PHARVARIS

Corporate Presentation

Pioneering science for patient choice

January 2025

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Pioneering science for patient choice for hereditary angioedema (HAE)

DEUCRICTIBANT

FDA orphan drug designation[1]

Robust IP on CoM (granted in multiple territories, initial term to 2038) and formulations[2,3]

TWO LATE-STAGE PROGRAMS

- Deucrictibant is an orally available small molecule targeting the **validated bradykinin B2 receptor**[4]
- Results from randomized Phase 2 trials [5,6] and their ongoing extensions[7,8] **demonstrate a differentiated profile** for both **preventing** and **treating** HAE attacks with **injectable-like efficacy**, **rapid onset of action**, a **favorable tolerability profile**, and **oral convenience** over current standard of care[9] for people living with HAE

LARGE GLOBAL HAE MARKET

- Predicted **$5.2B market** in 2036[10]
- While people living with HAE appear satisfied with their treatment, history has shown that the availability of a **more efficacious, better-tolerated** and/or **more convenient** alternative drives a **dynamic switch to the better product**[11]
- Internationally, the **long-term prevention** market is likely to **grow significantly**[10]

STRONG FUNDAMENTALS

- Two pivotal **Phase 3** studies **designed to differentiate** current standard of care in both prophylaxis and on-demand treatments
- Accomplished team with **track record in HAE drug development and commercialization**
- Approximately **€305M** cash and cash equivalents as of September 30, 2024

Source: [1]U.S. FDA OOPD listing. [2]World Intellectual Property Organization. [3]European Patent Office. [4]Lesage et al. *Int. Immunopharmacology*. 2022. [5]Riedl MA et al. AAAAI 2024. [6]Maurer M et al. AAAAI 2023. [7]Riedl MA et al. BKS 2024. [8]Maurer M et al. BKS 2024. [9]Riedl MA at al. BKS 2024. [10]IQVIA predictions. [11]Evaluate Pharma Uptake Curves 2008-2023.

HAE: A rare, life-long genetic condition with significant burden

Unpredictable attacks

Frequency, location, severity[1]

- Often, unknown triggers[1,2]
- If untreated, **attacks may last up to 5 days**[3]

Painful and debilitating

Leading to hospitalization[1]

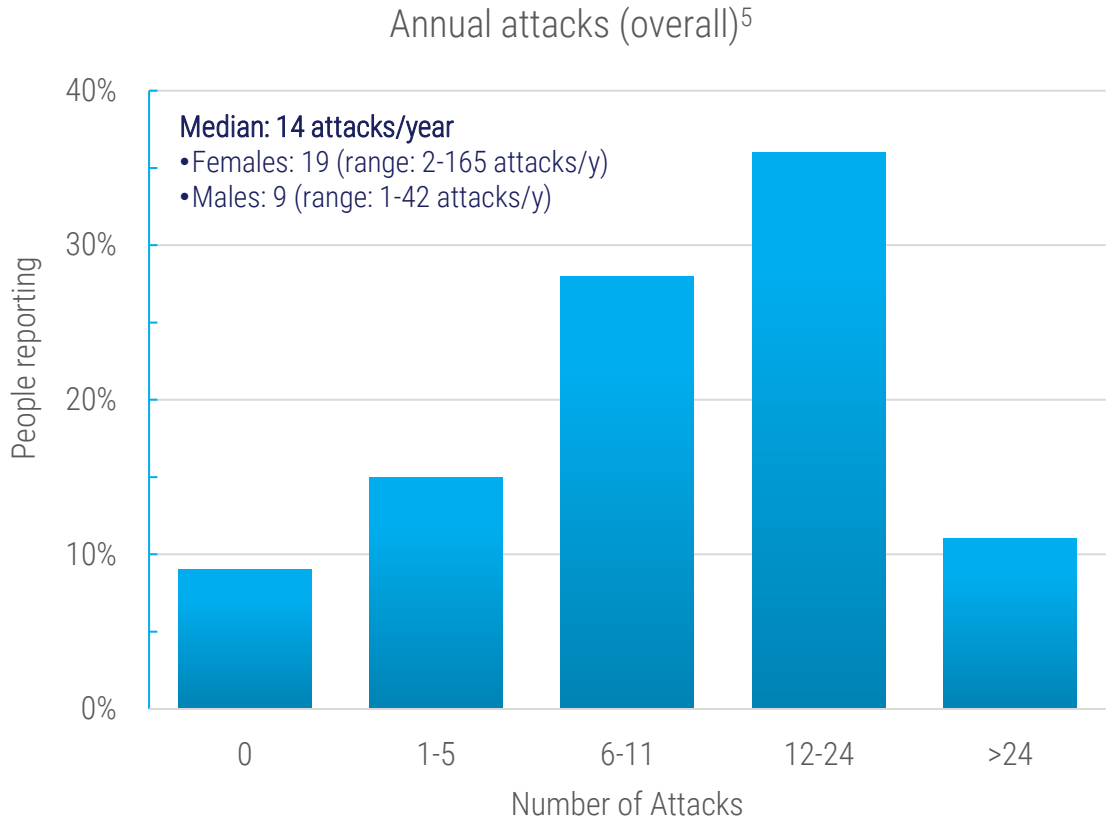
- **Potentially life-threatening** due to asphyxiation[1]

Rare

1:30,000 to 1:80,000 individuals globally[4]

United States[4]
~7,000 individuals

Europe[4]
~15,000 individuals



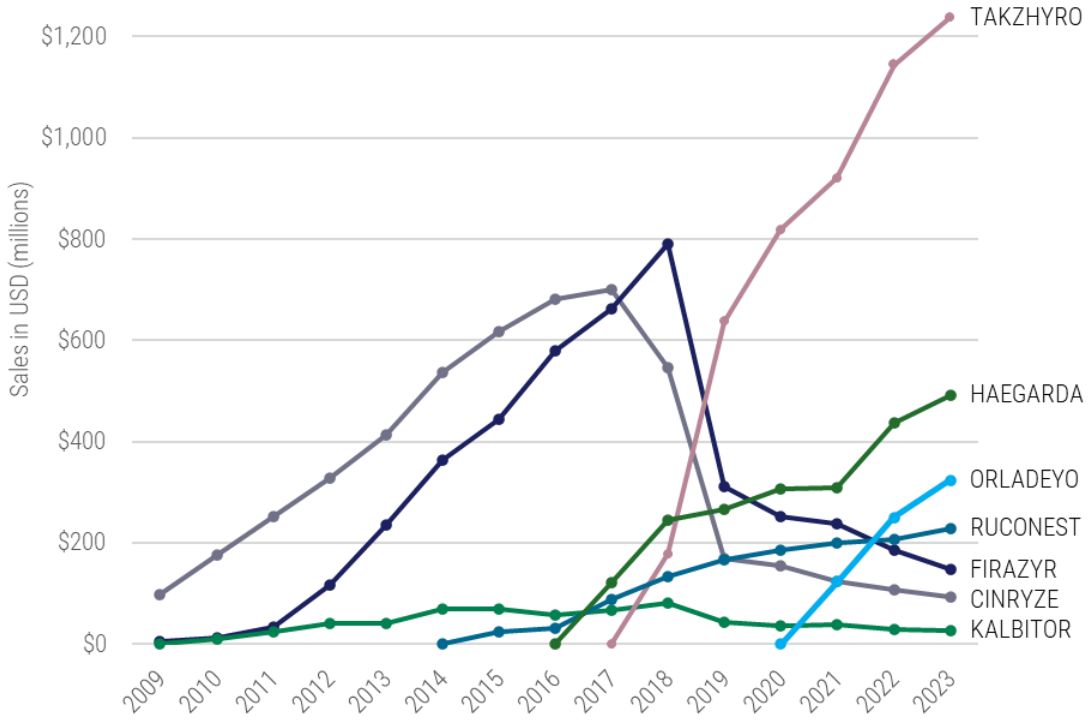
HAE: hereditary angioedema

Source: [1]Betschel SD, et al. *J Allergy Clin Immunol Pract*. 2023. [2]Christiansen SC, et al. *Ann Allergy Asthma Immunol*. 2023. [3]Bork K et al. *Allergy Asthma Clin Immunol*. 2021. [4]Lumry WR *Front. Med*. 2018. [5]Nordenfelt P et al. *Acta Derm. Venereol* 2016.

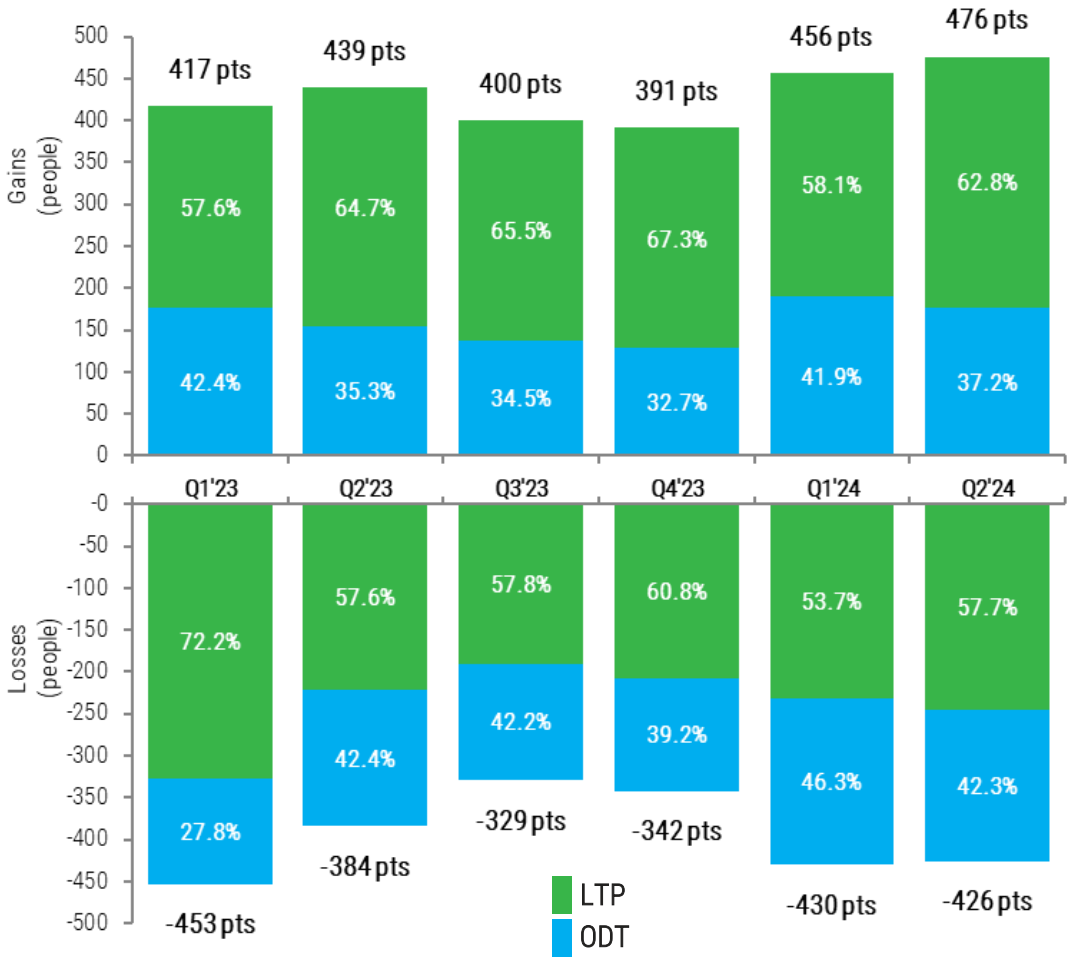
The HAE market is dynamic, with people actively seeking a better* product

