
**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 January 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

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):

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):

On January 10, 2022, Pharvaris N.V. made available an investor presentation on its website. A copy of the investor presentation is attached hereto as Exhibit 99.1.

EXHIBIT INDEX

<u>Exhibit No.</u>	<u>Description</u>
99.1	Investor Presentation, dated January 10, 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: January 10, 2022

PHARVARIS N.V.

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

PHARVARiS

Pioneering science for patient choice

January 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 other than statements of historical factors contained in this Presentation, including statements regarding our future financial condition, results of operations and/or business achievements, including, without limitation, statements containing the words “believe,” “anticipate,” “expect,” “estimate,” “may,” “could,” “should,” “would,” “will,” “intend” and similar expressions are forward-looking statements. 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, risks associated with the COVID-19 pandemic, 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, and the other factors described under the heading “Risk Factors” in our registration statement 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



Large market opportunity

Large global HAE market of \$2+ billion with predicted 13% 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)

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

Cash runway to early 1Q24: €209.4 million as of December 31, 2021

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

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**



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

JERINI



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

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



Anna Nijdam
Principal Accounting Officer

EY

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

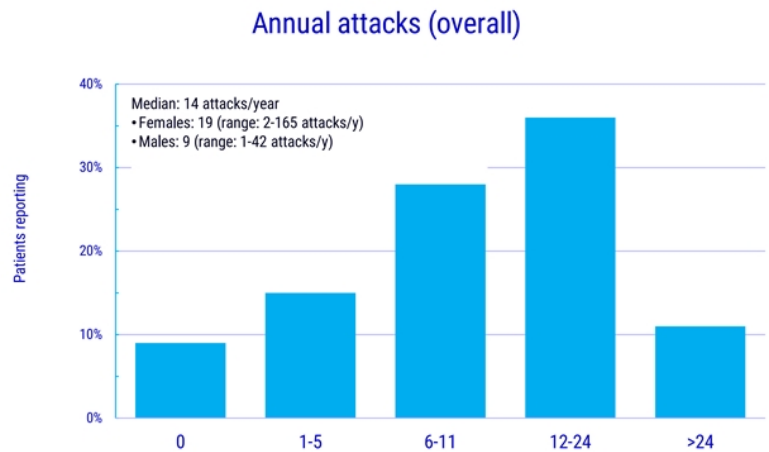
- Rare and potentially life-threatening genetic condition
- 1:10,000 to 1:50,000 Individuals affected by HAE globally
 - At least 6,600 patients in the U.S.
 - At least 8,900 patients in Europe
 - Globally, under-diagnosed/treated



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

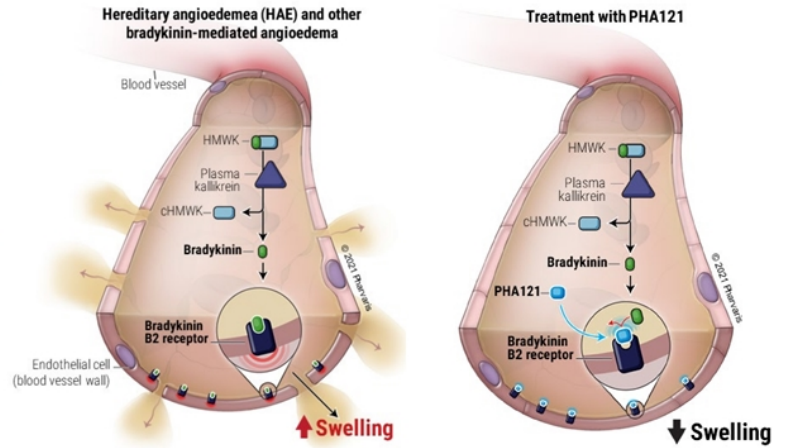
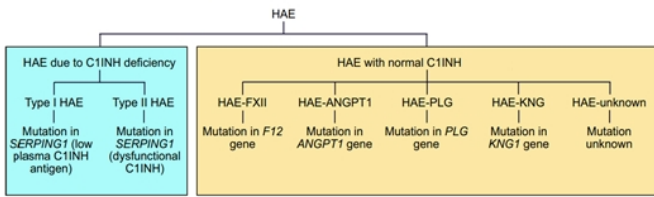
HAE attacks are unpredictable, debilitating and potentially lethal

