Pharvaris Announces Positive Top-line Phase 2 Data from the CHAPTER-1 Study of Deucrictibant for the Prophylactic Treatment of HAE Attacks

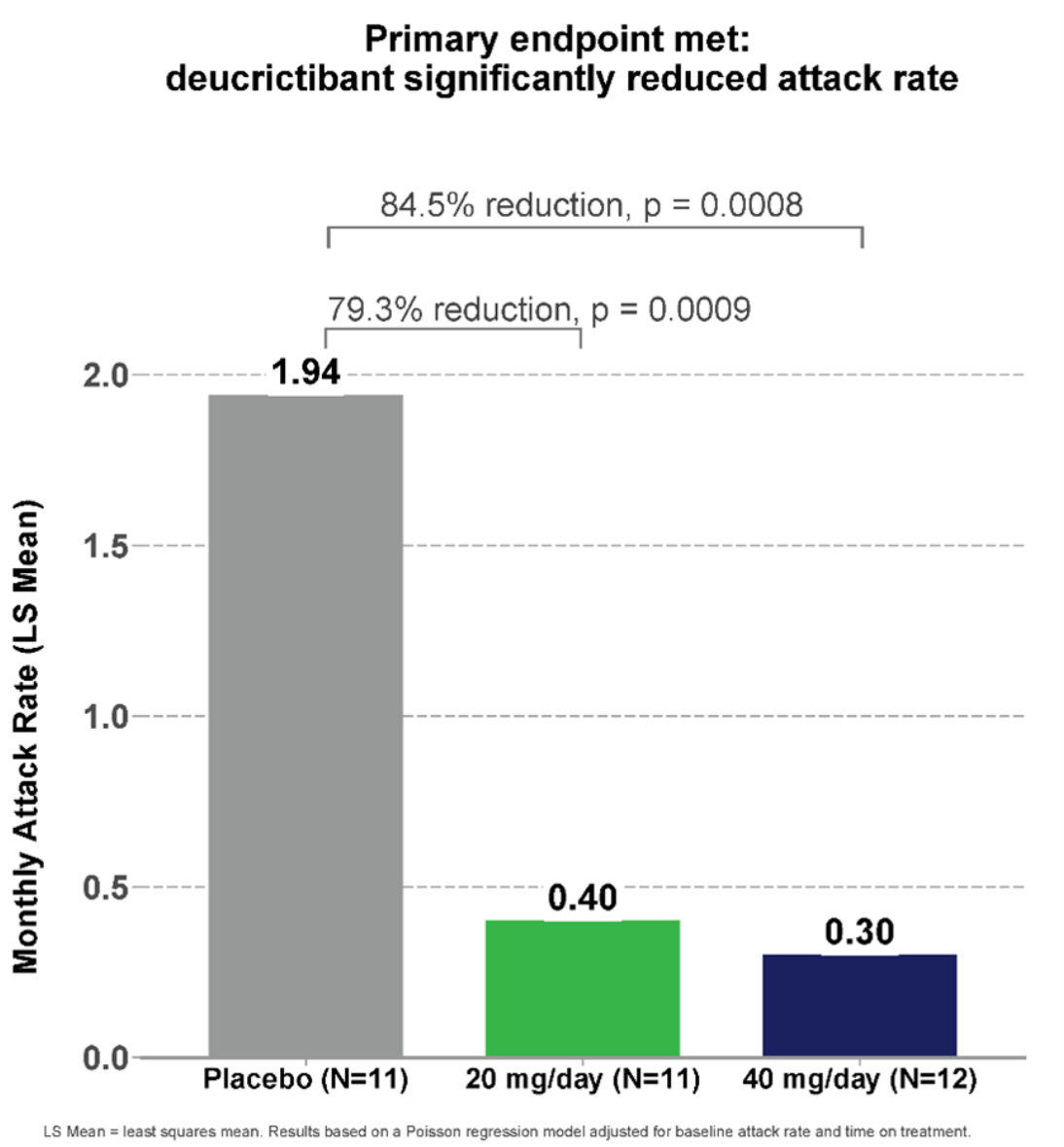
December 6, 2023

- **Primary endpoint met; 40 mg/day orally administered deucrictibant significantly reduced mean monthly attack rate by 84.5% (p=0.0008) compared to placebo**
- 92.3% reduction in occurrence of moderate and severe attacks
- 92.6% fewer attacks treated with on-demand medication by participants
- Deucrictibant well-tolerated
- Pharvaris to host a conference call today at 8:00 a.m. EST

ZUG, Switzerland, Dec. 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 positive top-line data from the CHAPTER-1 Phase 2 clinical study meeting its primary endpoint, with deucrictibant demonstrating statistically significant and clinically meaningful results of deucrictibant as an oral preventative treatment for people living with HAE. Pharvaris plans to present data from the study at future medical meetings.

CHAPTER-1 Clinical Study Design and Results
CHAPTER-1 (NCT05047185) is a double-blind, placebo-controlled Phase 2 study evaluating the efficacy as well as the safety and tolerability of deucrictibant for long-term prophylaxis against angioedema attacks in HAE-1/2. In the study, 34 participants were enrolled globally and randomized to receive one of two doses of deucrictibant (20 mg/day or 40 mg/day) or placebo for 12 weeks of treatment. Deucrictibant immediate-release capsule (PHVS416) was dosed twice-a-day as a proof-of-concept for the once-daily deucrictibant extended-release tablet (PHVS719), which is the intended formulation for the prophylactic treatment of HAE. The open-label portion of the CHAPTER-1 study is ongoing at the 40 mg/day dose.