People living with HAE actively switch therapies[1,2]: first-to-market is no guarantee for long-term market leadership

Evolution of HAE product sales[1,2]



U.S. HAE switches, gains ↑ and losses ↓[3]

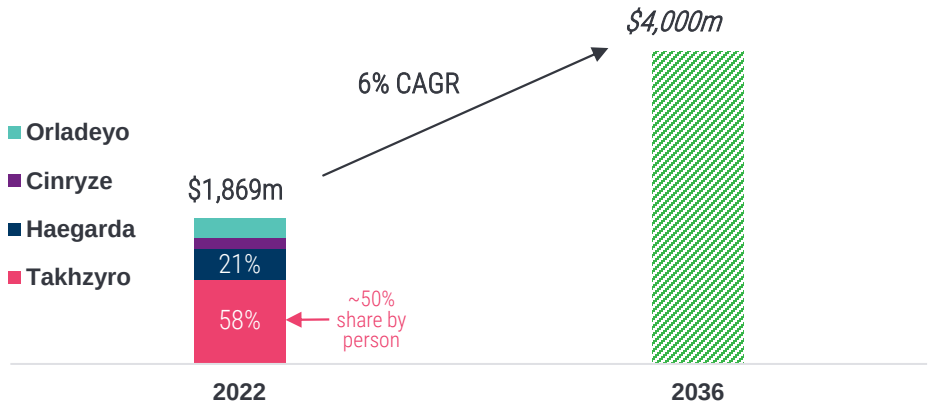


HAE: hereditary angioedema. *Treatment selection is driven by physicians and patient preference.

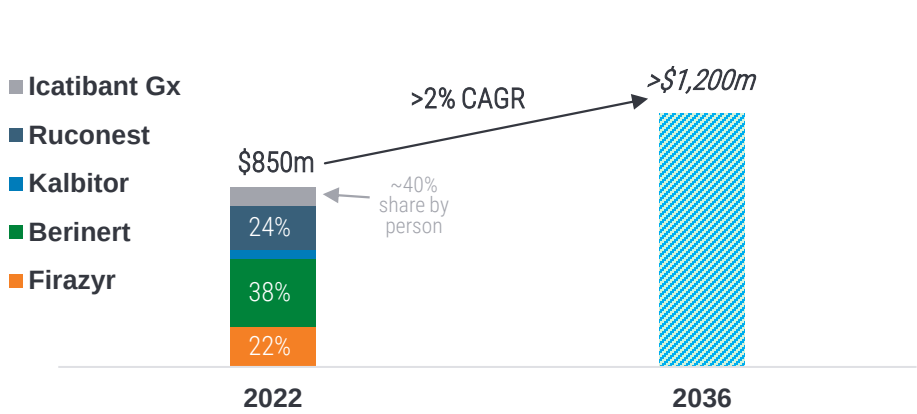
Source: [1]Evaluate Pharma uptake curves 2008-2023 [2]SEC filings (BioCryst, CSL Behring, Pharming, Takeda). [3]U.S. Chart Audit 2023-2024, ADIVO.

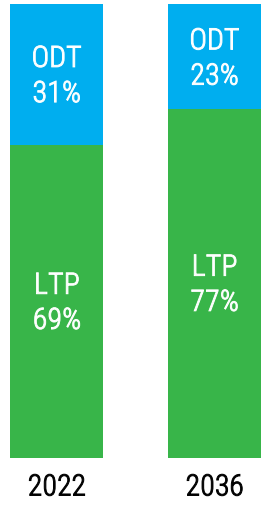
In the U.S., significant growth in the long-term prophylaxis (LTP) and on-demand therapy (ODT) market is expected over the next decade[1]

Value of prophylaxis[1-3]



Value of on-demand[1-3]





Growth expected to be driven by:

- New options
- Increased convenience
- Continued paradigm shift from ODT to LTP

Growth expected to be driven by:

- New options
- Increased convenience
- Increased treatment rate

LTP to further grow as the dominant treatment paradigm in the U.S. market through to 2036[1]

HAE market growth will be driven by increased efficacy and convenience of new therapies

Source: [1]IQVIA market evolution and company data. [2]Evaluate Pharma uptake curves 2008-2023. [3]SEC filings (BioCryst, CSL Behring, Pharming, Takeda).

People living with HAE are seeking a life not defined by their condition nor burdened by its management[1]

Efficacy is a prime driver…

but **safety and tolerability** cause exploration of alternatives…

…while **convenience** is a key driver for overall preference[2]

People living with HAE actively switch between products[3], seeking improvement in efficacy, safety/tolerability, and convenience

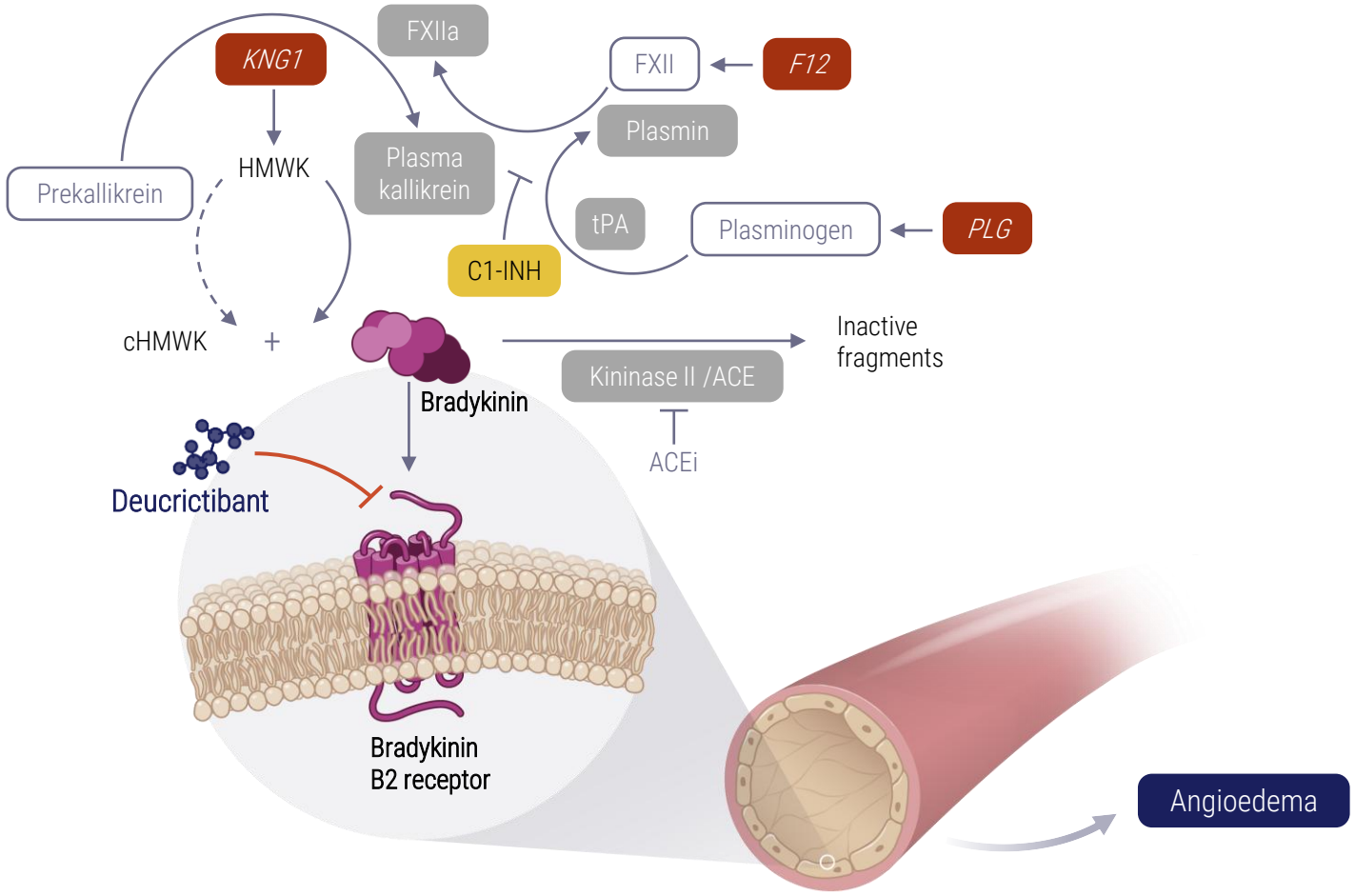
Source: [1]Lumry WR et al. *Allergy Asthma Proc*. 2020. [2]Geba et al, *J Drug Access*.2021. [3]U.S. Chart Audit 2023-2024, ADIVO.

