Pharvaris Presents Data Supporting Ongoing Clinical Development of Deucrictibant in Bradykinin-Mediated Angioedema

June 2, 2025

- Deucrictibant data shows single-dose durability without symptom reoccurrence in the majority of HAE attacks treated
- First-ever bradykinin B2 receptor mechanism-on-mechanism prophylactic/on-demand data supports potential for deucrictibant portfolio
- Clinically validated biomarker assay has potential to eventually expand treatment opportunities of deucrictibant into additional forms of bradykinin-mediated angioedema
- Epidemiologic data and cognitive interviews further elucidate the unmet needs in bradykinin-mediated angioedema

ZUG, Switzerland, June 02, 2025 (GLOBE NEWSWIRE) -- Pharvaris (Nasdaq: PHVS), a late-stage biopharmaceutical company developing novel, oral bradykinin B2 receptor antagonists to help address unmet needs of those living with bradykinin-mediated diseases such as hereditary angioedema (HAE) and acquired angioedema due to C1 inhibitor deficiency (AAE-C1INH), today announced a summary of data that were presented at the 14th C1-Inhibitor Deficiency and Angioedema Workshop.

"Additional analyses of deucrictibant data demonstrate consistency in the clinical profile shown in both the prophylactic and on-demand treatment settings," said Berndt Modig, Chief Executive Officer of Pharvaris. "Deucrictibant's early-onset and durable treatment response in the on-demand setting, the maintenance of attack reduction for over a year and a half in the prophylactic setting, and the potential for deucrictibant to be used together in both the prophylactic and on-demand settings, if needed, provide additional evidence of deucrictibant's potential in the treatment of bradykinin-mediated angioedema. Pharvaris continues to diligently execute on the deucrictibant clinical program and is planning for two pivotal data readouts in the next 18 months."

Details of the presentations are outlined below:

Prophylaxis

Long-Term Safety and Efficacy of Oral Deucrictibant for Prophylaxis in Hereditary Angioedema: Data Snapshot Results of the CHAPTER-1 Open-Label Extension Study, an oral presentation by Emel Aygören-Pürsün, M.D. The ongoing Phase 2 CHAPTER-1 open-label extension (OLE) study provides further evidence on the long-term safety and efficacy of oral deucrictibant for prevention of HAE attacks. The attack rate has remained low, irrespective of baseline attack rate, for over a year and a half in OLE participants. When evaluating mechanism-on-mechanism responses, the response to icatibant for on-demand treatment of breakthrough attacks appeared to be maintained when used for breakthrough attacks during prophylactic treatment with deucrictibant.

Peng Lu, M.D., Ph.D., Chief Medical Officer of Pharvaris, stated, "Deucrictibant remains the only drug in development for bradykinin-mediated angioedema that has the potential to both prevent attacks and treat them when they occur. The data from the ongoing study further bolsters the potential value proposition of deucrictibant as it provides initial evidence that a bradykinin B2 receptor antagonist can effectively manage a breakthrough attack during treatment with a B2 receptor antagonist, if it were to occur. We believe further confirming these post-hoc open-label findings in our ongoing CHAPTER-3 study would provide additional evidence on the potential of deucrictibant to help address unmet needs of people living with bradykinin-mediated angioedema."

Long-Term Prophylactic Treatment with Oral Deucrictibant Improves Health-Related Quality of Life and Disease Control in Participants with Hereditary Angioedema: CHAPTER-1 Open-Label Extension Study, a poster presentation by Markus Magerl, M.D. The impact of deucrictibant treatment on health-related quality of life (HRQoL), disease control, and treatment satisfaction during the ongoing CHAPTER-1 OLE was evaluated. All of the participants who received deucrictibant reported clinically meaningful improvements in HRQoL at the end of the randomized portion of the trial, which was maintained at week 62 of the OLE. All of the participants in the OLE reported well controlled HAE and a high level of satisfaction with treatment.

Sustained Therapeutic Exposure with Once-Daily Oral Deucrictibant XR Tablet for Prophylaxis of Hereditary Angioedema Attacks: Results of a Pharmacokinetics Study in Healthy Volunteers, a poster presentation by Zhi-Yi Zhang, Ph.D. To confirm its potential for once-daily prophylactic treatment, a Phase 1 pharmacokinetic study was conducted to compare the profile of the XR formulation (40 mg) to the immediate-release (IR) formulation (2 x 20 mg in a single administration), which was shown to be efficacious and well tolerated in the proof-of-concept CHAPTER-1 prophylaxis study. Deucrictibant extended-release (XR) tablet was well tolerated with no adverse events. Deucrictibant XR's pharmacokinetic profile demonstrated sustained exposure for over 24 hours, supporting once-daily dosing, and showed, on average, approximately a four-fold higher mean plasma concentration than therapeutic threshold (EC_{85}) at 24 hours, supporting its further investigation as a potential oral once-daily prophylactic therapy for bradykinin-mediated angioedema.

