
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 6-K

**REPORT OF FOREIGN PRIVATE ISSUER
PURSUANT TO RULE 13A-16 OR 15D-16 UNDER
THE SECURITIES EXCHANGE ACT OF 1934**

For the month of February 2023
Commission File Number: 001-40010

Pharvaris N.V.

(Translation of registrant's name into English)

Emmy Noetherweg 2
2333 BK Leiden
The Netherlands

(Address of principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Note: Regulation S-T Rule 101(b)(1) only permits the submission in paper of a Form 6-K if submitted solely to provide an attached annual report to security holders.

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

Note: Regulation S-T Rule 101(b)(7) only permits the submission in paper of a Form 6-K if submitted to furnish a report or other document that the registrant foreign private issuer must furnish and make public under the laws of the jurisdiction in which the registrant is incorporated, domiciled or legally organized (the registrant's "home country"), or under the rules of the home country exchange on which the registrant's securities are traded, as long as the report or other document is not a press release, is not required to be and has not been distributed to the registrant's security holders, and, if discussing a material event, has already been the subject of a Form 6-K submission or other Commission filing on EDGAR.

PHARVARIS N.V.

On February 14, 2023 in connection with an investor event, Pharvaris N.V. provided a corporate update included in a corporate presentation on its website in which, among other things, Pharvaris disclosed that it has finalized the protocol for a 26-week rodent toxicology study with the FDA and that the 26-week study will initiate soon. The presentation is attached as Exhibit 99.1 hereto and is incorporated by reference herein.

A copy of the corporate presentation is attached hereto as Exhibit 99.1. This Report on Form 6-K (excluding Exhibit 99.1) shall be deemed to be incorporated by reference into the registration statements on Form F-3 (Registration Number 333-263198) and Form S-8 (Registration Number 333-252897). Exhibit 99.1 to this Report on Form 6-K shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended or the Exchange Act.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

PHARVARIS N.V.

Date: February 14, 2023

By: /s/ Berndt Modig
Name: Berndt Modig
Title: Chief Executive Officer

EXHIBIT INDEX

Exhibit No.	Description
99.1	Corporate Presentation, dated February 14, 2023

PHARVARiS

Pioneering science for patient choice

February 2023

Disclaimer

This Presentation may contain certain "forward-looking statements" within the meaning of the federal securities laws that involve substantial risks and uncertainties. All statements contained in this Presentation 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. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. Such forward-looking statements involve unknown risks, uncertainties and other factors which may cause our actual results, financial condition, performance or achievements, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Factors that might cause such a difference include, but are not limited to, uncertainty in the outcome of our interactions with regulatory authorities, including the FDA with respect to the clinical hold 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 FDA clinical hold, risks arising from epidemic diseases, such as 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 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. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Certain information contained in this Presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this Presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

Pharvaris: Focused on unmet need in the treatment of hereditary angioedema (HAE) and other bradykinin-mediated diseases



Competitive product profile

Convenient, orally available, small molecule targeting the **validated bradykinin B2 receptor pathway**

Clinical proof-of-mechanism using surrogate endpoint with higher potency and duration than previously observed for icatibant

Positive top-line Phase 2 data from RAPIDe-1 study of PHVS416 for the on-demand treatment of HAE attacks

PK/PD profile supports use in both **on-demand and prophylactic settings; Phase 2 studies underway***

*The FDA has placed a hold on the clinical trials of PHA121 in the U.S.; see slide 15 for an update on our clinical program



Large market opportunity

Large global HAE market: >\$2 billion with predicted 9% CAGR over 5 years

Potential portfolio expansion into other BK-mediated angioedema and diseases through **B2-receptor pathway expertise**



Strong fundamentals

Novel lead series with strong IP (primary CoM granted in multiple territories; initial term to 2038); FDA **orphan drug designation**

World-wide operations: the Netherlands, USA, and Switzerland (headquarters)

Strong financial position; **cash runway into 4Q24**

Experienced management **team with successful track record** in HAE drug design and development

Experienced management with deep expertise in development and rare diseases



Berndt Modig
Chief Executive Officer




Anne Lesage, Ph.D.
Chief Early Development Officer




Morgan Conn, Ph.D.
Chief Business Officer




Wim Souverijns, Ph.D.
Chief Community Engagement and Commercial Officer




Includes the leaders behind the **discovery, development, and approval** of Firazyr® (icatibant), and a key member of the Takhzyro® (lanadelumab) development team




Jochen Knolle, Ph.D.
Chief Scientific and Operating Officer




Peng Lu, M.D., Ph.D.
Chief Medical Officer

Joan Schmidt, J.D.
Chief Legal Officer



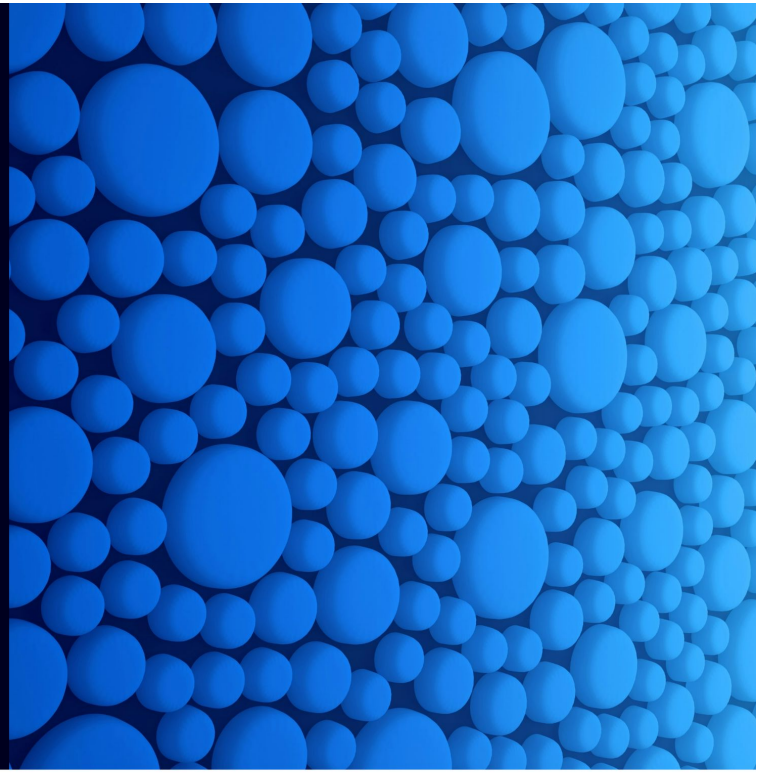

Anna Nijdam
Principal Accounting Officer




Annick Deschoolmeester
Chief Human Resources Officer

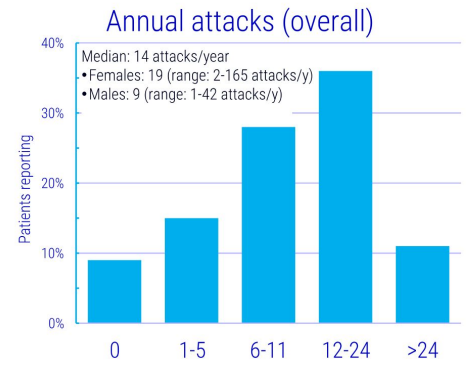


Hereditary Angioedema (HAE)



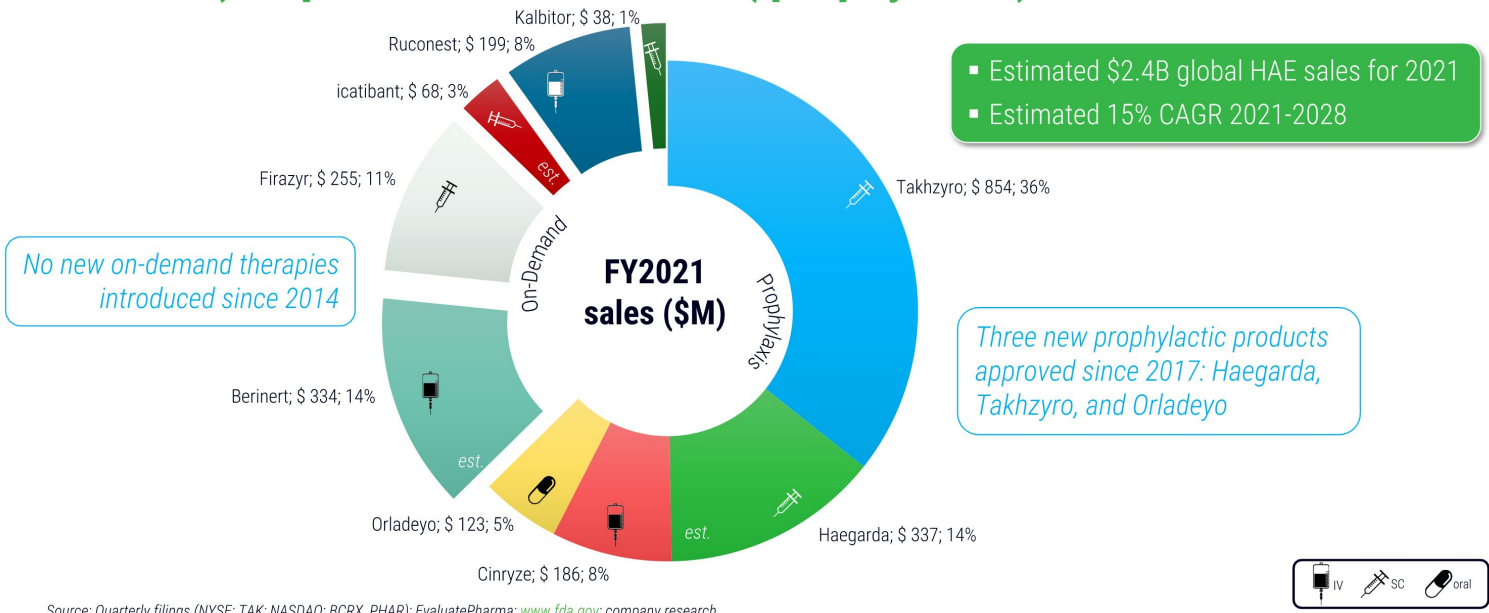
HAE: A rare, life-long genetic condition with significant burden from unpredictable, debilitating, and potentially lethal attacks of swelling