Bradykinin B2 receptor antagonism is a foundational mechanism to treat and prevent bradykinin-mediated angioedema attacks[1,2]

Deucrictibant is a bradykinin B2 receptor antagonist in development for prevention and treatment of HAE attacks

Directly blocks the main mediator of swelling and inflammation[1,3]

Has potential to prevent or treat bradykinin-mediated angioedema **irrespective of source of bradykinin**[4-6]

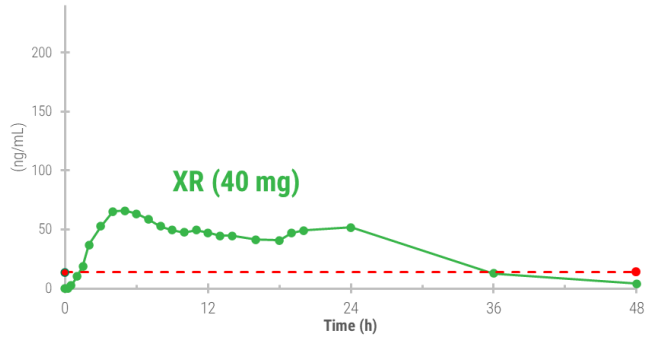


Source: [1]Maurer M, et al. *Allergy*. 2022. [2]Zuraw BL *World Allergy Orphan J*. 2010. [3]Lumry WR et al. *Allergy Asthma Proc*. 2020. [4]Riedl MA et al. AAAAI 2024. [5]Maurer M et al. AAAAI 2023. [6]Petersen RS et al. *J Allergy Clin Immunol*. 2024.

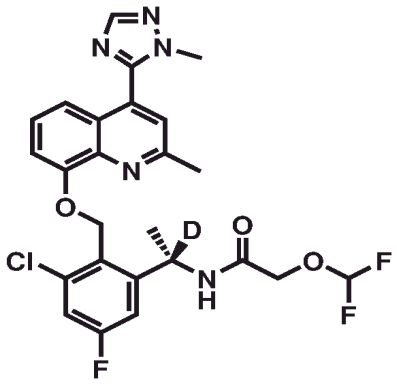
Deucrictibant has the potential to address unmet needs of people living with HAE

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



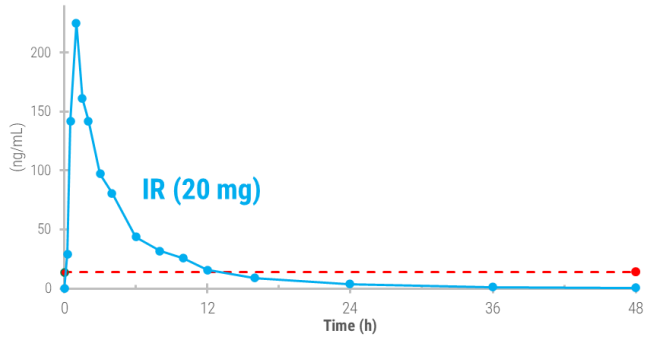
Maintains sustained therapeutic exposure over 24 hours[2] from day one, allowing for once-daily oral treatment to prevent HAE attacks*



deucrictibant

DEUCRICTIBANT immediate-release (IR) capsule

rapid absorption[3]



Rapidly reaches therapeutic exposure within 15-30 minutes[4], making it optimal for on-demand oral treatment of HAE attacks*

Two oral products with the same active ingredient for the prevention and treatment of HAE attacks

HAE: hereditary angioedema. *To be confirmed with clinical data from Phase 3 studies

Source: [1]Company data: single-dose cross-over PK study in healthy volunteers (n=14) under fasting conditions. [2]Lesage A et al. IDDST 2024. [3]Crabbe et al. AAAAI 2021. [4]Maurer M et al. AAAAI 2023.

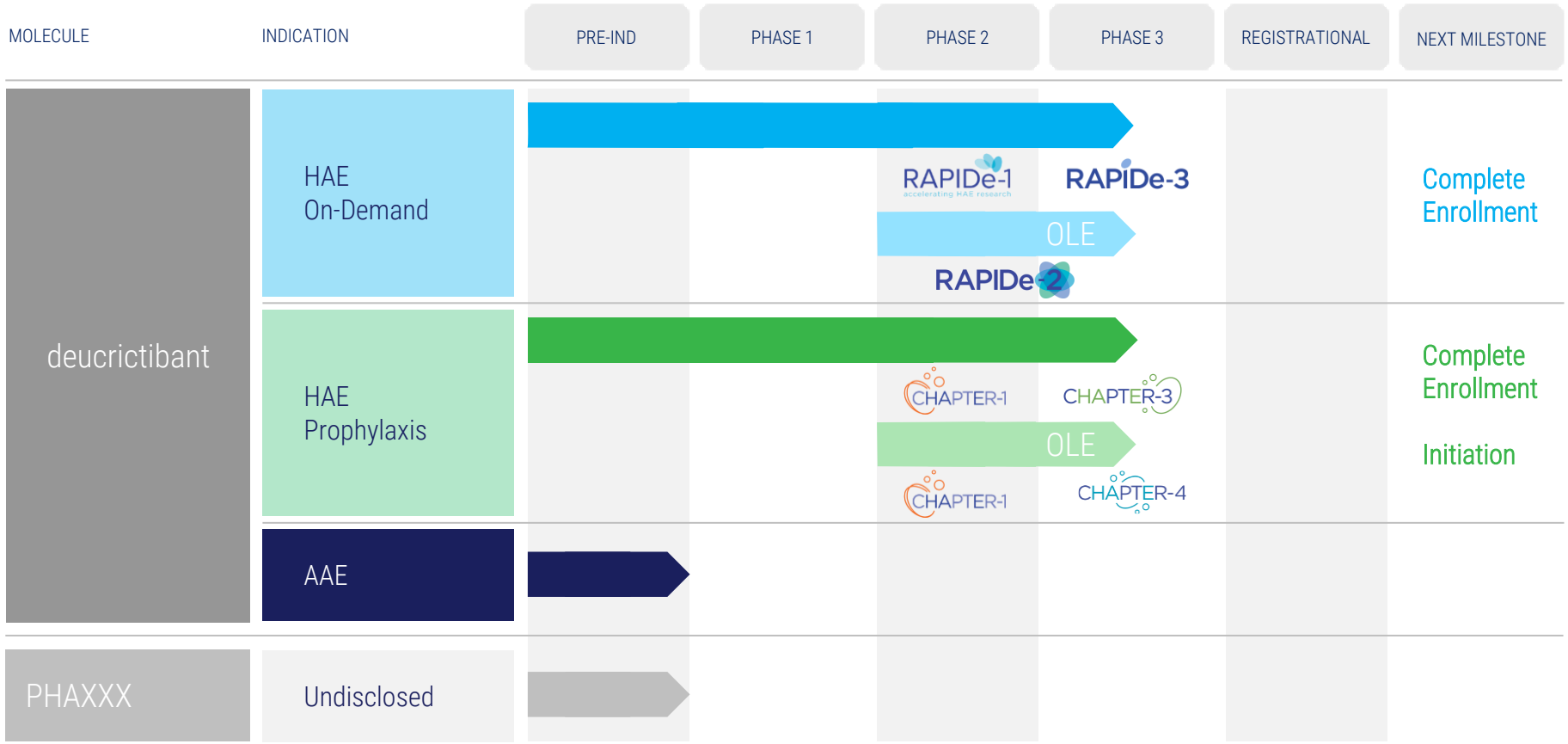
Deucrictibant differentiated profile for LTP and ODT

		LTP	ODT
Oral ODT or LTP Formulations	**Deucrictibant is the only HAE therapy**[1] in development that allows for oral administration **in both prophylaxis and on-demand**[2]	✓	✓
Single Oral Pill	**Specific formulations** allow for **once-daily dosing**[3] (XR for LTP) or **rapid, single-dose resolution**[4] of HAE attacks (IR for ODT)	✓	✓
Rapid to Steady State	Deucrictibant XR has the potential to achieve steady state within 2-3 days[5], providing **protection against HAE attacks on the initial day**[3] of LTP initiation	✓	
Rapid Absorption	Within 15-30 minutes[6], deucrictibant IR reaches therapeutic exposure resulting in the halt of attack progression within **30 minutes**[7]		✓
Longer Effective Exposure	A longer effective exposure can potentially result in a **high rate of single-dose attack resolution**[8]		✓

LTP: long-term prophylaxis. ODT: on-demand therapy. XR: extended-release tablet formulation of deucrictibant. IR: immediate-release capsule formulation of deucrictibant.

Sources: [1]Company research. [2]Leasge et al. IDDST 2024. [3]Groen K et al. ACAAI 2022. [4]Li H et al. EAC 2024. [5]Maurer M et al. HAEi Workshop, 2022. [6]Maurer M et al. AAAAI 2023. [7]Riedl et al. WSAAI 2024. [8]Maurer M et al. BKS 2024.

Wholly-owned pipeline focused on bradykinin B2 receptor mechanism



HAE: hereditary angioedema. AAE: acquired angioedema. OLE: open-label extension

Deucrictibant clinical development program

Long-Term Prophylaxis (LTP)

CHAPTER-1	Phase 2[1]	Part 1: randomized controlled primary analysis (complete) Part 2: open-label extension (ongoing)
CHAPTER-3	Phase 3 pivotal[2]	Ongoing
CHAPTER-4	Phase 3 OLE[3]	Start-up

On-Demand Treatment (ODT)

RAPIDe-1	Phase 2[4]	Complete
RAPIDe-2	Phase 2/3 LTE[5]	Ongoing
RAPIDe-3	Phase 3 pivotal[6]	Ongoing

OLE: open-label extension. LTE: long-term extension.
Source: [1]NCT05047185. [2]NCT06669754. [3]NCT06679881. [4]NCT04618211. [5]NCT05396105. [6]NCT06343779.

