
**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 July 2022

Commission File Number: 001-40010

Pharvaris N.V.

(Translation of registrant's name into English)

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 Form 20-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.

In connection with an investor event, on July 13, 2022, Pharvaris N.V. (the “Company”) provided a corporate update included in a corporate presentation on its website, which, among other things, contains updated guidance with respect to the Company’s Phase 2 clinical trial for the prophylactic treatment of hereditary angioedema using twice-daily dosing of the PHVS416 softgel capsules (CHAPTER-1). Based on projected enrollment rates, the Company has now refined timing of full trial enrollment and believes a more conservative estimate for reporting topline data for this trial is the first quarter of 2023.

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.

EXHIBIT INDEX

<u>Exhibit No.</u>	<u>Description</u>
99.1	Corporate Presentation, dated July 13, 2022

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.

Date: July 13, 2022

PHARVARIS N.V.

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

PHARVARiS

Pioneering science for patient choice

July 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, the expected timing, progress, or success of our clinical development programs especially for PHVS416 and PHVS719 which are in mid-stage clinical trials, 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: Fulfilling an 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 with superior potency and duration against surrogate endpoint, when compared to icatibant

Favorable PK/PD profile supporting both **on-demand and prophylactic treatment**; **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 into 1Q24:** €194.8 million as of March 31, 2022

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




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




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




Joan Schmidt
Chief Legal Officer




Anna Nijdam
Principal Accounting Officer



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

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

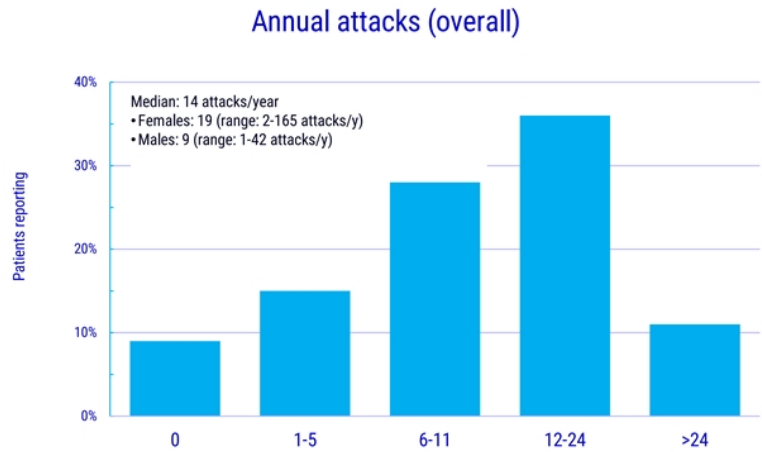


Nordenfelt et al, Acta Derm. Venereol 2016; 96: 540-545

HAE attacks are unpredictable, debilitating and potentially lethal

Attacks are unpredictable in frequency, location, timing, and severity

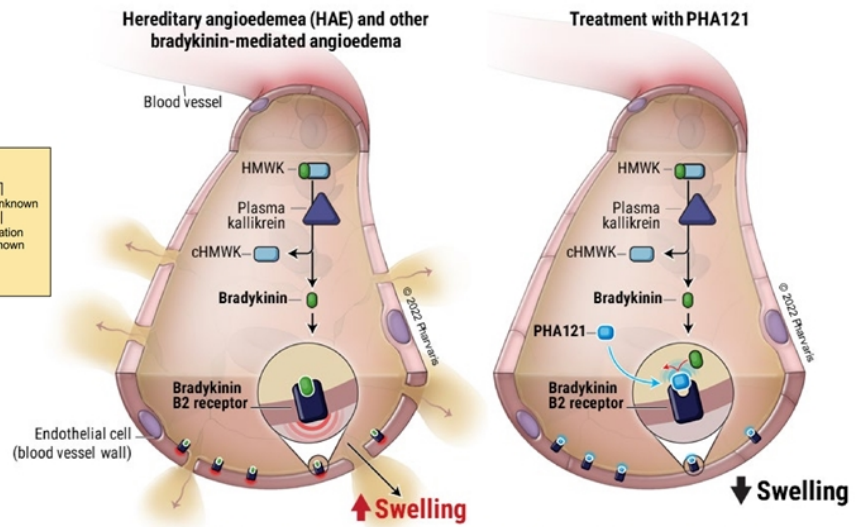
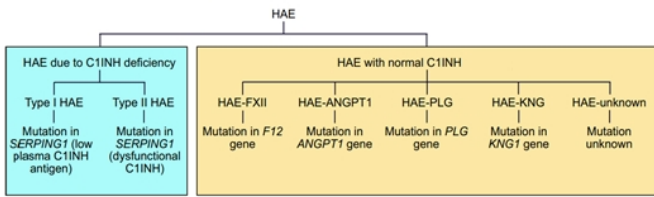
- Multiple types of triggers
- If untreated, attacks last multiple days
- Attacks are commonly painful, leading to hospitalization or multiple sick days
- Half of people living with HAE experience a potentially life-threatening laryngeal attack at least once in their lifetime