- Unpredictable frequency, location, timing, and severity
 - Multiple types of triggers
 - If untreated, attacks last multiple days
- Attacks are commonly painful, leading to hospitalization or multiple sick days
 - Half of people living with HAE experience a potentially life-threatening laryngeal attack at least once in their lifetime
- 1:10,000 to 1:50,000 Individuals affected by HAE globally
 - At least 6,600 people living with HAE in the U.S.
 - At least 8,900 people living with HAE in Europe
 - Globally, under-diagnosed/treated



Nordenfelt et al, Acta Derm. Venereol 2016; 96: 540-545

People living with HAE use approved therapeutics for treatment ('on demand') or prevention of attacks ('prophylaxis')



Source: Quarterly filings (NYSE: TAK; NASDAQ: BCRX, PHAR); EvaluatePharma; www.fda.gov; company research

People living with HAE actively switch products, seeking improvement in efficacy, safety/tolerability, and convenience



Efficacy is patients' prime concern ...



... but **safety & tolerability** are pushing patients to explore alternatives ...

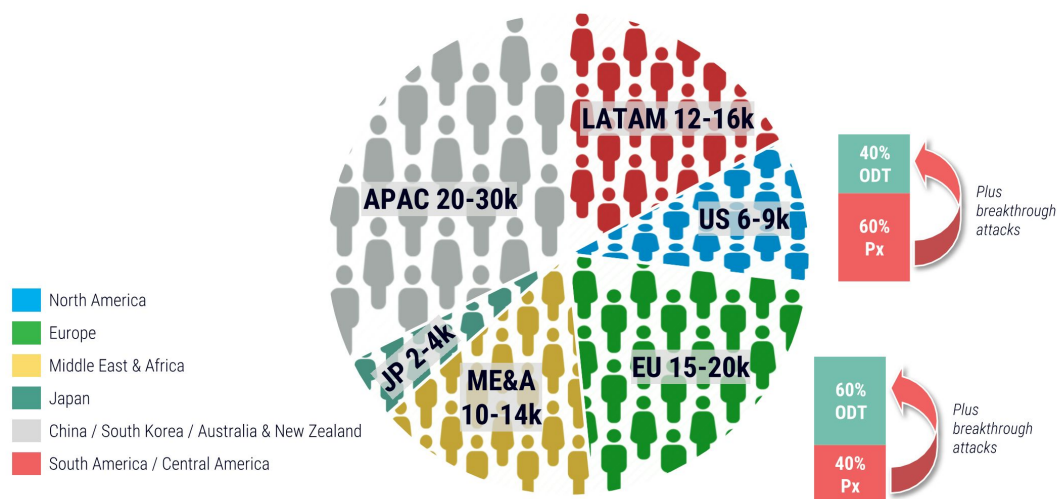


... while **convenience** has become a key driver for patient preference

People living with HAE desire HAE therapy that can deliver on ALL fronts

Proprietary company research 2022

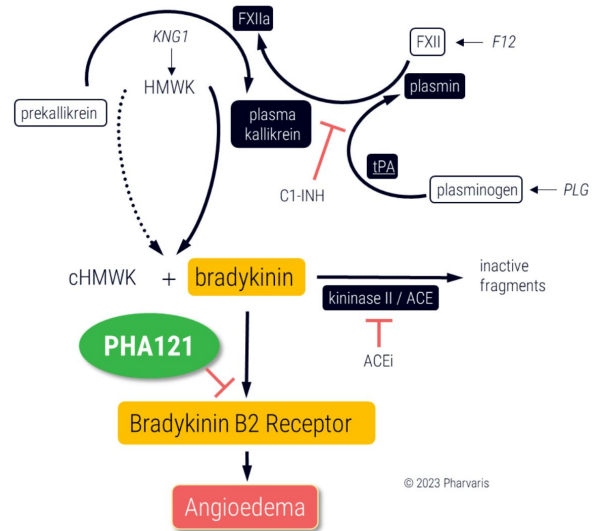
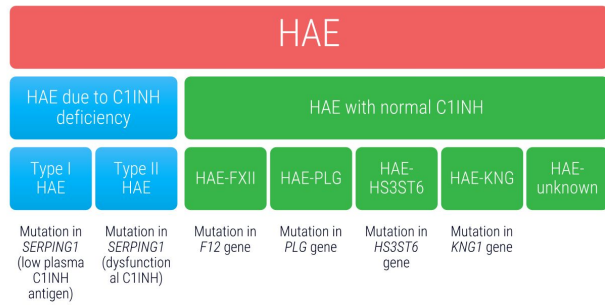
Significant global unmet need: Potentially up to 100,000 people living with HAE



Proprietary company research 2022; Maurer et al. Consensus on diagnosis and management of Hereditary Angioedema in the Middle East: A Delphi initiative. World Allergy Organization Journal (2023);16:1-2; Zuraw et al. NEJM 2008;359:1027-1036; HAEi (haei.org), The State of Management of HAE in Latin America (2015); <https://haei.org/potentially-28000-hae-patients-in-china/dj>; Ann Allergy Asthma Immunol 2015;114(6), 492-498; Allergol Int. (2020) Nov 6;S1323-8930(20)30135-0

The swelling of an HAE attack is caused by excess levels of bradykinin

Genetic causes lead to elevated levels of bradykinin

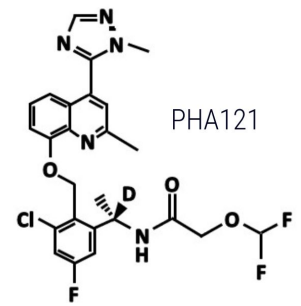


HMWK: high-molecular-weight kininogen; cHMWK: cleaved high-molecular-weight kininogen; FXII(a): Factor XII(a); ACE(i): angiotensin-converting enzyme (inhibitor); tPA: tissue plasminogen activator; KNG1: gene encoding HMWK; PLG: gene encoding plasminogen; F12: gene encoding FXII

Busse 2020 J Allergy Clin Immunol Pract; Bork et al 2021 J Allergy Clin Immunol

Pharvaris has discovered the first orally bioavailable bradykinin B2 receptor antagonist

- New molecular entity, orally administered
- Potent inhibition of the bradykinin B2 receptor to compete with bradykinin, the ultimate driver of swelling attacks
- Results from Phase 1 healthy volunteer studies demonstrate rapid absorption, exposure, and tolerability
- Dose and exposure threshold predicted from human surrogate endpoint for both on-demand and prophylaxis
 - Bradykinin challenge in healthy volunteers

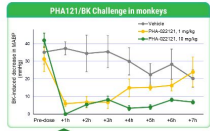


We aspire to develop **novel, oral alternatives** that **improve** the **standard of care** for people living with HAE

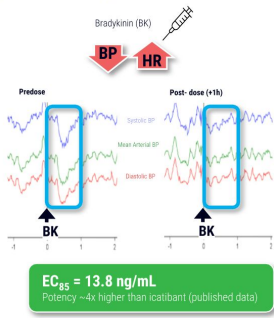
Lesage et al, *Frontiers in Pharmacology* 2020, doi: 10.3389/fphar.2020.00916; ; Lesage et al, *Int. Immunopharmacology* 2022, doi.org/10.1016/j.intimp.2022.108523; <https://ir.pharvaris.com/static-files/0361cd85-6000-490b-932b-d305e1f3ca1b>; <https://ir.pharvaris.com/static-files/81a9499d-0769-4b89-8ecd-8ace5ca521d3>; <https://ir.pharvaris.com/static-files/33217945-6893-4f49-8a93-c80ea6fb2a31>; <https://doi.org/10.1016/j.jaci.2019.12.094>

Predictive value of our unique *in vivo* surrogate-marker model, the BK challenge, allows for derisking of our clinical studies