Deucrictibant shows the potential to address unmet needs of people living with HAE

Long-Term Prophylaxis (LTP)

Efficacy	Early-onset attack reduction sustained for over one year in ongoing OLE study[1]
Quality of Life	Improvement in disease control and health-related quality of life paralleled attack reduction in Phase 2[2,3]
Safety & Tolerability	Phase 2 safety and tolerability profile confirmed in ongoing OLE study[1,4]
Formulation	Intended commercial formulation for once-daily dosing ready for Phase 3

Potential preferred option for LTP

On-Demand Treatment (ODT)

Efficacy	▪ Onset of symptom relief with median PGI-C "a little better" ~ 1.1 hour ▪ Symptom resolution with PGI-S "none" ~ 11.5 hours in ongoing LTE study[5] ▪ 85.8% of attacks achieved complete symptom resolution within 24 hours in ongoing LTE; 90.2% of which with single dose[5]
Safety & Tolerability	Phase 2 safety and tolerability profile confirmed in ongoing LTE study[5,6]

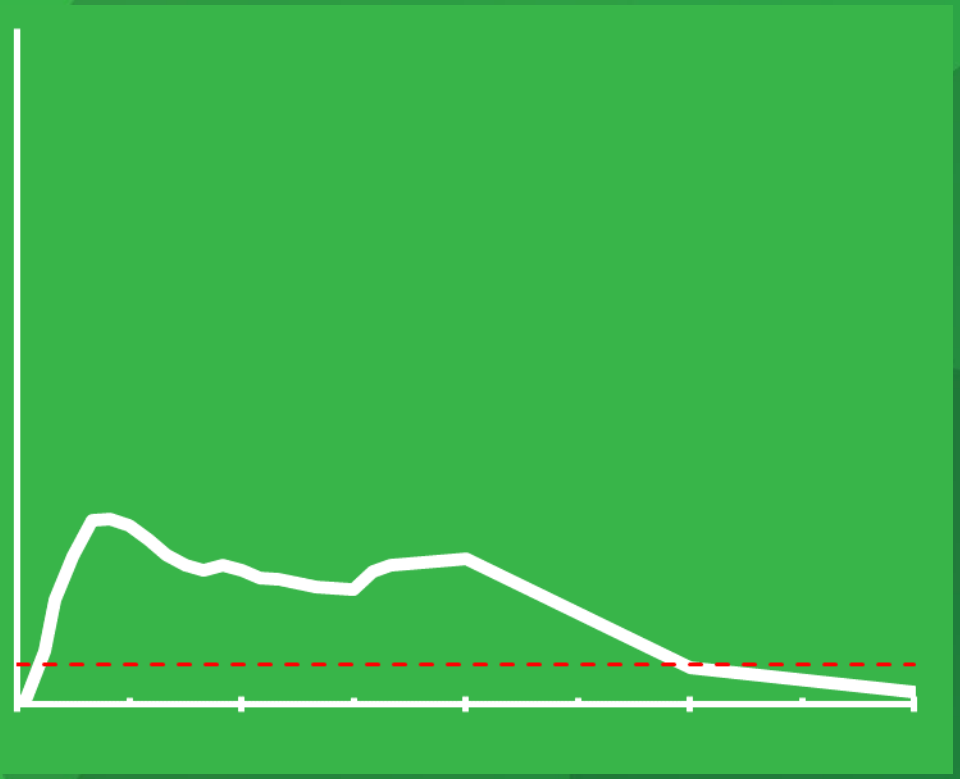
Potential preferred option for ODT

HAE: hereditary angioedema. OLE: open-label extension. LTE: long-term extension. PGI-C: patient global impression of change. PGI-S: patient global impression of severity.

Source: [1]Riedl MA et al. BKS 2024. [2]Valerieva A et al. EAACI 2024. [3]Magerl M et al. BKS 2024. [4]Riedl MA et al. AAAAI 2024. [5]Maurer M et al. BKS 2024. [6]Maurer M et al. AAAAI 2023.

Deucrictibant extended-release tablets

Long-Term Prophylaxis



Deucrictibant clinical development for LTP and ODT

Long-Term Prophylaxis (LTP)

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Positive topline data from CHAPTER-1, a Phase 2 study of deucrictibant the for prophylaxis of HAE attacks

Primary endpoint met: **84.5%** reduction in monthly attack rate versus placebo at week 12 (p=0.0008)*

92.3%
reduction in occurrence of **moderate and severe attacks***

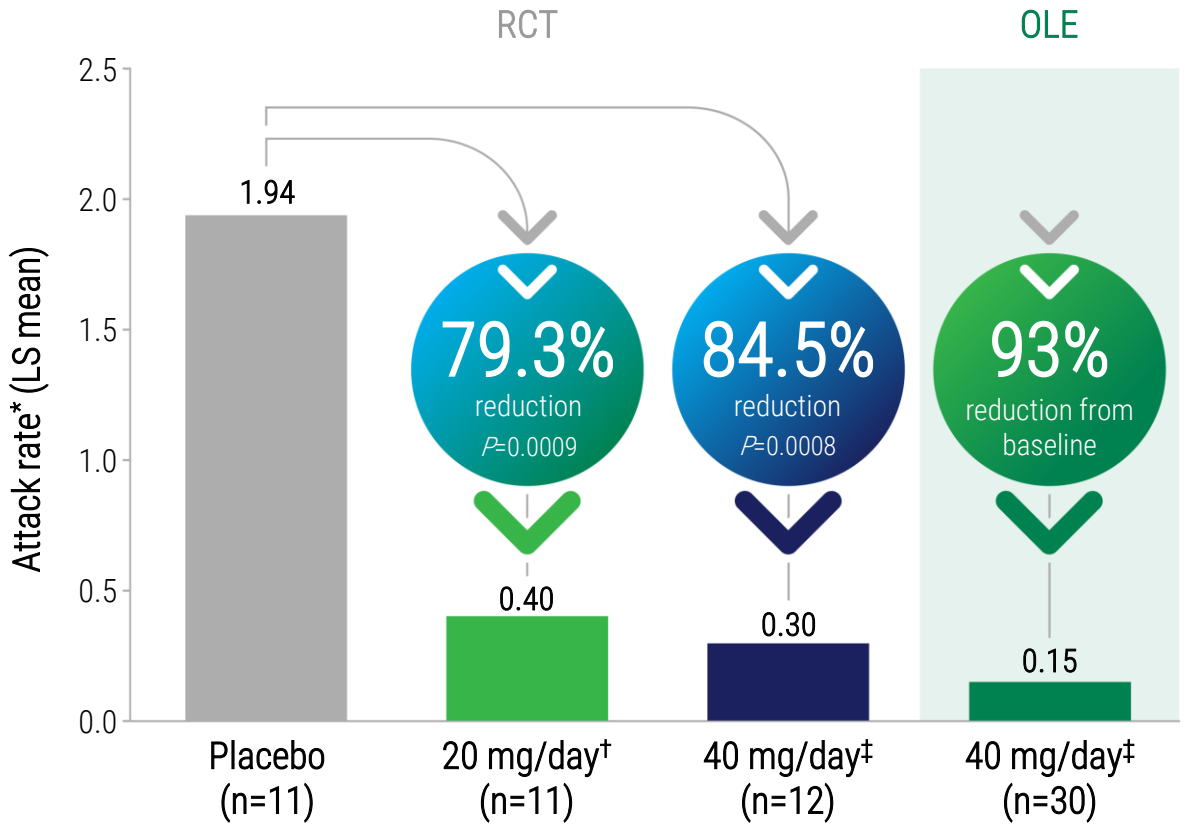
92.6%
reduction in occurrence of **attacks treated with on-demand medication***

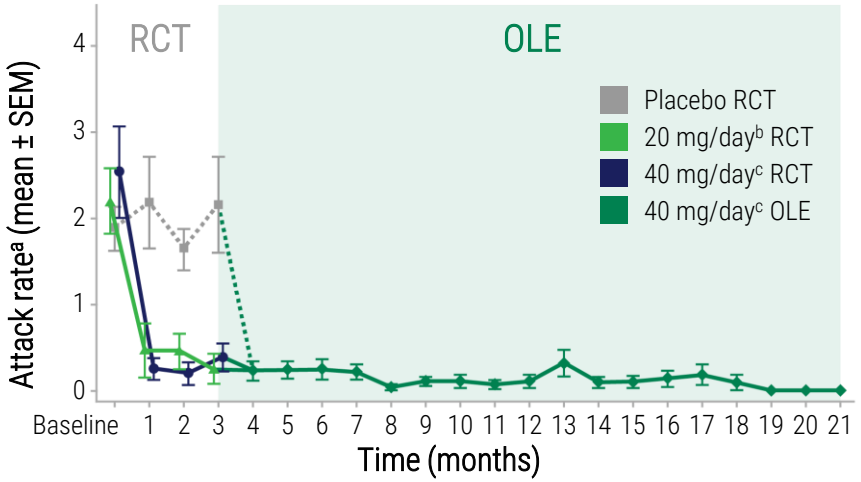
Clinically **meaningful results** across primary, secondary, and health-related quality of life endpoints

Deucrictibant **well-tolerated** at both doses

*40 mg/day deucrictibant treatment group; %reduction in monthly attack rate is based on a Poisson regression model. All attacks reported herein are investigator-confirmed; attack rate is number of attacks per month of exposure, also referred to as time-normalized number of attacks; all statistical analyses comparing deucrictibant and placebo are made without adjustment for multiplicity. HAE: hereditary angioedema.
Source: Aygören-Pürsün E et al. EAACI 2024.

Continuing deucrictibant treatment sustained the early-onset attack reduction for over one year





In the open-label extension up to 18 months:

- **93% attack rate reduction from baseline**
- Median attack rate = 0 for every month
- 99% of days symptom free

IR, immediate release; OLE, open label extension; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in Part 1 of the study. N' = number of participants in the OLE. [a]1 month = 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily. **Source:** Riedl MA et al. BKS 2024.