- 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 patients experience a potentially life-threatening laryngeal attack at least once in their lifetime



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

HAE patients actively switch products seeking improvement in efficacy, safety/tolerability, and convenience

1



Efficacy is patient's prime concern ...

2



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

3








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

Patients desire HAE therapy that can deliver on ALL fronts

Source: Company research 2021

HAE is a valuable, growing market

(US approved)	On-Demand	Prophylaxis
B2 receptor	 firazyr \$772M 2018 (icaltiban injection) + generic	<i>open ground</i>
C1-INH	 BERINERT \$251M 3Q21 (est) C1 Esterase Inhibitor, Human	 HAEGARDA \$253M 3Q21 (est) C1 Esterase Inhibitor Subcutaneous (Human)
	 RUCONEST \$152M 3Q21 C1 esterase inhibitor (recombinant)	 CINRYZE \$137M 3Q21 C1 esterase inhibitor (human)
plasma kallikrein	 KALBITOR \$28M 3Q21 ecallantide	 TAKHZYRO \$633M 3Q21 (lanadelumab-flyo) injection
		 orladeyo \$76M 3Q21 (berotralstat) capsules 150 mg

Source: Sales trends from quarterly filings (ASX: CSL; NYSE: TAK; AMS: PHARM; NASDAQ: BCRX); EvaluatePharma

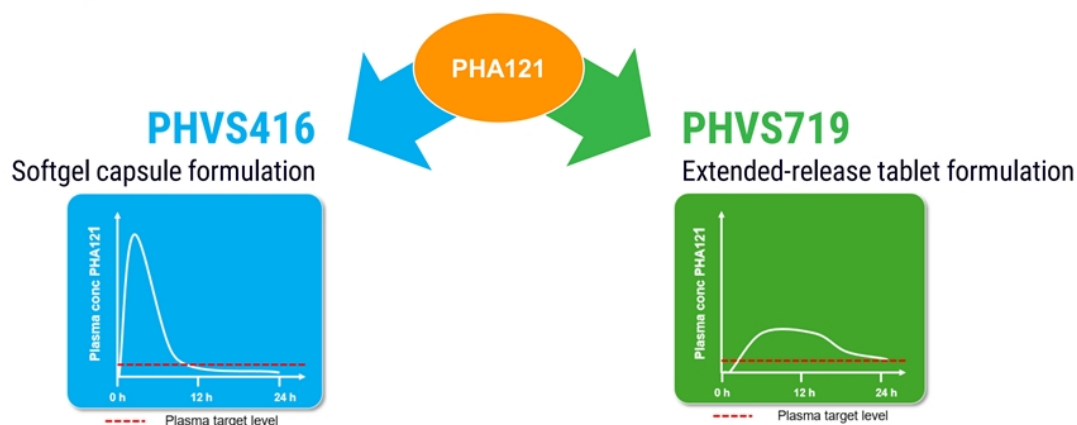
- \$2B+ market in 2018 growing ~13% annually
- Significant unmet need for an oral solution
- Most approved products are injectable
 - Efficacious, but often with injection-site reactions (leads some patients to delay treatment and risk attacks)
 - Time consuming to receive
 - Difficult to carry and/or store
- One oral product recently approved
 - Early sales validate patient demand for oral therapy