Primate bradykinin challenge



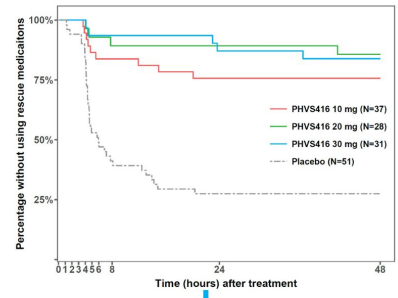
Healthy volunteer bradykinin challenge



Phase 2 clinical dose selection
On-demand (RAPIDe-1) Prophylaxis (CHAPTER-1)

On-demand dose confirmation

RAPIDe-1 on-demand study in people living with HAE



https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022150Orig1s000ClinPharmR.pdf; Maurer et al 2020: Long-term effectiveness and safety of icaltibat for the on-demand treatment of hereditary angioedema attacks: 10 years of the icaltibat outcome survey (EAACI Poster #1118, June 6-8, 2020); <https://clinicaltrials.gov/ct2/show/NCT01034969>; <https://ir.pharvaris.com/static-files/33217945-6893-4f49-8a93-c80ea6fb2a31>; <https://doi.org/10.1016/j.jaci.2019.12.094>

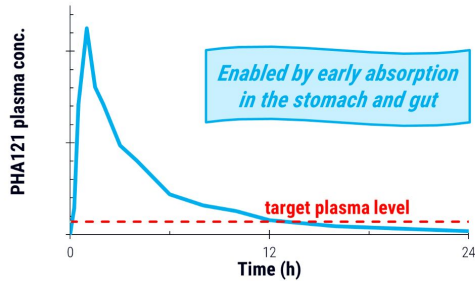
Product Strategy

On-demand and prophylaxis: Developing two oral products utilizing the same active ingredient



PHVS416

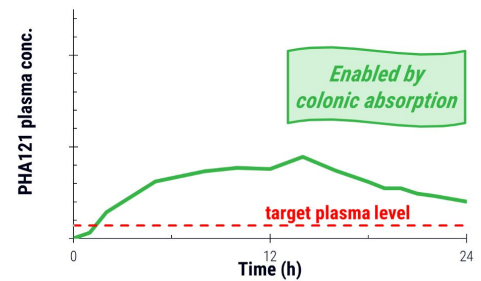
Softgel capsule formulation



Potential to provide rapid, easy, and reliable symptom relief for all attacks*

PHVS719

Extended-release tablet formulation



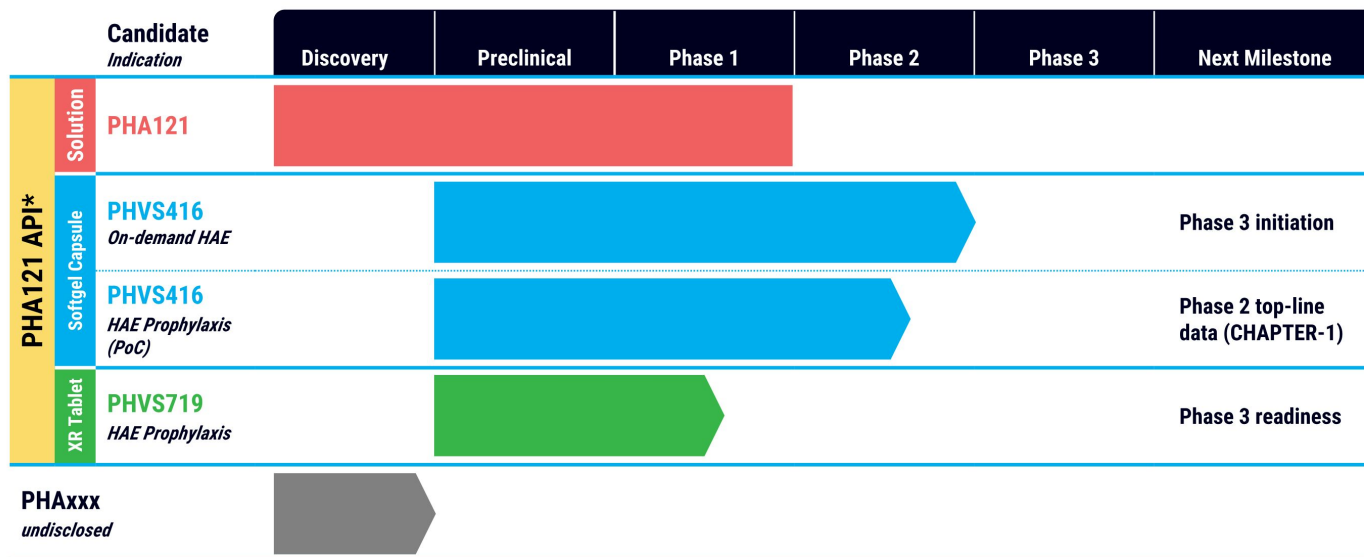
Aim to maintain compound exposure to prevent attacks, for convenient and effective control*

*Aspirational; to be confirmed with clinical data

Regulatory update

- In August 2022, the U.S. Food & Drug Administration (FDA) placed a hold on the clinical trials of PHA121 in the U.S. based on its review of nonclinical data
 - The agency requested that Pharvaris conduct an additional long-term rodent toxicology study and update the Investigator's Brochure
 - Pharvaris participated in a Type A meeting with the FDA to discuss paths to address the on-demand and prophylactic holds
- A protocol for a 26-week rodent toxicology study has been finalized with the FDA and the study will initiate soon
- FDA has agreed to partially lift the clinical hold on on-demand
 - Two remaining U.S. participants in RAPIDe-1 allowed to complete treatment of a final HAE attack per protocol
 - All other clinical studies of PHA121 are currently on hold in the U.S.
- Outside the U.S., the regulatory status remains unchanged for the CHAPTER-1 study and other studies, including long-term extension RAPIDe-2 study
 - Pharvaris notified country-specific regulatory authorities in Canada, Europe, Israel, and the UK of the U.S. clinical holds
 - All active sites outside of the U.S. continue to recruit participants in the CHAPTER-1 clinical study

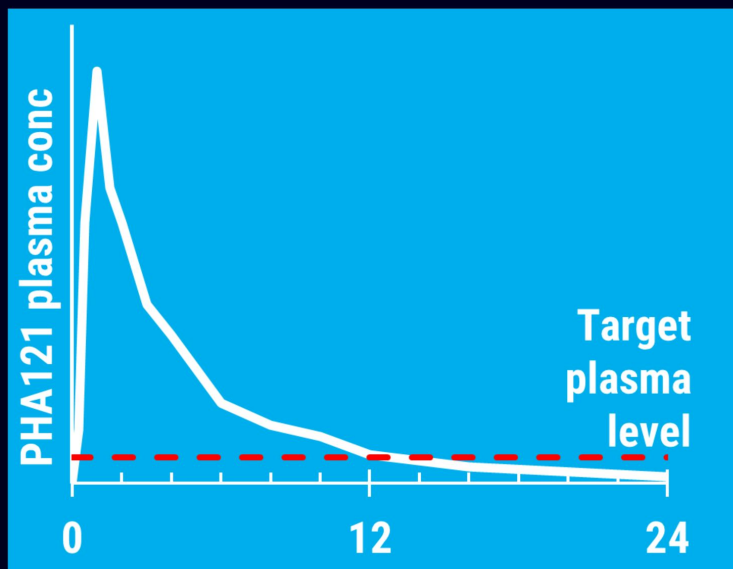
Wholly-owned pipeline focused on bradykinin B2 receptor mechanism



* The FDA has placed a clinical hold on the clinical trials of PHA121 in the U.S.; timeline based on studies ongoing outside the U.S.; see slide 15 for an update on our clinical program

PHVS416/On-Demand

Softgel capsule formulation of PHA121



On-demand treatment of HAE attacks: No new approvals beyond injectable options have left a significant unmet need



Treatment today means **painful** injections ...



... and often **one dose does not suffice** ...



... while finding a place to administer the drug causes an **extra burden**

As a result, people living with HAE often delay or even avoid therapy against clinical guideline recommendations

Proprietary Pharvaris research, 2022 (representative sample of patients, n = 103, and doctors, n = 100)

People living with HAE are hoping for better on-demand therapies that offer rapid symptom relief with one single, oral dose



Patients want **rapid onset of symptom relief** ...

1

... with **single dose durability** ...