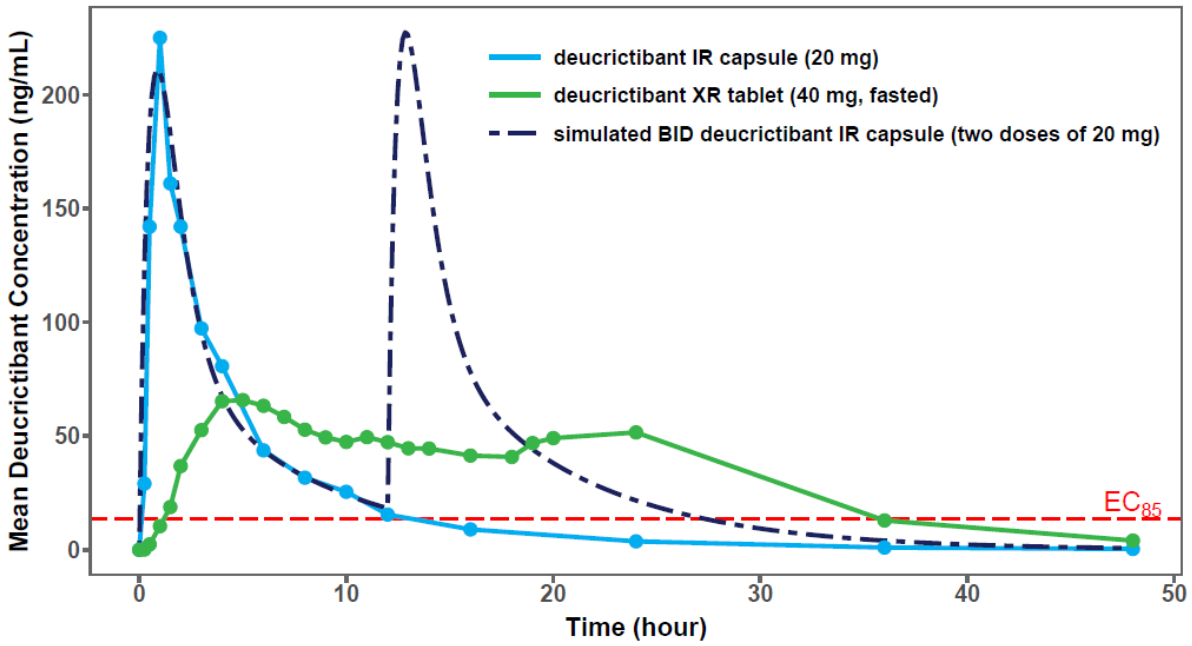
Deucrictibant efficacy and tolerability profile could address unmet needs in the prophylactic setting, with the convenience of a daily tablet

	Cinryze® (pdC1INH)	Haegarda® (pdC1INH)	Takhzyro® (lanadelumab)	Orladeyo® (berotralstat)	garadacimab	donidalorsen	deucrictibant	
Mechanism of Action	Plasma-derived C1NH	Plasma-derived C1INH	Anti-plasma kallikrein mAb	Plasma kallikrein inhibitor	Anti-FXIIa mAb	Plasma kallikrein inhibitor	Bradykinin B2 receptor antagonist	
Clinical Trial(s)	Ph 3§ (500 U, 1,000 U)	Ph 3§§ (60 IU/Kg)	Ph 3† (300mg q2w / q4w)	Ph 3†† (150mg daily)	Ph 3†	Ph 3¶ (80 mg q4w, q8w)	Ph 2‡ (40mg/day)	Ph 2/3 OLE
Mean monthly attack reduction vs. placebo	71-85%[1]	84%[2]	73-87%[4]	44%[6,7]	89%[8]	55-81%[9]	85%[10,11]	93%¤[12]
Mean reduction in use of ODT vs. placebo	-	89%[2]	74-87%[4]	54%[7]	88%[8]	67-92%¶¶[9]	93%[10,11]	pending publication
≥50% attack reduction	-	90%#[2,3]	100-100% vs. 32%[4,5]	58% vs. 25%[6,7]	95% vs. 33%[8]	83-93% vs. 27%¶¶[9]	90% vs. 18%[11]	pending publication
≥70% attack reduction	-	83%#[2,3]	76-89% vs. 10%[4,5]	50% vs. 15%[6,7]	92% vs. 17%[8]	65-92% vs. 18%¶¶[9]	80% vs. 18%[11]	pending publication
≥90% attack reduction	-	58%#[2,3]	55-67% vs. 5%[4,5]	23% vs. 8%[6,7]	74% vs. 8%[8]	48-62% vs. 9%¶¶[9]	60% vs. 0%[11]	pending publication
% patients attack-free vs. placebo	-	40% vs. 0%[2,3]	31-44% vs. 2%[4,5]	10% vs. 2.5%[6]	62% vs. 0%[8]	35-53% vs. 9%¶¶[9]	40% vs. 0%[11]	pending publication

§ Crossover, 12 weeks/treatment. §§ Crossover, 16 weeks/treatment (results reported for weeks 3-16 for each treatment arm). † Parallel-arms, 26 weeks. †† Parallel-arms, 24 weeks. ¶ Parallel-arms, 25 weeks. ‡ Parallel-arms, 12 weeks. # vs. placebo. ¶¶ Weeks 5-25. ¤ vs. RCT Part 1 baseline.

Source: [1]Cinryze® US PI, Feb 2023. [2]Longhurst H et al. *N Engl J Med*. 2017. [3]Haegarda® US PI, Jan 2022. [4]Takhzyro® US PI, Feb 2023. [5]Banerji A et al. *JAMA*. 2018. [6]Zuraw B et al. *J Allergy Clin Immunol*. 2021. [7]Orladeyo® US PI, Nov 2023. [8]Craig TJ et al. *Lancet*. 2023. [9]Riedl MA et al. *N Engl J Med*. 2024. [10]Aygören-Pürsün E et al. EAACI 2024. [11]Aygören-Pürsün E et al. BKS 2024. [12]Riedl MA et al. BKS 2024.

Commercial XR formulation maintains exposure above therapeutic level for at least 24 hours



- **Extended-release** matrix controls release and absorption of compound in small intestine as well as in colon
- Supports **once-daily** dosing while maintaining exposure more consistently versus twice-daily IR (used in proof-of-concept Phase 2 CHAPTER-1 study)
- **Formulation patent** applications filed with broad coverage of worldwide pharmaceutical markets

XR: extended-release tablet formulation of deucrictibant. IR: immediate-release capsule formulation of deucrictibant.
Source: Company data: single-dose cross-over PK study in healthy volunteers (n=14) under fasting conditions

CHAPTER-3 RCT and CHAPTER-4 OLE

Two-part, global Phase 3 study of deucrictibant for prophylaxis of HAE attacks

Enrollment

- Target enrollment of approximately 81 adolescents and adults living with HAE
- Top-line data anticipated in the second half of 2026

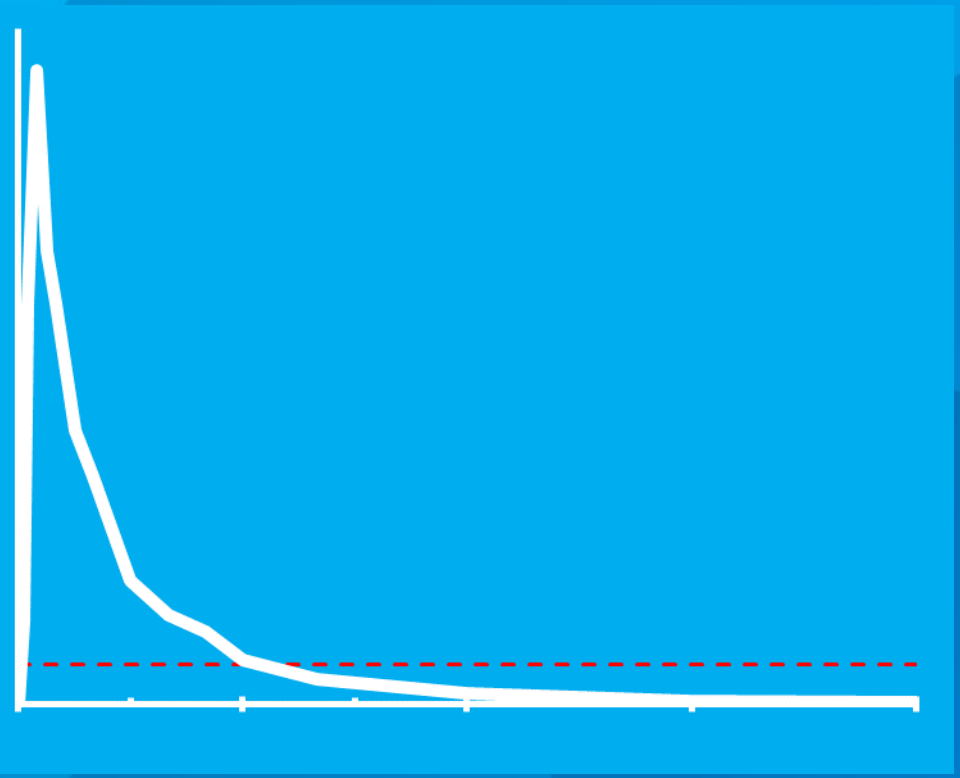
Objectives

- Evaluation and characterization of investigator-confirmed HAE attacks during 24-week treatment period
- Incidence of treatment-emergent adverse events
- Evaluation of deucrictibant XR pharmacokinetics
- Measure of change in participant-reported quality of life

RCT: randomized clinical trial. OLE: open-label extension. HAE: hereditary angioedema. XR: extended-release tablet.

Deucrictibant immediate-release capsules

On-Demand



Deucrictibant clinical development for LTP and ODT

Long-Term Prophylaxis (LTP)

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RAPIDe-3	Phase 3 pivotal[6]	Ongoing

OLE: open-label extension. LTE: long-term extension.

Source: [1]NCT05047185. [2]NCT06669754. [3]NCT06679881. [4]NCT04618211. [5]NCT05396105. [6]NCT06343779.

RAPIDe-1, a Phase 2 on-demand study of deucrictibant in HAE

Primary endpoint met: deucrictibant IR significantly reduced attack symptoms versus placebo*[1]

Deucrictibant IR **substantially reduced** the use of **rescue medications**[1]

Deucrictibant IR **well-tolerated** at all doses[1]

Deucrictibant IR showed rapid onset of action, symptom relief, and resolution of HAE attacks

End of symptom progression in **25-26 minutes*** (based on AMRA-3)†[2]

5-fold reduction in use of rescue medication*[1]

Onset of symptom relief achieved in **2.4 hours*** (≥30% reduction in AMRA-3)[1]

HAE: hereditary angioedema. IR: immediate-release. AMRA, Angioedema Symptom Rating Scale.
*pooled 10, 20, 30 mg deucrictibant treatment group †based on post-hoc analysis.
Source: [1]Maurer M et al. AAAAI 2023. [2] Riedl MA et al. ACAAI 2023.