Product Strategy

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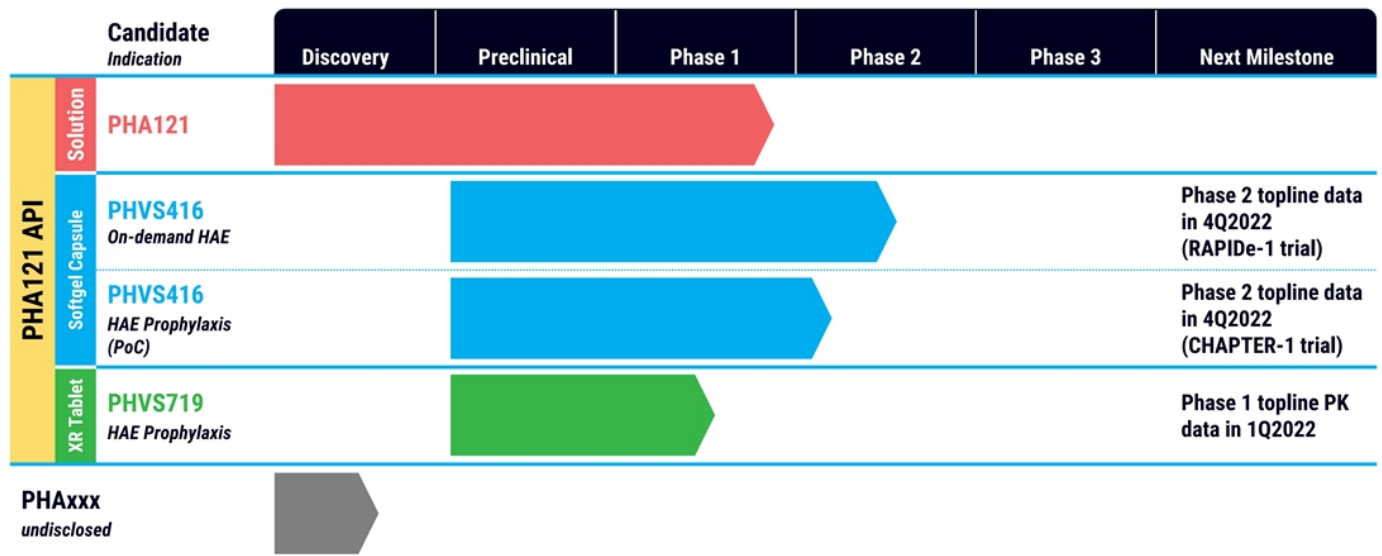
On-demand and prophylaxis: Developing two oral products utilizing the same active ingredient



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

Aim to maintain compound exposure to prevent attacks, providing an easy and effective way for patients to live

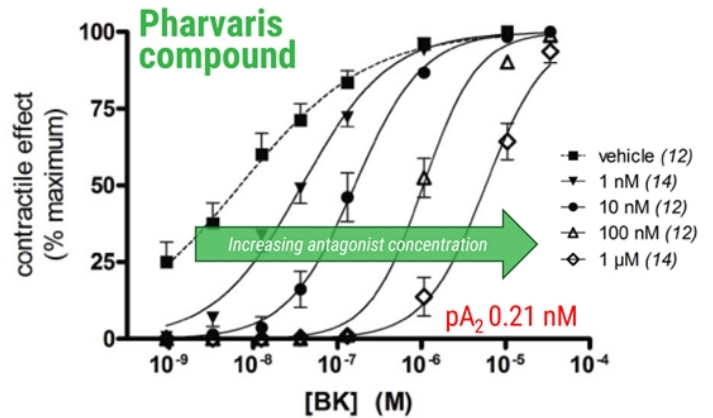
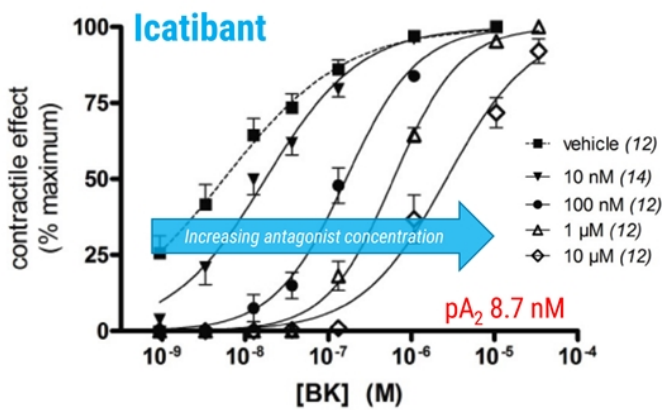
Wholly-owned pipeline focused on bradykinin B2 receptor mechanism



