Metagenomi Presents New Preclinical Data from MGX-001 Hemophilia A Program Supporting Advancement into Clinical Development

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MGX-001 demonstrated curative FVIII activity in non-human primates

Pre-IND regulatory meeting expected in Q4 2025 with investigational new drug (IND) and clinical trial application (CTA) submissions expected in 4Q 2026

EMERYVILLE, Calif., Nov. 11, 2025 (GLOBE NEWSWIRE) -- Metagenomi, Inc. (Nasdaq: MGX) (the “Company”), an in vivo genome editing company capitalizing on its proprietary technologies to create curative genetic medicines for patients, today reported new dose range finding data from the Company’s MGX-001 hemophilia A program. The data demonstrated curative factor VIII (FVIII) activity in non-human primates (NHPs) and informs a clinical dose regimen strategy for a therapy with best-in-class treatment potential. Metagenomi intends to advance MGX-001 into clinical development.

“We are highly encouraged by the dose range finding results observed in this study where we have seen clear dose-dependent activity across both the AAV and LNP components of MGX-001, resulting in therapeutically relevant FVIII activity in each animal treated in all but the lowest AAV dose,” said Jian Irish, Ph.D., M.B.A., President and CEO of Metagenomi. “In contrast to bispecific FVIII mimetics or rebalancing therapies, MGX-001 enables endogenous production of FVIII for hemostatic regulation and restores the body’s own ability to produce FVIII for a potentially lifelong cure. Our new data builds upon an earlier study demonstrating durable and stable FVIII activity in NHPs over an approximately 19-month study, giving us confidence that our novel approach has the potential to be a curative, one-and-done treatment for patients suffering from hemophilia A. We are leveraging these results in discussions with regulators and our IND/CTA submissions are expected by the end of 2026.”

NHP study design and results:

In this preclinical dose range finding study, a single dose of AAV containing a B-domain deleted human FVIII gene was administered to 24 NHPs in six dose cohorts at varying doses from 5.0e11 vg/kg to 4.0e13 vg/kg followed by a single dose of LNP delivering the proprietary MG29-1 nuclease mRNA and associated guide RNA at either 0.2, 0.6 or 2.0 mg/kg. Each animal received a single dose of corticosteroids prior to both AAV and LNP doses.

A functional cure is generally defined as FVIII levels of 50% to 150% of normal human levels. Key highlights from the study are below:

- Therapeutically relevant levels of FVIII activity were achieved in the five highest AAV doses of the six dose cohorts
  - At a fixed LNP dose of 0.6 mg/kg and a variable AAV dose of 1.6e12 to 4e13, MGX-001 achieved average per cohort FVIII activity of 49% - 81%
  - At a fixed AAV dose of 5e12 vg/kg and a variable LNP dose of 0.2 to 2.0 mg/kg, MGX-001 achieved average per cohort FVIII activity of 17% - 72%
  - FVIII activity exhibited both AAV and LNP dose dependency with no animal exceeding 150% of normal, the maximum acceptable level of human FVIII activity
  - The treatment was well tolerated in all animals without significant elevation of liver enzymes except in the highest dose of LNP where transient elevations in liver enzymes were observed
- At a proposed clinical dose of AAV at 5e12 vg/kg and LNP at 0.6 mg/kg, MGX-001 achieved average FVIII activity of 49% within a range of 29.3% - 59.5%

The new data demonstrated improved FVIII activity with reduced variability, building upon previously announced results with the B-domain deleted FVIII construct that demonstrated durable FVIII activity over an approximately 19-month study. This earlier NHP study used a cynomolgus version of the FVIII gene (cFVIII) to avoid the confounding effects of anti-human FVIII antibodies. MGX-001 has also shown no identifiable off-target editing in a series of orthogonal assays employed to discover and validate potential off-target sites.

“The MGX-001 approach represents a potential paradigm shift for the treatment of hemophilia A patients who, even with currently approved therapies, are subject to rare but serious spontaneous bleeding events and must always ensure access to their treatment,” said Glenn F. Pierce, M.D., Ph.D., an expert in the treatment of hemophilia. “As a physician scientist, drug developer, and former hemophilia A patient myself, I can speak firsthand to the impact that a potential one-and-done curative treatment can have in enabling a new standard of life with a hemophilia-free mindset.”

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, with the vast majority of patients being male.

About Metagenomi

Metagenomi is an in vivo genome editing company capitalizing on its proprietary technologies to create curative genetic medicines for patients. The Company was founded on the science of metagenomics, the study of genetic materials recovered from the natural environment, to discover and develop a suite of novel editing tools potentially capable of correcting any type of genetic mutation found anywhere in the human genome. The Company focuses on high value programs in disease indications with well-understood biology and clearly defined clinical development and regulatory pathways. Going forward, the Company intends to continue to expand its pipeline by leveraging its proprietary genetic editing capabilities in site

specific deletion, integration and correction.

MGX-001, the Company's lead, wholly-owned development program in hemophilia A, has demonstrated a preclinical profile potentially competitive with best-in-class treatment options, including targeted genome editing and durable gene expression in a one-time treatment. MGX-001 is designed to provide curative, life-long protection from bleeding events and joint damage in adults and children with hemophilia A. The Company is also currently pursuing other secreted protein deficiencies leveraging the MGX-001 site-specific genome integration system and partnered assets targeting cardiometabolic diseases. For more information, please visit https://metagenomi.co.

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 product development programs, including the timing of and our ability to conduct IND-enabling studies and make regulatory filings such as INDs, statements concerning the potential of therapies and product candidates, expectations regarding MGX-001, including the preclinical profile being potentially competitive with best-in-class treatment options, benefits of the approach and timing to submit the IND/CLA packages, 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 IND submissions and 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 and the current regulatory environment; patent and intellectual property matters; competition; the volatility of capital markets and other adverse macroeconomic factors; as well as other risks described in "Risk Factors," in our most recent Form 10-K and other risk factors set forth from time to time in our filings with the Securities and Exchange Commission made pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended. 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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