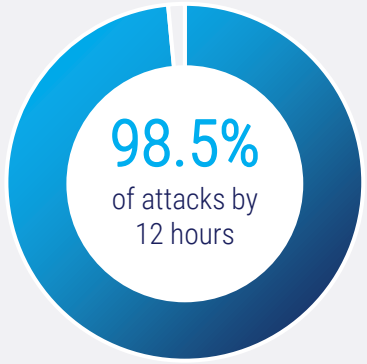
RAPIDe-2*, a long-term extension of RAPIDe-1

In the current analysis of the ongoing RAPIDe-2 Phase 2/3 extension study, **deucrictibant IR capsule was well-tolerated** for all studied doses with no new safety signals observed

Efficacy analysis showed:

Results from the ongoing RAPIDe-2 extension are consistent with the Phase 2 RAPIDe-1 study and provide **evidence on the long-term safety and efficacy of deucrictibant IR** capsule for repeat treatment of HAE attacks

1.1 hours median time to **onset of symptom relief** by PGI-C



2.6 hours median time to **reduction in attack severity** by PGI-S

11.5 hours median time to **complete attack resolution** by PGI-S[1]

86.0%

of attacks were treated with a single dose of deucrictibant IR capsule

*A total of 265 attacks from 17 participants were included in the modified intention-to-treat efficacy analysis set (data cutoff: 1 March 2024); a total of 337 attacks from 19 participants were included in the safety analysis set (data cutoff: 10 June 2024). HAE: hereditary angioedema. IR: immediate-release capsule formulation of deucrictibant. PGI-C: Patient Global Impression of Change. PGI-S: Patient Global Impression of Severity.

Source: Maurer M et al. BKS 2024.

Deucrictibant's rapid-onset and complete symptom resolution may address unmet medical need in HAE with a single oral capsule

		sebetralstat tablet	deucrictibant IR capsule			Standard of Care Berinert® (pdC1INH), Firazyr® (icatibant), Ruconest® (rhC1INH)
Mechanism of Action		Plasma kallikrein inhibitor	Bradykinin B2 receptor antagonist			Plasma-derived C1NH (23%) - Icatibant (60%) – Recombinant hC1INH (9%) - Other (9%)
Clinical Trial(s)		Ph 3* (300mg, 600mg)	Ph 2 (10mg, 20mg, 30 mg pooled)	Ph 2/3 Ext.* (10mg, 20mg, 30mg pooled)	Ph 2/3 Ext. PSM Analysis (10mg, 20mg, 30mg pooled)	PSM Analysis of Mixed Methods Study[9]
Time to onset of symptom relief (median)	VAS/AMRA[a]	-	2.4 vs. 8.0 h[3]	-	-	-
	TOS[b]	-	2.0 vs. 7.6 h[4,5]	-	-	-
	PGI-C[c]	1.6-1.8 vs. 6.7 h[1]	-	1.1 h[7]	1.1 h[8]	2.4 h[8]
Time to ≥50% VAS reduction (median)		Not reported yet[2]	3.9 vs. 22.8 h[3]	-	-	-
Time to reduction in attack severity (median)[d]		7.7-9.3 vs. > 12 h[1]	-	2.6 h[7]	2.1 h[8]	4.0 h[8]
Time to symptom resolution (median)	VAS/AMRA[e]	-	7.5 vs. 42.0 h[3]	-	-	-
	TOS[f]	-	5.2 vs. 23.3 h[4,5]	-	-	-
	PGI-S[g]	≥24.0 vs. >24 h[1]	-	11.5 h[7]	12.3 h[8]	13.5 h[8]
% attacks resolved within 24 h with 1 dose		42.5-49.5% vs. 27.4%#[1]	75.0% vs. 15.7†[6] 81.7% vs. 22.4%‖[6]	90.2%[7]	-	-
% attacks treated with 1 dose of study drug (no additional doses of study drug and/or rescue med.)		≤60.2-≤60.9 vs. ≤44.0%[1]	pending publication	86.0%§[7]	-	-

References on following slide

This presentation includes data for an investigational product not yet approved by regulatory authorities.

ODT comparison data references

* Non-laryngeal and laryngeal attacks included for treatment with study drug. # Symptom resolution assessed by PGI-S. † Symptom resolution assessed by VAS/AMRA. ‖ Symptom resolution assessed by TOS.

a. Time to onset of symptom relief by VAS/AMRA defined as 'VAS-3 ≥30% reduction from pre-treatment score' in [3].
b. Time to onset of symptom relief by TOS defined as 'The time point when TOS PRO first reaches at least "A little better" for all symptom complexes affected at baseline, 'and no new symptom in any other symptom complex is reported. Relief is confirmed if the improvement is sustained at 2 consecutive time points' in [4,5].
c. Time to beginning (*or* onset) of symptom relief by PGI-C defined as 'beginning of symptom relief as assessed in a time-to-event analysis. The beginning of symptom relief was defined as a rating of "a little better" on the 7-point Patient Global Impression of Change (PGI-C) scale (ratings range from "much better" to "much worse") at two or more consecutive time points within 12 hours after the first administration of the trial agent' in [1] and as 'Patient Global Impression of Change (PGI-C) rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment' in [7,8].
d. Time to reduction in attack severity defined as 'reduction in the severity of the attack, defined as an improved rating on the 5-point Patient Global Impression of Severity (PGI-S) scale (ratings range from "none" to "very severe") at two or more consecutive time points within 12 hours after the first administration' in [1] and 'achieving ≥1 point reduction in the Patient Global Impression of Severity (PGI-S) from pretreatment for 2 consecutive timepoints by 12 hours post-treatment' in [7,8].
e. Time to symptom resolution by VAS/AMRA defined as 'all 3 individual VAS items ≤10' in [3].
f. Time to symptom resolution by TOS defined as 'The time point when TOS PRO first reaches "A lot better or resolved" for all symptom complexes affected at baseline, and no new symptom in any other symptom complex is reported' in.[4,5]
g. Time to symptom resolution by PGI-S defined as 'achieving PGI-S rating of "none" at 24 hours post-treatment' in [1] and as 'achieving PGI-S rating of "none" at 24 hours post-treatment' in [7,8] .

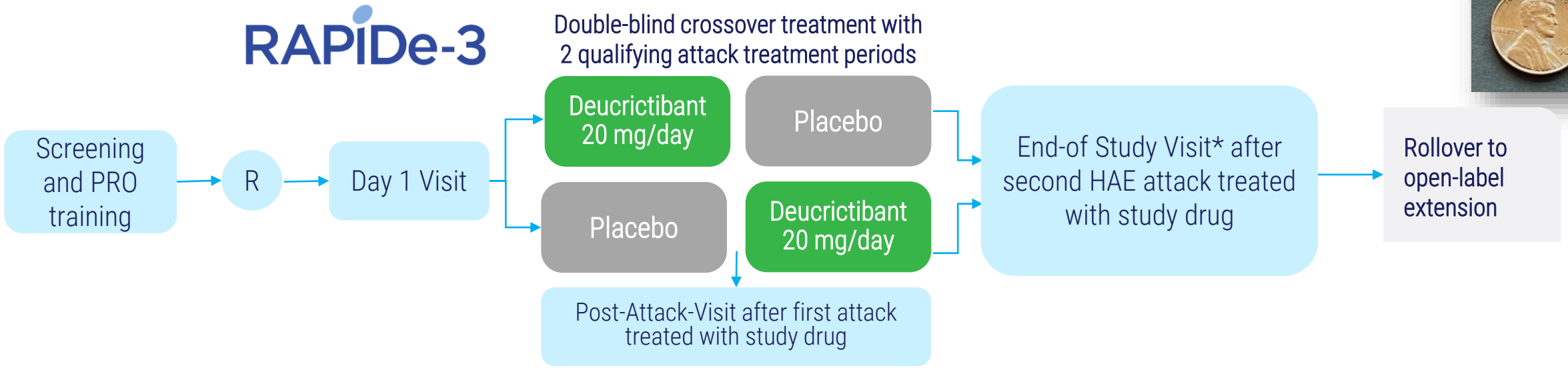
[1]Riedl MA et al. *N Engl J Med*. 2024. [2]EudraCT: 2021-001226-21. [3]Maurer M et al. AAAAI 2023. [4]Riedl MA et al. C1-INH Workshop 2023. [5]RAPIDe-1 Phase 2 Top-line data presentation. [6]Li HH et al. EAC 2024. [7]Maurer M et al. BKS 2024. [8]Riedl MA et al. BKS 2024. [9]Mendivil et al. GA²LEN UCARE 2023.

RAPIDe-3[1] RCT

Global Phase 3 study of deucrictibant for on-demand treatment of HAE attacks

RAPIDe-3

20 mg capsule



Enrollment

- Target enrollment of approximately 120 adolescents and adults living with HAE
- Top line data anticipated in 1Q2026

Primary Endpoints

- Onset of symptom relief
- Patient Global Impression of Change (PGI-C) rating of at least "a little better" for two consecutive timepoints within 12 hours post-treatment

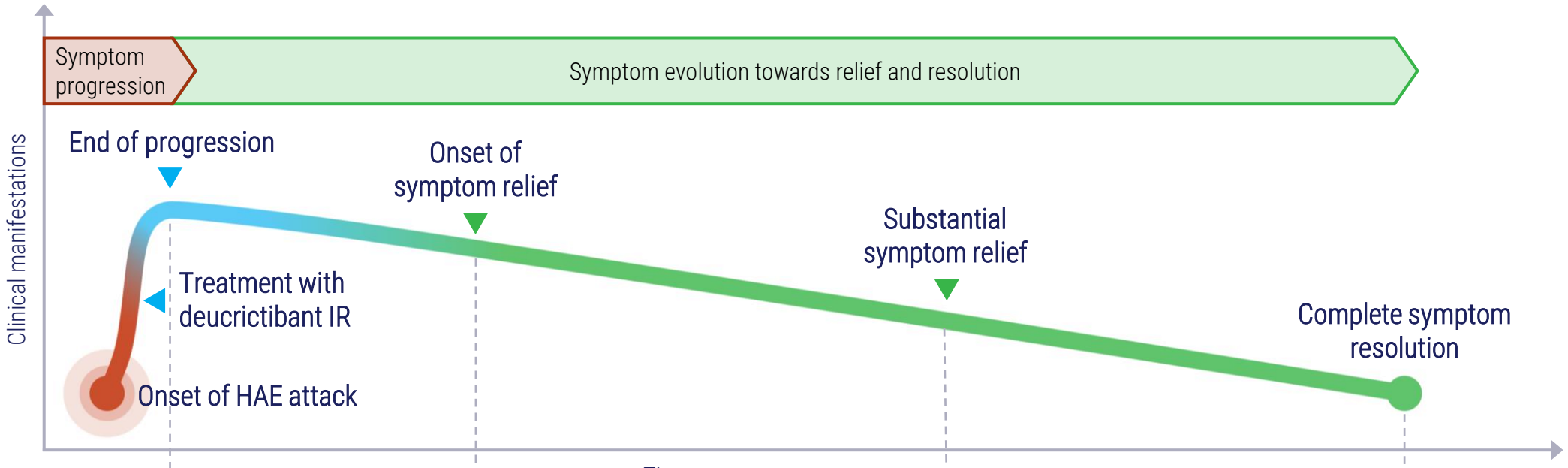
Secondary Endpoints

- Time to end of progression of attack symptoms, substantial symptom relief, and symptom resolution
- PGI-C, Patient Global Impression of Severity (PGI-S), Angioedema syMptom Rating scAle (AMRA)
- Use of rescue medication
- Incidence of treatment-emergent adverse events

RCT: randomized clinical trial. *Adolescent patients receive a non-attack dose for PK sampling prior to randomization.