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 (11), 916, doi: 10.3389/fphar.2020.00916

PHA121

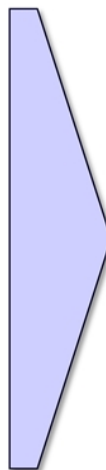
PK/PD in humans

PHA121 was well tolerated in Phase 1 SAD and MAD trials

PHA121 (oral solution) has completed SAD and MAD Phase 1 studies

- Single ascending dose: 1-50 mg; double-blind, placebo-controlled
- Food effect: 22-50 mg; fasting, high-fat diet, normal diet
- Bradykinin challenge: 12/22 mg; Proof-of-mechanism
- Multiple ascending dose: 12-50 mg; double-blind, placebo-controlled

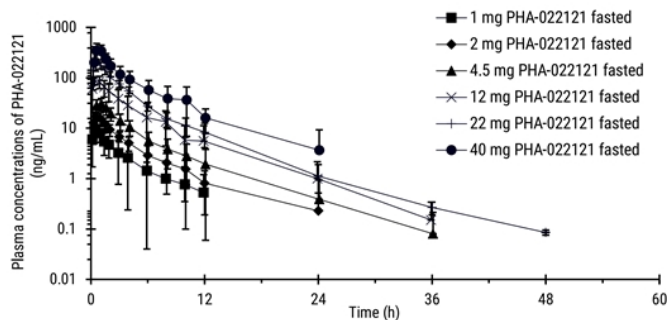
No clinically significant changes were observed for physical exams, vitals, ECG, and safety lab assessments



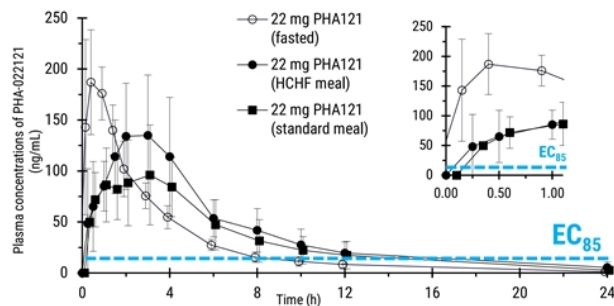
All doses were well tolerated in SAD, SADext, and MAD studies (oral solution)

- No SAEs or severe AEs were reported with no treatment discontinuations
- Total incidence of AEs was similar between active and placebo groups
- Most AEs observed were of mild severity
- No clear differences for AE patterns between different dosing regimens vs. placebo

