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Pharvaris Announces Positive Top-line Phase 2 Data from RAPIDe-1 Study of PHVS416 for the On-Demand Treatment of HAE Attacks

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- Primary endpoint met, substantially reducing HAE attack symptoms
- All secondary endpoints met
- PHVS416 was well tolerated at all dose levels
- Pharvaris to host a conference call today at 8:00 a.m. ET

ZUG, Switzerland, Dec. 08, 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 positive top-line data from the RAPIDe-1 Phase 2 clinical study, demonstrating statistically significant results of PHVS416 as an oral on-demand treatment for HAE attacks. Pharvaris plans to present data from the study at future medical meetings.

RAPIDe-1 Clinical Study Design and Results
RAPIDe-1 is a Phase 2, double-blind, placebo-controlled, randomized, crossover, dose-ranging study of PHVS416 softgel capsule for the acute treatment of angioedema attacks in patients with Type I or II HAE. Seventy-four patients were enrolled across 13 countries and were randomized into one of three single dose levels of PHVS416 and placebo. The study compares symptom relief during HAE attacks and the safety of each dose of PHVS416 with placebo. In Part I of the study, participants in a non-attack state received the assigned single dose of PHVS416 at the study center to assess its pharmacokinetics and safety. In Part II, participants self-administer blinded study drug at home to treat three physician-confirmed HAE attacks with PHVS416 or placebo. Additional information on the study can be found at: NCT04618211.

The primary endpoint of the study (Table 1) is the change of a three-symptom composite (skin pain, skin swelling, abdominal pain) visual analogue scale (VAS-3) score from pre-treatment to four hours post-treatment, as captured electronically using numerically assisted input. Topline data from 147 attacks collected by 62 patients show that dose levels of PHVS416 significantly reduces attack symptoms.
The statistical tests for the primary and all key secondary endpoints followed a pre-specified multiple comparison procedure to assess statistical significance for PHVS416 20 mg and 30 mg, supported by a nominal statistical analysis for PHVS416 10 mg.

Table 1 Results of the Primary Endpoint

	Placebo	PHVS416 10 mg	PHVS416 20 mg	PHVS416 30 mg	Combined PHVS416*
	N=51	N=37	N=28	N=31	N=96
Mean VAS-3 at pre-treatment	27.76	26.16	25.46	29.73	27.11
Change in VAS-3 at 4 hours					
LS mean difference: PHVS416 - Placebo		-16.75	-15.02	-16.28	-16.08
p-value		<0.0001†	<0.0001	<0.0001	

N = The number of attacks included in the mITT analysis set
p-values for PHVS416 20mg and PHVS416 30mg are based on statistical tests in the pre-specified multiple comparison procedure, and other p-values are nominal
LS = Least squares. The LS mean differences and p-values are based on mixed model for repeated measures
*The combined PHVS416 results are based on post-hoc analyses to provide a reference of the result by pooling all attacks treated with active doses
†Nominal p-value

All key secondary endpoints of the study (Table 2) were met, demonstrating that PHVS416 significantly:

- Shortens the time to onset of symptom relief by a ≥30% reduction in VAS-3 score from the pre-treatment score
- Decreases time to a ≥50% reduction in VAS-3 score from the pre-treatment score
- Reduces time to almost complete or complete symptom relief by VAS-3
- Reduces mean symptom complex severity (MSCS) score from pre-treatment to four hours post-treatment
- Improves treatment outcome score (TOS) at four hours post-treatment

Table 2 Results of Key Secondary Endpoints

	Placebo	PHVS416 10 mg	PHVS416 20 mg	PHVS416 30 mg	Combined PHVS416*
	N=51	N=37	N=28	N=31	N=96
Time to onset of symptom relief by 30% reduction in VAS-3[a]					
Median time (hours)	8.0	2.1	2.7	2.5	2.4