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



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

Busse 2020 J Allergy Clin Immunol Pract

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 ...

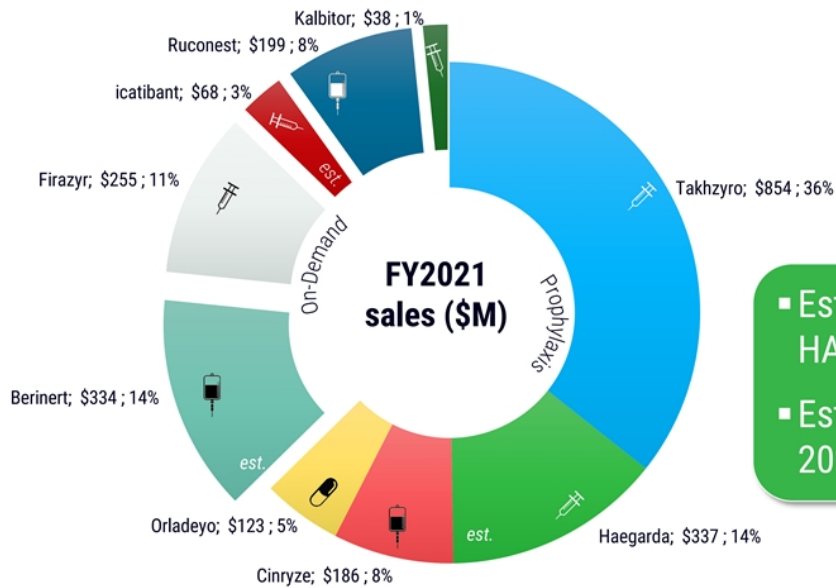


... while **convenience** has become a key driver for patient preference

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

Source: Company research

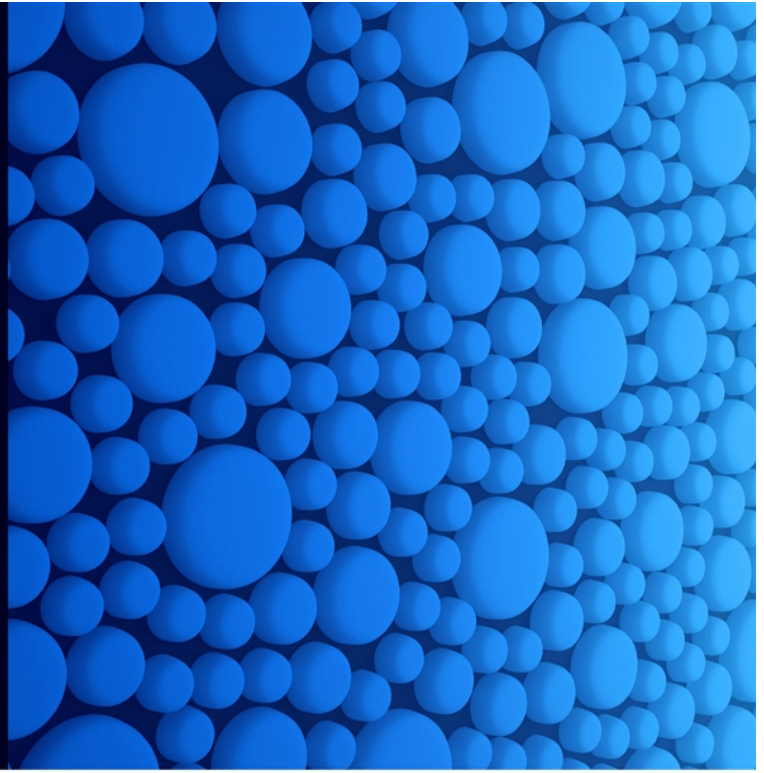
HAE is a valuable, growing market



