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

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**FORM 6-K**

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**REPORT OF FOREIGN PRIVATE ISSUER  
PURSUANT TO RULE 13A-16 OR 15D-16 UNDER  
THE SECURITIES EXCHANGE ACT OF 1934  
For the month of November 2022  
Commission File Number: 001-40010**

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**Pharvaris N.V.**

(Translation of registrant's name into English)

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**J.H. Oortweg 21  
2333 CH 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.

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**PHARVARIS N.V.**

In connection with an investor event on November 1, 2022, Pharvaris N.V. (the “Company”) provided a corporate update included in a corporate presentation on its website, which, among other things, (i) reported that the Company held cash and cash equivalents of approximately \$198 million as of September 30, 2022, (ii) provided an update with respect to the Company’s clinical programs, including that a Type A meeting has been scheduled with the U.S. Food & Drug Administration for discussion of the on-demand and prophylactic proposals to address the hold on the clinical trials of PHA121 in the U.S., (iii) provided additional information on the endpoints in the Company’s Phase 2 clinical study for the on-demand treatment of hereditary angioedema using the Company’s investigational drug PHVS416 soft gel capsule (RAPIDe-1), and (iv) provided an update with respect to the Company’s expectations for the announcement of topline data for the RAPIDe-1 clinical study (the Company now expects to announce RAPIDe-1 topline data in December 2022).

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: November 1, 2022

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

EXHIBIT INDEX

Exhibit No.	Description
99.1	<a href="#">Press release, dated November 1, 2022</a>



# PHARVARiS

Pioneering science for patient choice

November 2022

# 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 clinical trials and are currently on hold in the U.S. as a result of the FDA clinical hold, 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. 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

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



## 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 through 1Q24:** ~€198 million as of September 30, 2022

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

\*The FDA has placed a hold on the clinical trials of PHA121 in the U.S.; see slide 14 for an update on our clinical program

# Experienced management with deep expertise in development and rare diseases



**Berndt Modig**  
Chief Executive Officer

**JERINI** **PRO S ENSA**



**Anne Lesage, Ph.D.**  
Chief Early Development Officer

**Johnson & Johnson**



**Morgan Conn, Ph.D.**  
Chief Business Officer

**PTC**  
THERAPEUTICS



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

**AMGEN** **Celgene** **Obseva**  
laboratory solutions

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

**JERINI**



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

**Roche** **Takeda** **Shire**  
**abbvie**



**Joan Schmidt, J.D.**  
Chief Legal Officer

**nova nordisk** **dbv** **ARENA**  
PHARMACEUTICALS



**Anna Nijdam**  
Principal Accounting Officer

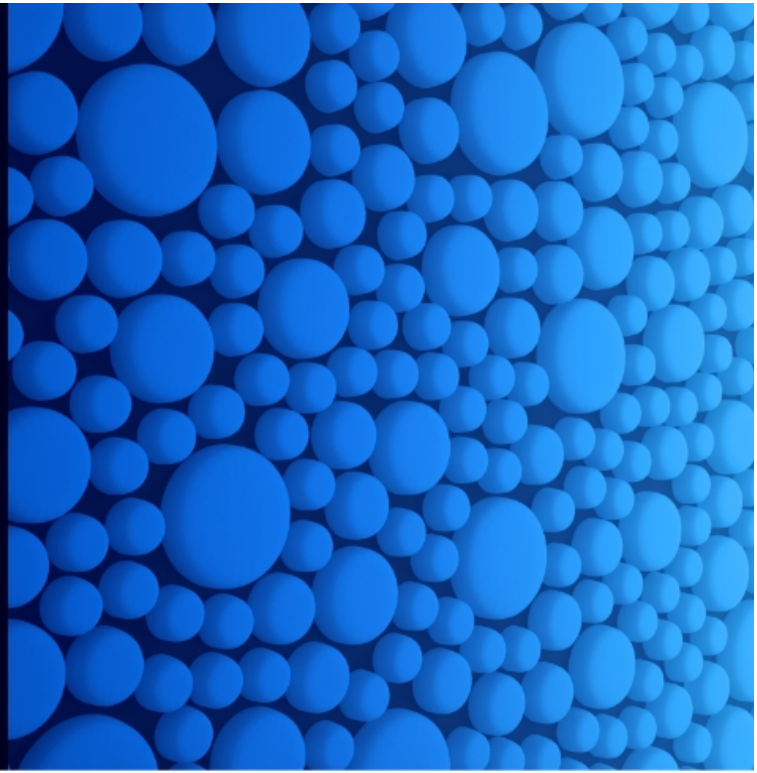
**EY**



**Annick Deschoolmeester**  
Chief Human Resources Officer

**Allergan** **Shire**  
**pwc** **Y!** **Takeda**

# Hereditary Angioedema (HAE)



## HAE is a rare, life-long condition characterized by attacks of swelling

- Rare and potentially life-threatening genetic condition
- 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

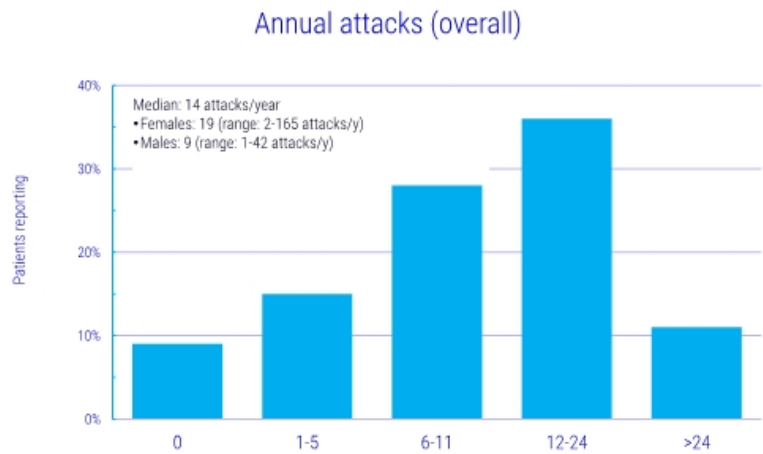


*Nordenfelt et al, Acta Derm. Venereol 2016; 96: 540-545*

# HAE attacks are unpredictable, debilitating and potentially lethal

Attacks are unpredictable in 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

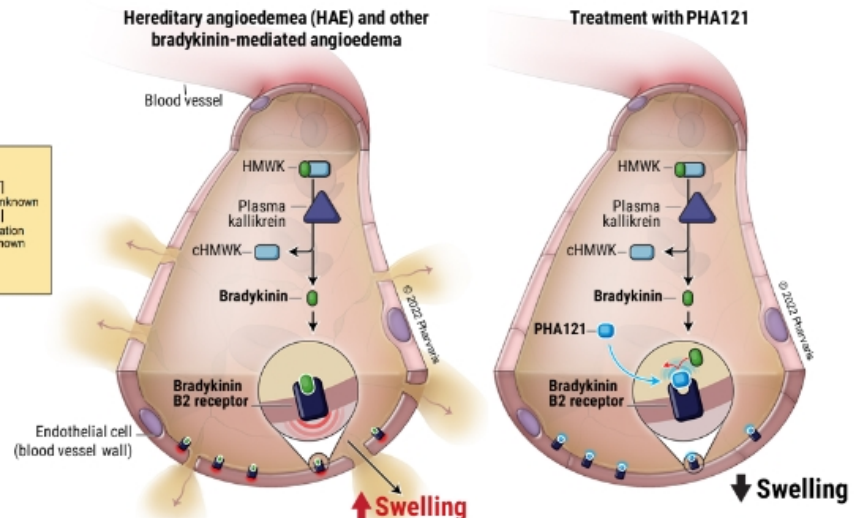
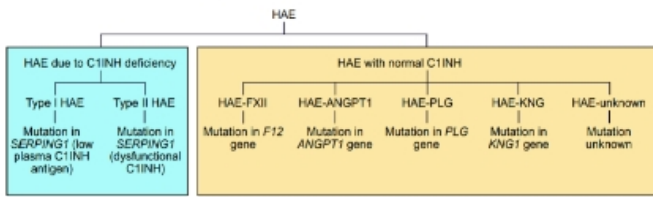