Hazard ratio		3.81	3.08	3.61	
p-value		<0.0001†	0.0021	<0.0001	
Time to VAS-3 50% reduction[a]					
Median time (hours)	22.8	3.3	4.0	4.0	3.9
Hazard ratio		4.55	3.65	3.87	
p-value		<0.0001†	0.0003	<0.0001	
Time to almost complete or complete symptom relief by VAS[a]					
Median time in hours (95% CI)	42	5.8	20	20	7.5
Hazard ratio		5.09	2.25	2.65	
p-value		<0.0001†	0.0127	0.0001	
Change in MSCS score at 4 hours[b]					
LS mean difference: PHVS416 - Placebo		-0.79	-0.61	-0.39	-0.61
p-value		<0.0001†	0.0008	0.0291	
TOS at 4 hours[b]					
LS mean difference: PHVS416 - Placebo		64.13	62.69	71.06	66.05
p-value		<0.0001†	<0.0001	<0.0001	

N = The number of attacks included in the mITT analysis set

[a]Hazard ratios and p-values are based on marginal Cox proportional hazards models

[b]p-values are based on mixed models for repeated measures

*The combined PHVS416 results are based on post-hoc analyses to provide a reference of the result by pooling all attacks treated with active doses

†Nominal p-value

All other secondary endpoints were met. Participants on PHVS416 also used substantially less rescue medication compared to placebo (10 mg=18.9%, p<0.0001†; 20 mg=10.7%, p=0.0007†; 30 mg=6.5%, p<0.0001†, placebo=60.8%).

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†Nominal p-value

PHVS416 was generally well tolerated with no treatment-related serious adverse events and no adverse events leading to treatment discontinuation. In the non-attack phase, two treatment-related adverse events were experienced by two patients; in the attack treatment phase, three treatment-related adverse events were reported for one attack treated with PHVS416 30mg (2.8%) and one treatment-related adverse event was reported for one attack treated with placebo (1.9%).

Marcus Maurer, M.D., Professor of Dermatology and Allergy at the Charité – Universitätsmedizin Berlin, and principal investigator on the RAPIDe-1 study, commented, "The expectation of people living with HAE is that next-generation HAE therapies should achieve the same or better efficacy than current standard of care while offering an improved duration of effect and better convenience. Given the study design with physician-confirmed attacks, these data showing consistent results across all endpoints are an encouraging step in that direction for PHVS416."

Peng Lu, M.D., Ph.D., Chief Medical Officer of Pharvaris, stated, "The data demonstrate rapid onset of action, symptom relief, and resolution of attacks, which support the further development of PHVS416 as a potential on-demand therapy for HAE. Further, study participants used substantially less rescue medication when taking PHVS416 to treat attacks versus when treating with placebo. The strength and durability of effect shown in the top-line data from RAPIDe-1, as well as the observed safety profile, has further enhanced our confidence in the clinical development strategy."

Berndt Modig, Chief Executive Office of Pharvaris, added, "Seven years ago, we embarked on our journey to bring novel, oral therapies to people living with HAE based on our deep insight into the biology of HAE and an experiment, the bradykinin challenge, that guided our trial design and dose selection. The results of the RAPIDe-1 study represent another step towards a potential new, oral on-demand HAE treatment. We sincerely thank the clinical trial participants and their families, the site investigators and staff, the HAE community, and the Pharvaris team for their contributions to the RAPIDe-1 study."

In August 2022, the U.S. Food & Drug Administration (FDA) placed clinical studies of PHA121 in the U.S., including RAPIDe-1, on hold. Pharvaris had previously announced the achievement of target enrollment across 33 sites in Canada, Europe, Israel, the UK, and the U.S. Subsequent to the clinical holds, the company continues to evaluate PHVS416 for the treatment of acute attacks for continuing participants enrolled outside the U.S.

Conference Call

Pharvaris will host a live conference call and webcast to discuss the RAPIDe-1 study top-line data in greater detail at 8:00 a.m. ET today. To access the conference call and webcast, you must first register through this link. A live webcast of the conference call and presentation slides may be accessed on the "Events and Presentations" page of the Pharvaris investor relations website. An archived replay will also be available on the website for 90 days following the event.

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 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 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 safe, effective and convenient alternatives to treat attacks, for 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 holds 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 holds; 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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