Source: [1]Maurer M et al. EAACI 2024.

Clinical trial endpoints span the entire attack timecourse

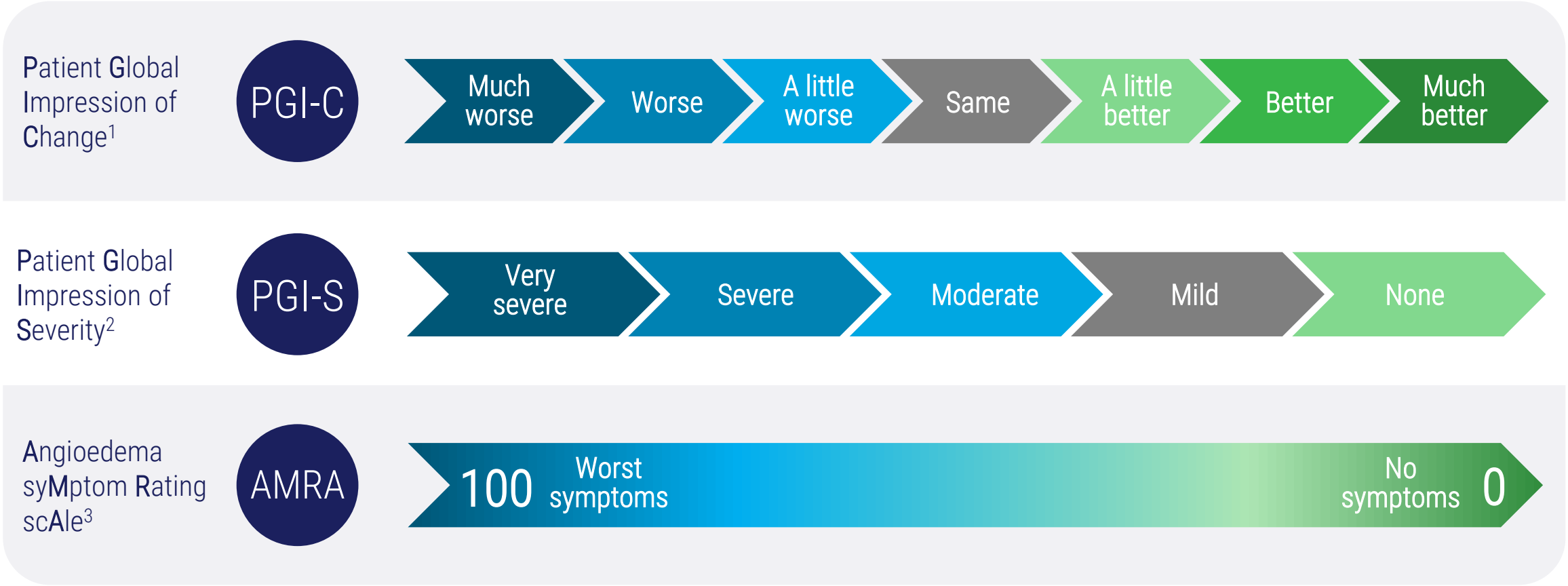


RAPIDe-1[1,2,3]	Time to EoP by AMRA *Post-hoc*	AMRA-3 ≥30% reduction	AMRA-3 ≥50% reduction	AMRA all 3 items ≤10
RAPIDe-2[4]		PGI-C "a little better" AMRA ≥30% reduction;	PGI-C "better"; PGI-S ≥1 point reduction; AMRA ≥50% reduction	PGI-S "none"; AMRA all 3 items ≤10
RAPIDe-3[5,6]	Time to EoP by PGI-C	**Primary endpoint** PGI-C "a little better"	PGI-C "better"; PGI-S ≥1 point reduction; AMRA ≥50% reduction	PGI-S "none"; AMRA all 3 items ≤10

AMRA, Angioedema Symptom Rating Scale; EoP, end of progression; HAE, hereditary angioedema; IR, immediate release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity.

Source: [1]NCT04618211. [2]Riedl et al. ACAAI 2023. [3]Medivil et al. GA²LEN UCARE 2023. [4]NCT05396105. [5]NCT06343779. [6]Maurer et al. EAACI 2024.

Patient-reported outcomes (PRO) assessments

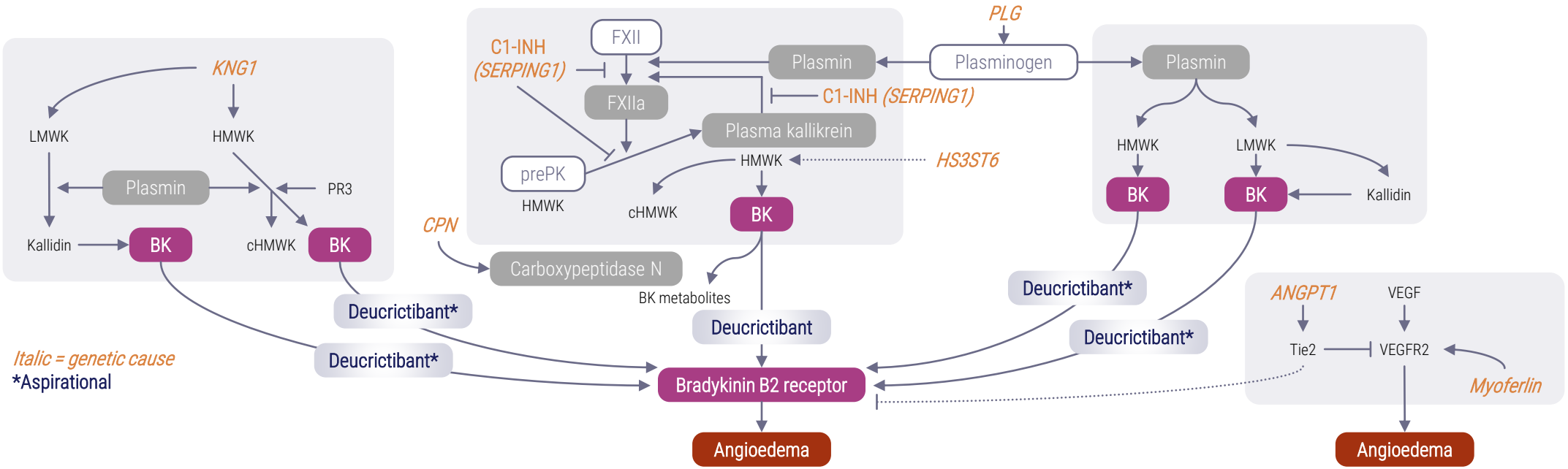


Source: Riedl MA et al. BKS 2024.

Acquired Angioedema

Bradykinin B2 receptor inhibition broadly applicable across angioedema

Types of angioedema	AE-MC Mast-cell mediated		AE-BK Bradykinin mediated			AE-VE Vascular endothelium	AE-DI Drug induced	AE-UNK Unknown
Mechanism	Mast cell degranulation		Hereditary C1INH deficiency	Acquired C1INH deficiency	KKS pathway mutations	Intrinsic vascular endothelium dysfunction	Drug adverse reactions (various mechanisms)	Unknown aetiology or mechanism
Name/ Acronym	AE-URT	AE-ANA	HAE-C1INH (Type 1, 2)	AAE-C1INH	HAE-FXII†, HAE-PLG†, HAE-KNG†	HAE-ANGPT†, HAE-MYOF†, HAE-HSST†, SCLS	AE-ACEI, AE-tPA, AE-DPPIV, AE-NSAID, etc.	AE-UNK, HAE-UNK†, EAE



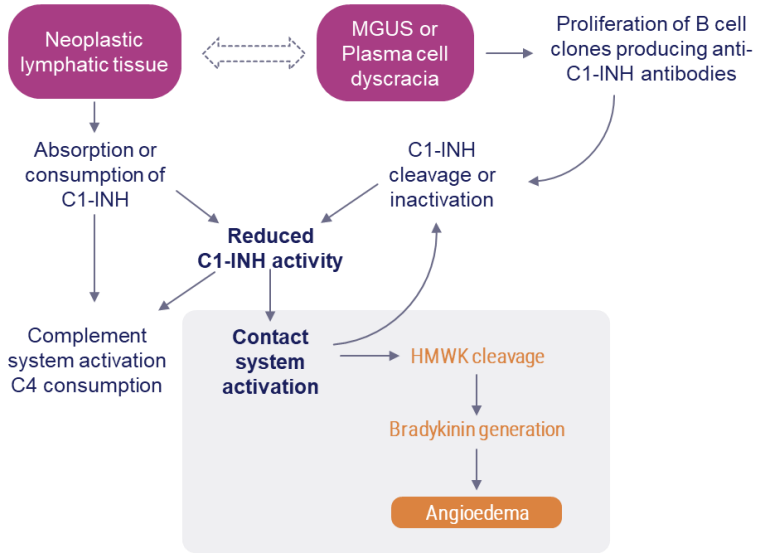
Notes: bold = known or potential role for bradykinin involvement in disease. †also designated as Normal C1INH Angioedema (HAE-nC1INH)
HMWK: high-molecular-weight kininogen; cHMWK: cleaved high-molecular-weight kininogen; FXII(a): Factor XII(a); ACE(i): angiotensin-converting enzyme (inhibitor); tPA: tissue plasminogen activator; KNG1: gene encoding HMWK; PLG: gene encoding plasminogen; FXII: gene encoding FXII; ANGPT: gene encoding angiopoietin; MYOF: gene encoding myoferlin; HSST: gene encoding heparan sulfate sulfotransferase; SCLS: systemic capillary leak syndrome.
Source: Busse 2020 *J Allergy Clin Immunol Pract*; Bork et al 2021 *J Allergy Clin Immunol*; Zanichelli et al 2012 *Allergy*; Longhurst et al 2017 *Clin. Exp. Immunol.*; Otani, Banerji 2017 *Immunol. Allergy Clin. N. Am.*; Bova et al 2018 *Int. Arch. Allergy Immunol.*; Petersen et al 2024 *J Allergy Clin Immunol*