Nordenfelt et al, Acta Derm. Venereol 2016; 96: 540-545



# The swelling of an HAE attack is caused by excess levels of bradykinin: PHA121 is designed to block signaling by bradykinin

Most genetic causes lead to elevated levels of bradykinin



Busse 2020 J Allergy Clin Immunol Pract

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



# 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 ...

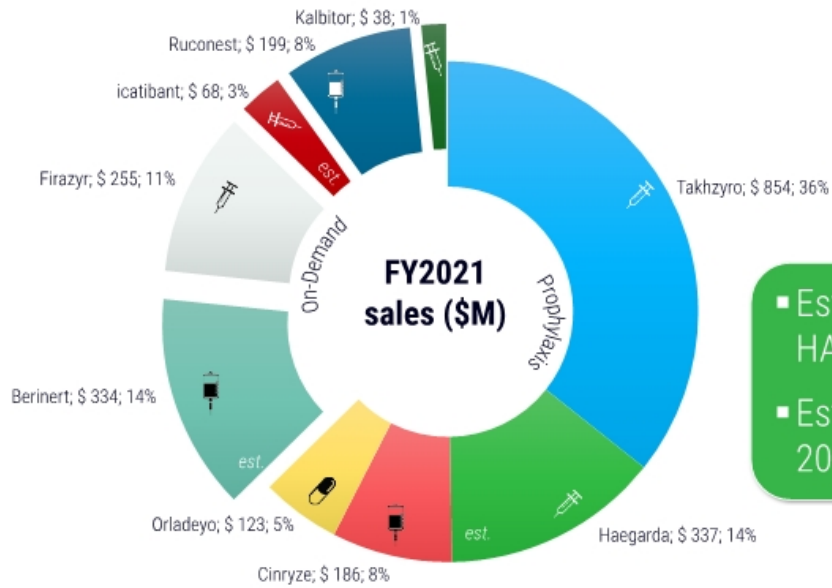


... while **convenience** has become a key driver for patient preference

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

Source: Company research

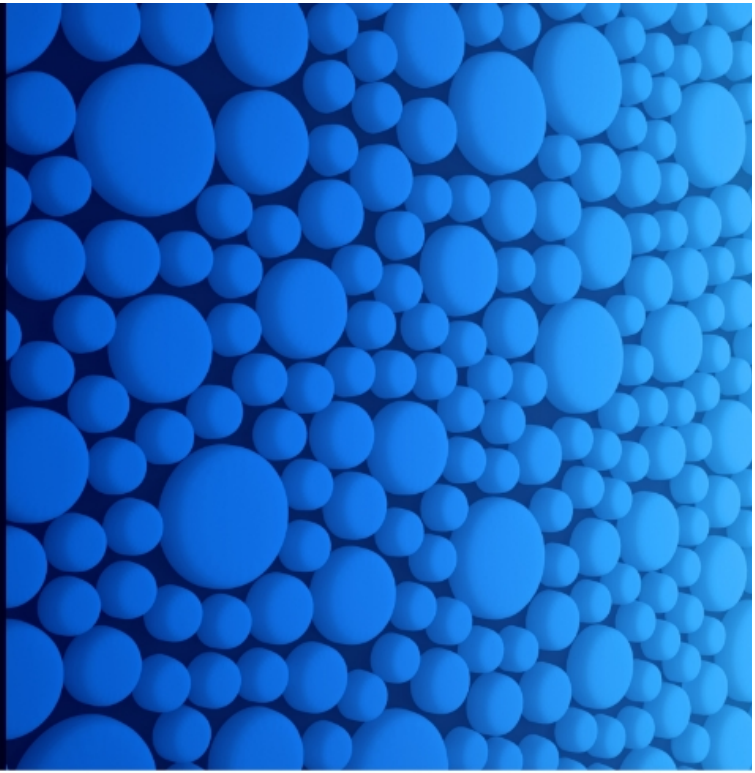
# HAE is a meaningful and growing global market



