Metagenomi Announces Preclinical Data for Lead Hemophilia A Program Demonstrating Durable Factor VIII (FVIII) Activity Levels through Twelve Months

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Twelve-month durability data from Metagenomi's ongoing nonhuman primate (NHP) study in hemophilia A remains generally consistent with data previously released at 4.5 months

NHPs remain healthy and exhibit normal weight gain; treatment is generally well tolerated

Program on track for IND filing in 2026

Company to host conference call with management and Dr. Glenn Pierce, international thought leader in hemophilia A

EMERYVILLE, Calif., Sept. 03, 2024 (GLOBE NEWSWIRE) -- Metagenomi, Inc. (Nasdaq: MGX), a precision genetic medicines company committed to developing curative therapeutics for patients using its proprietary gene editing toolbox, today announced data from an ongoing preclinical study designed to provide evidence supporting the potential durability and safety of the company's hemophilia A gene editing investigational therapy, MGX-001.

"We are thrilled to achieve this preclinical milestone supporting our recent decision to declare MGX-001 as our development candidate for hemophilia A," said Brian C. Thomas, PhD, CEO and founder of Metagenomi. "We conducted this NHP study in response to a competitive landscape where gene therapies have been unable to achieve long term persistence of FVIII activity levels in patients. Establishing proof-of-concept of site specific gene integration and durable activity levels of FVIII in NHPs over twelve months in hemophilia A represents an important validation of our platform. Our goal for MGX-001 is to provide a one-time, curative treatment for adults and children with hemophilia A. Furthermore, we intend to leverage the MGX-001 editing platform to pursue additional therapies for secreted protein disorders."

The NHP study involved treating three NHPs with a single intravenous dose of an adeno associated virus (AAV) containing a FVIII donor template followed 35 days later by a single intravenous dose of a lipid nanoparticle (LNP) containing a novel Metagenomi nuclease and associated guide RNA targeting the first intron of the albumin gene. Each animal received only a single dose of dexamethasone prior to the AAV and LNP doses. The NHPs were then followed for safety and donor FVIII activity. The NHPs also underwent liver biopsy on Day 7 to evaluate editing and integration efficiency. The study remains ongoing.

All NHPs demonstrated durable FVIII activity levels over the twelve-month period. At the twelve-month time point two of the NHPs had FVIII activity levels within normal/near normal range (82% and 41%) while the third NHP had FVIII activity level in the mild hemophilia range (9%). Comparisons of mean values from the three to six month time points to the nine to twelve month time points were highly consistent, demonstrating no significant decline in donor-derived FVIII activity levels. Liver biopsy data demonstrated gene integration in the forward orientation at a frequency of 0.7% to 2.9%; these values positively correlated with FVIII activity levels. Treatment was generally well tolerated with findings limited to moderate transient elevation of liver transaminases following AAV and LNP administration. There were no notable findings in total bilirubin or albumin levels or adverse clinical observations.

This early NHP study was conducted without the benefit of several subsequent optimizations of the therapeutic candidate designed to enhance safety and efficacy in the clinic. For the development candidate MGX-001, the company selected a bioengineered FVIII construct designed to improve FVIII activity levels, optimized the ratio of different LNP components and timing between AAV and LNP administration, and enhanced aspects of the manufacturing processes.

"The treatment of hemophilia, which has undergone many transformative changes over the past 60 years, is poised for yet another disruptive change: the use of genome editing, with site specific integration of FVIII, to produce functional cures in patients with hemophilia A. I am encouraged by the preclinical progress in the genome editing space to potentially provide a new path to a one-time, curative treatment option for both adults and children in hemophilia A in the future," said Dr. Glenn Pierce, member of the Metagenomi Scientific Advisory Board.

The company will host a conference call at 8:30am ET, on Wednesday, September 4, 2024. The registration link to the webcast can be found at https://ir.metagenomi.co/.

About Hemophilia A

Hemophilia A is the most common X-linked inherited bleeding disorder, caused by a large variety of mutations in the FVIII gene leading to a loss of functional FVIII protein. Intracranial bleeding is of greatest concern as this can lead to major morbidity and mortality. Bleeding into joints leads to cumulative joint damage and is a major cause of morbidity. Diagnosis typically occurs in infancy due to exaggerated bleeding in response to minor injury or routine medical procedures. Prevalence is estimated to be up to 26,500 patients in the US and more than 500,000 patients globally according to the World Federation of Hemophilia (WFH), with the vast majority of patients being male.

About Metagenomi

Metagenomi is a precision genetic medicines company committed to developing curative therapeutics for patients using its proprietary, comprehensive metagenomics-derived toolbox. Metagenomi is harnessing the power of metagenomics, the study of genetic material recovered from the natural environment, to unlock four billion years of microbial evolution to discover and develop a suite of novel editing tools capable of correcting any type of genetic mutation found anywhere in the genome. Its comprehensive genome editing toolbox includes programmable nucleases, base editors, and RNA and DNA-mediated integration systems (including prime editing systems and clustered regularly interspaced short palindromic repeat associated transposases). Metagenomi believes its diverse and modular toolbox positions the company to access the entire genome and select the optimal tool to unlock the full potential of genome editing for patients. For more information, please visit https://metagenomi.

Cautionary Note Regarding Forward- Looking Statements

This press release contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. Such statements, which are often indicated by terms such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “goal,” “intend,” “look forward to,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” and similar expressions include, but are not limited to, any statements relating to our growth strategy and product development programs, including the timing of and our ability to conduct IND-enabling studies, make regulatory filings such as INDs, statements concerning the potential of therapies and product candidates, including our development candidate, MGX-001, statements concerning the timing of data presentations and publications, and any other statements that are not historical facts. Forward looking statements are based on management’s current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition, and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to our growth strategy; our ability to obtain, perform under, and maintain financing and strategic agreements and relationships; risks relating to the results of research and development activities; risks relating to the timing of starting and completing clinical trials; uncertainties relating to preclinical and clinical testing; our dependence on third party suppliers; our ability to attract, integrate and retain key personnel; the early stage of products under development; our need for substantial additional funds; government regulation; patent and intellectual property matters; competition; as well as other risks described in “Risk Factors,” in our most recent Form 10-K and our most recent 10-Qs on file with the Securities and Exchange Commission. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

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