Metagenomi Presents Updated Preclinical Data in Hemophilia A at American Society of Hematology (ASH) 66th Annual Meeting

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Therapeutically relevant levels of Factor VIII (FVIII) activity sustained in ongoing nonhuman primate (NHP) study through more than sixteen months of follow up

MGX-001 bioengineered FVIII construct exhibited higher FVIII activity at similar integration rates compared to wild type FVIII construct in preclinical studies; program on track for IND filing in 2026

EMERYVILLE, Calif., Dec. 09, 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 presented updated preclinical NHP data for its hemophilia A program in an oral presentation (link here) at the American Society of Hematology (ASH) 66th Annual Meeting and Exposition in San Diego.

“The distinguishing feature of our gene editing approach to hemophilia A, compared to conventional gene therapies, lies in our ability to achieve durable Factor VIII activity levels through precise *in vivo* integration of the FVIII gene. Today, we shared updated preclinical data demonstrating durable FVIII activity over 16 months in an ongoing NHP study. Additionally, we are pleased to highlight our lead development candidate, MGX-001, which uses a B domain deleted bioengineered FVIII construct, achieved higher levels of FVIII activity versus wild type FVIII, with preclinical evidence of durable FVIII activity levels. Together, these studies help support proof-of-concept as we progress MGX-001 toward the clinic. MGX-001 represents a potentially one-time curative treatment for both adults and children, with the goal to change the treatment paradigm for patients living with hemophilia A,” said Brian C. Thomas, PhD, CEO and Founder of Metagenomi.

NHP durability study update:

In a preclinical study, a cynomolgus version of the FVIII gene (cFVIII), used to avoid the confounding effects of anti-human FVIII antibodies, was administered to three NHPs via AAV at a dose of 2.0E13 vg/kg. Five weeks later, each NHP was administered an LNP at a dose of 1.0 mg/kg, delivering the MG29-1 nuclease mRNA and associated guide RNA. Each animal received only a single dose of dexamethasone prior to the AAV and LNP doses. Plasma was collected and assayed for safety parameters and FVIII activity. Data was generated over 16 months and the study remains ongoing.

Results of the study suggest that FVIII activity was maintained over the 16-month study duration. Mean FVIII activity of months 13-16.5 following LNP dosing was 71%, 7%, and 27% compared to mean FVIII activity of months 3-6 of 76%, 8% and 30%, and mean FVIII activity of months 7-12 of 77%, 8% and 32% respectively, in animals 1001, 1002 and 1003. At the 16.5-month time point, FVIII levels were 72%, 9%, 30% in each of the three animals, respectively. FVIII activity levels correlated with gene integration frequency from day 7 liver biopsy of 0.7%, 1.3%, 3.1% in each of the three animals, respectively. The FVIII knock-in was achieved with only transient elevation of liver transaminases at the time of AAV and LNP administration, and with no other safety findings and no impact to circulating albumin levels and no significant change in total bilirubin post AAV and LNP.

MGX-001 update:

A separate NHP study designed to support the company’s lead hemophilia A development candidate, MGX-001, which uses a B-domain deleted bioengineered FVIII construct, demonstrated significantly higher FVIII activity compared to wild type FVIII, despite similar integration frequency between the bioengineered construct and wild type gene. This result suggests the MGX-001 bioengineered construct may enable therapeutic FVIII activity at lower AAV doses with the potential for associated safety benefits. In addition, MGX-001 showed no identifiable off-target editing to-date in a series of orthogonal assays employed to discover and validate potential off-target sites.

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 of severe disease 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 (CAST)). 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.c

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 e include, but are not limited to, any statements relating to 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, 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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