PHA121 demonstrates a well-behaved dose-proportional PK profile



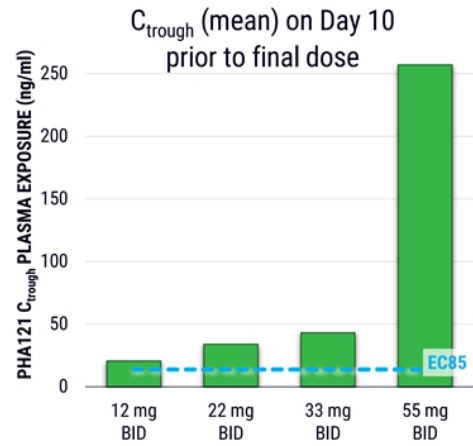
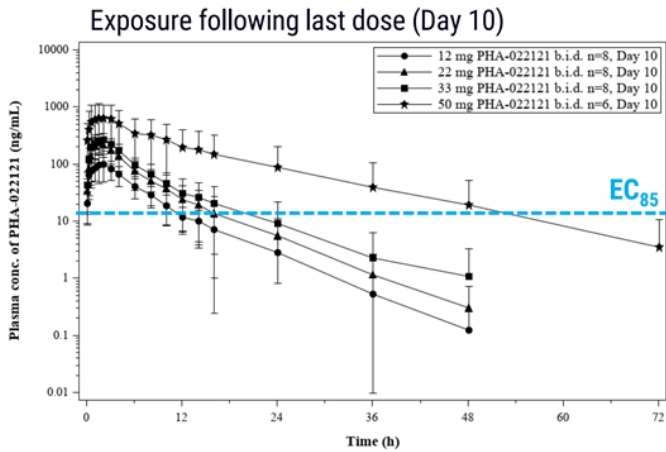
- Approximately dose-proportional PK with single and multiple oral administration
- Half-life approximately 3.4-5.6 hours (approximately three-fold longer than icanitabant)



- Rapid exposure under both fasted and fed status (EC₈₅ within 15 min); T_{max} delayed by ~2 hours with food
- Lower C_{max} and comparable AUC_{0-24h} under fed (standard and high-calorie, high-fat) compared to fasted status

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

In multiple-dose studies, when dosed with food, BID doses of PHA121 solution maintain exposure above predicted efficacious levels



Steady state reached within 72 hours; plasma trough levels on Day 10 remained well above EC_{85}

<https://ir.pharvaris.com/static-files/81a9499d-0769-4b89-8ecd-8ace5ca521d3>

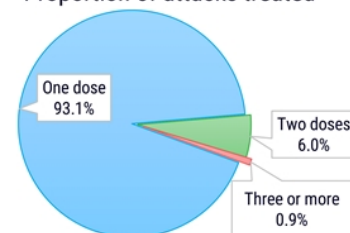
Inhibition of bradykinin-induced hemodynamic effects is a validated surrogate assessment



- 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

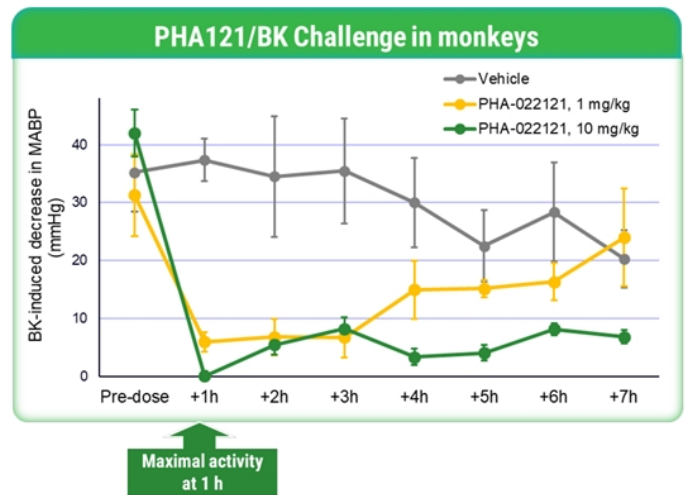
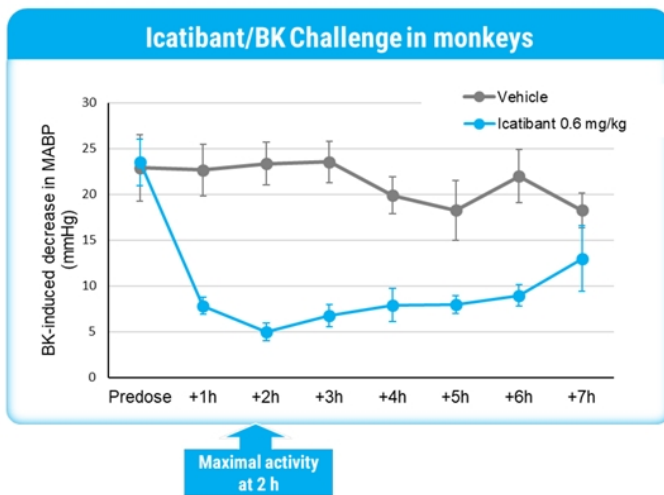
- Icatibant's clinical dose, established with the BK challenge, has demonstrated successful resolution of HAE attacks in randomized clinical trials and over 10 years of data post-approval
 - Icatibant Outcome Survey: Longitudinal survey over 10 years; more than 5000 HAE attacks treated with 30 mg SC

