Homology Medicines Presents Preclinical Data Supporting Immunosuppression Regimen in Ongoing PKU and Hunter Syndrome Clinical Trials, and Details Optimized MLD Gene Therapy Candidate at the 19th Annual WORLDSymposium™ Meeting

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Preclinical Studies Demonstrated a Targeted Immunosuppression Approach Led to Reduced Immune Response to AAVHSC Administration and Improved Gene Expression

In Vivo *Gene Therapy Candidate HMI-204 for MLD Showed Robust CNS Distribution and Expression with Improved Packaging Productivity*

BEDFORD, Mass., Feb. 22, 2023 (GLOBE NEWSWIRE) -- Homology Medicines, Inc. (Nasdaq: FIXX), a genetic medicines company, announced today the presentation of preclinical data that supports the targeted, prophylactic immunosuppression regimen in the ongoing pheEDIT gene editing clinical trial in adults with phenylketonuria (PKU) and juMPStart gene therapy trial in adults with Hunter syndrome (MPS II). Homology also shared additional details of the optimized, *in vivo* gene therapy candidate HMI-204 for metachromatic leukodystrophy (MLD) during the 19th Annual WORLD*Symposium* ™ Meeting.

"We are pleased to share our work outlining the impact immunosuppression regimens had on outcomes following AAVHSC dosing in NHPs, as it contributes to a key area of research in the gene therapy and gene editing field," stated Albert Seymour, Ph.D., President and Chief Executive Officer of Homology Medicines. "In this study, we evaluated multiple regimens, including the combination of a T-cell inhibitor and steroid, and reported that the combination was the most effective in reducing B- and T-cell activity, reducing neutralizing antibody formation and improving gene expression. This targeted, prophylactic approach is part of our ongoing pheEDIT and juMPStart trials, from which we expect to share initial clinical data mid-year and in the second half of the year, respectively."

Dr. Seymour continued, "Also at WORLD, we presented the details of our optimized gene therapy development candidate for MLD, which showed the ability to cross the blood-brain-barrier following a single I.V. administration in the murine disease model and resulted in levels of enzyme activity predicted to lead to efficacy *in vivo*. The data also included HMI-204's optimized tissue expression profile and improvements in productivity packaging. We continue to seek a partner for this candidate, which is ready to enter IND-enabling studies."

Details of Homology's Presentations at WORLD *Symposium* ™
In the poster titled, "Tacrolimus Administration in Combination with Dexamethasone Reduces Neutralizing Antibody Formation Against AAV Vector and Increases Transgene Expression in Cynomolgus Macaques," data showed that administration of the T-cell inhibitor tacrolimus with dexamethasone in AAVHSC-*PAH*-treated non-human primates (NHPs) resulted in:

- Lowered secretion of inflammatory cytokines and activation state of CD8+ T cells compared to the no immunosuppression (IS) group;
- Reduced AAVHSC neutralizing antibody (nAb) formation compared to NHPs treated with each agent alone and by 4.8-fold compared to the no IS group; and
- Increased *PAH* gene expression, as measured by mRNA, compared to each agent alone and by two-fold compared to the no IS group.

In the poster titled, "Gene Therapy for Metachromatic Leukodystrophy: Lead Candidate Optimization," a single I.V. administration of optimized HMI-204 in the murine model of MLD showed:

- Systemic and central nervous system (CNS) biodistribution, including robust expression in the CNS;
- Human ARSA cellular expression patterns in the brain that were nearly identical to that of murine Arsa distribution in wildtype age-matched controls; and
- Sustained levels of ARSA activity reaching normal adult ARSA brain activity levels.

Additionally, packaging productivity of HMI-204 demonstrated a substantial improvement in vector genome yields, compared to the earlier MLD gene therapy candidate.

For more information, please visit the Publications and Presentations page on Homology's website.

About Metachromatic Leukodystrophy (MLD)
MLD is a rare lysosomal storage disorder primarily caused by a mutation in the *ARSA* gene. *ARSA* is responsible for the creation of the arylsulfatase A (ARSA) protein, which is required for the breakdown of sulfatides in cells. In MLD, sulfatides accumulate and destroy myelin-producing cells in the peripheral and central nervous systems leading to progressive and serious neurological deterioration. The late infantile form of the disorder is estimated to affect 1 in 40,000 people, and it is fatal within 5-10 years after onset.

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 nuclease-free gene editing modality, gene therapy, or GTx-mAb, which is designed to produce antibodies throughout the body. 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 plans to engage in future collaborations and strategic partnerships; 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; 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: 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; the impact of the COVID-19 pandemic on our business and operations, including our preclinical studies and clinical trials, and on general economic conditions; 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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