Pharvaris Announces Preclinical Pharmacological Data for Small Molecule PHA121 Published in International Immunopharmacology

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Data demonstrate PHA121 to be a potent human bradykinin B2 receptor antagonist

ZUG, Switzerland, March 22, 2022 (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, has published pharmacological data for the novel small molecule bradykinin (BK) B2-receptor antagonist PHA121 (PHA-022121) and its active metabolite PHA-022484, in a recent open-access article in *International Immunopharmacology* and will be published in the April 2022 issue of the journal.

The preclinical data demonstrate PHA121 specificity and potency for both recombinant and endogenous B2 receptor, including 20-fold higher potency than icatibant, an approved injectable B2-receptor antagonist. Relative to icatibant, PHA121 exhibited improved intrinsic clearance, which predicted the improved in vivo half-life and oral bioavailability seen in clinical studies to date. This novel small molecule bradykinin B2 receptor antagonist is in clinical development for the treatment and prevention of hereditary angioedema attacks. Early clinical data in healthy participants indicate that PHA121 is orally bioavailable, with rapid absorption, favorable pharmacokinetics, and good tolerance.

"To our knowledge, PHA121 is the most potent, and the only oral, small-molecule human bradykinin B2 receptor antagonist that has ever been reported," said Anne Lesage, Ph.D., Chief Early Development Officer of Pharvaris and lead author on the publication. "PHA121 acts as a selective and competitive antagonist of the bradykinin B2 receptor, blocking the effect of elevated bradykinin levels that lead to angioedema. This specificity is shown through large margins of inhibition at other targets. Its high potency allows for oral administration with a small dose, and supports Pharvaris' development of this compound for on-demand and prophylactic treatment of HAE."

The dataset in this publication demonstrates the *in vitro* pharmacological characteristics of PHA121 and its active metabolite, PHA-022484. Both compounds show high affinity for the recombinant human bradykinin B2 receptor. In contractility assays, both PHA121 and PHA-022484 demonstrate potent and reversible B2 antagonist activity. The data support a high degree of selectivity over a wide range of molecular targets, including the bradykinin B1 receptor.

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 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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