Deucrictibant proof-of-concept in acquired angioedema due to C1-INH deficiency (AAE-C1INH)[1,2]

Investigator-initiated trial (IIT) by the Amsterdam UMC

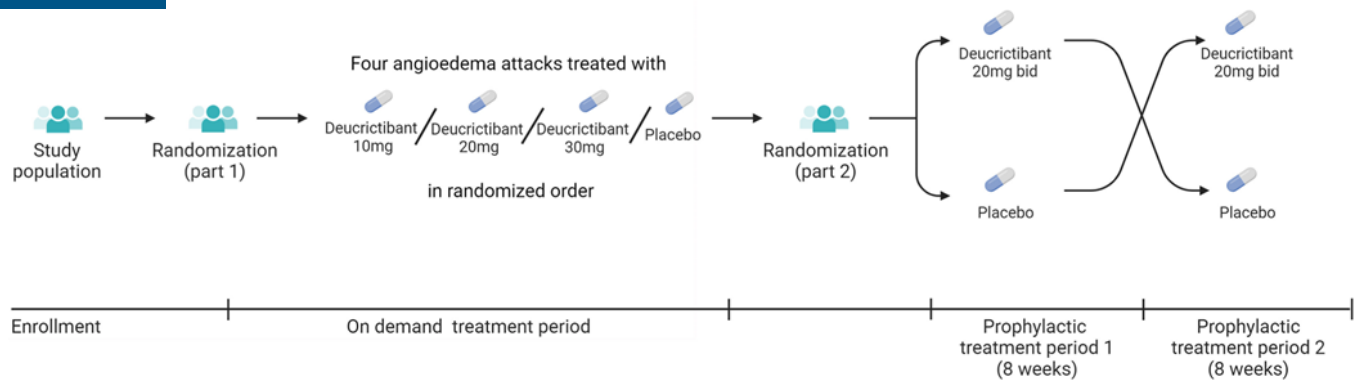
Currently, no therapies approved for AAE

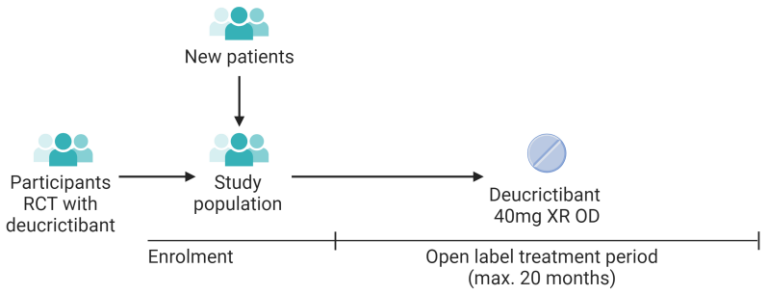
Estimated prevalence of 1:100,000 to 1:500,000 or ~10% of HAE type 1/2



JACI The Journal of Allergy and Clinical Immunology

POP-AID		ONCE-AID
Part 1: On-demand treatment	Part 2: Prophylactic treatment	Long-term extension (XR tablet)



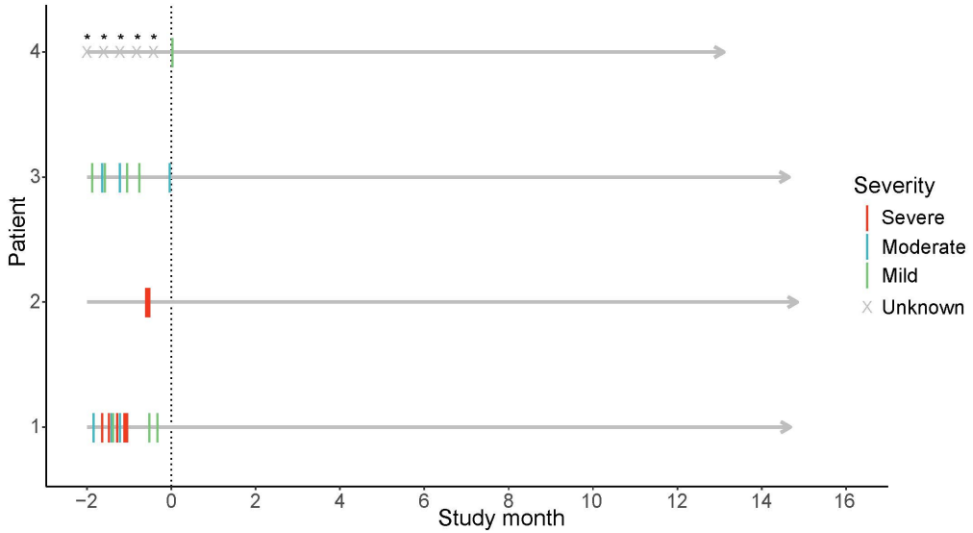


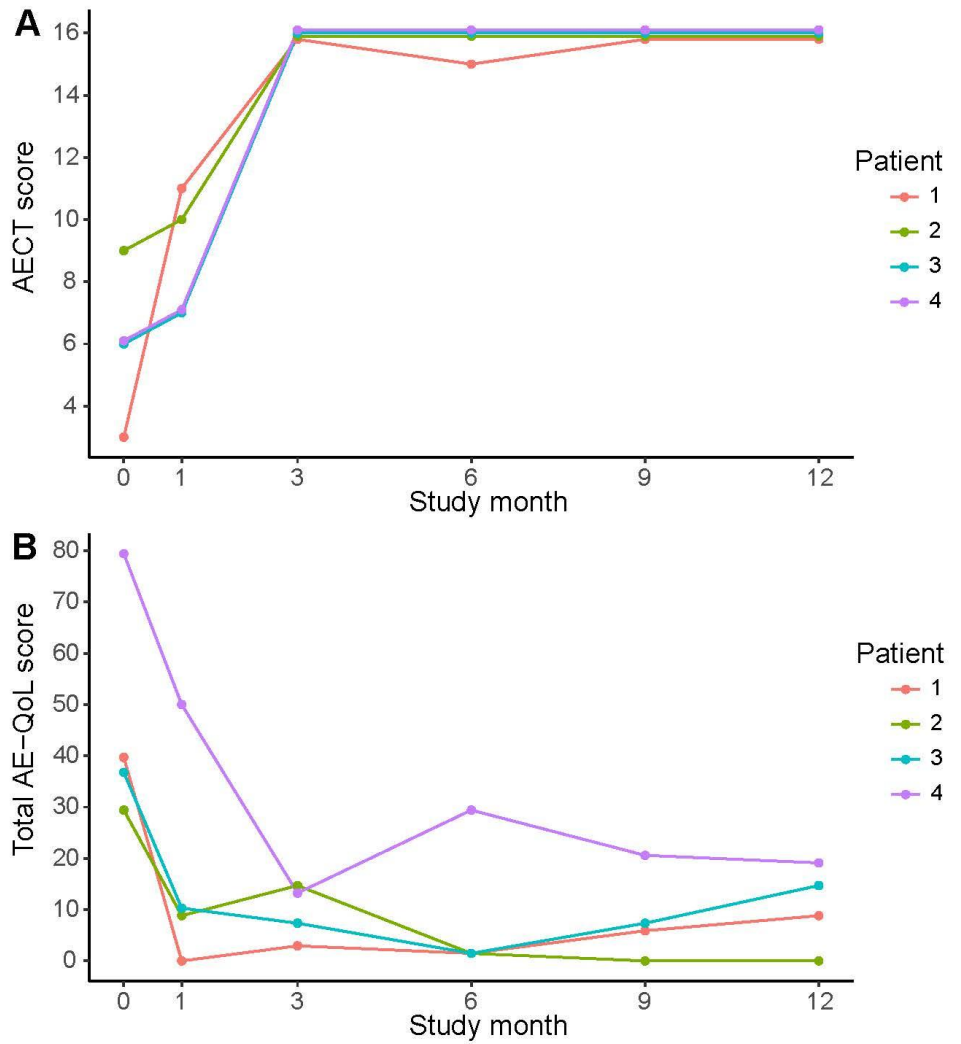
Source: [1]Petersen RS et al. *J Allergy Clin Immunol*. 2024. [2]Petersen RS et al. BKS 2024.

Deucrictibant XR tablet for the prevention of acquired angioedema (AAE-C1INH) attacks[1,2]

Attacks per month	Patient 1	Patient 2	Patient 3	Patient 4
Baseline	1.2	1.2	0.9	2.2
Placebo	2.0	0.6	1.0	N/A
Deucrictibant	0	0	0	0.1

Attacks before and during deucrictibant XR treatment





Notes: the baseline attack rate covers 90 days prior to randomization for prophylactic treatment in the randomized controlled trial for Patients 1,2, and 3, and 90 days prior to enrollment in the open-label portion for Patient 4. *Patient 4 reported five angioedema attacks in the two months prior to enrollment, but did not recall the exact dates on which these attacks occurred. Graph A: Angioedema Control Test (AECT) score during prophylactic treatment with deucrictibant XR tablet. Graph B: Angioedema Quality of Life (AE-QoL) score during prophylactic treatment with deucrictibant XR tablet. **Source:** [1]Petersen RS et al. *J Allergy Clin Immunol*. [2]Petersen RS et al. BKS 2024.

Our aspiration is to become a market leader in HAE

Rooted in a deep commitment to engage with the HAE community

Notes: Aspirational, to be confirmed with Phase 3 clinical data

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