- 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

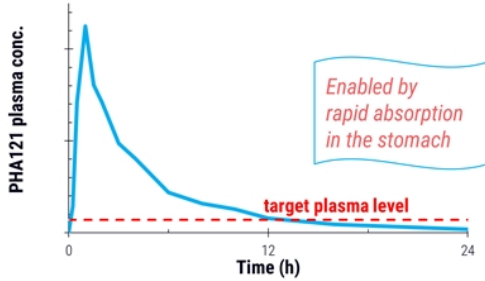


On-demand and prophylaxis: Developing two oral products utilizing the same active ingredient



PHVS416

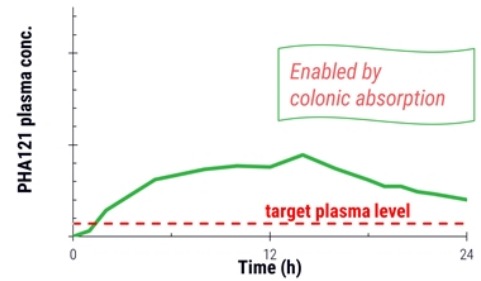
Softgel capsule formulation



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

PHVS719

Extended-release tablet formulation

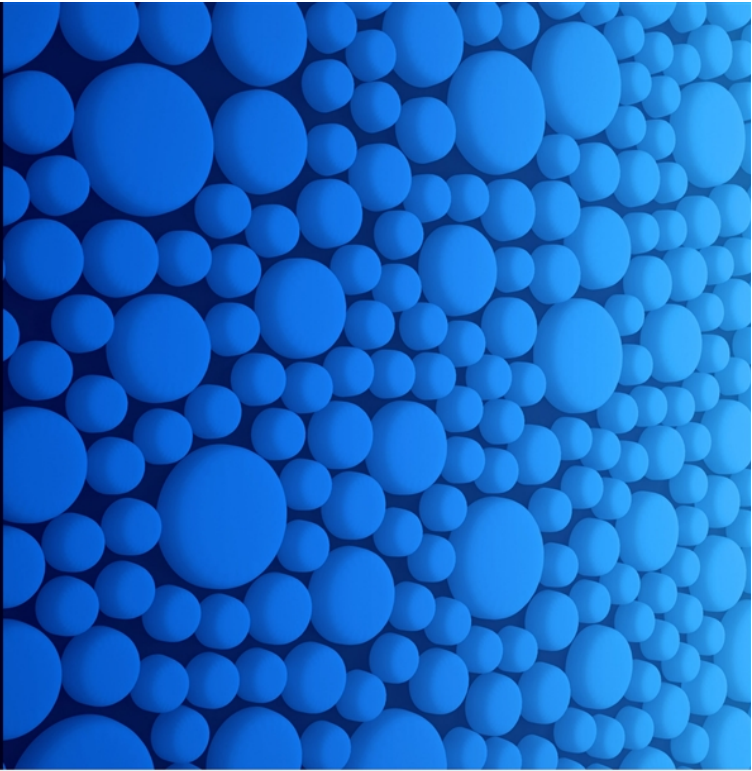


Aim to maintain compound exposure to prevent attacks, for easy and effective control