Proportion of attacks treated



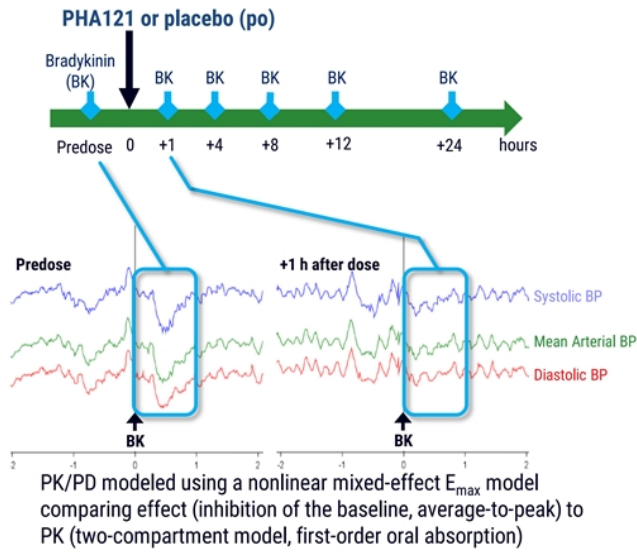
https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022150Orig1s000ClinPharmR.pdf; Maurer et al 2020: Long-term effectiveness and safety of icatibant for the on-demand treatment of hereditary angioedema attacks: 10 years of the icatibant outcome survey (EAACI Poster #1118, June 6-8, 2020); <https://clinicaltrials.gov/ct2/show/NCT01034969>

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



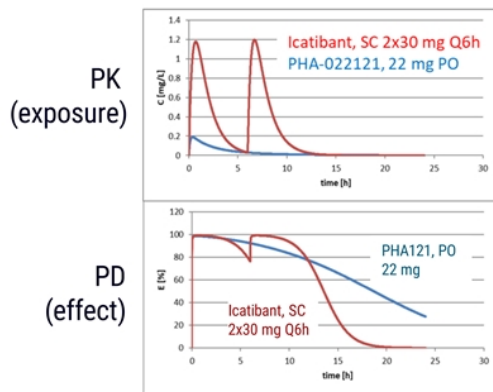
<https://epostersonline.com/acaai2020/node/1369>; <https://doi.org/10.1016/j.jaci.2019.12.094>; https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022150Orig1s000ClinPharmR.pdf

Human BK challenge	PHA121
EC_{50} (ng/mL)	2.4
EC_{85} (ng/mL)	13.8

Potency ~4x higher than icatibant based on plasma concentration (published data)

- ~24x more potent on molecule-by-molecule basis (170 pM for PHA121 vs. 4.1 nM for icatibant)
- Consistent with *in vitro* measurement: PHA121 demonstrates K_b 150 pM (recombinant) and 350 pM (endogenous) at the human bradykinin B2 receptor

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



The PK/PD model was used to simulate PK profiles (N=1000) and calculate probability of durations of effect as well as to visualize effect-time profiles

Estimated duration of effect (icatibant versus PHA121)

Response	Icatibant 30 mg SC	PHA121 12 mg PO	PHA121 22 mg PO
Time (h) plasma level above EC_{85} at 50% confidence level			
DBP	5.5	7.5	10
MABP	5.5	7	10
HR	5.5	6.5	9.5