- Estimated \$2.4B global HAE sales for 2021
- Estimated 15% CAGR 2021-2028

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

# Product Strategy

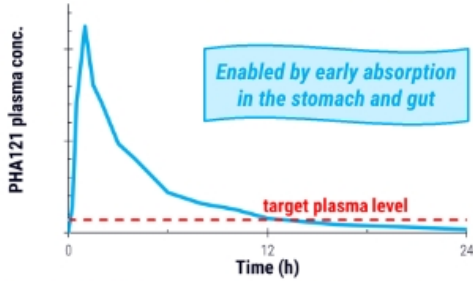


# On-demand and prophylaxis: Developing two oral products utilizing the same active ingredient



## PHVS416

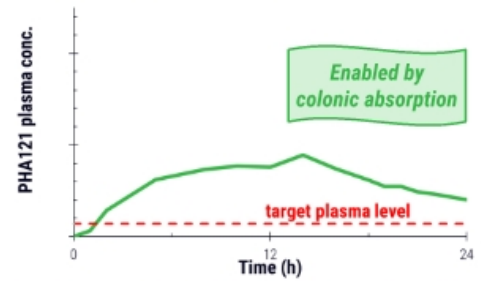
Softgel capsule formulation



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

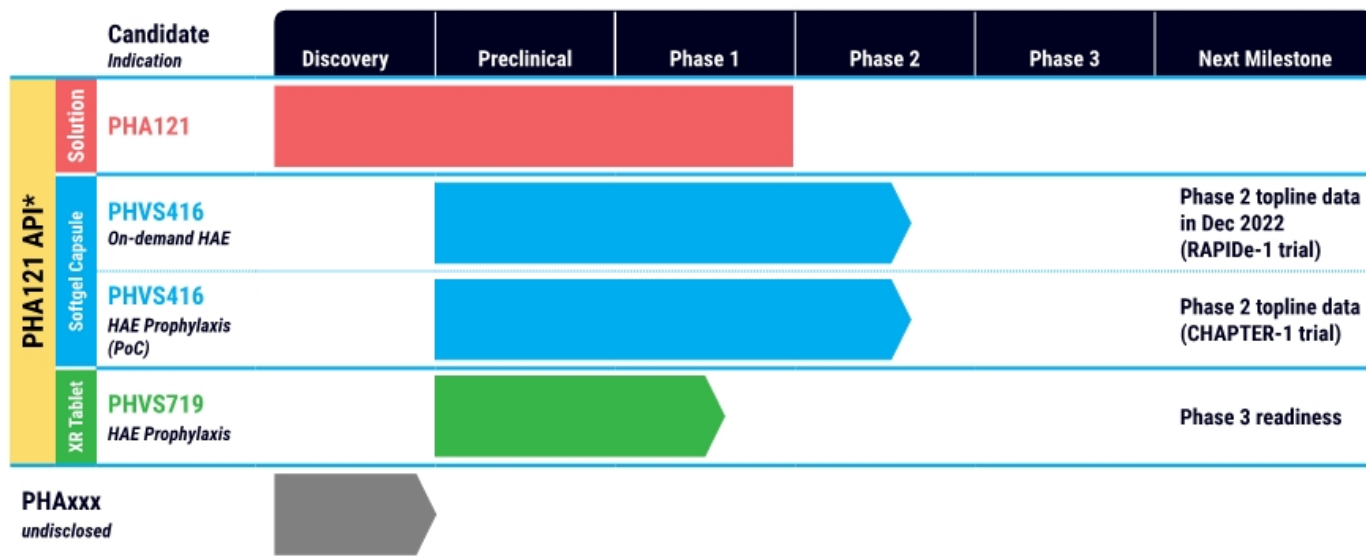
## PHVS719

Extended-release tablet formulation



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

# 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 14 for an update on our clinical program

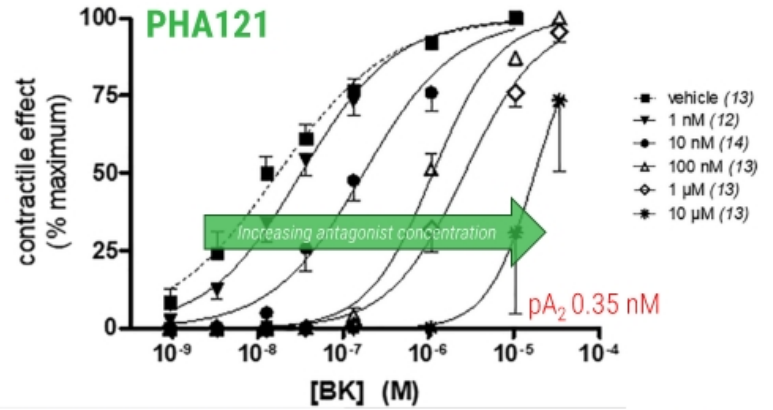
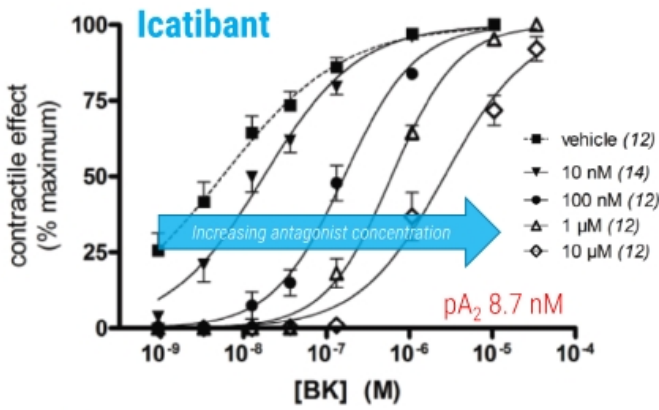
## Update on clinical programs

- 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
  - The FDA stated that the nonclinical observations are unlikely due to bradykinin B2 receptor antagonism
  - A Type A meeting has been scheduled with the FDA to discuss on-demand and prophylactic proposals to address the holds
- Clinical studies continue in Canada, Europe, Israel, and the UK as Pharvaris works with country-specific regulatory authorities
- In our completed Phase 1 trials and ongoing Phase 2 trials to date, we have observed that PHA121 was well tolerated at all doses studied

# Programs

# Pharvaris compounds are potent, orally available competitive inhibitors of the bradykinin B2 receptor

Competitive antagonism of bradykinin-induced contraction  
(human umbilical vein preparation)



PHA121 is 25-fold more potent than icatibant at the endogenous human B2 receptor

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



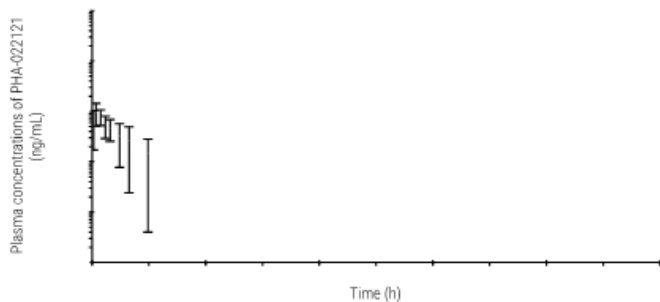
PHA121

PK/PD in humans

© 2022

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## PHA121 was well tolerated in Phase 1 SAD and MAD trials



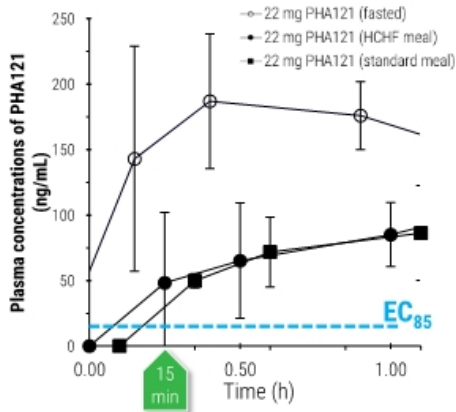
- **Approximately dose-proportional PK** with single and multiple oral doses
- **Half-life approximately 3.4-5.6 hours** (approximately three-fold longer than icatibant)

### PHA121 (oral solution)

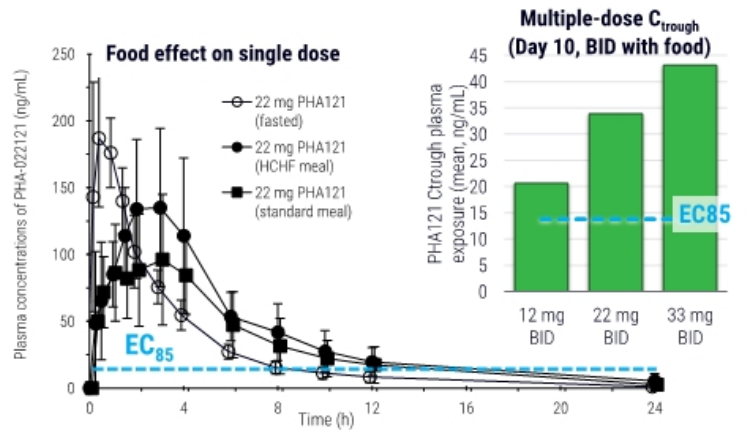
- **No clinically significant changes** were observed for physical exams, vitals, ECG, and safety lab assessments
- **No SAEs or severe AEs** were reported with no treatment discontinuations
- Most AEs observed were of **mild severity**
- Total incidence of AEs was **similar between active and placebo** groups
- No clear differences for AE patterns between different dosing regimens vs. placebo

<https://epostersonline.com/acaai2020/node/1384>

# Phase 1 pharmacokinetics offer options for on-demand and prophylactic development



Surpasses target exposure ( $EC_{85}$ ) within 15 minutes under both fasted and fed status



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

<https://eostersonline.com/acaai2020/node/1384>; <https://r.pharvaris.com/static-files/81a9499d-0769-4b89-8ecd-8ace5ca521d3>

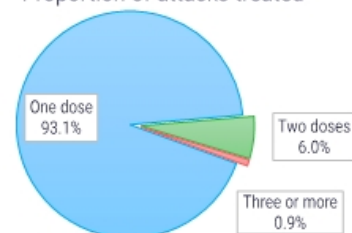
# Inhibition of bradykinin-induced hemodynamic effects is a validated surrogate assessment



- In healthy volunteers, pre-dosing a bradykinin-B2-receptor antagonist blocks the hemodynamic effects of bradykinin
  - Bradykinin effects restored as single-dose eliminated
- Used to select clinical dose in the original icatibant development program, as reviewed by FDA and EMA