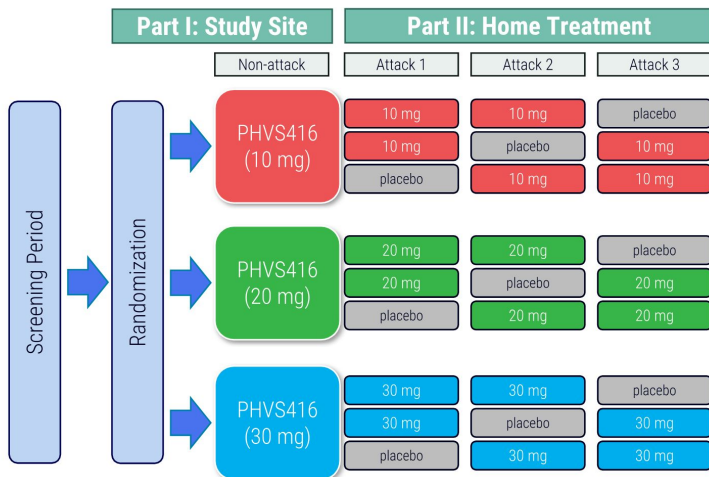


... in an **oral** pill

Effectively targeting the **bradykinin receptor** with a **small molecule** has the potential to deliver on their hopes

Proprietary Pharvaris research, 2022 (representative sample of patients, n = 103, and doctors, n = 100)

HAE RAPIDe-1 study: Phase 2 study of on-demand treatment of angioedema attacks in patients with Type I or II HAE



- **Primary objective:** to evaluate angioedema symptom relief within four hours in acute attacks of patients with HAE type 1 or 2
- **Study design:** Placebo-controlled, three dose levels
 - Part I: patients randomized and received a single dose of PHA121 in clinic for PK and safety assessment
 - Part II: patients treated three attacks with two PHA121 vs. one placebo
 - Before an attack was treated, one of the VAS-3 elements had to be at least hit a score of 30 and it had to be qualified by the clinician
- 74 HAE patients enrolled from ~30 sites in US, Canada, Europe, Israel, and UK

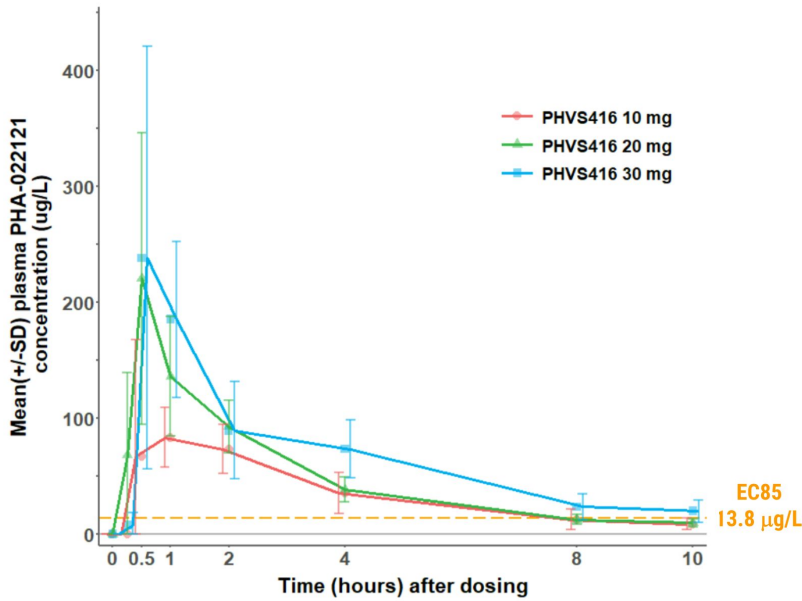
www.hae-rapide.com; <https://clinicaltrials.gov/ct2/show/NCT04618211>; <https://hae-rapide.us/>; <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2020-003445-11>

Positive top-line Phase 2 data from RAPIDe-1 study of PHVS416 for the on-demand treatment of HAE attacks

- A total of 74 patients from 13 countries were enrolled to the study, 62 of them had 147 attacks that were treated with blinded study drug and included in efficacy evaluation
- The **primary endpoint** and all **key secondary endpoints** were **met**
- PHVS416 demonstrated **rapid onset of action, symptom relief, and resolution** of HAE attacks
- PHVS416 **substantially reduced** the use of **rescue medications**
- PHVS416 was **well tolerated** at all dose levels
 - There were no treatment-related SAEs, no treatment-related AEs of severe severity, and no AEs leading to treatment discontinuation

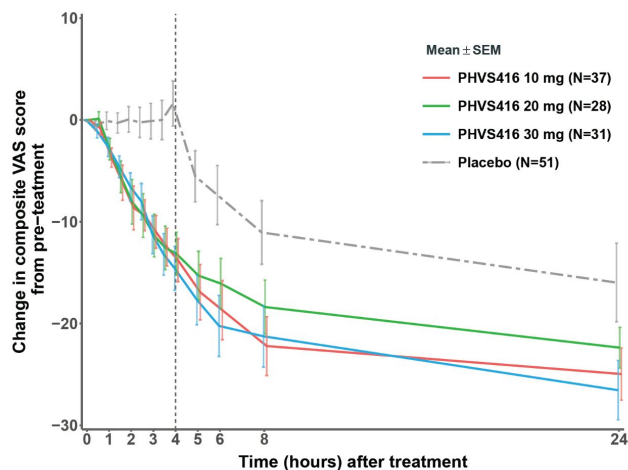
Consistent outcomes observed
across all endpoints and types of measurements

PK profile in HAE patients: Rapid absorption confirmed on oral dosing, consistent with Phase 1 healthy volunteer studies



- **Rapid absorption** with mean plasma levels exceeding EC_{85} (13.8 ng/mL) within 30 min
- Mean **plasma levels maintained** $>EC_{85}$ for approximately
 - 8 h at 10 mg or 20 mg
 - >10 h at 30 mg dose
- **EC_{85} levels established using bradykinin challenge**, a human surrogate endpoint study in healthy volunteers

Primary endpoint: PHVS416 significantly reduces attack symptoms by VAS-3 at 4h



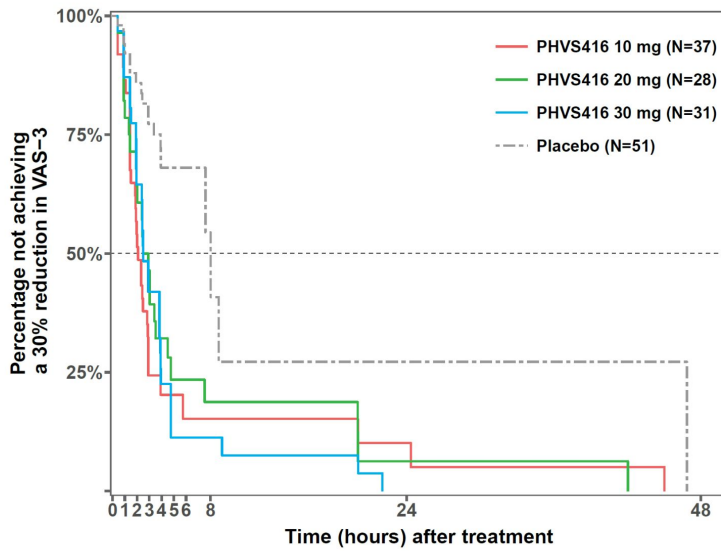
Difference from placebo in change from pre-treatment to 4 h post-treatment, least-squares mean (95% CI)

PHVS416 10 mg	-16.75 (-21.52, -11.97)	p < 0.0001†
PHVS416 20 mg	-15.02 (-20.22, -9.81)	p < 0.0001
PHVS416 30 mg	-16.28 (-21.27, -11.29)	p < 0.0001
Combined PHVS416	-16.08 (-19.87, -12.29)	

Median VAS-3 at pre-treatment ranges from 24.33-27.00 across different dose levels

†Nominal p-value; VAS assessed every 30 minutes up to 4 hours post-treatment, then at 5, 6, 8, 24, 48 hours; N = The number of attacks in the mITT Analysis Set. Attacks in mITT Analysis Set refer to attacks treated with blinded study drug that had non-missing VAS result at pre-treatment and at least one non-missing VAS result post-treatment. VAS-3 = electronically captured, numerically assisted visual analogue scale. Figure is based on descriptive summary of mean and SEM (standard error of the mean). Least-squares mean differences, CIs, and p-values come from a mixed-effects model with repeated measures (MMRM). Data after rescue medication use is not included. The combined PHVS416 result is based on post-hoc analysis using a similar MMRM with all three active doses combined vs placebo

PHVS416 significantly shortened time to onset of symptom relief (30% reduction in VAS-3)



Median time in hours (95% CI)

Placebo	8.0 (7.6, 46.9)	
PHVS416 10 mg	2.1 (1.5, 2.9)	$p < 0.0001^\dagger$
PHVS416 20 mg	2.7 (1.9, 3.5)	$p = 0.0021$
PHVS416 30 mg	2.5 (1.9, 3.8)	$p < 0.0001$
Combined PHVS416	2.4 (2.0, 2.9)	

VAS assessed every 30 minutes up to 4 hours post-treatment, then at 5, 6, 8, 24, 48 hours

†Nominal p-value; N = The number of attacks in the mITT Analysis Set. Median time based on Kaplan-Meier estimates. p-values based on a marginal Cox proportional hazards model. The combined PHVS416 results are based on post-hoc analyses to provide a reference of the result by pooling all three active doses.