Wholly-owned pipeline focused on bradykinin B2 receptor mechanism

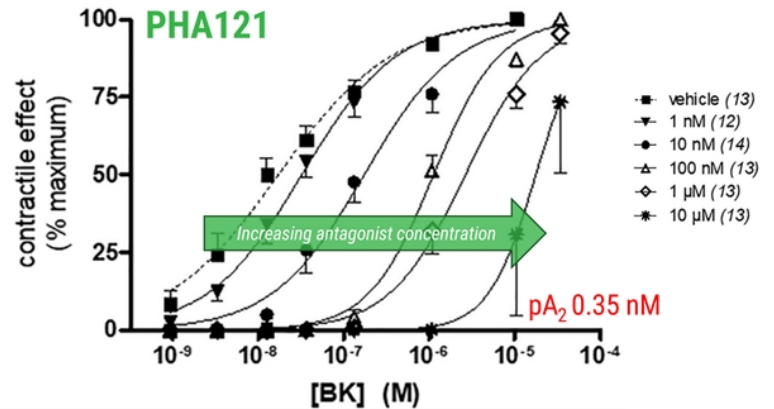
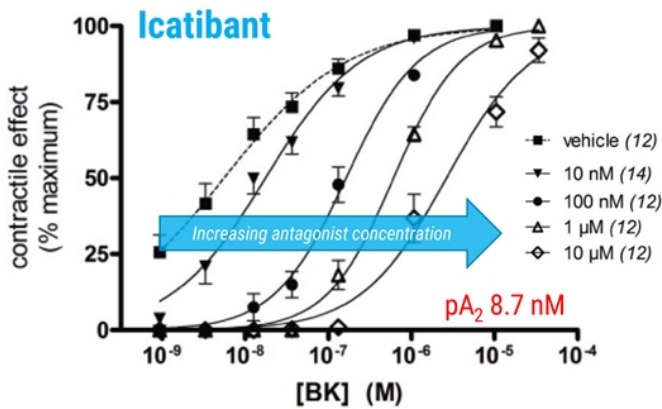


Programs



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

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



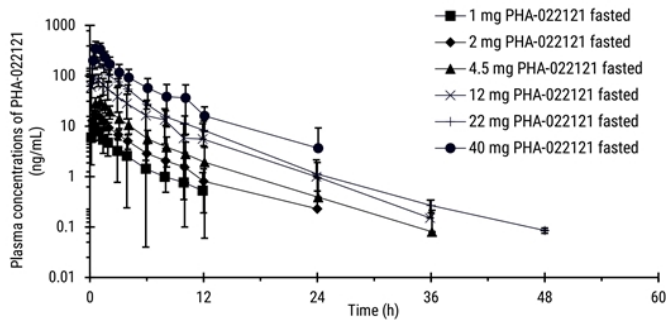
PHA121 is 25-fold more potent than icatibant at the endogenous human B2 receptor

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

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)

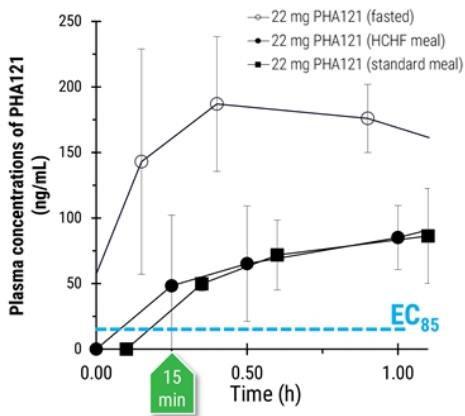


PHA121 (oral solution)

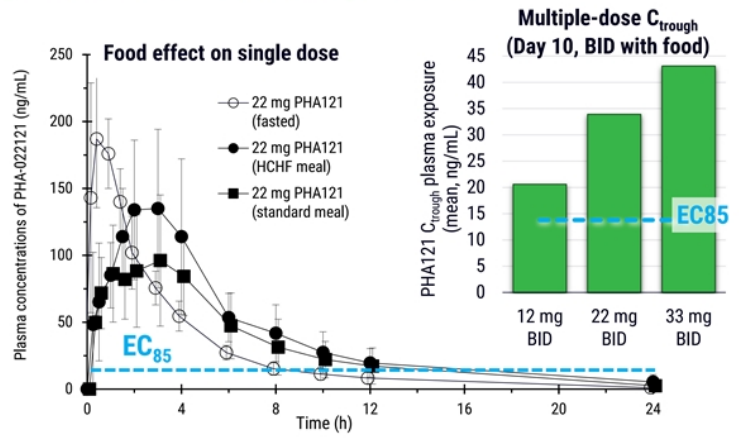
- **No clinically significant changes** were observed for physical exams, vitals, ECG, and safety lab assessments
- **No SAEs or severe AEs** were reported with no treatment discontinuations
- Most AEs observed were of **mild severity**
- Total incidence of AEs was **similar between active and placebo** 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 development



