PepGen Announces Clearance of CTA by UK Medicines & Healthcare Products Regulatory Agency to Begin CONNECT2-EDO51, a Phase 2 Clinical Trial designed to support potential accelerated approval of PGN-EDO51 for the Treatment of Duchenne Muscular Dystrophy

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BOSTON, March 04, 2024 (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 UK Medicines & Healthcare products Regulatory Agency (MHRA) has authorized its Clinical Trial Application (CTA) to initiate the CONNECT2-EDO51 Phase 2 clinical trial of PGN-EDO51 in patients with Duchenne muscular dystrophy (DMD) amenable to an exon 51-skipping approach.

“We are excited to take the next step forward in our development of PGN-EDO51, which we believe to be a potentially transformative investigational candidate for people living with DMD and are pleased the MHRA authorized our CTA. We believe this study, together with the data generated in our ongoing CONNECT1-EDO51 trial, could potentially support accelerated approval of EDO51, subject to alignment with regulators,” said James McArthur, Ph.D., President and CEO of PepGen. “We are grateful to continue our work with the DMD community to develop this therapy.”

The CONNECT2-EDO51 Phase 2 clinical trial is a multinational, randomized, double-blind, placebo-controlled, multiple ascending dose (MAD) study, that will enroll approximately 20 ambulatory and non-ambulatory boys and young men living with DMD amenable to exon 51-skipping, who are at least six years of age. Participants will receive seven doses of either PGN-EDO51 or placebo at approximately four-week intervals for 24 weeks. Per the protocol, the starting dose will escalate from 5 mg/kg to 10 mg/kg, and potentially higher; the same dose levels are being evaluated in the ongoing CONNECT1-EDO51 trial. Further dose escalation will be determined based on evaluation of safety data from prior dose cohort(s). Participants will provide a muscle biopsy at baseline and then at week 25. The trial will assess exon skipping, dystrophin production, and safety and tolerability. All participants will have the opportunity to participate in an open-label extension.

About PGN-EDO51

PGN-EDO51, PepGen’s lead clinical candidate 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. In preclinical studies, PepGen observed that treatment of non-human primates with PGN-EDO51 resulted in greater levels of exon 51 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 we believe 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 at tolerable target dose levels, based on cross-trial comparisons of publicly available data. In humans, in a Phase 1 single ascending dose study in healthy volunteers, PGN-EDO51 also exhibited six times higher mean exon 51 skipping as compared to a naked oligonucleotide following a single dose, based on cross-trial comparisons of publicly available data.

About Duchenne Muscular Dystrophy (DMD)

Duchenne muscular dystrophy (DMD) is an X-linked recessive, progressive, muscle-wasting disease that predominantly affects boys. This debilitating disease is caused by genetic mutations in the gene encoding dystrophin, a protein necessary for normal 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 exon skipping 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.

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, our technology, including our EDO platform, the design, initiation and conduct of clinical trials, including the CONNECT1-EDO51 and CONNECT2-EDO51 trials, expected timelines and preliminary data reports from our clinical trials, regulatory interactions, including the development pathway for our product candidates and the potential for an accelerated approval pathway for PGN-EDO51, assuming alignment with regulators, 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; our ability to

enroll patients in our clinical trials, including CONNECT1-EDO51 and CONNECT2-EDO51; 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; our product candidates, including PGN-EDO51, 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, such as PGN-EDO51, or other regulatory feedback requiring modifications to our development programs, including in each case with respect to CONNECT1-EDO51 and CONNECT2-EDO51; 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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