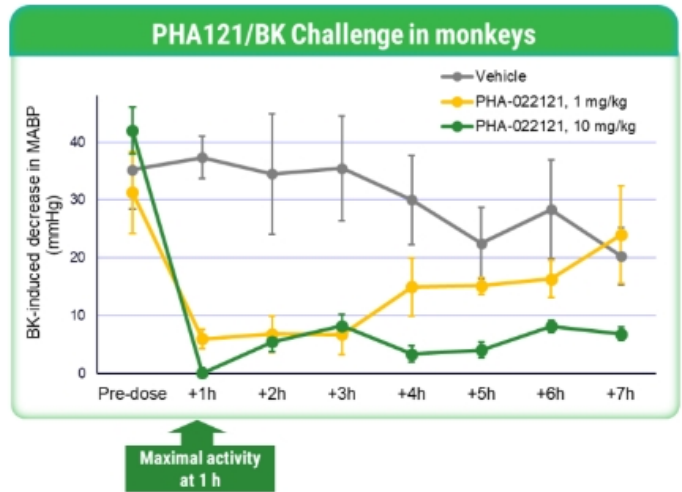
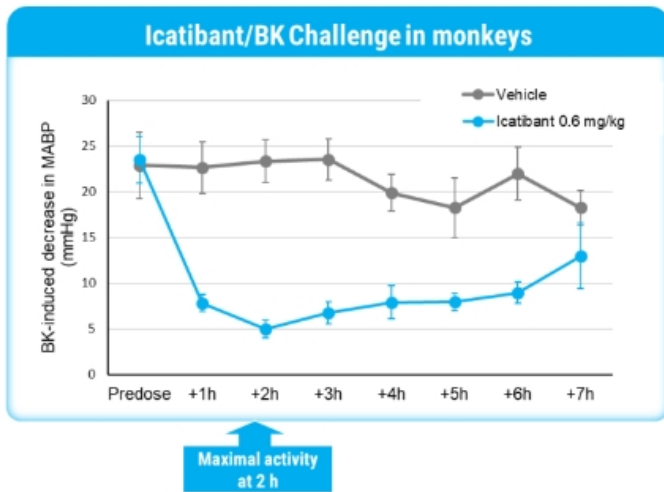
- Icatibant's clinical dose, established with the BK challenge, has demonstrated successful resolution of HAE attacks in randomized clinical trials and over 10 years of data post-approval
  - Icatibant Outcome Survey: Longitudinal survey over 10 years; more than 5000 HAE attacks treated with 30 mg SC

Proportion of attacks treated



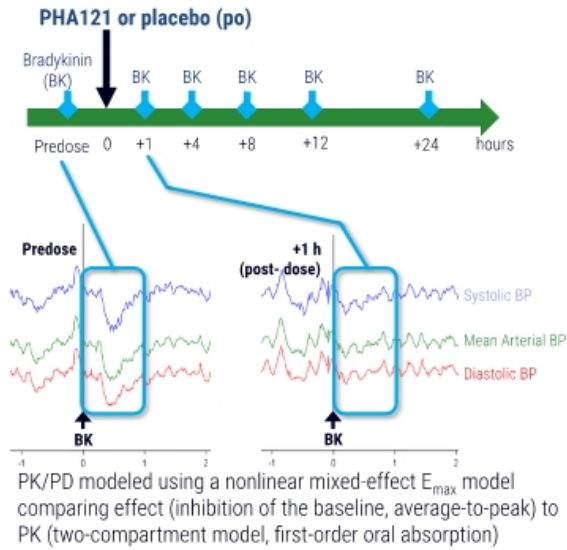
[https://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2011/022150Orig1s000ClinPharmR.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022150Orig1s000ClinPharmR.pdf); Maurer et al 2020: Long-term effectiveness and safety of icatibant for the on-demand treatment of hereditary angioedema attacks: 10 years of the icatibant outcome survey (EAACI Poster #1118, June 6-8, 2020); <https://clinicaltrials.gov/ct2/show/NCT01034969>

# In preclinical in vivo studies, oral PHA121 inhibits challenge by bradykinin with longer duration and faster onset than SC icatibant



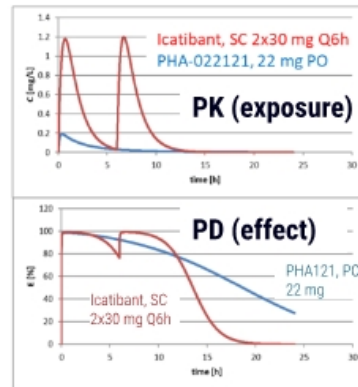
[https://education.aaaai.org/sites/default/files/L37%20Lesage\\_1.pdf](https://education.aaaai.org/sites/default/files/L37%20Lesage_1.pdf)

# In healthy volunteers, oral pre-treatment with PHA121 blocks the effect of bradykinin-induced hemodynamic changes



$EC_{50}$  (ng/mL) **2.4**  
 $EC_{85}$  (ng/mL) **13.8**

**Potency ~4x higher than icatibant**  
 (published data)

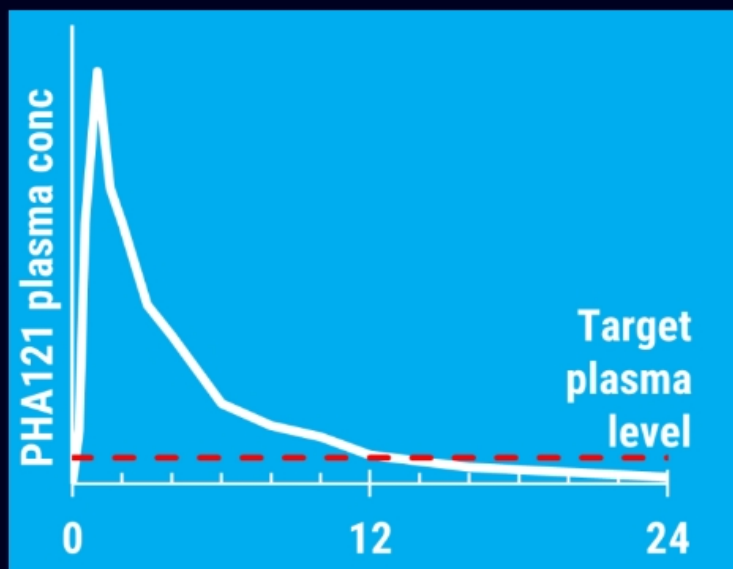


A **single** PHA121 dose predicted to provide **similar PD effect** as two injections of icatibant

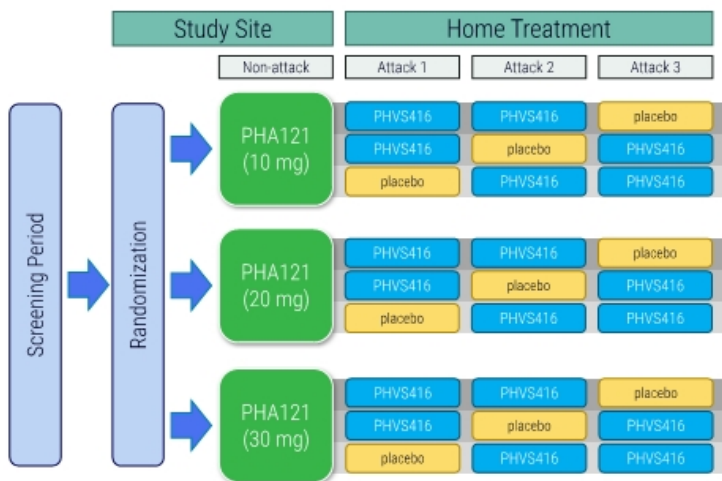
<https://epostersonline.com/acaai2020/node/1369>; <https://doi.org/10.1076/1.jaci.2019.12.094>; [https://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2011/022150Orig1s000ClinPharmR.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022150Orig1s000ClinPharmR.pdf)

## PHVS416/On-Demand

Softgel capsule formulation of PHA121



# HAE RAPIDe-1 study: Dose-ranging study for acute treatment of angioedema attacks in patients with hereditary angioedema