Surpasses target exposure (EC₈₅) 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://epostersonline.com/acaai2020/node/1384>; <https://ir.pharvaris.com/static-files/81a9499d-0769-4b89-8ecd-8ace5ca521d3>

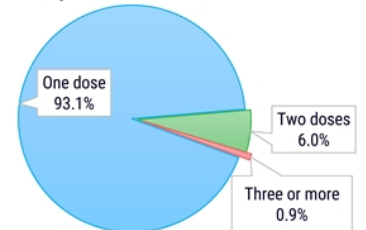
Inhibition of bradykinin-induced hemodynamic effects is a validated surrogate assessment



- 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

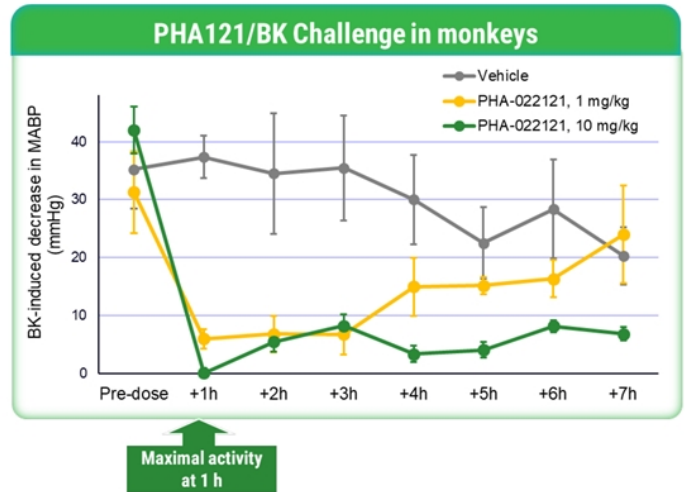
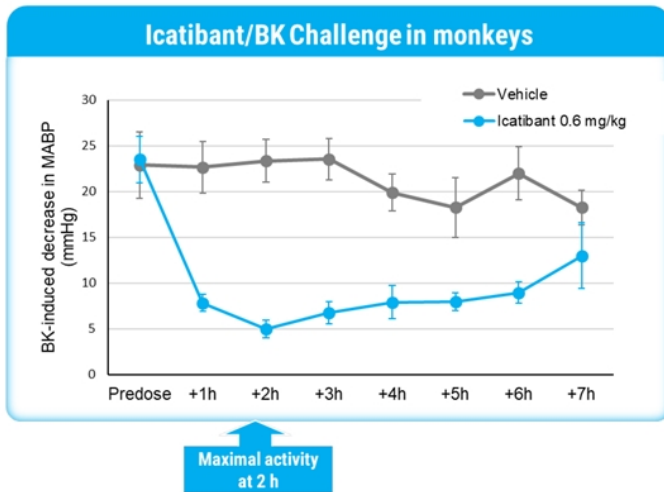
- Icatibant's clinical dose, established with the BK challenge, has demonstrated successful resolution of HAE attacks in randomized clinical trials and over 10 years of data post-approval
 - Icatibant Outcome Survey: Longitudinal survey over 10 years; more than 5000 HAE attacks treated with 30 mg SC

