PepGen Reports Positive Data from Phase 1 Trial of PGN-EDO51 for the Treatment of Duchenne Muscular Dystrophy

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- PGN-EDO51 exhibited the highest levels of oligonucleotide delivery and exon skipping in a clinical study following a single dose when compared to publicly available clinical data for other exon 51 skipping approaches -

- PGN-EDO51 was generally well-tolerated -

- PepGen plans to initiate a Phase 2a multiple ascending dose (MAD) clinical trial in Duchenne muscular dystrophy (DMD) patients in 1H 2023 -

- Data supports the potential of PepGen's Enhanced Delivery Oligonucleotide (EDO) platform in neuromuscular diseases -

- Company to host conference call today at 8:00 a.m. ET to discuss these results -

BOSTON, Sept. 28, 2022 (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 results from its completed Phase 1 healthy normal volunteer (HNV) trial of PGN-EDO51, the company's lead product candidate for the treatment of DMD patients whose mutations are amenable to an exon 51 skipping approach.

PepGen's Phase 1 HNV trial of PGN-EDO51 was a single ascending dose (SAD) clinical trial evaluating the safety and tolerability of PGN-EDO51 in 32 healthy adult males. Oligonucleotide tissue concentration and exon skipping were also assessed. Following intravenous administration of PGN-EDO51, safety data were evaluated by a Safety Review Committee prior to progressing to the next dose level. Volunteers were dosed with either 1, 5, 10 or 15 mg/kg of PGN-EDO51 or placebo. The trial met its primary endpoint assessing the safety profile of PGN-EDO51 at pharmacologically relevant doses.

"We are thrilled to announce that we have observed very high levels of oligonucleotide delivery and exon skipping in muscle in our Phase 1 HNV trial. The EDO technology performed above our expectations," said James McArthur, Ph.D., President and CEO of PepGen. "In biopsies taken from biceps, PGN-EDO51 exhibited mean exon 51 skipping levels of 1.4% following a single dose of 10 mg/kg, and mean levels of 2.0% following a single dose of 15 mg/kg. Based on cross-trial comparisons with publicly available data, we believe that these results are unprecedented and reflect the highest level of *DMD* exon 51 skipping observed in a clinical trial following a single dose. With the very encouraging outcome of this trial, PepGen plans to initiate a Phase 2a multiple ascending dose clinical trial in DMD patients in the first half of 2023. We extend our heartfelt appreciation to the participants in our Phase 1 HNV trial for their role in supporting our mission to develop transformative therapies for people living with DMD and other devastating neuromuscular diseases."

Dr. McArthur added: "We are particularly pleased with the high levels of exon skipping observed for PGN-EDO51 at 28 days. Exon skipping was higher on Day 28 than at Day 10, which we believe, in conjunction with our tissue concentration data, suggests both sustained drug exposure and pharmacodynamic effect. Furthermore, we believe that these results could signal the potential for the accumulation of exon 51 skipped transcript and dystrophin protein in muscle tissue with repeated doses of PGN-EDO51 in people living with DMD."

Safety and Tolerability Data

The trial met its primary endpoint providing evidence that PGN-EDO51 was generally well tolerated at pharmacologically relevant doses.

- All participants completed the trial; there were no discontinuations.
- The majority of treatment-emergent adverse events (TEAEs) were assessed as mild and resolved without any intervention. At 10 mg/kg, there were only Grade 1 (mild) adverse events (AEs).
- At 15 mg/kg, there were mild, transient, reversible changes in kidney biomarkers that resolved without intervention in all but one HNV who received IV hydration. This event was recorded as a non-life-threatening serious adverse event (SAE).
- Transient mild (Grade 1) to moderate (Grade 2) hypomagnesemia was observed in two participants at the 15 mg/kg dose and did not require any intervention.
- Serum cystatin C, the recommended biomarker to assess renal function in DMD, showed minimal change at the highest dose.

Oligonucleotide Tissue Concentration and Exon Skipping Results

A dose dependent increase in PGN-EDO51 tissue concentration and exon skipping was observed in biceps.

