Deucrictibant Data Highlighted in Multiple Presentations at the C1-Inhibitor Deficiency and Angioedema Workshop

May 6, 2023

ZUG, Switzerland, May 06, 2023 (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 two oral presentations and three poster presentations highlighting data from non-clinical and clinical studies of deucrictibant at the 13th C1-inhibitor Deficiency and Angioedema Workshop, being held from May 4-7, 2023, in Budapest, Hungary.

"Today, two sequential presentations showed how PHVS416 (immediate-release deucrictibant capsules) provided symptom relief and resolution in the treatment of HAE attacks using the doses projected through the bradykinin challenge, our *in vivo* surrogate marker model," said Peng Lu, M.D., Ph.D., Chief Medical Officer of Pharvaris. "The RAPIDe-1 study showed consistent and clinically meaningful results across all endpoints supporting the further development of PHVS416 as a potential on-demand therapy for HAE. We plan to leverage these findings to prepare for RAPIDe-3, our Phase 3 clinical study evaluating PHVS416 for the treatment of on-demand HAE attacks."

Anne Lesage, Ph.D., Chief Early Development Officer of Pharvaris, added, "The outcomes of the cardiovascular assessments in non-clinical studies, combined with the data from our clinical studies to date, support the cardiovascular tolerability and safety profile of deucrictibant for the potential treatment of HAE and other bradykinin-mediated diseases with unmet need."

Presentation details and key data highlights include:

- **Title:** The EC_{85} Derived from the Oral Bradykinin B2 Receptor Antagonist Deucrictibant (PHA121) Against Bradykinin Effects in Healthy Volunteers Predicts the Onset and Duration of Its Clinical Effects in Hereditary Angioedema
  Presentation ID: O-18
  Presenter: Prof. Marcus Maurer, M.D.
  Date and Time: Saturday, May 6, 08:45-09:00 CEST (2:45-3:00 a.m. EDT)
  A bradykinin challenge model developed in non-human primates and healthy volunteers was employed to determine the plasma effective threshold for the bradykinin-antagonistic properties of deucrictibant in HAE and to predict the duration of the clinical effects of deucrictibant. Consistent with the modeling from the bradykinin challenge, a single dose of each of the PHVS416 (immediate-release deucrictibant capsules) doses in the RAPIDe-1 trial reached therapeutic threshold within 15-30 minutes in trial participants and was maintained for approximately 8-10 hours. In the same study, rapid onset of PHVS416 clinical effect was observed, with clinically meaningful improvements within four hours for all doses. Rescue medication was used for a lower proportion of PHVS416-treated attacks compared to placebo-treated attacks.

- **Title:** Efficacy and Safety of the Oral Bradykinin B2 Receptor Antagonist Deucrictibant Immediate Release Capsule (PHVS416) in Treatment of Hereditary Angioedema Attacks: Topline Results of RAPIDe 1 Phase 2 Trial
  Presentation ID: O-19
  Presenter: Prof. Henriette Farkas, M.D., Ph.D.
  Date and Time: Saturday, May 6, 09:00-09:15 CEST (3:00-3:15 a.m. EDT)
  Analysis of the primary endpoint of RAPIDe-1 demonstrated that PHVS416 (immediate-release deucrictibant capsules) significantly reduced attack symptoms at four hours when compared to placebo, measured as change in the mean 3-symptom composite (skin pain, skin swelling, abdominal pain) visual analogue scale (VAS-3) score during HAE attacks. All key secondary efficacy endpoints were also met and participants on PHVS416 also used substantially less rescue medication compared to placebo. In the attack-treatment phase, PHVS416 was generally well tolerated with three treatment-related adverse events (TRAEs) reported for one PHVS416 30-mg-treated attack and one TRAE reported for one placebo-treated attack.

- **Title:** Early symptom relief following treatment with the oral bradykinin 2 receptor antagonist deucrictibant immediate-release capsule (PHVS416) in patients with hereditary angioedema attacks
  Presentation ID: P-25
  Presenter: Prof. Marc A. Riedl, M.D.
  Date and Time: Friday, May 5, 14:00-16:00 CEST (8:00-10:00 a.m. EDT)
  Improvements in secondary endpoints Mean Symptom Complex Severity (MSCS, score decreased) and Treatment Outcome Score (TOS, score increased) during the first four hours after administration was observed in all three doses of PHVS416 (immediate-release deucrictibant capsules)-treated attacks, as compared to placebo-treated attacks.