Proportion of attacks treated



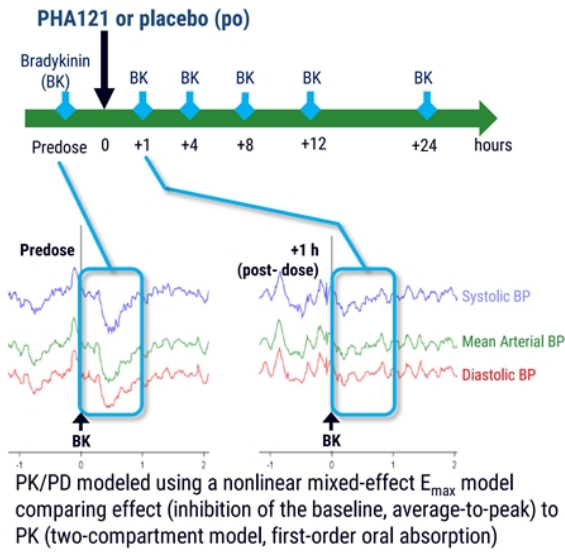
https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022150Orig1s000ClinPharmR.pdf; Maurer et al 2020: Long-term effectiveness and safety of icatibant for the on-demand treatment of hereditary angioedema attacks: 10 years of the icatibant outcome survey (EAACI Poster #1118, June 6-8, 2020); <https://clinicaltrials.gov/ct2/show/NCT01034969>

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



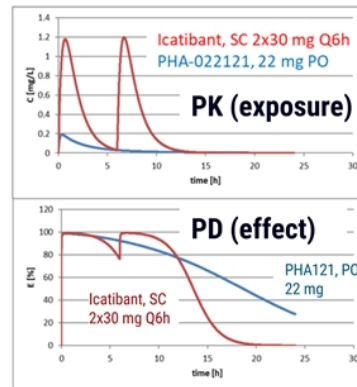
https://education.aaaai.org/sites/default/files/L37%20Lesage_1.pdf

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)

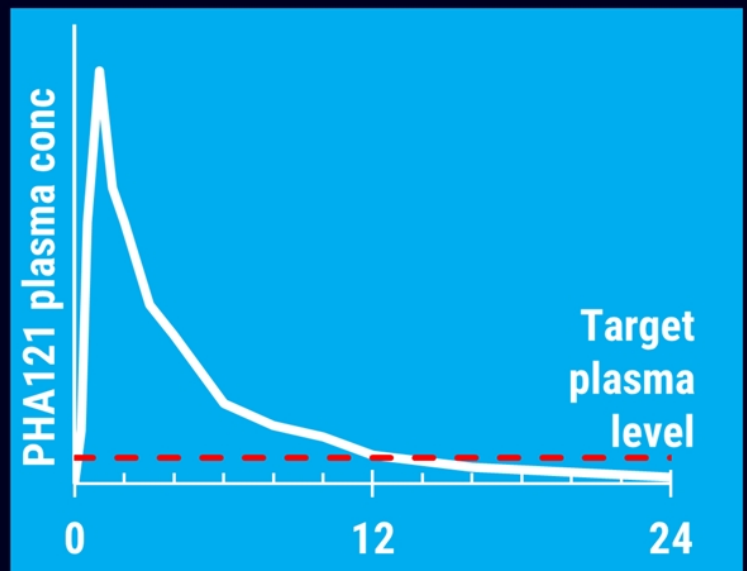


A single PHA121 dose predicted to provide similar PD effect as two injections of icatibant

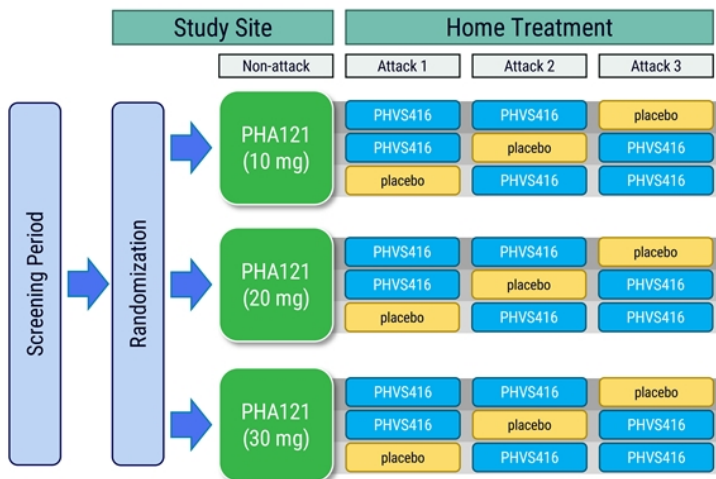
<https://epostersonline.com/acaai2020/node/1365>; <https://doi.org/10.1016/j.jaci.2019.12.094>; https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022150Orig1s000ClinPharmR.pdf