- Phase 2 double-blind placebo-controlled cross-over
  - Patients randomized to one of three doses
  - Each patient receives dosage to treat three attacks, two active and one placebo (2:1 treatment to placebo)
- Primary objective: evaluate efficacy of single treatment of three doses against placebo for treatment of HAE attacks
- Attacks qualify for treatment when at least one attack symptom (skin pain, skin swelling, abdominal pain) becomes moderate (VAS  $\geq 30$ )**
  - Early treatment: treatment must start no later than 6 h after first onset of symptoms at any location

[www.hae-rapide.com](http://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>



## HAE RAPIDe-1 study: Topline data expected Dec 2022



### Enrollment target achieved

- 72 HAE patients enrolled from ~30 sites in U.S.\*, Canada, Europe, Israel, and UK



### Primary topline data expected Dec 2022 based on collected dataset of attacks

- Continued monitoring of attacks of enrolled patients in countries outside the U.S. in RAPIDe-1 and RAPIDe-2 (open-label extension)

\*The FDA has placed a hold on the clinical trials of PHA121 in the U.S.; see slide 14 for an update on our clinical program

## RAPIDe-1: Primary and secondary endpoints

- Primary
  - Change of VAS-3 from pre-treatment to 4h post-treatment
- Secondary
  - Time to onset of symptom relief (VAS-3;  $\geq 30\%$  reduction from pre-treatment score)
  - Time to almost complete and complete symptom relief (VAS; all three components  $< 10$  mm)
  - Time to a  $\geq 50\%$  reduction in VAS-3 from pre-treatment score
  - Change of MSCS from pre-treatment to 4h post-treatment
  - TOS at 4h post-treatment

VAS: visual analogue score; MSCS: mean symptom complex severity; TOS: treatment outcome score

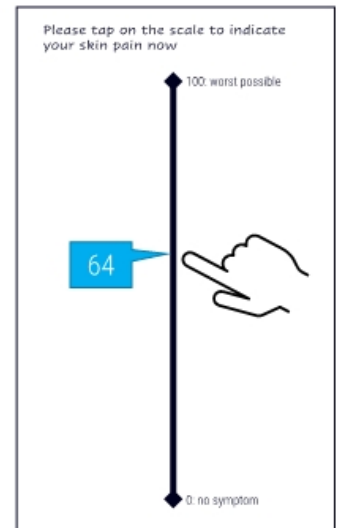
## RAPIDe-1: Other secondary endpoints include:

- Time to onset of primary symptom relief (leading component of VAS)
- Proportion of IMP-treated attacks requiring the use of HAE rescue medication
- Time to the first use of HAE rescue medication
- Safety
- PK, dose-effect relationship, and concentration-effect relationship
- TSQM score at 48 h post-treatment

VAS: visual analogue score; IMP: investigational medicinal product; MCSC: mean symptom complex severity; TOS: treatment outcome score; TSQM: treatment satisfaction questionnaire for medication

## VAS-3 is a measure of HAE attack severity, used in past registrational studies

- 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 up to 48 hours post-treatment
- Used in approval of two most recently approved on-demand therapies
  - FIRAZYR® icatibant and RUCONEST® C1 esterase inhibitor [recombinant]
- VAS, MCSC, 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

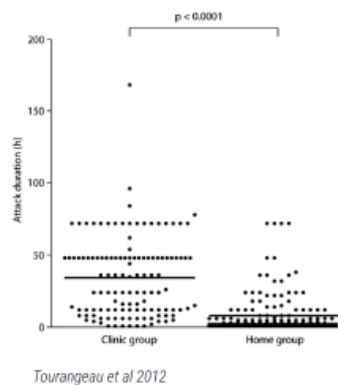
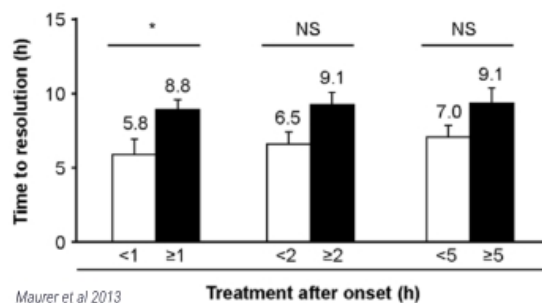


*Firazyr is a registered trademark of Shire, and marketed by Takeda; Ruconest is a registered trademark of and marketed by Pharming; FDA 2021 COA compendium: <https://www.fda.gov/drugs/development-resources/clinical-outcome-assessment-compendium>*

## Clinical practice: Earlier treatment reduces time to resolution

HAE attacks should be treated early (US, Canada, WHO guidelines)

- Associated with shorter time to resolution and total attack duration



Maurer et al 2022 *Allergy*; Busse et al 2021 *J. Allergy Clin Immunol Pract*; Betschel et al 2019 *Allergy Asthma Clin Immunol*; Maurer et al 2013 *PLOSone*; Tourangeau et al 2012 *Int Arch Allergy Immunol*

# Prior studies showed higher baseline and changes in VAS-3 scores, with treatment at clinic

icatibant (FAST-3 Ph3): Travel to clinic <6 hours after symptoms become moderate (high baseline VAS-3)

rC1-INH (Ph2): Travel to clinic <5 hours after symptoms become moderate (high baseline VAS-3)

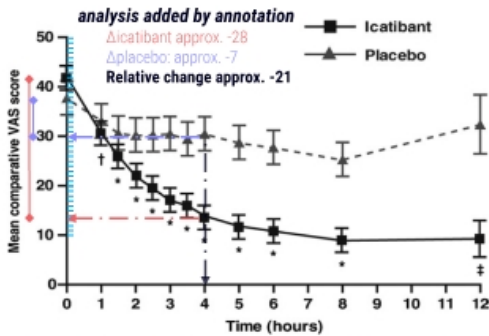
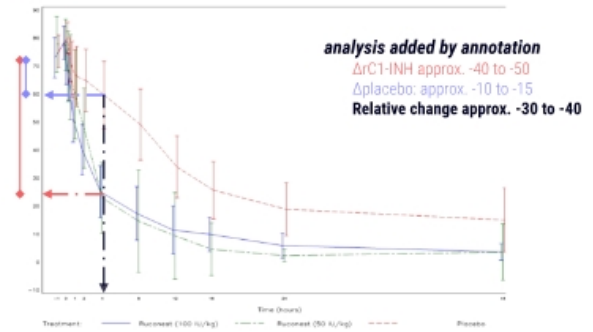


Figure 3. Mean composite VAS-3 score for the first 12 hours after treatment (nonlaryngeal ITT population). \* $P \leq .001$ ; † $P = .003$ ; ‡ $P = .041$ , vs placebo. Sixteen subjects (icatibant  $n = 5$ ; placebo  $n = 11$ ) who had not achieved relief by hour 8 had nonmissing data for hour 12.