CHAPTER-3 Phase 3 Trial Design: Efficacy and Safety of the Oral Bradykinin B2 Receptor Antagonist Deucrictibant Extended-Release Tablet for Prophylaxis of Hereditary Angioedema Attacks, a poster presentation by Andrea Zanichelli, M.D., Ph.D. CHAPTER-3 is an ongoing, global, Phase 3 study designed to evaluate the efficacy and safety of once-daily, oral deucrictibant (40 mg/day) XR tablet for prophylaxis of attacks in adolescents and adults with HAE. Results from the Phase 2 CHAPTER-1 study support the CHAPTER-3 study design.

On-Demand

Durability Of Response to a Single Dose of Oral Deucrictibant for On-Demand Treatment of Hereditary Angioedema Attacks, a poster presentation by Anna Valerieva, M.D., Ph.D. A post-hoc analysis of the placebo-controlled RAPIDe-1 trial and the RAPIDe-2 extension study assessed the durability of effects in HAE attacks treated with a single dose of deucrictibant. In both studies, the majority of attacks were treated with a single dose of deucrictibant. In RAPIDe-1, 95-100% of the attacks and, in RAPIDe-2, 98-100% of the attacks that achieved symptom relief and resolution had a durable response without symptom reoccurrence.

Dr. Lu continued, "The ideal on-demand treatment for people living with HAE should offer both rapid symptom relief and complete symptom resolution with a single dose; this can only be achieved if the response to treatment is sustained without attack symptom reoccurrence. We believe the recently presented data on durability of response could be compelling to multiple stakeholders in the HAE community, including those living with HAE, their prescribing physicians, and the payor community. We aim to further evaluate deucrictibant's ability to rapidly and completely address bradykinin-mediated angioedema attack symptoms in our ongoing Phase 3 RAPIDe-3 clinical study."

Long-Term Safety and Efficacy of Oral Deucrictibant for Treatment of Hereditary Angioedema Attacks: Results of the RAPIDe-2 Extension Study, an oral presentation by Marc A. Riedl, M.D., M.S. Following the closure of Part A of RAPIDe-2, a Phase 2/3 study of deucrictibant for the on-demand treatment of HAE attacks, an analysis of 465 attacks from 19 participants, including 14 upper airway attacks from seven participants, was conducted. The final results from Part A of the RAPIDe-2 extension are consistent with the Phase 2 RAPIDe-1 randomized study. Deucrictibant continued to be well tolerated across all doses. The median time to onset of symptom relief was 1.1 hours, and 97.8% of attacks achieved onset of symptom relief in 12 hours. The median time to complete attack resolution was 10.6 hours, and 86.9% of attack achieved complete resolution at 24 hours. Eighty-nine percent of the attacks that achieved symptom resolution at 24 hours were treated with a single dose of deucrictibant.

Safety and Efficacy of Oral Deucrictibant for Treatment of Upper Airway and Laryngeal Hereditary Angioedema Attacks: Results from the RAPIDe-2 Extension Study, a poster presentation by Ramón Lleonart, M.D. The final data from Part A of the RAPIDe-2 study showed that safety and efficacy outcomes of treatment with deucrictibant IR were consistent for both HAE attacks affecting the upper airways, including laryngeal attacks, and HAE attacks occurring in other locations. Deucrictibant was generally well tolerated with no treatment-related treatment-emergent adverse events reported across upper airway and non-upper airway attacks. Fourteen upper airway attacks were treated by 7 participants; the median time to onset of symptom relief, as measured by Patient Global Impression of Change (PGI-C) of "a little better", was 1.4 hours (n=14) for upper airway attacks compared to 1.1 hours for non-upper airway attacks (n=451). Endpoint measurements taken throughout the span of an entire attack until and including complete resolution were similar for both upper airway and non-upper airway attacks. Importantly, 92.9% of the upper airway attacks were treated with a single dose of deucrictibant.

Expansion Beyond HAE
Clinical Validation of a Novel Biomarker Assay to Characterize Bradykinin-Mediated Angioedema in Prospective and Biobank Plasma Samples, an oral presentation by Evangelia Pardali, Ph.D. Assays for an early and accurate diagnosis of bradykinin-mediated angioedema are lacking. Cold activation of plasma from people living with HAE resulted in increased levels of bradykinin compared to cold-activated plasma of healthy volunteers, resulting in a qualified kinin assay that can be used to reliably characterize people with bradykinin-mediated angioedema and could become a key tool aiding identification, study, and management of bradykinin-mediated pathologies including angioedema.

