Homology Medicines Provides Update on pheEDIT and juMPStart Clinical Trials and Announces Expected 2023 Milestones, Including Initial Data Read-Outs from Both Programs

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Strong Cash Position with Runway into Fourth Quarter 2024

Non-Clinical Data on Immunosuppression Regimen Supportive of Clinical Programs

Preclinical Data from HMI-103 Gene Editing Program Utilizing a Unique Mechanism of Action Demonstrated Significantly Increased Potency in PKU Model

BEDFORD, Mass., Jan. 04, 2023 (GLOBE NEWSWIRE) -- Homology Medicines, Inc. (Nasdaq: FIXX), a genetic medicines company, announced today enrollment and site status updates from the pheEDIT Phase 1 gene editing trial with HMI-103 for phenylketonuria (PKU) and the juMPStart Phase 1 gene therapy trial with HMI-203 for Hunter syndrome (MPS II).

The first participant was recently dosed in the pheEDIT trial, with additional participants in screening. Homology expects to provide initial data from the trial mid-year 2023. There are nine active clinical trial sites with more expected to be initiated throughout 2023. The juMPStart trial has five clinical sites in the U.S. and Canada with more expected to be initiated, and initial data is expected in the second half of 2023.

“With a solid financial position, our focus is and will continue to be centered on clinical trial execution,” said Albert Seymour, Ph.D., President and Chief Executive Officer. “HMI-103 and HMI-203 represent differentiated one-time approaches to PKU and MPS II, respectively, designed to address key unmet medical needs. Building on the interest from the physician and patient communities, we look forward to progressing these programs. Importantly, we plan to share initial clinical data from both trials in 2023, including the first data from our nuclease-free gene editing technology in humans.”

Homology shared new preclinical data today supporting the immunosuppression regimen incorporated in both the pheEDIT and juMPStart trials. In non-human primates (NHPs), use of a prophylactic T-cell inhibitor combined with steroids reduced the neutralizing antibody (nAb) response to the AAVHSC vector and increased mRNA expression, compared to NHPs not receiving the regimen and to those receiving each agent alone. Homology plans to present these data at an upcoming scientific conference.

Building on the unique mechanism of action of gene editing candidate HMI-103, Homology today shared preclinical potency data. HMI-103 is designed to use homologous recombination to integrate the *PAH* gene and a liver-specific promoter into the genome and to maximize PAH expression in all transduced liver cells. In the preclinical PKU model, the murine surrogate of
HMI-103 was ten times more potent than non-integrating gene therapy vector HMI-102.

“We believe HMI-103 has the potential to treat both children and adults with PKU by maximizing PAH through genome integration and episomal expression. Optimizing HMI-103, including vector design, integration of a strong liver-specific promoter, and enhanced packaging, resulted in increased potency, which is what you strive for with one-time genetic medicines,” concluded Dr. Seymour.

In 2023, Homology plans to progress its pipeline of genetic medicines, including conducting IND-enabling studies of HMI-104, a one-time GTx-mAb development candidate for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). The Company is also focused on efforts to partner the optimized HMI-204 gene therapy candidate for metachromatic leukodystrophy (MLD), with near-term plans to present preclinical data from the program for the first time. The Company will continue to work with Oxford Biomedica Solutions, the AAV manufacturing and innovation business Homology established with Oxford Biomedica and that supplies Homology’s programs. Oxford Biomedica Solutions recently announced that its platform has produced high-quality titers of E15 vg/L and achieved over 90% fully intact vector.

About HMI-103
Homology is conducting a Phase 1, open-label, dose-escalation clinical trial (called the pheEDIT study). HMI-103 is a one-time, *in vivo,* nuclease-free gene editing candidate for PKU designed to harness the body's natural DNA repair process of homologous recombination to replace the disease-causing gene with a functional gene and liver-specific promoter and to maximize PAH expression in all transduced liver cells.

About PKU
PKU is a rare inborn error of metabolism caused by a mutation in the *PAH* gene. PKU results in a loss of function of the enzyme phenylalanine hydroxylase, which is responsible for the metabolism of Phe, an amino acid obtained exclusively from the diet. If left untreated, toxic levels of Phe can accumulate in the blood and result in progressive and severe neurological impairment. Currently, there are no treatment options for PKU that target the underlying genetic cause of the disease. According to the National PKU Alliance, PKU affects nearly 16,500 people in the U.S. with approximately 350 newborns diagnosed each year. The worldwide prevalence of PKU is estimated to be 50,000 people.