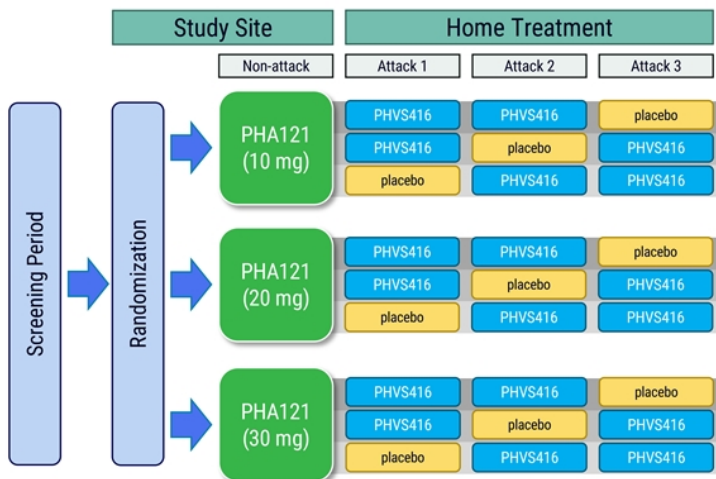
DBP: diastolic blood pressure; MABP: mean arterial blood pressure; HR: heart rate

<https://epostersonline.com/acaai2020/node/1369>; https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022150Orig1s000ClinPharmR.pdf

PHVS416/On-Demand

Softgel capsule formulation of PHA121

HAE RAPIDe-1 study underway: On-demand treatment of acute attacks in Type 1 or 2 HAE patients



- 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 at 4hr post-dose
 - VAS, MSCS, TOS will be assessed up to 48 hr post-dose
- Up to 72 HAE patients to enroll from ~30 sites in US, Canada, Europe, Israel, and UK
- Topline data anticipated 4Q2022

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

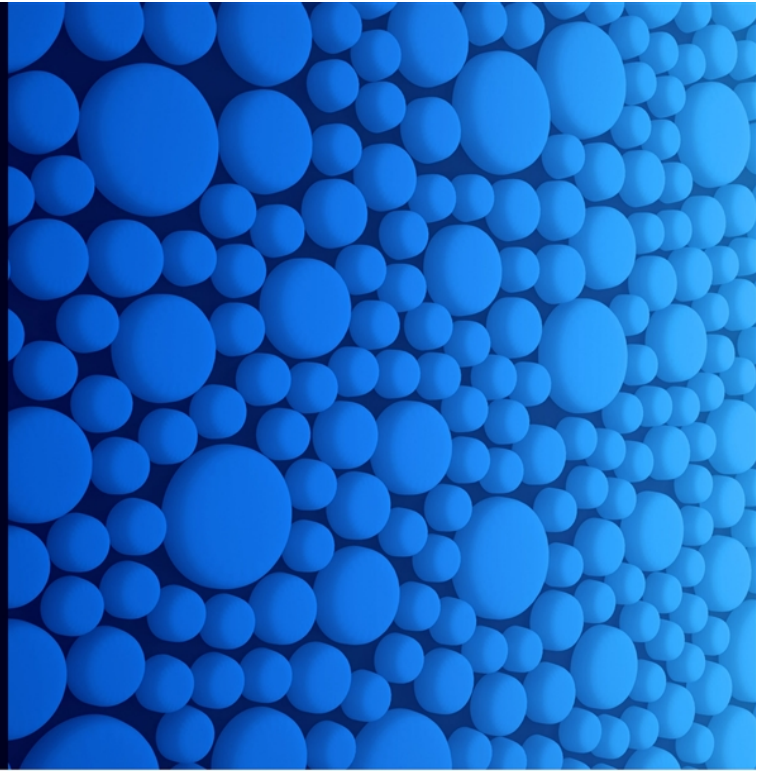
On-Demand: PHVS416 aims to provide clear differentiation for efficacy and convenience