- **Title:** Cardiovascular safety of the orally administered bradykinin B2 receptor antagonist, deucrictibant (PHA121, PHA-022121)
  Presentation ID: P-27
  Presenter: Brigitte Loenders, Ph.D.

Date and Time: Saturday, May 6, 16:00-18:00 CEST (10:00a.m.-12:00 p.m. EDT)
The cardiovascular safety of deucrictibant was assessed in non-clinical studies using *in vitro* cardiac ion channel and off-target receptor screenings, and *in vivo* acute and chronic studies in non-human primates, a pharmacologically active species. The occurrence of cardiovascular events was monitored in Phase 1 and Phase 2 studies of deucrictibant and continues to be monitored in ongoing and future clinical studies in HAE. Deucrictibant showed no *in vitro* alerts and no effect on cardiovascular function in *in vivo* non-clinical studies, and in clinical studies completed to date, including acute on-demand and repeat administration up to 10 days at anticipated therapeutic doses.

- **Title:** Efficacy of the oral bradykinin B2 receptor antagonist deucrictibant immediate-release capsule (PHVS416) by attack location in the RAPIDe-1 Phase 2 clinical trial for treatment of hereditary angioedema attacks
  Presentation ID: P-38
  Presenter: Prof. Anna Valerieva, M.D., Ph.D.
  Date and Time: Saturday, May 6, 16:00-18:00 CEST (10:00a.m.-12:00 p.m. EDT)
  Treatment outcomes by attack location (abdominal and peripheral) were analyzed in post-hoc analyses of RAPIDe-1. PHVS416 (immediate-release deucrictibant capsules) demonstrated consistent rapid onset of symptom relief and resolution of HAE attacks across attack location. These results are consistent with results of RAPIDe-1 primary analyses.

Additionally, data were presented from an independent investigator-initiated trial (IIT) in the Netherlands evaluating deucrictibant as a prophylactic treatment for acquired C1-inhibitor deficiency. Pharvaris provided PHVS416 (immediate-release deucrictibant capsules) for this study. Details of the presentation were:

- **Title:** Prophylaxis of angioedema attacks due to acquired C1-Inhibitor deficiency with PHA121, a novel oral bradykinin B2 receptor antagonist
  Presentation ID: O-26
  Presenter: Remy S. Petersen, M.D.
  Date and Time: Saturday, May 6, 11:45-12:00 CEST (5:45-6:00 a.m. EDT)

About RAPIDe-1
RAPIDe-1 is a Phase 2, double-blind, placebo-controlled, randomized, cross-over, dose-ranging trial of PHVS416 (immediate-release deucrictibant capsules) for the treatment of HAE type 1 and type 2 (HAE-1/2) attacks. The trial enrolled participants in Canada, Europe, Israel, the United Kingdom, and the United States. Eligible participants were between the ages of 18 and 75 years, diagnosed with HAE type I or II and experienced three or more attacks in the last four months or two or more attacks in the last two months prior to screening. Seventy-four participants were enrolled and 62 of them experienced 147 qualifying HAE attacks that were treated with double-blinded study drug (either placebo or PHVS416 10, 20, or 30 mg doses).

About PHVS416 (immediate-release deucrictibant capsules)
PHVS416 (immediate-release deucrictibant capsules) is an investigational medicine intended to treat acute attacks of hereditary angioedema (HAE) containing deucrictibant, a highly potent, specific, and orally bioavailable competitive antagonist of the bradykinin B2 receptor. Pharvaris aims to develop this formulation to provide rapid and reliable symptom relief, through rapid exposure of attack-mitigating therapy in a convenient, small oral dosage form. 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 (extended-release deucrictibant tablets)
PHVS719 (extended-release deucrictibant tablets) is an investigational medicine intended to prevent attacks of hereditary angioedema (HAE) containing deucrictibant, 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 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 Pharvaris
Building on its deep-seated roots in HAE, Pharvaris is a clinical-stage company developing novel, oral bradykinin-B2-receptor antagonists to treat and prevent HAE attacks. 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 safe, 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 relating to our future plans, studies and trials, and any 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 holds on deucrictibant 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 holds; risks arising from epidemic diseases, such as the COVID-19 pandemic, which may adversely impact our business, nonclinical studies, and clinical trials; the expected timing and results of the rodent toxicology study; 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 weaknesses in our internal control over financial reporting and to maintain an effective system of internal control over financial reporting; changes and uncertainty in general market, political and economic conditions, including as a result of inflation and 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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