PHVS416/On-Demand

Softgel capsule formulation of PHA121



HAE RAPIDe-1 study: Treating patients on-demand for acute attacks in Type 1 or 2 HAE



- Primary objective: to evaluate angioedema symptom relief within four hours in acute attacks of patients with HAE type 1 or 2
- Placebo-controlled, three doses
- Primary endpoint: Δ VAS-3 at 4hr post-dose
 - VAS, MSCS, TOS will be assessed up to 48 hr post-dose
- Enrollment target achieved; 72 HAE patients enrolled from ~30 sites in US, Canada, Europe, Israel, and UK
- Topline data anticipated 4Q22

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>

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

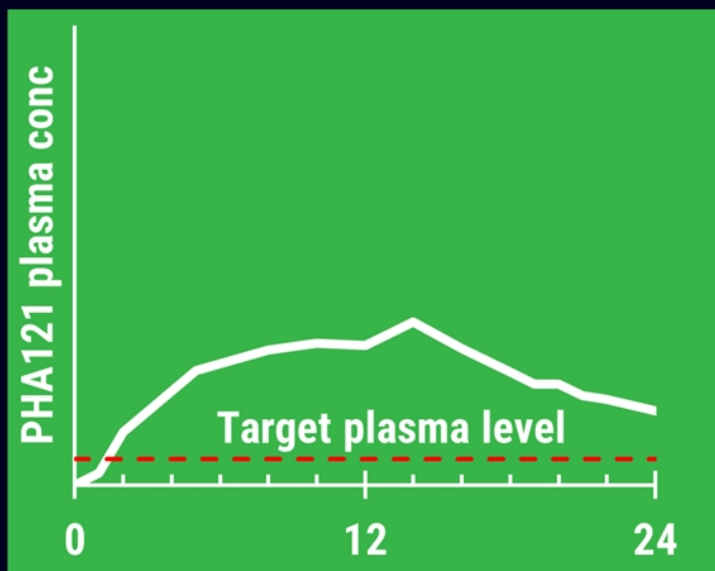
On-Demand: PHVS416 aims to provide clear differentiation for efficacy and convenience

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% ^{5d}	21% ^{24h}	30% ^{24h}	11-20%	11%	14-33%
Initial relief (h)		0.8-1.5 ^{VAS}	1.6 ^{PGI-C} /6 ^{VAS}	5	0.25	1.5 ^{PGI-C}	--
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: Firazy, 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; EAAACI 2020 Poster #1118; Zanichelli et al, C1 Inhibitor Workshop 2021 (https://www.kalvista.com/sites/default/files/presentations/zoom_0.mp4)

PHVS719/Prophylaxis

Extended-release tablet formulation of PHA121

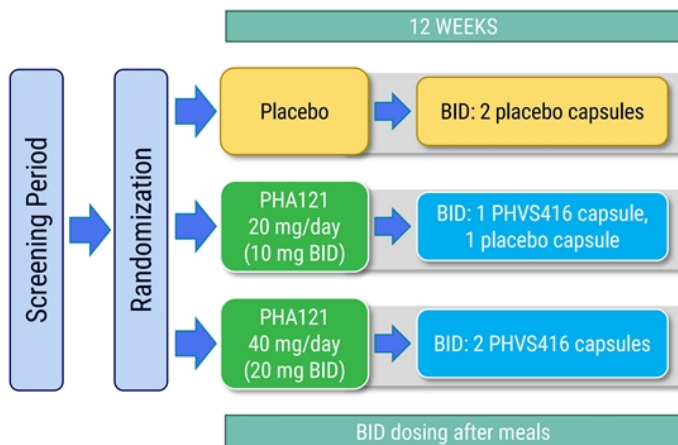


Data from prophylactic proof-of-concept study (PHVS416) and PHVS719 tablet PK to enable Phase 3 development

	Candidate Indication	Phase 1	Phase 2	Phase 3
Softgel	PHVS416 <i>Prophylaxis HAE</i> (PoC)		Data 1Q23	
XR Tablet	PHVS719 <i>Prophylaxis HAE</i>	Data 1Q22		