About HMI-203
Homology is conducting a Phase 1, open-label, dose-escalation clinical trial (called the juMPStart study). HMI-203 is a one-time, *in vivo* gene therapy candidate for Hunter syndrome designed to use one of Homology’s AAVHSC vectors to deliver functional copies of the iduronate-2-sulfatase (*IDS)* gene to multiple organs where there are missing or mutated copies of the gene.

About Hunter Syndrome, or MPS II
Hunter syndrome is a rare, X-linked lysosomal storage disorder caused by mutations in the *IDS* gene, which is responsible for producing the I2S enzyme that breaks down large sugar molecules, or cellular waste, called glycosaminoglycans (GAGs). Severe Hunter syndrome results in toxic lysosomal accumulation of GAGs that causes progressive debilitation and decline in intellectual function. Hunter syndrome occurs in approximately 1 in 100,000 to 1 in 170,000 males, and the severe form leads to life expectancy of 10 to 20 years.

About Homology Medicines, Inc.
Homology Medicines, Inc. is a clinical-stage genetic medicines company dedicated to transforming the lives of patients suffering from rare diseases by addressing the underlying cause of the disease. The Company's clinical programs include HMI-103, a gene editing candidate for phenylketonuria (PKU); HMI-203, an investigational gene therapy for Hunter syndrome; and HMI-102, an investigational gene therapy for adults with PKU. Additional programs focus on metachromatic leukodystrophy (MLD), paroxysmal nocturnal hemoglobinuria (PNH) and other diseases. Homology's proprietary platform is designed to utilize its family of 15 human hematopoietic stem cell-derived adeno-associated virus (AAVHSCs) vectors to precisely and efficiently deliver genetic medicines *in vivo* through a gene therapy or nuclease-free gene editing modality, as well as to deliver one-time gene therapy to produce antibodies throughout the body through the GTx-mAb platform. Homology established an AAV manufacturing and innovation business in partnership with Oxford Biomedica, which was based on Homology's internal process development and manufacturing platform. Homology has a management team with a successful track record of discovering, developing and commercializing therapeutics with a focus on rare diseases. Homology believes its initial clinical data and compelling preclinical data, scientific and product development expertise and broad intellectual property position the Company as a leader in genetic medicines. For more information, visit www.homologymedicines.com.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding: our expectations surrounding the potential, safety, efficacy, and regulatory and clinical progress of our product candidates; the potential of our gene therapy and gene editing platforms, including our GTx-mAb platform; our plans and timing for the release of additional preclinical and clinical data; our plans to progress our pipeline of genetic medicine candidates and the anticipated timing for these milestones; the sufficiency of our cash and cash equivalents to fund our operations; our expectations surrounding our relationship with Oxford Biomedica Solutions; and our position as a leader in the development of genetic medicines. The words "believe," "may," "will," "estimate," "potential," "continue," "anticipate," "intend," "expect," "could," "would," "project," "plan," "target," and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the impact of the COVID-19 pandemic on our business and operations, including our preclinical studies and clinical trials, and on general economic conditions; we have and expect to continue to incur significant losses; our need for additional funding, which may not be available; failure to identify additional product candidates and develop or commercialize marketable products; the early stage of our development efforts; potential unforeseen events during clinical trials could cause delays or other adverse consequences; risks relating to the regulatory approval process; interim, topline and preliminary data may change as more patient data become available, and are subject to audit and verification procedures that could result in material changes in the final data; our product candidates may cause serious adverse side effects; inability to maintain our collaborations, or the failure of these collaborations; our reliance on third parties, including for the manufacture of materials for our research programs, preclinical and clinical studies; failure to obtain U.S. or international marketing approval; ongoing regulatory obligations; effects of significant competition; unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives; product liability lawsuits; securities class action litigation; failure to attract, retain and motivate qualified personnel; the possibility of system failures or security breaches; risks relating to intellectual property and significant costs incurred as a result of operating as a public company. These and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 and our other filings with the Securities and Exchange Commission could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

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