Mean VAS scores over time with 95% Confidence Intervals (Study 2 and 3, RCT Phase)

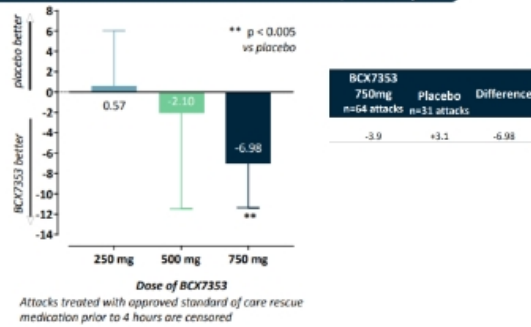


Lumry et al 2011 Ann Allergy Asthma Immunol; Riedl et al 2014 Ann Allergy Asthma Immunol; RUCONEST prescribing information

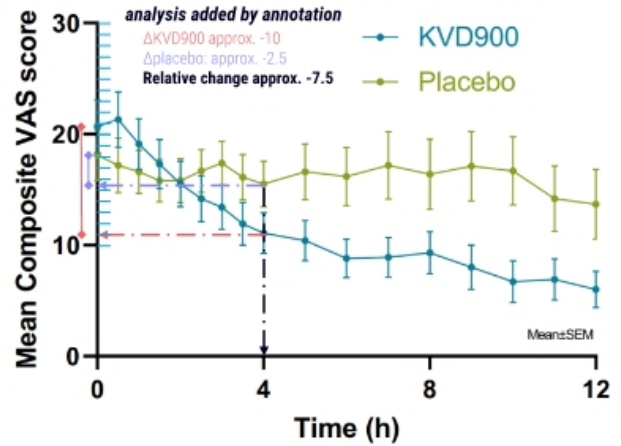
# Recent on-demand HAE trials treat sooner in home setting, with lower baseline and smaller absolute changes in VAS-3 at 4 hours

## BCX7353 (ZENITH-1 Ph2): Dosing within 1 hour of symptoms

Change from Baseline in 3-Composite VAS at 4 hours Post-dose (LS Mean Difference from Placebo in mm, 95% CI)



## KVD900 (Ph2): Dosing within 1 hour of symptoms



BCRX poster #110 AAAAI 2019-02-23 <https://ic.biocryst.com/static-files/2b3e13b9-ad24-432c-9ac5-15711d954d88>; KALV presentation 2021-02-09

# Initial relief: Relative change in VAS-3 may depend on baseline

## icatibant (FAST-3 Ph3)

- 2.0 h (VAS-3, 50% reduction)
- 1.5 h (VAS-3, 30% reduction)

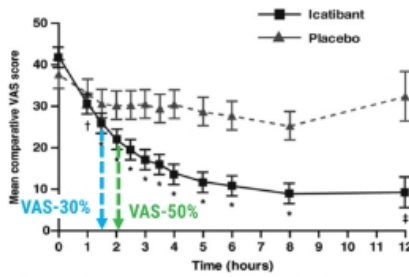
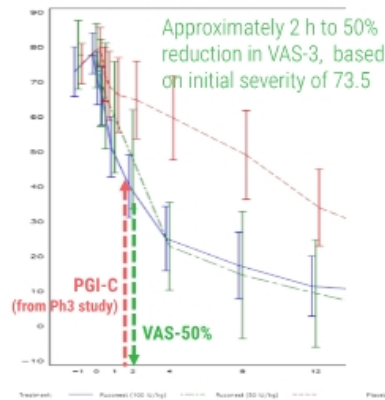


Figure 3. Mean composite VAS-3 score for the first 12 hours after treatment (nonlaryngeal ITT population). \* $P \leq .001$ ; † $P = .003$ ; ‡ $P = .041$  vs placebo. Sixteen subjects (icatibant  $n = 5$ ; placebo  $n = 11$ ) who had no achieved relief by hour 8 had nonmissing data for hour 12.

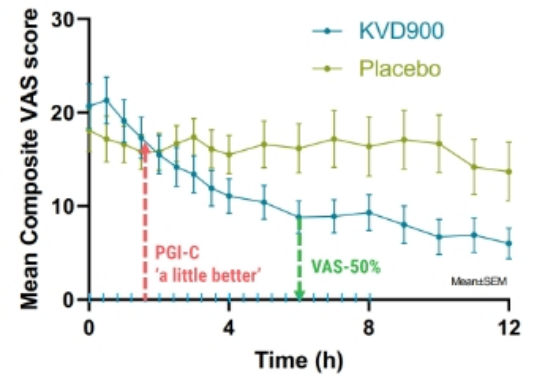
## rC1-INH

- Ph2: approx. 2 h (VAS-3, 50%)
- Ph3: 1.5 h (two-question TEQ)



## KVD900 (Ph2)

- 6 h (VAS-3, 50% reduction from pretreatment)
- 1.6 h (PGI-C, at least "a little better")
- ~5-6h (PGI-C, at least "better")



Lumry et al 2011 Ann Allergy Asthma Immunol; Riedl et al 2014 Ann Allergy Asthma Immunol; RUCONEST prescribing information; KALV presentation 2021-02-09



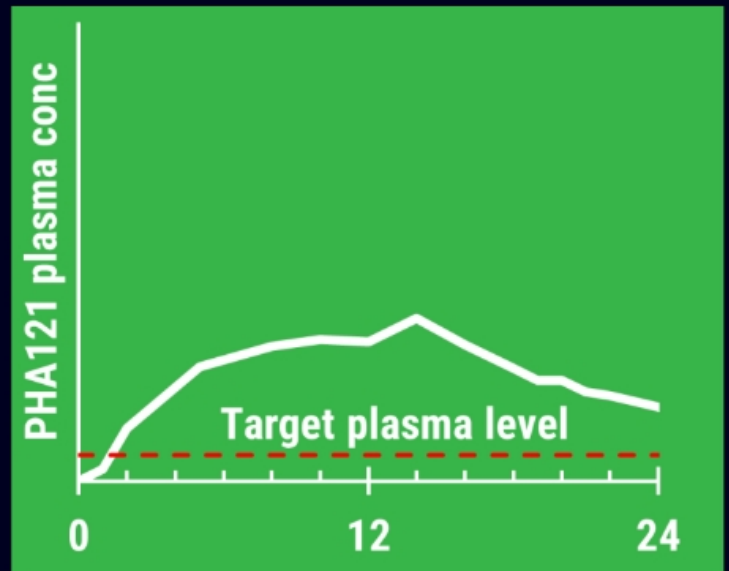
## On-Demand: PHVS416 aims to provide clear differentiation for efficacy and convenience

Clinical data	PHVS416	icatibant	sebetralstat	berotralstat	BERINERT®	RUCONEST®	KALBITOR®
FDA Approval	(Phase 2)	2011	(Phase 3)	(EOP2, dropped)	2009	2014	2009
Mechanism	B2R	B2R	pKi	pKi	C1INH	C1INH	pKi
Dose	≤30 mg	30 mg	1-2x300 mg	750 mg	20 IU/kg	50 IU/kg	3x10 mg
Form	Soft capsule	SC	Tablet	Oral, suspension	IV (10 mL/2.5 min)	IV (14 mL/5 min)	SC, 3 doses
Storage	Room temp	Room temp	Room temp		Room temp	Room temp	Fridge
Administered	Patient	Patient	Patient	Patient	Patient	HCP/Patient	HCP
Time to 2x IC50	<15 min		10 min	<30 min	48 min		
Half-life (h)	3.4-5.6	1.4	~2	93	18	2.5	2
Single-dose resolution		93%		64%	80-89%	90%	67-86%
Rescue or re-dose?		7% <sup>5d</sup>	21% <sup>24h</sup>	30% <sup>24h</sup>	11-20%	11%	14-33%
Initial relief (h)		0.8-1.5 <sup>VAS-50%</sup>	1.6 <sup>PGI-C/6VAS-50%</sup>	5	0.25	1.5 <sup>PGI-C</sup>	--
50% VAS reduction (h)		2	6	8	--	3.5	--
Almost-complete symptom relief (h)		8		23	8.4	--	--
Side effects		Injection site reaction		Nasopharyngitis, diarrhea, headache	Thromboembolic events	Headache, rabbit allergy	Anaphylaxis, pruritus, rash, nausea


Source: Firazyr, Ruconest, Kalbitor prescribing information; Pharming release 2018-12-07; BioCryst release 2018-09-04; Kalvista corporate presentation 2021-02-09; <https://www.clinicaltrials.gov/ct2/show/NCT05259917>; Lumry 2013 Allergy Asthma Proc. 34(2), 155-161; EAACI 2020 Poster #1118; Zanichelli et al, C1 Inhibitor Workshop 2021 ([https://www.kalvista.com/sites/default/files/presentations/zoom\\_0.mp4](https://www.kalvista.com/sites/default/files/presentations/zoom_0.mp4))

