Pharvaris Presents Data Supporting HAE Drug Development Strategy at the 2022 HAEi Global Leadership Workshop

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ZUG, Switzerland, Oct. 07, 2022 (GLOBE NEWSWIRE) -- Pharvaris (Nasdaq: PHVS), a clinical-stage company developing novel, oral bradykinin-B2-receptor antagonists to treat and prevent hereditary angioedema (HAE) attacks, today announced the presentation of preclinical and clinical data of PHA121, and its two formulations – softgel capsule PHVS416 and extended-release tablet PHVS719, for the treatment of HAE at the 2022 HAEi Global Leadership Workshop being held October 6-9, 2022, in Frankfurt, Germany. The poster, titled "Development of two novel oral formulations of a first-in-class bradykinin B2 receptor antagonist for on-demand and prophylactic treatment of hereditary angioedema," was presented by Marcus Maurer, M.D., Professor of Dermatology and Allergy, Executive Director of the Institute of Allergology at the Charité – Universitätsmedizin Berlin, and Co-Director of Allergology and Immunology at the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP.

"Treating HAE requires addressing excess bradykinin in the body as bradykinin is the direct cause of HAE attacks," said Dr. Maurer. "Although there are approved therapies for people living with HAE around the globe, there is still an unmet need related to treatment efficacy, tolerability, and administration preference. Novel, safe, and effective treatments are in development to address the need of the HAE community."

The poster included preclinical and clinical data supporting Pharvaris' development strategy for two oral therapies, one for on-demand treatment and one for prophylactic treatment of HAE attacks. Preclinical *in-vitro* and *ex-vivo* studies demonstrate that PHA121, the active ingredient in PHVS416 and PHVS719, is 25-fold more potent than icatibant at inhibiting bradykinin activation of the endogenous human B2 receptor. Tailored formulations of PHA121 achieved exposure levels predicted from a human bradykinin challenge study to be effective in treating acute HAE attacks and reducing the likelihood of HAE attacks with a convenient single-dose oral administration. The poster included data supporting the suitability of the pharmacokinetics of PHVS416 for the on-demand treatment of HAE with therapeutic exposure above EC_{85} within 30 minutes and of PHVS719 daily for the prophylactic treatment of HAE with extended release and absorption from the GI tract providing the necessary therapeutic exposure for more than 24 hours.

Peng Lu, M.D., Ph.D., Chief Medical Officer of Pharvaris, added, "By tailoring the formulations of PHA121, Pharvaris has developed two distinct oral therapeutic candidates to specifically address the unmet need of those living with HAE. The softgel capsule, PHVS416, has shown to have a rapid onset of action, which is preferred for the on-demand treatment of HAE, while the extended-release tablet formulation, PHVS719, has shown sustained therapeutic exposure, which supports its use in prophylaxis. We remain ever grateful to the HAE community, clinical trial participants, and site investigators and staff, without whom we would not be able to continue to advance science as we strive to improve treatment options for people living with HAE."

About PHVS416
PHVS416 is an investigational softgel capsule formulation containing PHA121, a highly potent, specific, and orally bioavailable competitive antagonist of the bradykinin B2 receptor. Pharvaris aims to develop this formulation to provide fast and reliable symptom relief, through rapid exposure of attack-mitigating therapy in a convenient, small oral dosage form. In healthy volunteers, a single dose of PHVS416 showed rapid exposure exceeding predicted therapeutically efficacious levels within 30 minutes. PHVS416 is currently in Phase 2 clinical development outside the U.S. for the on-demand and proof-of-concept prophylactic treatment of HAE.

About PHVS719
PHVS719 is an investigational extended-release tablet formulation containing PHA121, a highly potent, specific, and orally bioavailable competitive antagonist of the bradykinin B2 receptor. Pharvaris is developing this formulation to provide an easy way to prevent attacks with sustained exposure of attack-preventing medicine in a convenient, small oral dosage form. PHVS719 is currently in Phase 1 clinical development for the prophylactic treatment of HAE. In healthy volunteers, a single dose of PHVS719 was well tolerated with an extended-release profile supporting once-daily dosing.

