Homology Medicines Presents on Design of pheEDIT Trial Evaluating One-Time Nuclease-Free Gene Editing Candidate HMI-103 for PKU at American Society of Human Genetics Meeting

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- Additional Presentation Focused on Use of Single-Molecule, Modified Base Sequencing to Support Vector Design -

BEDFORD, Mass., Oct. 27, 2022 (GLOBE NEWSWIRE) -- Homology Medicines, Inc. (Nasdaq: FIXX), a genetic medicines company, announced today a presentation on the design of pheEDIT, a Phase 1, open-label, dose-escalation study evaluating one-time gene editing candidate HMI-103 in adults with phenylketonuria (PKU). The presentation included preclinical data demonstrating efficacy in a PKU murine model and precision of editing in a humanized murine model. During the American Society of Human Genetics (ASHG) Annual Meeting, the Company also presented data that demonstrated single-molecule, modified base sequencing can aid in the characterization, design and optimization of AAV vectors.

"The pheEDIT dose-escalation clinical trial is the first gene editing study for PKU, and investigational HMI-103 has the potential to treat adult and pediatric PKU with its unique dual mechanism of action designed to integrate the *PAH* gene and liver-specific promoter into the genome and to maximize PAH expression in all transduced liver cells," said Albert Seymour, Ph.D., President and Chief Executive Officer of Homology Medicines. "The program's preclinical data showed long-term Phe normalization in the PKU model following a single I.V. administration, and a genome-wide integration assay demonstrated the precision of homologous recombination with no off-target integration in a humanized liver model. Together, these data supported the initiation of pheEDIT and highlight our commitment to leading the field with an unbiased approach to evaluating on-and off-target integrations."

The poster presentation titled, "A Phase 1, Open-Label, Dose-Escalation Study to Evaluate the Safety and Efficacy of HMI-103, a One-Time Gene-Editing Vector in Adult Participants with Classical PKU Due to PAH Deficiency," outlined the design of the pheEDIT trial, which is:

- A Phase 1, open label, sequential dose-escalation trial evaluating safety and efficacy of a single I.V. administration of HMI-103, including tolerability and Phe levels;
- Designed to enroll three dose cohorts with up to three patients with uncontrolled PKU in each cohort; and
- Incorporating a steroid-sparing prophylactic immunosuppression regimen, including a T-cell inhibitor, to temporarily dampen potential immune response to the capsid.

A second presentation titled, "Single-Molecule, Modified Base Sequencing to Identify Frequency and Cause of rAAV Vector Breakpoints," demonstrated that use of next-generation sequencing can lead to improved vector design by identifying the locations and frequency of potential breakpoints that can be addressed by optimizing the vectors.

For more information, please visit www.homologymedicines.com/publications.

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 phenylketonuria (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 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. 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: 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; and our position as a leader in the development of genetic medicines. 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 June 30, 2022 and our other filings with the Securities and Exchange Commission (SEC) 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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