Further applications of this biomarker assay will be explored during Pharvaris' R&D call on June 4 (register here).

Acquired Angioedema Due to C1-Inhibitor Deficiency: Patient Experience and Assessment of Patient-Reported Outcome Measures, a poster presentation by Andrea Zanichelli, M.D., Ph.D. There are currently no approved therapies for the treatment of AAE-C1INH attacks, nor patient-reported outcome measures validated in AAE-C1INH. Concept elicitation and cognitive interviews were performed to develop a conceptual model of AAE-C1INH that could reveal important disease concepts supporting a clinical outcome assessment strategy, as well as evaluating the comprehension and interpretation of PGI-C, PGI-Severity (PGI-S), patient global assessment of change (PGA-C), and PGA-Status (PGA-S), and explore perceptions of meaningful change using these measures. One hundred percent of participants considered PGI-C "better" to be a meaningful change four hours post-treatment.

Epidemiology of Bradykinin-Mediated Angioedema in the European Population, a poster presentation by Emel Aygören-Pürsün, M.D. A systematic literature review was conducted to summarize epidemiologic data on bradykinin-mediated angioedema, including HAE due to C1 inhibitor deficiency (HAE-C1INH Type 1 and Type 2), HAE due to other mutations in people with normal C1 levels and function (HAE-nC1INH), and AAE-C1INH, in the European Union (EU) and United Kingdom (UK). The review of 14 peer-reviewed scientific articles allowed to estimate the prevalence of HAE-C1INH (Type 1/2) as ranging between 0.05-0.33/10,000 individuals, the prevalence of HAE-nC1INH ranging between <0.01-0.07/10,000 individuals, and the prevalence of AAE-C1INH ranging between 0.01-0.02/10,000 individuals in European countries.

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

About Deucrictibant
Deucrictibant is a novel, potent, orally bioavailable small-molecule bradykinin B2 receptor antagonist currently in clinical development. Deucrictibant is being investigated for its potential to prevent the occurrence of bradykinin-mediated angioedema attacks and to treat the manifestations of attacks if/when they occur by inhibiting bradykinin signaling through the bradykinin B2 receptor. Pharvaris is developing two formulations of deucrictibant for oral administration: an extended-release tablet to enable sustained absorption and efficacy as prophylactic treatment, and an immediate-release capsule to enable rapid onset of activity for on-demand treatment. Deucrictibant has been granted orphan drug designation for the treatment of bradykinin-mediated angioedema by the U.S. Food and Drug Administration and orphan designation by the European Commission.

About Pharvaris
Pharvaris is a late-stage biopharmaceutical company developing novel, oral bradykinin B2 receptor antagonists to potentially address all types of bradykinin-mediated angioedema. Pharvaris intends to provide injectable-like efficacy™ and placebo-like tolerability with the convenience of oral therapies to prevent and treat bradykinin-mediated angioedema attacks. With positive data in both Phase 2 prophylaxis and on-demand studies in HAE, Pharvaris is currently evaluating the efficacy and safety of deucrictibant in a pivotal Phase 3 study for the prevention of HAE attacks (CHAPTER-3) and a pivotal Phase 3 study for the on-demand treatment of HAE attacks (RAPIDe-3). 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; the

expected timing, progress, or success of our clinical development programs, especially for deucrictibant immediate-release capsules and deucrictibant extended-release tablets, which are in late-stage global clinical trials; our ability to replicate the efficacy and safety demonstrated in the RAPIDe-1, RAPIDe-2, and CHAPTER-1 Phase 2 and Phase 3 studies in ongoing and future nonclinical studies and clinical trials; risks arising from epidemic diseases, which may adversely impact our business, nonclinical studies, and clinical trials; our ability to potentially use deucrictibant for alternative purposes, for example to treat C1-INH deficiency (AAE-C1INH); the outcome and 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, 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, including with respect to existing therapies, emerging potentially competitive therapies and with competitive generic products; our ability to market, commercialize and achieve market acceptance for our product candidates; our ability to produce sufficient amounts of drug product candidates for commercialization; 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 (including the Biosecure Act), 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 conditions; disruptions at the FDA and other agencies; political conditions, such as the current war between Russia and Ukraine; economic conditions, including continuing inflation concerns; 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 U.S. 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.

Contact Maggie Beller Executive Director, Head of Corporate and Investor Communications maggie.beller@pharvaris.com