TOS Patient Reported Outcome (PRO)

- TOS PRO captures change in five symptom complexes of HAE attacks

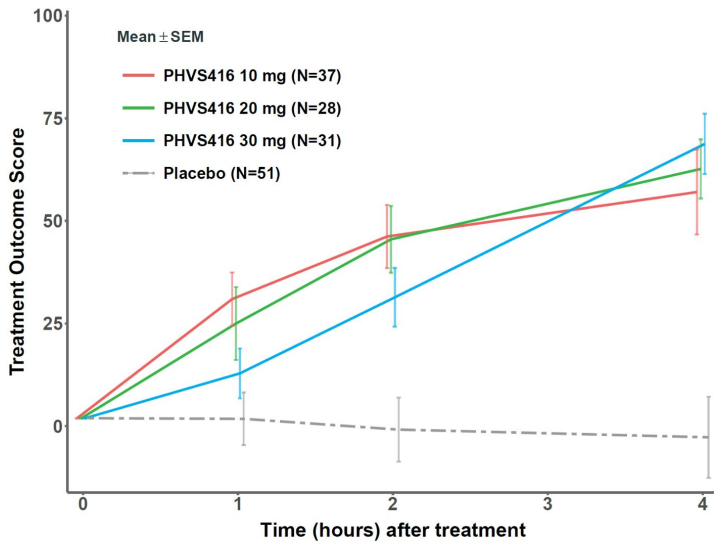
Internal head/neck	Stomach/GI	Genital/buttocks	External head/neck	Cutaneous
---------------------------	-------------------	-------------------------	---------------------------	------------------

- At each timepoint, the change in attack symptom from pre-treatment is reported by patient

PRO – how do you feel now compared to before receiving study drug?

A lot better or resolved	A little better	Same	A little worse	A lot worse
---------------------------------	------------------------	-------------	-----------------------	--------------------

TOS endpoint shows early response to treatment: Significant at 4h



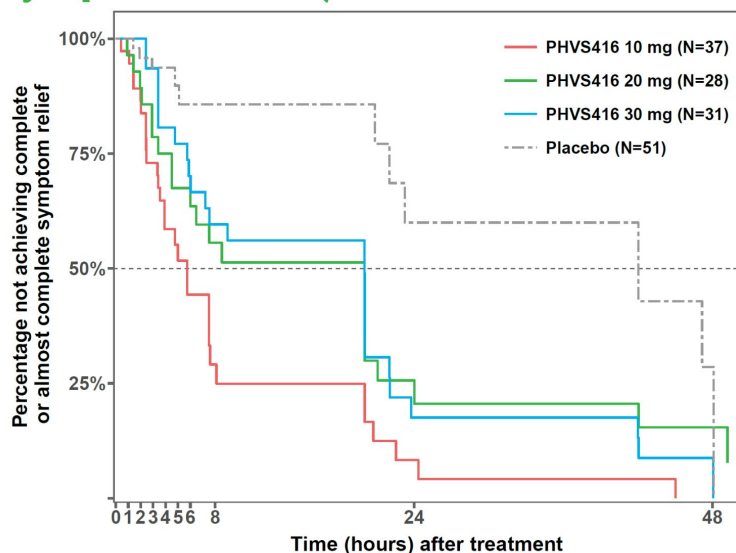
Difference from placebo in 4 h post-treatment least-squares mean (95% CI)

PHVS416 10 mg	64.13 (40.35, 87.91)	p < 0.0001 [†]
PHVS416 20 mg	62.69 (36.71, 88.67)	p < 0.0001
PHVS416 30 mg	71.06 (46.09, 96.03)	p < 0.0001
Combined PHVS416	66.05 (47.42, 84.69)	

Minimally Important Difference (MID)
for TOS is **30**

Source: Vernon M, Rentz AM, Wyrwich KW, et al. *Qual Life Res.* 2009; †Nominal p-value; N = The number of attacks in the mITT Analysis Set. TOS = Treatment Outcome Score. Figure is based on descriptive summary of mean and SEM. The least-squares mean differences, CIs, and p-values come from an MMRM. Data after rescue medication use is not included. The combined PHVS416 result is based on post-hoc analysis using a similar MMRM with all three active doses combined vs placebo

PHVS416 significantly reduces time to almost complete or complete symptom relief (all individual VAS ≤ 10)



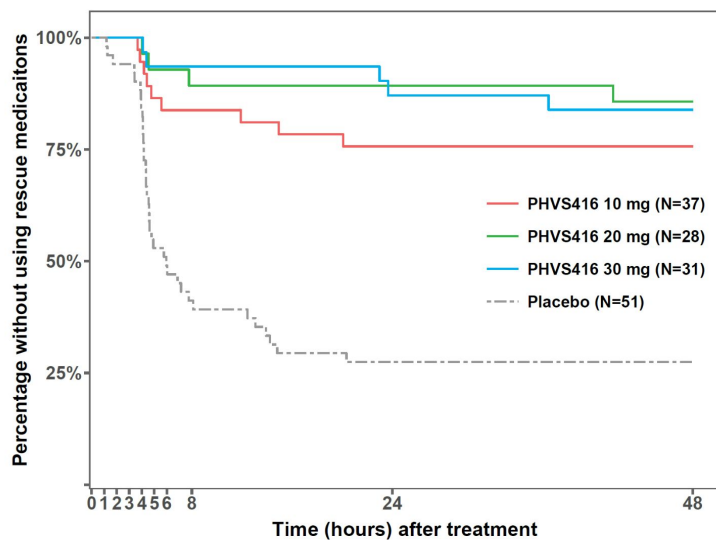
Median time in hours (95% CI)

Placebo	42.0 (22.0, 48.1)	
PHVS416 10 mg	5.8 (3.6, 7.5)	$p < 0.0001^{\dagger}$
PHVS416 20 mg	20.0 (4.5, 20.0)	$p = 0.0127$
PHVS416 30 mg	20.0 (6.0, 20.1)	$p = 0.0001$
Combined PHVS416	7.5 (5.9, 20.0)	

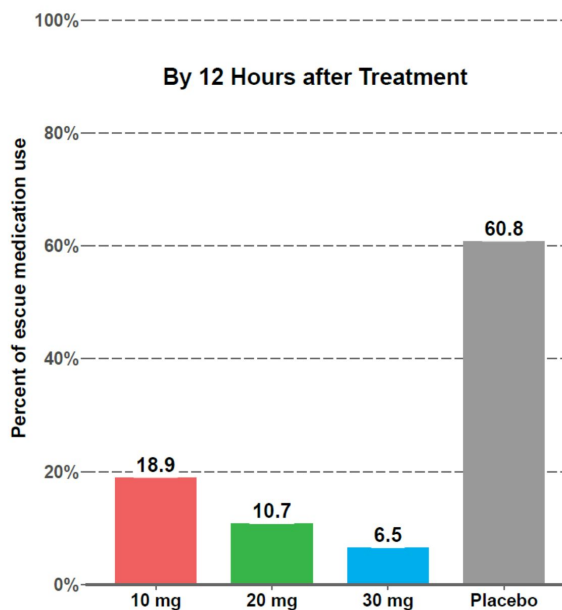
VAS assessed every 30 minutes up to 4 hours post-treatment, then at 5, 6, 8, 24, 48 hours

[†]Nominal p-value; N = The number of attacks in the mITT Analysis Set. Median time based on Kaplan-Meier estimates. p-values based on a marginal Cox proportional hazards model. The combined PHVS416 results are based on post-hoc analyses to provide a reference of the result by pooling all three active doses.

Patients treating with PHVS416 used substantially less rescue medication



N = The number of attacks in the mITT Analysis Set



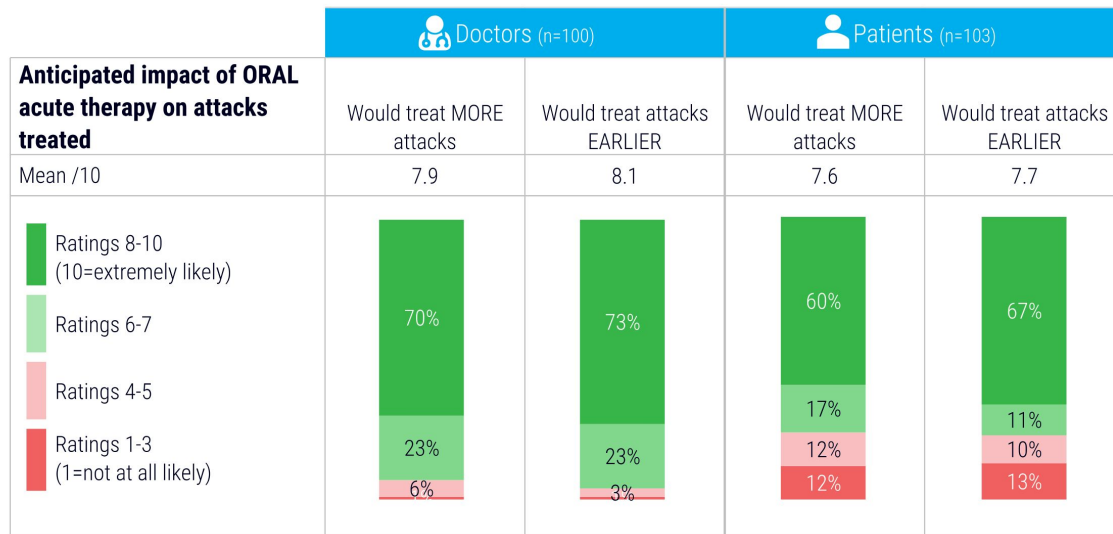
PHVS416 was well tolerated at all doses

- No treatment-related SAEs or AEs of severe severity
- No AEs leading to treatment discontinuation
- No treatment-related AEs of laboratory parameters, vital signs, or ECG parameters
- Few treatment-related AEs reported within 48 h after administration of study drug

