Pharvaris Presents Pharmacokinetic and Pharmacodynamic Data for Oral PHA121, Under Development for the Treatment of HAE, at 12th C1 Inhibitor Deficiency and Angioedema Workshop

June 4, 2021

ZUG, Switzerland, June 04, 2021 (GLOBE NEWSWIRE) -- Pharvaris (Nasdaq: PHVS), a clinical-stage company focused on the development and commercialization of novel oral bradykinin-B2-receptor antagonists for the treatment of hereditary angioedema (HAE) and other bradykinin-B2-receptor-mediated indications, today announced that Anne Lesage, Ph.D., chief early development officer at Pharvaris, will present bradykinin challenge data supporting the pharmacokinetic (PK) and pharmacodynamic (PD) profile of PHA121 (PHA-022121) for the treatment of hereditary angioedema (HAE), at the 12th C1 Inhibitor Deficiency and Angioedema Workshop, to be held virtually June 3-6, 2021.

"Pharvaris is proud to be a sponsor for the 12th C1 Inhibitor Deficiency and Angioedema Workshop," said Dr. Lesage. "Findings presented here from pre-clinical and clinical studies, particularly from in vivo bradykinin challenge studies, show that PHA121 demonstrates faster onset than icatibant in head-to-head preclinical studies and, compared to published data, is consistently more potent showing longer duration bradykinin-BR2-antagonist activity than icatibant in human pharmacodynamic studies. These data position PHA121 as a potentially valuable treatment option for both on-demand and prophylactic treatment of HAE."

Berndt Modig, chief executive officer and co-founder of Pharvaris added, "Our data demonstrate a favorable pharmacokinetic and pharmacodynamic profile of PHA121 – providing strong proof of mechanism for PHA121 and a foundation for the dose regimens to be further evaluated for HAE as Pharvaris continues progressing our clinical programs using our PHVS416 and PHVS719 product formulations."

Pharvaris established a proof-of-concept model for HAE in non-human primates using bradykinin, an endogenous peptide known to mediate signs and symptoms of HAE. The model was validated utilizing icatibant, a marketed injectable B2 receptor antagonist, providing back-translation from human clinical experience with icatibant. The objective of the study was to investigate the ability of PHA121 to attenuate blood-pressure changes induced by bradykinin injection. In this model, PHA121 inhibited bradykinin-induced changes in blood pressure at all doses tested (0.1, 0.3, 1, 3, and 10 mg/kg given orally) with a faster onset of action than icatibant and the duration of the effect was dose dependent.

PHA121 was also orally administered in two double-blind, placebo-controlled single-ascending-dose studies up to 50 mg, with pharmacokinetics (PK) and safety observed for 72 hours, in healthy volunteers. Pharmacodynamic (PD) effects were evaluated with a nonlinear mixed-effect PK/PD model using 12 mg and 22 mg doses and compared to historical icatibant data. PK/PD analysis showed significant inhibition of bradykinin-induced hemodynamic changes with an average composite EC_{50} of 2.4 ng/mL and EC_{85} of 13.8 ng/mL. Single-dose treatment of PHA121 demonstrated effective bradykinin inhibition. Quantitative modeling indicates that single oral doses of PHA121 will maintain pharmacologically active drug levels for a substantially longer time than 30 mg of subcutaneous icatibant.

A copy of the oral presentation can be viewed on the investor section of our website.

About PHVS416
PHVS416 is a softgel capsule formulation containing PHA121, a highly potent, specific, and orally bioavailable competitive antagonist of the bradykinin B2 receptor. Pharvaris is developing this formulation to provide rapid exposure of attack-mitigating medicine in a convenient, small oral dosage form. PHVS416 is currently in Phase 2 clinical development for the on-demand treatment of HAE.

About PHVS719
PHVS719 is an 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 sustained exposure of attack-preventing medicine in a convenient, small oral dosage form. PHVS719 is currently in preclinical development for the prophylactic treatment of HAE.

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 for the treatment of HAE. 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 predictable 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 pharmacologically active drug levels for a substantially longer time than 30 mg of subcutaneous icatibant. PHA121 has been observed to be well-tolerated at all doses studied to date.

About Pharvaris
Pharvaris is a clinical-stage company focused on bringing oral bradykinin-B2-receptor antagonists to patients. By targeting this clinically proven therapeutic target with novel small molecules, the Pharvaris team is advancing new alternatives to injected therapies for all sub-types of HAE and other bradykinin-mediated diseases. The Company brings together executives with a breadth of expertise across pharmaceutical development and rare disorders, including 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: the expected timing,

progress, or success of our clinical development programs, especially for PHVS416 and PHVS719, which are in early-stage clinical trials; risks associated with the COVID-19 pandemic, which may adversely impact our business, preclinical 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; and the other factors described under the heading “Risk Factors” in our registration statement 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.

Investor Contact
Sarah McCabe
Stern Investor Relations, Inc.
+1-212-362-1200
sarah.mccabe@sternir.com

Media Contact
Maggie Beller
Russo Partners, LLC
+1-646-942-5631
maggie.beller@russopartnersllc.com