yet to establish meaningful clinical benefit for DMD patients.

About PepGen

PepGen Inc. 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 Enhanced Delivery Oligonucleotide, or 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 that are designed to target the root cause of serious diseases. For additional information, visit www.pepgen.com.

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 our product candidates including PGN-EDO51 and PGN-EDODM1, our technology, including our EDO platform, the design, initiation and conduct of clinical trials, including expected timelines, regulatory interactions, including development pathway for our product candidates, and our financial resources and cash runway.

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; 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; our product candidates 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, including PGN-EDO51 and PGN-EDODM1, or other regulatory feedback requiring modifications to our development programs; 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.

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