About PHA121
PHA121 (PHA-022121) is a highly potent, specific, and orally bioavailable competitive antagonist of the bradykinin B2 receptor that has completed Phase 1 clinical development. PHA121 utilizes the same mechanism as icatibant, the leading therapy for on-demand treatment of HAE. Pharvaris is developing this novel small molecule for on-demand and prophylactic treatment of HAE and other bradykinin-mediated diseases through formulations optimized for each setting. Data from single- and multiple-ascending-dose Phase 1 studies in healthy volunteers demonstrate rapid exposure and linear pharmacokinetics at doses up to 50 mg. In a bradykinin-challenge study in healthy volunteers, PHA121 showed significant inhibition of bradykinin-induced hemodynamic changes with an average composite EC50 of 2.4 ng/mL and EC85 of 13.8 ng/mL, approximately four-fold more potent than historical data for icatibant. Quantitative modeling indicates that single oral doses of PHA121 will maintain pharmacological effectiveness for a substantially longer time than 30 mg of subcutaneous icatibant. In clinical studies, PHA121 has been observed to be well-tolerated at all doses studied to date.

About Pharvaris
Pharvaris is a clinical-stage company developing novel, oral bradykinin-B2-receptor antagonists to treat and prevent HAE attacks, building on its deep-seated roots in HAE. By directly targeting this clinically proven therapeutic target with novel small molecules, the Pharvaris team aspires to offer people with all sub-types of HAE effective and convenient alternatives to treat attacks, both on-demand and prophylactically. The company brings together the best talent in the industry with deep expertise in rare diseases and HAE. For more information, visit https://pharvaris.com/.

Forward-Looking Statements
This press release contains certain forward-looking statements that involve substantial risks and uncertainties. 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 containing the words "believe," "anticipate," "expect," "estimate," "may," "could," "should," "would," "will," "intend" and similar expressions. These forward-looking statements are based on management's current expectations, are neither promises nor guarantees, and involve known and unknown risks, uncertainties and other important factors that may cause Pharvaris' actual results, performance or achievements to be materially different from its expectations expressed or implied by the forward-looking statements. Such risks include but are not limited to the following: uncertainty in the outcome of our interactions with regulatory authorities, including the FDA with respect to the clinical hold on PHA121 clinical trials in the U.S.; the

expected timing, progress, or success of our clinical development programs, especially for PHVS416 and PHVS719, which are in mid-stage global clinical trials and are currently on hold in the U.S. as a result of the clinical hold; risks associated with the COVID-19 pandemic, which may adversely impact our business, nonclinical studies, and clinical trials; the timing of regulatory approvals; the value of our ordinary shares; the timing, costs and other limitations involved in obtaining regulatory approval for our product candidates PHVS416 and PHVS719, or any other product candidate that we may develop in the future; our ability to establish commercial capabilities or enter into agreements with third parties to market, sell, and distribute our product candidates; our ability to compete in the pharmaceutical industry and with competitive generic products; our ability to market, commercialize and achieve market acceptance for our product candidates; our ability to raise capital when needed and on acceptable terms; regulatory developments in the United States, the European Union and other jurisdictions; our ability to protect our intellectual property and know-how and operate our business without infringing the intellectual property rights or regulatory exclusivity of others; our ability to manage negative consequences from changes in applicable laws and regulations, including tax laws, our ability to successfully remediate the material weakness in our internal control over financial reporting and to maintain an effective system of internal control over financial reporting; changes in general market, political and economic conditions, including as a result of the current conflict between Russia and Ukraine; and the other factors described under the headings "Cautionary Statement Regarding Forward-Looking Statements" and "Item 3. Key Information—D. Risk Factors" in our Annual Report on Form 20-F and other periodic filings with the Securities and Exchange Commission.

These and other important factors 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. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. While Pharvaris may elect to update such forward-looking statements at some point in the future, Pharvaris disclaims any obligation to do so, even if subsequent events cause its views to change. These forward-looking statements should not be relied upon as representing Pharvaris' views as of any date subsequent to the date of this press release.

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