## PHVS719/Prophylaxis

Extended-release tablet formulation of PHA121



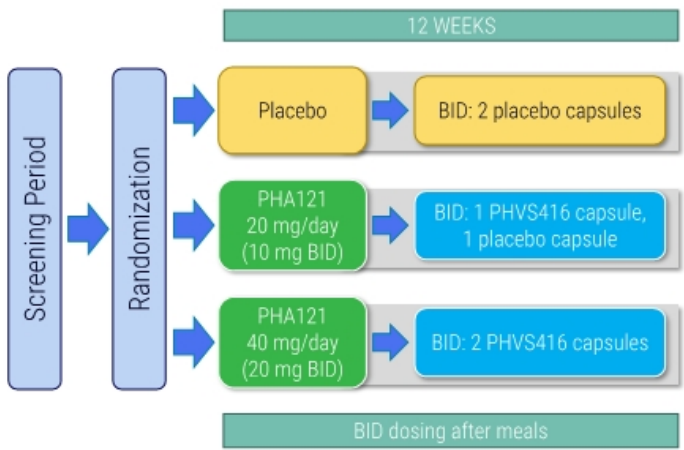
# Data from prophylactic proof-of-concept study (PHVS416) and PHVS719 tablet PK to inform Phase 3 development

	Candidate* Indication	Phase 1	Phase 2	Phase 3
Softgel	<b>PHVS416</b> Prophylaxis HAE (PoC)		Top-line Data	
XR Tablet	<b>PHVS719</b> Prophylaxis HAE	Data 1Q22		

Utilizing the food effect observed in Phase 1, PK/PD modeling suggests that twice-daily dosing of PHVS416 can maintain PHA121 exposure  $>EC_{85}$

\*The FDA has placed a hold on the clinical trials of PHA121 in the U.S.; see slide 14 for an update on our clinical program

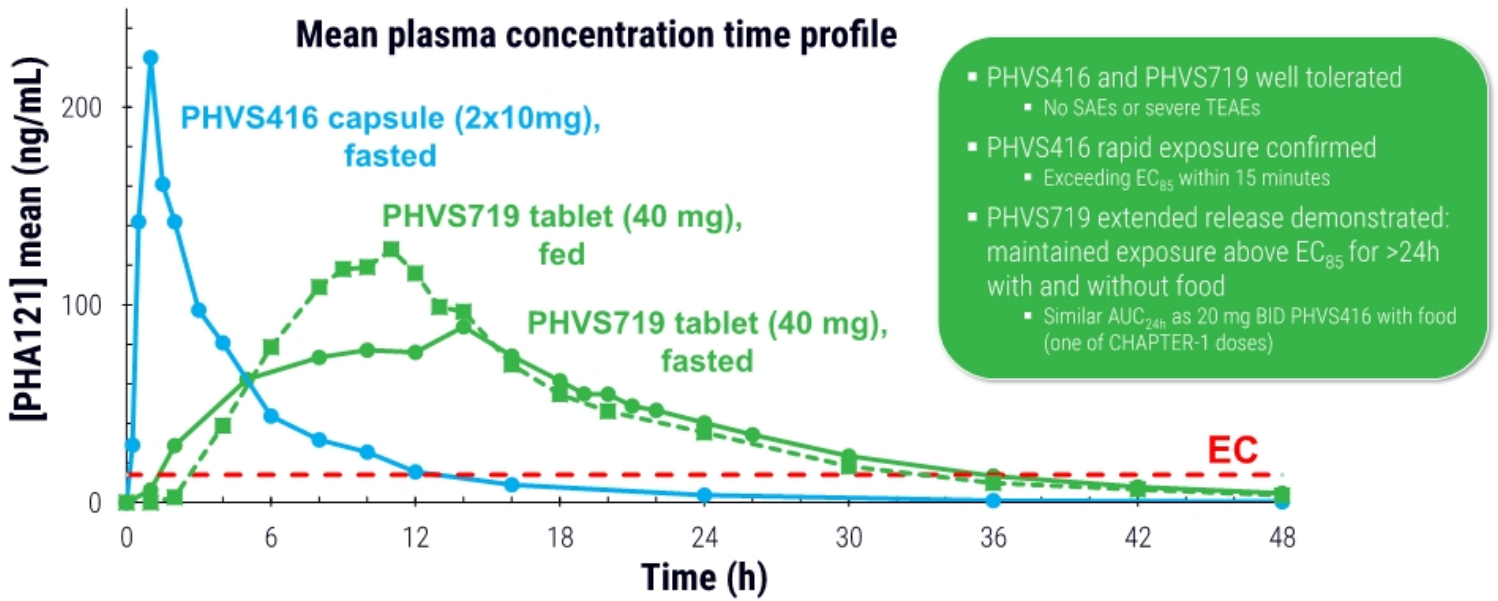
# HAE CHAPTER-1 study ongoing outside U.S.: Prevention of attacks in HAE (proof of concept with PHVS416 softgel capsule)



- 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; guidance on topline data timing to follow with more clarity regarding the impact of the U.S. clinical hold and additional feedback from global regulatory authorities

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

# PHVS719 single-dose PK study demonstrates QD potential



## Prophylaxis: PHVS719 aims to combine efficacy and convenience compared to approved therapies and oral pipeline

	PHVS719	KVD824	ORLADEYO®	TAKHZYRO®	HAEGARDA®	CINRYZE®
FDA Approval	(Phase 1/2)	(Phase 2)	2020	2018	2017	2008
Mechanism	B2R	pKi	pKi	pK mAb	C1INH	C1INH
Dose	40 mg (est.)	1-3x300 mg	150 mg, 110 mg	300 mg	60 IU/kg	1000-2500 IU
Form	XR tablet	Delayed-release tablet	Hard capsule	SC, 2 mL	SC, 6 mL	IV, 10-25 mL
Storage	room temp		room temp	fridge	room temp	fridge/room temp
Frequency	Once daily	Twice daily	Once daily	Semi-monthly	Semi-weekly	Semi-weekly
Attack reduction (mean)			44%	87%	84%	84.5%
≥50% reduction			58%	100%	90%	
≥70% reduction			50%	89%	83%	
≥90% reduction			23%	67%	58%	
Patients, attack-free (study)			--	44% (77-87% SS)	40%	
Steady-state	~2 d (est.)	~3 d (est.)	6-12 days	10 weeks	~14 d (est.)	~7 d (est.)
Side effects			GI effects, QTc on higher doses, moderate DDI	injection-site reaction	Injection-site reaction, thromboembolic events	Headache, nausea, thromboembolic events

Source: Takhzyro, Haegarda, Cinryze, Orladeyo prescribing information; Aygoren-Pursun 2018. NEJM 379(4), 352-62; ICER 2018 Final Evidence Report – Long-Term Prophylaxis in HAE; Kalvista corporate presentation March 2022 (<https://ir.kalvista.com/static-files/ed4489d4-70b7-4648-944f-76fe17d566842>), <https://clinicaltrials.gov/ct2/show/NCT05055258>

## Corporate Summary and Milestones

	HAE On-Demand (type 1 and type 2)	HAE Prophylaxis (type 1 and type 2)
PHVS416 soft capsule	RAPIDe-1 Ph2 topline data (expected Dec 2022)	CHAPTER-1 Ph2 topline data (timeline pending clarity on impact of U.S. clinical hold)
PHVS719 XR tablet	--	✓ Ph1 SD PK demonstrates once-daily potential

Financially strong: ~€198 million cash (Sep 30, 2022) provides runway through 1Q24