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

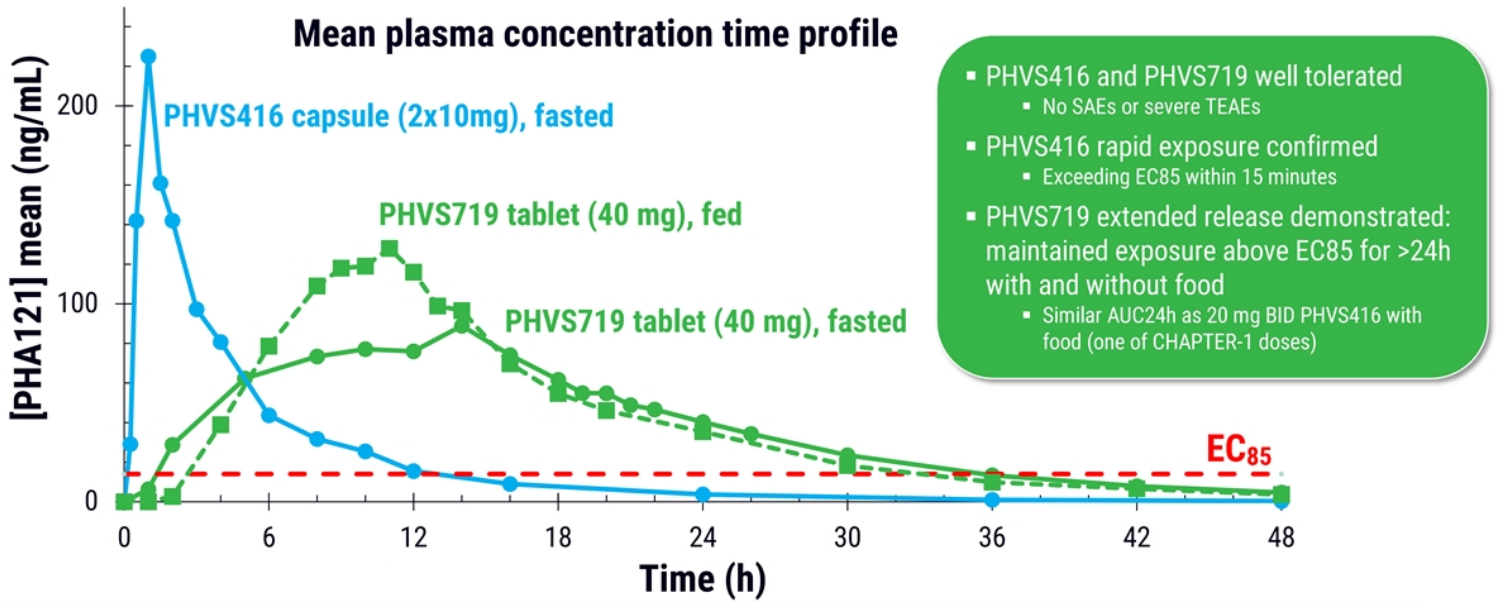
HAE CHAPTER-1 study enrolling: Prevention of attacks in HAE (proof of concept with PHVS416 softgel capsule)



- 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; cleared FDA review period of long-term non-clinical toxicology and safety data
- Primary endpoint: Number of investigator-confirmed HAE attacks
 - Secondary endpoints include moderate or severe HAE attacks, HAE attacks requiring acute treatment
- 30 HAE patients in US, Canada, Europe, Israel, and UK across 29 sites
- Topline data anticipated 1Q23

<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/edd489dd-70b7-4648-944f-76fe17d66842>), <https://clinicaltrials.gov/ct2/show/NCT05055258>

Pharvaris poised for multiple milestones

	HAE On-Demand (type 1 and type 2)	HAE Prophylaxis (type 1 and type 2)
PHVS416 soft capsule	RAPIDe-1 Ph2 topline data (anticipated 4Q22)	CHAPTER-1 Ph2 topline data (anticipated 1Q23)
PHVS719 XR tablet	--	✓ Ph1 SD PK demonstrates once-daily potential

Financially strong: €201 million cash (Jun 30, 2022) provides runway through 1Q24

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Nasdaq: PHVS