	Part I (Non-Attack)			Part II (Attack 1,2,3)			
	10 mg N=23	20 mg N=24	30 mg N=25	Placebo N=53	10 mg N=38	20 mg N=29	30 mg N=36
Subjects (Part I) or Attacks (Part II) with any treatment related AEs	1 (4.3%)	1 (4.2%)	-	1 (1.9%)	-	-	1 (2.8%)
Headache	-	1 (4.2%)	-	-	-	-	-
Nausea	1 (4.3%)	-	-	-	-	-	1 (2.8%)
Vomiting	-	-	-	-	-	-	1 (2.8%)
Fatigue	-	-	-	-	-	-	1 (2.8%)
Blister	-	-	-	1 (1.9%)	-	-	-

N= The number of subjects (Part I) and number of attacks (Part II) in the Safety Analysis Set. The Safety Analysis Set includes all randomized patients who received any dose of study drug. Treatment-related AEs within 48 h post-treatment are included

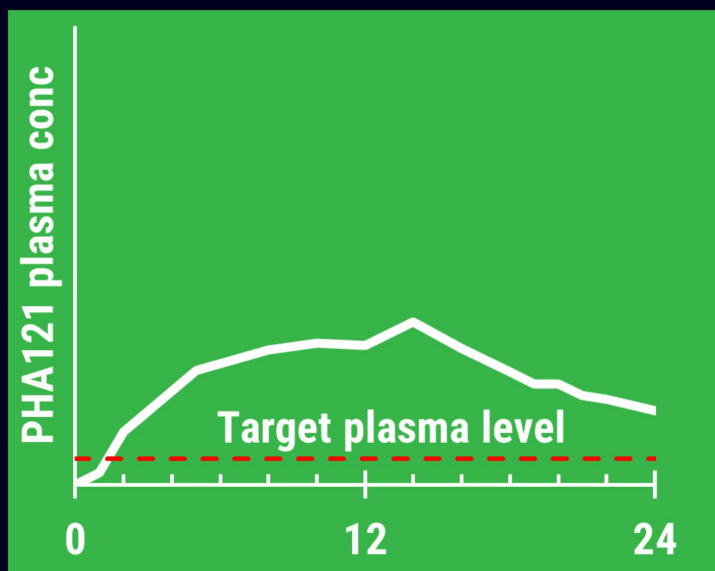
Both doctors and patients consider an oral acute therapy would increase likelihood that patients would treat more attacks, earlier



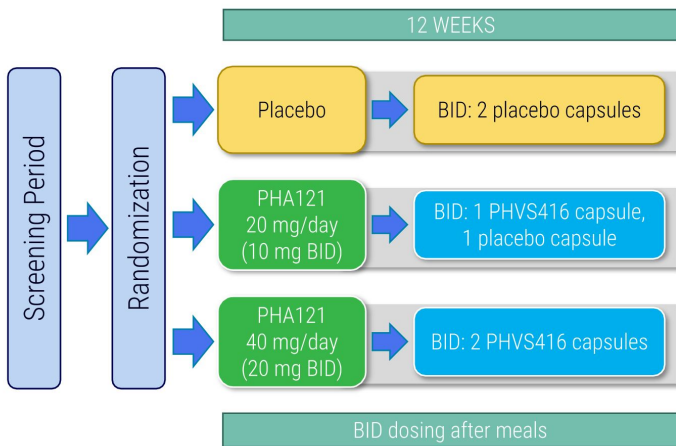
Proprietary Pharvaris research, 2022 (representative sample of patients, n = 103, and doctors, n = 100)

PHVS719/Prophylaxis

Extended-release tablet formulation of PHA121



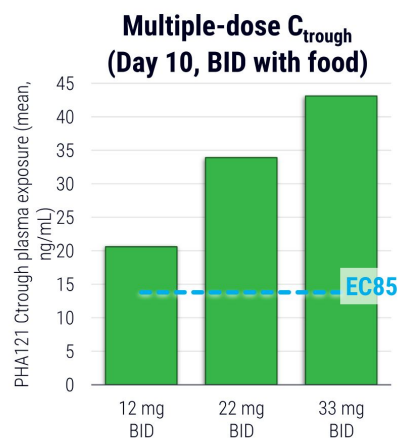
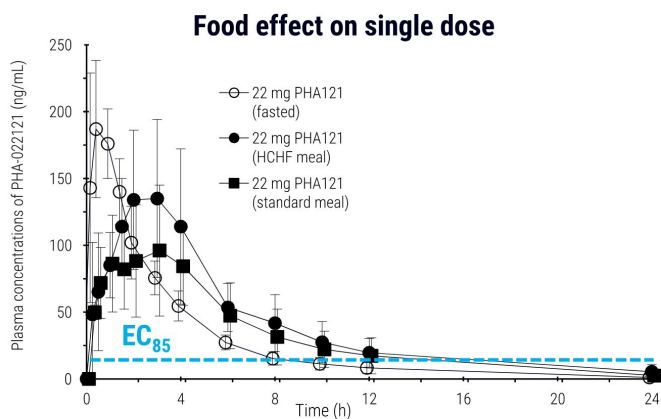
HAE CHAPTER-1 study ongoing outside U.S.: Prevention of attacks in HAE (proof of concept with PHVS416 softgel capsule)



- Primary objective: assessing safety and efficacy of PHA121 in preventing HAE attacks in patients with HAE type 1 or type 2
 - Placebo-controlled, 3 parallel arms, two doses
 - Includes open-label extension
- Primary endpoint: Number of investigator-confirmed HAE attacks
 - Secondary endpoints include moderate or severe HAE attacks, HAE attacks requiring acute treatment
- Target enrolment of 30 HAE patients globally
- Regulators in Canada, Europe, Israel, and the UK have been notified of U.S. clinical hold; the regulatory status of the CHAPTER-1 study outside the U.S. remains unchanged

<https://clinicaltrials.gov/ct2/show/NCT05047185>; <https://haechapter-1.com/>

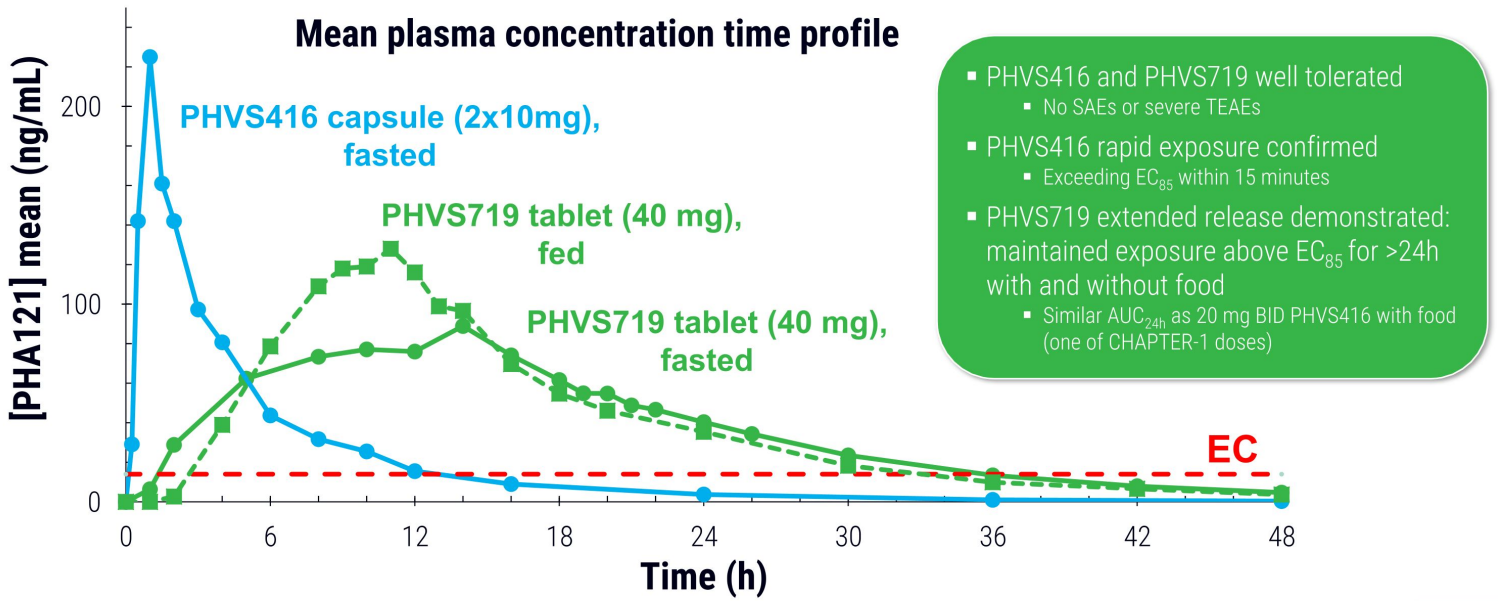
Phase 1 pharmacokinetics offer options to use softgel capsule as proof-of-concept in prophylactic development