# PHARVARiS

Nasdaq: PHVS



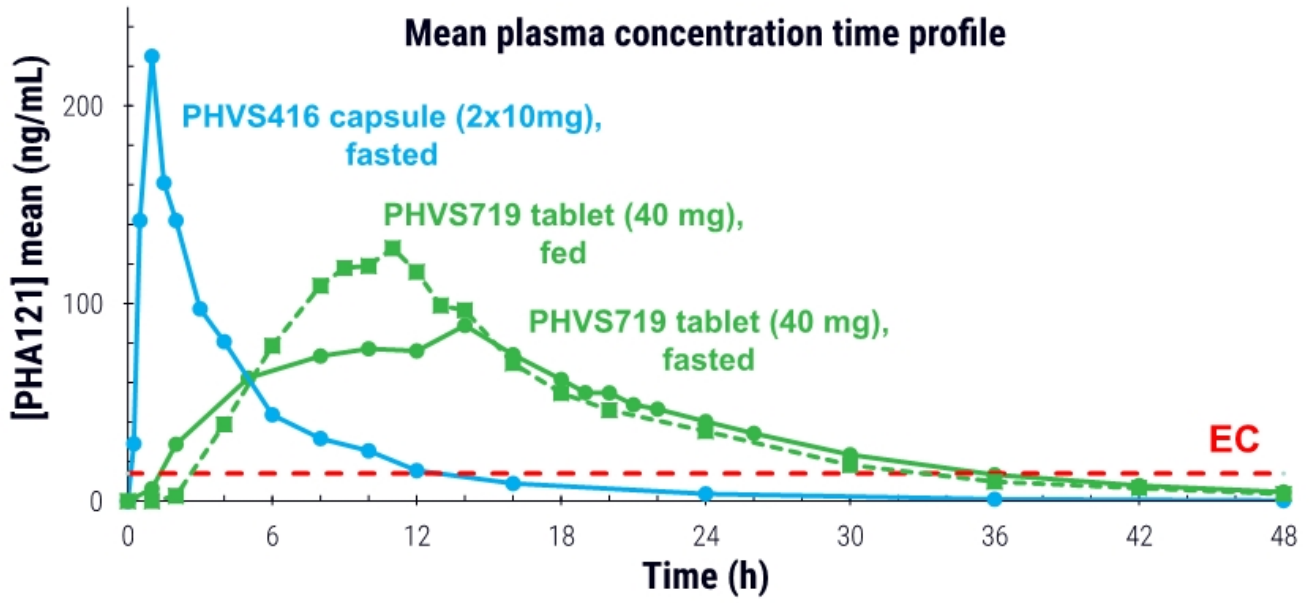
# PHVS719 single-dose PK study demonstrates QD potential

- Open-label, crossover comparison in 8 adult male healthy volunteers
- Sequential single doses (random order) of:
  - PHVS416: 20 mg dose (fasted)
  - PHVS719 prototypes
    - XR1: 20 mg dose (fasted, fed)
    - XR2: 40 mg dose (fasted, fed)

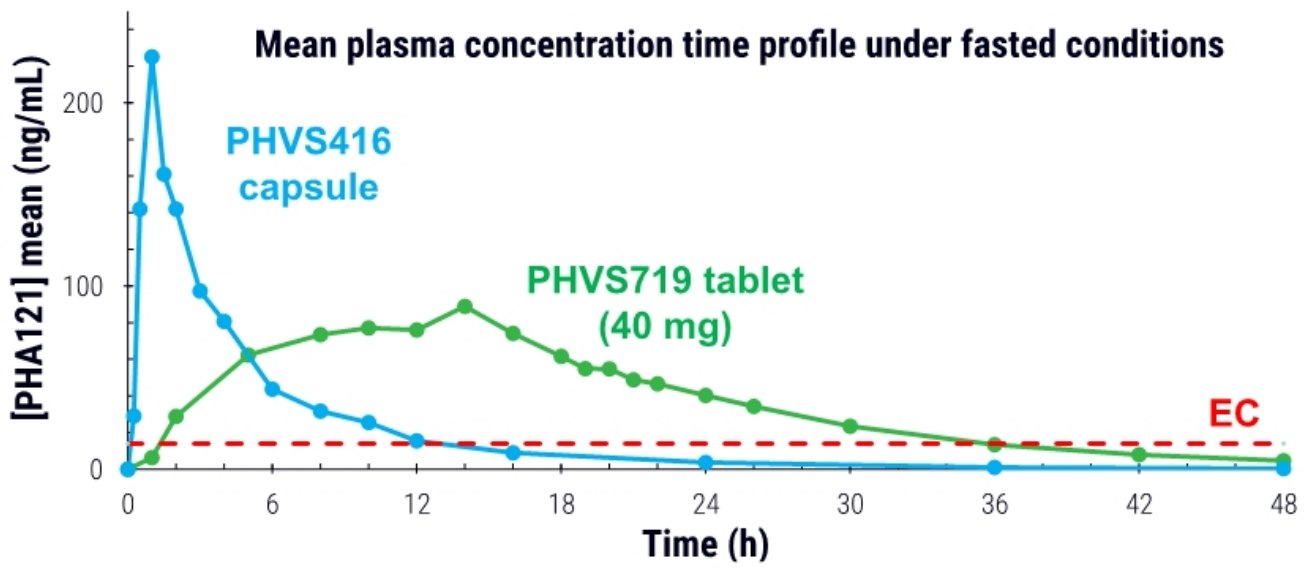


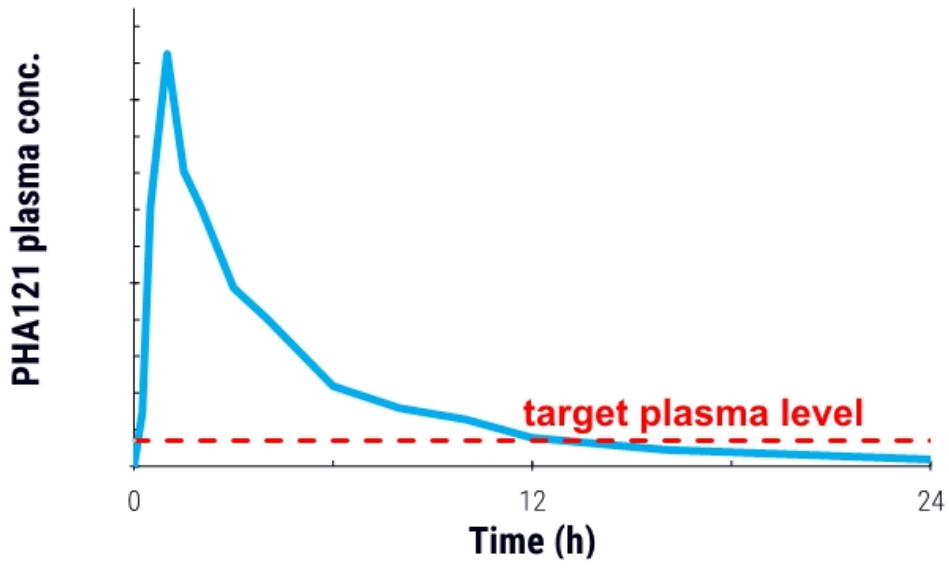
- PHVS416 and PHVS719 well tolerated
  - No SAEs or severe TEAEs
- PHVS416 rapid exposure confirmed
  - Exceeding  $EC_{85}$  within 15 minutes
- PHVS719 extended release demonstrated: maintained exposure above  $EC_{85}$  for >24h with and without food
  - Similar  $AUC_{24h}$  as 20 mg BID PHVS416 with food (one of CHAPTER-1 doses)

# PHVS719 single-dose PK study demonstrates QD potential



# PHVS719 single-dose PK study demonstrates QD potential





## PHVS719 single-dose PK study demonstrates QD potential

