Pharvaris to Present PHVS416 and PHVS719 Clinical Data for Treatment of HAE at the ACAAI Annual Scientific Meeting 2022

November 10, 2022

ZUG, Switzerland, Nov. 10, 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 it will be presenting two in-person "ePoster – Meet the Author" presentations at the American College of Allergy, Asthma & Immunology (ACAAI) Annual Scientific Meeting 2022, being held from November 10-14, 2022, in Louisville, Ky.

"The data presented at ACAAI demonstrate the optimized pharmacokinetic and tolerability profiles of Pharvaris' drug candidates that are in clinical development for the treatment of HAE," said Peng Lu, M.D., Ph.D., Chief Medical Officer of Pharvaris. "PHVS719 is designed to be a once-daily prophylactic treatment for the prevention of HAE attacks, as supported by data demonstrating compound absorption in the colon and maintained exposure above predicted therapeutic levels. The cross-over pharmacokinetic data described in the second poster support the dosing regimen in CHAPTER-1, a Phase 2 study evaluating PHVS416 as a proof of concept of PHVS719 for the prophylactic treatment of HAE."

Presentation details and key data highlights include:

- **Title:** Development of PHVS719: an Oral Extended-Release Bradykinin B2 Receptor Antagonist to Prevent Hereditary Angioedema Attacks
  Presentation ID: P064
  Date and Time: Saturday, November 12, 2022, 12:05 p.m. EST
  Location: Exhibition Hall (Upper Concourse), Monitor 10

Pharmacokinetic properties of PHA121 were evaluated to support the intended therapeutic use of PHVS719 for the prophylactic treatment of HAE attacks using preclinical and clinical experimental models. Colonic absorption of PHA121 was investigated as a requisite for prolonged absorption of the extended-release formulation under development. In rodents, plasma concentrations following oral and intracolonic administrations of PHA121 were comparable, providing evidence that PHA121 can be systemically absorbed by colonic mucosa. In humans, high oral bioavailability and low fecal excretion further indicate almost-complete absorption in the gastrointestinal tract. Together, these data support clinical development of the extended-release tablet PHVS719 as a once-daily prophylactic treatment of HAE attacks.

- **Title:** Pharmacokinetics of PHVS719, extended-release tablet formulation of PHA121, a first-in-class oral human bradykinin B2-receptor antagonist
  Presentation ID: P068
  Date and Time: Sunday, November 13, 2022, 11:50 a.m. EST
  Location: Exhibition Hall (Upper Concourse), Monitor 10

In the Phase 1 pharmacokinetic study of PHVS719, 10 healthy subjects received, in a randomized order, two different doses of PHVS719 extended-release tablets (XR1 at 20 mg and XR2 at 40 mg), in fasting and in fed conditions, and one dose of PHVS416 20 mg in fasting conditions. Measurement of time-to-reach-therapeutic-exposure-levels for PHA121 above the EC_{85} of 13.8 ng/mL showed that after administration of XR1 and XR2, therapeutic plasma concentrations were achieved within approximately two hours. Concentrations of PHA121 remained at therapeutic levels for at least 30 hours with XR2. Food intake did not have significant effects on the time to reach therapeutic exposure of PHA121 nor on the time at which concentrations remained at therapeutic levels. The 24-hour area-under-the-curve exposure of PHA121 after XR2 was comparable to that observed in Phase 1 studies with PHVS416 softgel capsules dosed at 20 mg bid with food. Administration of both PHVS719 and of PHVS416 were well tolerated. No severe nor serious treatment-emergent adverse events were reported, with no specific safety pattern or trend in number or type of events. The 10 treatment-emergent adverse events that were reported in 50% of the participating subjects were mainly of Grade 1 severity or of Grade 2 severity, occurred after only one of the administrations of study drugs, and all completely resolved. Two of these events, namely neck pain and post-procedural hypotension, were considered as not related to the study drug. PHVS416, a softgel capsule formulation of PHA121 is being evaluated for safety and efficacy outcomes in CHAPTER-1, a Phase 2 proof of concept clinical trial, which is currently ongoing in countries outside the U.S. The U.S. Food and Drug Administration has placed on hold on clinical trials of PHA121 in the U.S.

The posters are available on the Investors section of the Pharvaris website at: https://ir.pharvaris.com/news-events/events-presentations.

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 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 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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