Clinical data	PHVS416	icatibant	KVD900	berotralstat	BERINERT®	RUCONEST®	KALBITOR®
FDA Approval	(Phase 2)	2011	(end of Phase 2)	(EOP2, dropped)	2009	2014	2009
Mechanism	B2R	B2R	pKi	pKi	C1INH	C1INH	pKi
Dose	≤30 mg	30 mg	6x100 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.clinicaltrialsregister.eu/ctr-search/trial/2018-004489-32>; 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)

PHVS719/Prophylaxis

Extended-release tablet formulation of
PHA121



Prophylactic proof-of-concept study underway with PHVS416

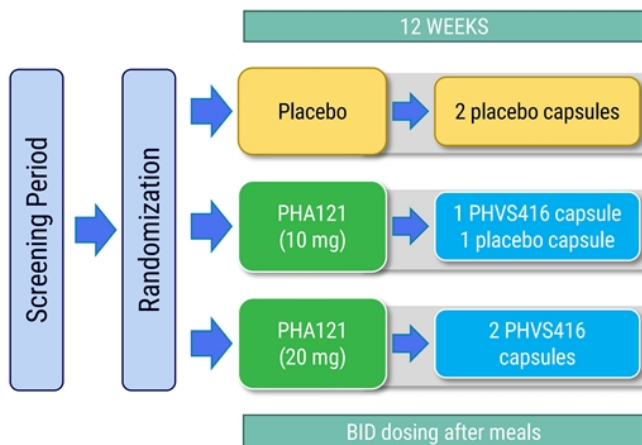
Candidate	Indication	Phase 1	Phase 2	Phase 3
Softgel	PHVS416 Prophylaxis HAE		Data 4Q22	
XR Tablet	PHVS719 Prophylaxis HAE	Data 1Q22		

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

Pharvaris is targeting to use PHVS719 for pivotal studies in HAE prophylaxis

- Combining exposure/efficacy data from PHVS416 Phase 2 (CHAPTER-1) study and exposure data from PHVS719 Phase 1 study

HAE CHAPTER-1 study recruiting: Prevention of attacks in HAE patients

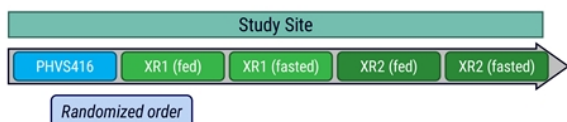


- Primary objective: assessing safety and efficacy of PHA121 in preventing HAE attacks in patients with HAE type 1 or type 2
- Placebo-controlled, 3 parallel arms, two doses
- Primary endpoint: Number of investigator-confirmed HAE attacks
 - Secondary endpoints include moderate or severe HAE attacks, HAE attacks requiring acute treatment
- 30 HAE patients across 24 sites in US, Canada, Europe, Israel, and UK
- Topline data anticipated 4Q22

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

PHVS719 PK study underway: Assessing QD potential

- Open-label, crossover comparison in 8 adult male healthy volunteers
- Sequential dosing (random order) of:
 - PHVS416: 20 mg dose (fasted)
 - PHVS719 prototypes
 - XR1: 20 mg dose (fasted, fed)
 - XR2: 40 mg dose (fasted, fed)
- Primary objective to assess PK under fasting conditions
 - Secondary objectives to assess food effect; compare exposure to PHVS416; evaluate safety and tolerability
- Key performance parameters
 - Mean plasma concentration maintained above 13.8 ng/mL at 12 or 24 hours
 - Extended-release profile enabling QD option for prophylactic use
- Topline results expected 1Q22



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	300-900 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	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	~3 d	~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 2020-12-16 and quarterly report 2021-09-09

Pharvaris poised for multiple milestones in 2022

	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 4Q22)
PHVS719 XR tablet	not applicable	Ph1 topline PK data (anticipated 1Q22)

€209.4 million cash (YE21) provides runway into early 1Q24

PHARVARiS

Nasdaq: PHVS