When dosed BID with food, exposure maintained above target levels, steady state reached within 72 hours

<https://ir.pharvaris.com/static-files/0361cd85-6000-490b-932b-d305e1f3ca1b>; <https://ir.pharvaris.com/static-files/81a9499d-0769-4b89-8ecd-8ace5ca521d3>

PHVS719 single-dose PK study demonstrates QD potential; target for Phase 3 dosage form



Corporate summary and milestones

	HAE On-Demand (type 1 and type 2)	HAE Prophylaxis (type 1 and type 2)
PHVS416 softgel capsule	<ul style="list-style-type: none">✓ RAPIDe-1 Ph2 top-line data meets all primary and key secondary endpoints▪ Phase 3 initiation	<ul style="list-style-type: none">▪ CHAPTER-1 Ph2 top-line data (expected 2H23)
PHVS719 XR tablet	--	<ul style="list-style-type: none">✓ Ph1 SD PK demonstrates once-daily potential▪ Phase 3 readiness

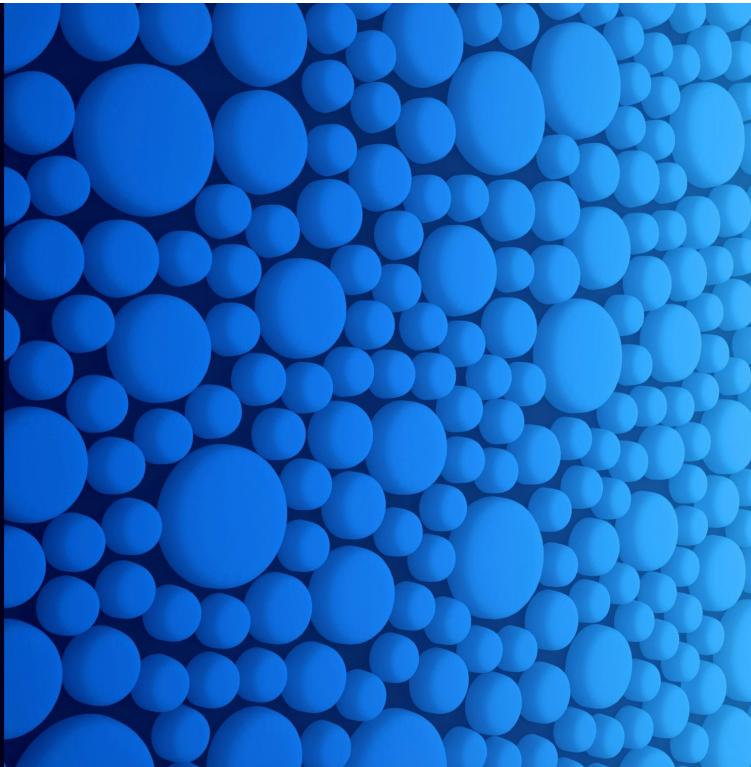
Financially strong: Cash runway into 4Q24

PHARVARiS

Nasdaq: PHVS

Appendix

Additional RAPIDe-1 top-line clinical data



RAPIDe-1: Primary, key secondary and other endpoints

Primary Endpoint

- Change in VAS-3 score from pre-treatment to 4h post-treatment

Key Secondary Endpoints

- Time to onset of symptom relief (VAS-3; $\geq 30\%$ reduction from the pre-treatment score)
- Time to a $\geq 50\%$ reduction in VAS-3 score from the pre-treatment score
- Time to almost complete and complete symptom relief (VAS; all 3 items ≤ 10)
- Change of MSCS (mean symptom complex severity) score from pre-treatment to 4h post-treatment
- TOS (treatment outcome score) at 4h post-treatment

Other Endpoints Included in the top-line Outputs

- Proportion of study-drug-treated attacks requiring the use of HAE rescue medication
- Time to the first use of HAE rescue medication
- Safety and PK assessments

Results summary of primary efficacy endpoint

	Placebo N=51	PHVS416 10 mg N=37	PHVS416 20 mg N=28	PHVS416 30 mg N=31	Combined PHVS416* 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					
least-squares mean difference: PHVS416 - Placebo		-16.75	-15.02	-16.28	-16.08
p-value		<0.0001 [†]	<0.0001	<0.0001	

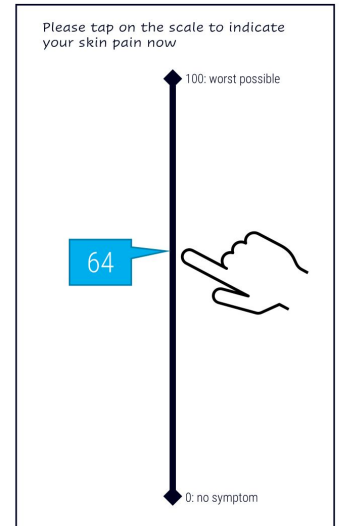
[†]nominal p-value; N = The number of attacks included in the mITT Analysis Set

p-values for PHVS416 20mg and PHVS416 30mg are based on statistical tests in the pre-specified multiple comparison procedure, other p-values are nominal least-squares = Least squares. The least-squares mean differences and p-values are based on mixed-effects model for repeated measures

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

VAS-3 is a measure of HAE attack severity, based electronically captured numerically assisted visual scale

- Electronically captured patient-reported assessment of three symptoms
 - Skin pain, skin swelling, abdominal pain
- Patient indicates the severity of symptom on a sliding scale, from 0-100
- Once an attack qualifies and is treated, VAS-3 assessed every ~30 min until 4 hours post-treatment and then at 5, 6, 8, 24, 48 hours post-treatment
- Used in approval of two most recently approved on-demand therapies
 - FIRAZYR® icatibant and RUCONEST® C1 esterase inhibitor [recombinant]
- VAS, MSCS, TOS are only endpoints listed for attacks in FDA compendium of clinical outcome assessments (2021) as listed by Division of Pulmonology, Allergy and Critical Care



Firazyr is a registered trademark of Shire, and marketed by Takeda; Ruconest is a registered trademark of and marketed by Pharming; FDA 2021 COA compendium: <https://www.fda.gov/drugs/development-resources/clinical-outcome-assessment-compendium>

Results summary of key secondary efficacy endpoints

	Placebo N=51	PHVS416 10 mg N=37	PHVS416 20 mg N=28	PHVS416 30 mg N=31	Combined PHVS416* N=96
Time to onset of symptom relief by VAS-3 30% reduction^a					
Median time in hours (95% CI)	8.0 (7.6, 46.9)	2.1 (1.5, 2.9)	2.7 (1.9, 3.5)	2.5 (1.9, 3.8)	2.4 (2.0, 2.9)
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 in hours (95% CI)	22.8 (20.0, 24.1)	3.3 (2.4, 3.9)	4.0 (2.9, 6.0)	4.0 (3.3, 5.8)	3.9 (3.0, 4.8)
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 (22.0, 48.1)	5.8 (3.6, 7.5)	20 (4.5, 20.0)	20 (6.0, 20.1)	7.5 (5.9, 20.0)
Hazard ratio		5.09	2.25	2.65	
p-value		<0.0001 [†]	0.0127	0.0001	
Change in MSCS score at 4 hours^b					
least-squares 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					
least-squares mean difference: PHVS416 - Placebo		64.13	62.69	71.06	66.05
p-value		<0.0001 [†]	<0.0001	<0.0001	

[†]nominal p-value; N = The number of attacks included in the mITT Analysis Set

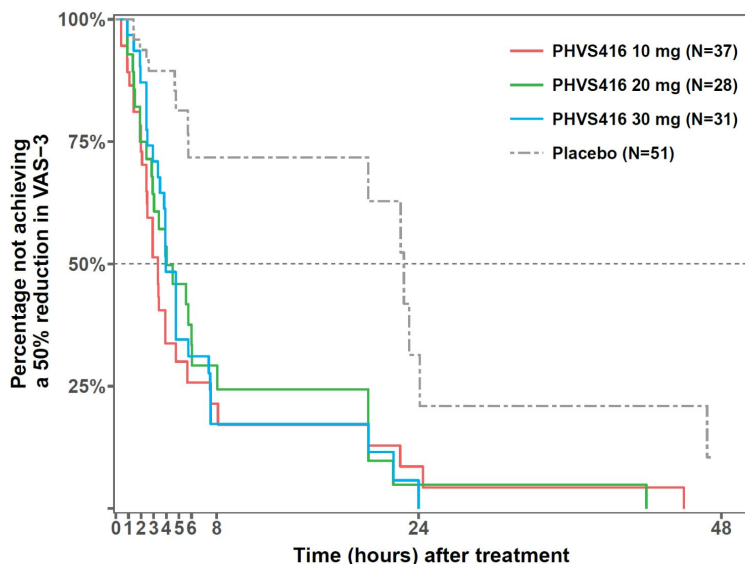
p-values for PHVS416 20mg and PHVS416 30mg are based on statistical tests in the pre-specified multiple comparison procedure, other p-values are nominal