The study's primary endpoint measured the time-normalized number of investigator-confirmed HAE attacks during the treatment period. The monthly attack rate was reduced by 84.5% (p=0.0008) compared to placebo in participants who received 40 mg/day of deucrictibant.



Marc A. Riedl, M.D., M.S., Professor of Medicine, Clinical Director of the US Hereditary Angioedema Association (HAEA) Angioedema Center at the University of California San Diego (UCSD), Clinical Service Chief for Allergy/Immunology at UCSD, and principal investigator in the CHAPTER-1 study, commented, "The HAE community is seeking highly effective, well-tolerated, and less burdensome therapies. The CHAPTER-1 data represent an important step forward in the evolution of HAE treatment. Given these encouraging results, deucrictibant has the potential to significantly improve clinical outcomes for people living with HAE."

Peng Lu, M.D., Ph.D., Chief Medical Officer of Pharvaris, stated, "Deucrictibant is the first HAE treatment with the potential to combine injectable-like efficacy and a favorable safety profile with the convenience of an oral therapy. The study demonstrates, for the first time ever, that antagonism of the bradykinin B2 receptor can provide early and sustained protection from HAE attacks, including substantial reduction of moderate and severe attacks, with clinically meaningful improvement in health-related quality of life. We look forward to advancing the development of deucrictibant for the prevention of HAE attacks."

Berndt Modig, Chief Executive Office of Pharvaris, added, "We sincerely thank the clinical trial participants and their caregivers, the site investigators and staff, the HAE community, and the Pharvaris team for their contributions to the CHAPTER-1 study. These study results, together with the compelling data from our on-demand program, further strengthens our confidence that deucrictibant can become the preferred option to treat as well as prevent HAE attacks."

In the analysis of the secondary endpoints, deucrictibant demonstrated clinically meaningful improvement in the severity of attacks and a decrease in the number of attacks treated with on-demand medication. Participants on deucrictibant treatment experienced a meaningful improvement in their quality of life. The table below lists additional study findings:

	Placebo N=11	20 mg/day N=11	40 mg/day N=12
Monthly attack rate – LS Mean (95% CI)*			
Moderate or severe attacks	1.50 (0.91, 2.50)	0.26 (0.08, 0.81)	0.12 (0.02, 0.67)

Attacks treated with on-demand medication	1.41 (0.88, 2.24)	0.35 (0.14, 0.85)	0.10 (0.02, 0.57)
Achieving threshold reduction of attack rate from baseline**			
>=50% reduction	2/11 (18%)	9/11 (82%)	9/10 (90%)
>=70% reduction	2/11 (18%)	8/11 (73%)	8/10 (80%)
>=90% reduction	0	6/11 (55%)	6/10 (60%)
Attack free during treatment period	0	6 /11(55%)	4/10 (40%)

LS = least squares; CI = confidence interval.
*Results of monthly attack rates are based on Poisson regression models adjusted for baseline attack rate and time on treatment. Nominal p-value < 0.01 for all endpoints included in this section comparing deucrictibant with placebo.
**Participants with <4 weeks of treatment (two participants on 40 mg/day) were not included in the summaries of proportions achieving threshold reduction of attack rate from baseline.
Nominal p-value < 0.05 for all endpoints included in this section comparing deucrictibant with placebo.

Throughout 12 weeks of treatment in CHAPTER-1, both doses of deucrictibant were well-tolerated. There were no serious adverse events, no severe treatment-emergent adverse events, and no adverse events leading to treatment discontinuation.

In August 2022, the U.S. Food & Drug Administration (FDA) placed clinical studies of deucrictibant, including CHAPTER-1, on hold. Pharvaris notified country-specific regulatory authorities in Canada, Europe, Israel, and the UK regarding the clinical holds in the U.S., and the regulatory status of deucrictibant outside the U.S. has not been affected. In June 2023, Pharvaris announced the removal of the clinical hold of deucrictibant for the on-demand treatment of HAE in the U.S. Pharvaris has completed the 26-week rodent toxicology study requested by the FDA, which we believe met its objective. Pharvaris is preparing to submit the study results to the FDA by the end of the year. However, neither the nature nor timing of the response from FDA is certain.

Conference Call
Pharvaris will host a live conference call and webcast to discuss the CHAPTER-1 study topline data in greater detail at 8:00 a.m. EST today via a live webcast; presentation slides may be accessed on the "Events and Presentations" page of the Pharvaris investor relations website. Participants interested in asking a verbal question during the Q&A may do so in the live conference call. An archived replay will also be available on the website for 90 days following the event.

About Deucrictibant
Deucrictibant is a potent, selective, and orally available antagonist of the bradykinin B2 receptor. By inhibiting bradykinin signaling through the bradykinin B2 receptor, deucrictibant has the potential to treat the clinical signs of an HAE attack and to prevent the occurrence of attacks. Based on its chemical properties, Pharvaris is developing two formulations of deucrictibant for oral administration; a capsule to enable rapid onset of activity for acute treatment, and an extended-release tablet to enable sustained absorption and efficacy in prophylactic treatment.

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 pursuing this clinically proven therapeutic target with novel small molecules, the Pharvaris team aspires to offer people with all sub-types of HAE efficacious, safe, and easy-to-administer 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 hold on prophylactic deucrictibant in the U.S.; the expected timing, progress, or success of our clinical development programs, especially for PHVS416 (immediate-release deucrictibant capsules) and PHVS719 (extended-release deucrictibant tablets), which are in mid-stage global clinical trials; 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 and our ability to resolve any issues to the satisfaction of the FDA or any regulatory agency in a timely manner; 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, 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 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 Hamas attack against Israel and the ensuing war; 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 External and Internal Communications maggie.beller@pharvaris.com