- Oligonucleotide Tissue Concentration:
    - In the 10 mg/kg dose cohort, PGN-EDO51 exhibited mean oligonucleotide tissue

concentrations of 19 nM and 11 nM in biceps biopsies taken at Day 10 (n=6) and Day 28 (n=6), respectively.
    - In the 15 mg/kg dose cohort, PGN-EDO51 exhibited mean oligonucleotide tissue concentrations of 50 nM and 50 nM in biceps biopsies taken at Day 10 (n=5) and Day 28 (n=6), respectively.
- Exon skipping:
    - In the 10 mg/kg dose cohort, PGN-EDO51 exhibited mean exon skipping of 1.1% and 1.4% in biceps biopsies taken at Day 10 (n=6) and Day 28 (n=6), respectively.
    - In the 15 mg/kg dose cohort, PGN-EDO51 exhibited mean exon skipping of 1.4% and 2.0% in biceps biopsies taken at Day 10 (n=5) and Day 28 (n=6), respectively.

PepGen believes that these data could indicate the potential for clinically meaningful accumulation of exon 51-skipped transcripts and dystrophin in tissue with repeated doses of PGN-EDO51.

PepGen plans to present the full results from the Phase 1 HNV trial of PGN-EDO51 at an upcoming medical meeting, and the company remains on track to initiate a planned Phase 2a MAD trial evaluating PGN-EDO51 in DMD patients in the first half of 2023.

Implications for PepGen's Myotonic Dystrophy Type 1 (DM1) program and EDO pipeline

We believe that these data also support the potential of PGN-EDODM1, PepGen's lead product candidate for the treatment of DM1, and our pipeline of EDO therapeutic candidates. The tissue concentrations observed in the Phase 1 HNV trial of PGN-EDO51 were similar to those seen in a single-dose study of PGN-EDODM1 conducted in HSA^{LR} mice, a murine model of DM1, at pharmacologically active dose levels. These tissue concentrations of PGN-EDODM1 resulted in significant correction of mis-splicing and myotonia in this mouse model of disease. Dr McArthur said, "We are encouraged by these results, which we believe support the potential of PGN-EDODM1 to treat the root cause of DM1 and drive meaningful clinical outcomes for individuals living with this disease. In addition, we are committed to the DMD community, with EDO candidates for patients amenable to an exon 53, 45 and 44 approach currently in development. We believe that these results provide robust support for the potential of these candidates to change the course of disease for those living with DMD."

Conference Call

PepGen will host a corresponding conference call and a live webcast at 8:00 a.m. ET on September 28, 2022, to discuss the topline results from its Phase 1 HNV trial of PGN-EDO51. Individuals interested in listening to the conference call by webcast may do so by registering via the webcast link in the investor relations section of the company's website at: www.pepgen.com.

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 diaphragm, reported for any approved therapeutic or known development candidate, based on cross-trial comparisons of publicly available data with preclinical PGN-EDO51 data.

About Duchenne Muscular Dystrophy

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 Myotonic Dystrophy Type 1

DM1 is a monogenic, autosomal dominant, progressive disorder that primarily affects skeletal, cardiac and smooth muscles as well as the CNS, resulting in significant physical, cognitive and behavioral impairments and disability. The burden of disease is significant, and many patients have a shortened lifespan. DM1 is caused by an abnormal trinucleotide repeat expansion in a region of the *DMPK* gene, with an estimated prevalence of approximately 1 in 8,000. However, under- and misdiagnosis is believed to be widespread, and genetic screening studies for *DMPK* triplet repeats have suggested that this rate may be as high as 1 in 2,100 people. There are currently no approved therapies for the treatment of DM1.

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 (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 engineered to target the root cause of serious diseases. For more information, visit www.pepgen.com or follow PepGen on Twitter and LinkedIn.

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 about our clinical and preclinical programs, product candidates, including their planned development and therapeutic potential, plans for future development and clinical trials in our programs, including the planned initiation of a Phase 2a MAD trial of PGN-EDO51 in DMD patients, achievement of milestones, and corporate and clinical/preclinical strategies.

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 that we may fail to successfully complete preclinical studies and clinical trials of our product candidates or to obtain regulatory approval for marketing of such products; initial clinical trial results for one or more of our product candidates may not be predictive of future trial results for such candidates; our product candidates may not be safe and effective; there may be delays in regulatory clearance or changes in regulatory framework that are out of our control; we may not be able to nominate new drug candidates within the estimated timeframes; our estimation of addressable markets of our product candidates may be inaccurate; we may need additional funding before the end of our expected cash runway and may fail to timely raise such additional required funding; more efficient competitors or more effective competing treatments may emerge; we may be involved in disputes surrounding the use of our intellectual property crucial to our success; we may not be able to attract and retain key employees and qualified personnel; earlier-stage trial results may not be predictive of later stage trial outcomes; and we are dependent 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 its most recent quarterly report on Form 10-Q on file 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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