^aHazard ratios and p-values are based on marginal Cox proportional hazards models

^bp-values are based on mixed-effects models for repeated measures

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

PHVS416 significantly reduces time to 50% reduction in VAS-3



Median time in hours (95% CI)

Placebo	22.8 (20.0, 24.1)	
PHVS416 10 mg	3.3 (2.4, 3.9)	p < 0.0001 [†]
PHVS416 20 mg	4.0 (2.9, 6.0)	p = 0.0003
PHVS416 30 mg	4.0 (3.3, 5.8)	p < 0.0001
Combined PHVS416	3.9 (3.0, 4.8)	

[†]Nominal p-value; VAS assessed every 30 minutes up to 4 hours post-treatment, then at 5, 6, 8, 24, 48 hours; N = The number of attacks in the mITT Analysis Set. Median time based on Kaplan-Meier estimates. p-values based on a marginal Cox proportional hazards model. The combined PHVS416 results are based on post-hoc analyses to provide a reference of the result by pooling all three active doses.

MSCS and TOS: definitions

- Validated patient-reported outcome measures to comprehensively capture symptom severity and change of HAE attacks
- MSCS (Mean Symptom Complex Severity) score is a point-in-time measure of symptom severity:
 - Patients rated the severity of each affected symptom on a categorical scale (0 = normal, 1 = mild, 2 = moderate, 3 = severe)
 - Calculated as average score from all affected anatomic sites of attack (symptom complexes or SC) pre-treatment
 - Decrease in MSCS score reflects improvement in symptom severity
- TOS (Treatment Outcome Score) is a measure of symptom response to treatment:
 - Patient assessment of response for each affected SC recorded on categorical scale (significant improvement [100], improvement [50], same [0], worsening [-50], significant worsening [-100])
 - Calculated as weighted average of the response at all SC using pre-treatment severity as the weight
 - TOS value >0 reflects improvement in symptoms from pre-treatment

Greater improvement in MSCS and TOS with PHVS416 than placebo

	Placebo	PHVS416 10 mg	PHVS416 20 mg	PHVS416 30 mg	Combined PHVS416
Change in MSCS score at 4 hours					
n	40	32	26	27	85
least-squares mean (95% CI)	-0.29 (-0.51, -0.08)	-1.08 (-1.33, -0.83)	-0.91 (-1.19, -0.62)	-0.68 (-0.95, -0.40)	-0.90 (-1.06, -0.75)
Difference (PHVS416 – Placebo, LSMD)		-0.79	-0.61	-0.39	-0.61
p-value		<0.0001 [†]	0.0008	0.0291	
TOS at 4 hours					
n	40	32	25	28	85
least-squares mean (95% CI)	-3.62 (-19.68, 12.45)	60.52 (41.74, 79.29)	59.08 (37.58, 80.57)	67.44 (47.15, 87.74)	62.57 (50.95, 74.19)
Difference (PHVS416 – Placebo, LSMD)		64.13	62.69	71.06	66.05
p-value		<0.0001 [†]	<0.0001	<0.0001	

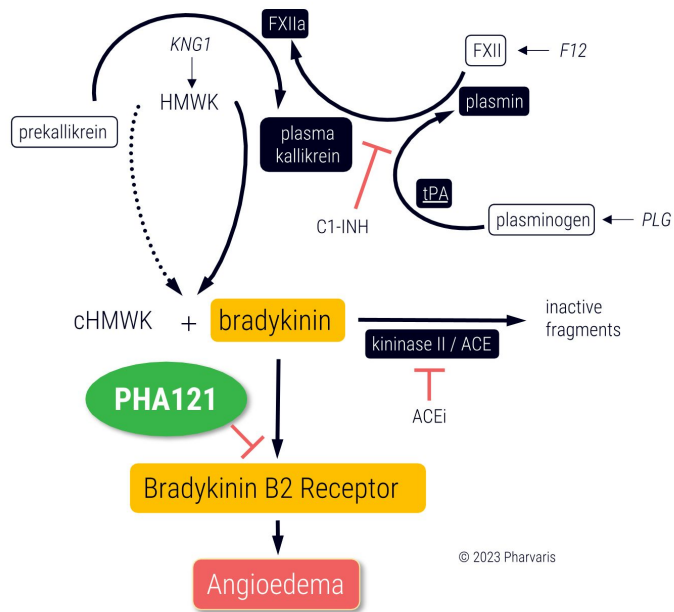
[†]Nominal p-value; MSCS = Mean Symptom Complex Severity, TOS = Treatment Outcome Score, CI = confidence interval, LSMD = least-squares mean difference; least-squares mean, LSMD, CIs, and p-values for MSCS change from pre-treatment/TOS come from mixed-effect models with repeated measures (MMRM). Data after rescue medication use is not included. The combined PHVS416 result is based on post-hoc analysis using similar MMRM with all three active doses combined vs placebo

Time to symptom relief by TOS PRO demonstrated consistent efficacy at all doses

	Placebo	PHVS416 10 mg	PHVS416 20 mg	PHVS416 30 mg	Combined PHVS416
Number of attacks	49	36	28	29	93
Attacks achieving <u>"a little better"</u> for all SCs at two consecutive time points - n (%) [*]	18 (36.7%)	32 (88.9%)	25 (89.3%)	27 (93.1%)	84 (90.3%)
Median (95% CI) time by KM estimate (hours)	7.62 (3.95, NE)	1.89 (0.97, 3.97)	2.15 (1.75, 4.00)	1.98 (1.80, 3.87)	1.98 (1.88, 3.87)
Attacks achieving <u>"a lot better or resolved"</u> for all SCs at any time point - n (%) [*]	13 (26.5%)	30 (83.3%)	23 (82.1%)	25 (86.2%)	78 (83.9%)
Median (95% CI) time by KM estimate (hours)	23.28 (5.78, 47.17)	4.02 (3.93, 5.77)	5.93 (3.90, 8.58)	4.12 (3.92, 7.22)	5.23 (3.98, 5.78)

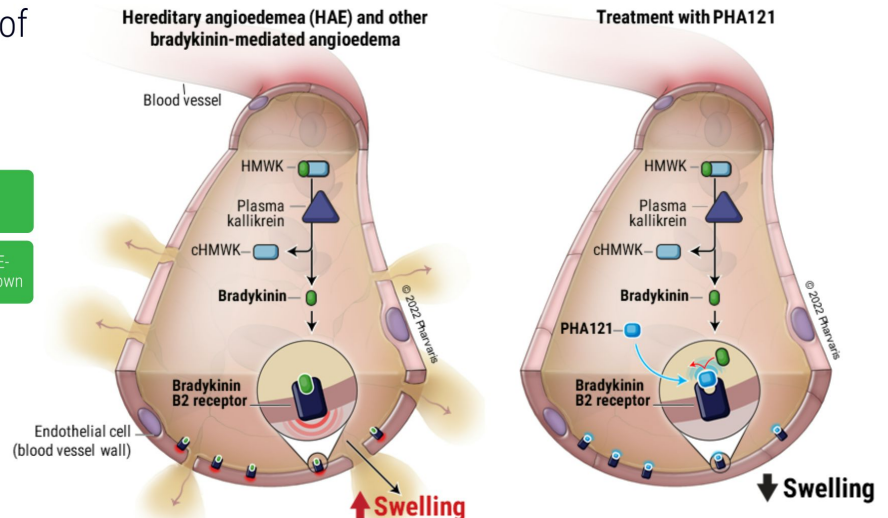
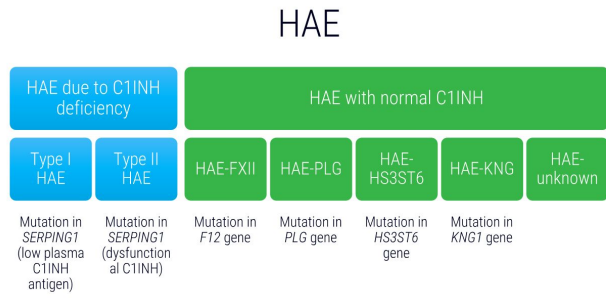
* Within 48 hours assessments

TOS = Treatment Outcome Score. PRO = Patient Reported Outcome. SC = Symptom Complex. KM = Kaplan-Meier. NE = Not Estimable



The swelling of an HAE attack is caused by excess levels of bradykinin

Genetic causes lead to elevated levels of bradykinin



Busse 2020 J Allergy Clin Immunol Pract; Bork et al 2021 J Allergy Clin Immunol

HMWK: high-molecular-weight kininogen; cHMWK: cleaved high-molecular-weight kininogen