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Pharmaceuticals

# Corporate Overview

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November 2023

# Forward-Looking Statements

This presentation and the accompanying oral presentation contain “forward-looking” statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as: “anticipate,” “intend,” “plan,” “goal,” “seek,” “believe,” “project,” “estimate,” “expect,” “strategy,” “future,” “likely,” “may,” “should,” “will” and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding our future financial performance, business plans and objectives, timing and success of our clinical trials, our ability to obtain regulatory approval or the timing of regulatory filings, the potential therapeutic benefits and economic value of our lead product candidates, financing plans, competitive position, industry environment and potential market opportunities.

Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, the following: those related to our future financial performance, our ability to raise additional funding when needed, our ability to develop and maintain partnerships, our ability to identify and develop new products in a timely manner, the outcome, cost and timing of our product development activities and clinical trials, market size and acceptance of our products, our ability to maintain, protect and enhance our brand and intellectual property, our ability to continue to stay in compliance with applicable laws and regulations, our ability to scale our business and make key hires and such other factors as discussed under the section titled “Risk Factors” and elsewhere in our Annual Report on Form 10-K, definitive proxy statement and quarterly reports on Form 10-Q that we file with the Securities and Exchange Commission (“SEC”) as well as our other filings and the documents incorporated by reference therein, with the SEC.

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# Company Highlights

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- Discovery, development, and commercialization of oral, small molecule protease inhibitors
- Lead program Sebetralstat for on-demand treatment of orphan disease hereditary angioedema (HAE)
- Achieved targeted number of on-treatment attacks to complete Sebetralstat phase 3 KONFIDENT trial; data expected early 2024, NDA H1 2024
- Sebetralstat would be first oral on-demand HAE therapy and has market transformation potential
- Preclinical oral Factor XIIa program advancing towards IND
  - Initial development in HAE, additional potential indications include thrombosis, inflammation
- All programs internally developed, with full rights and IP protection to at least late-2030s
- Funded into 2025 with \$123 million at July 31, 2023

# Program Portfolio

Product	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Status
Sebetralstat	On-Demand HAE	KONFIDENT				Data early 2024
		KONFIDENT-S (Open-Label Extension)				Trial ongoing
		Orally Disintegrating Tablets				Advancing to sNDA as lifecycle extension
Oral Factor XIIIa	HAE Prophylaxis					Advancing towards IND
Oral Factor XIIIa	Thrombosis, inflammation					Future opportunities under evaluation



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# Hereditary Angioedema (HAE)

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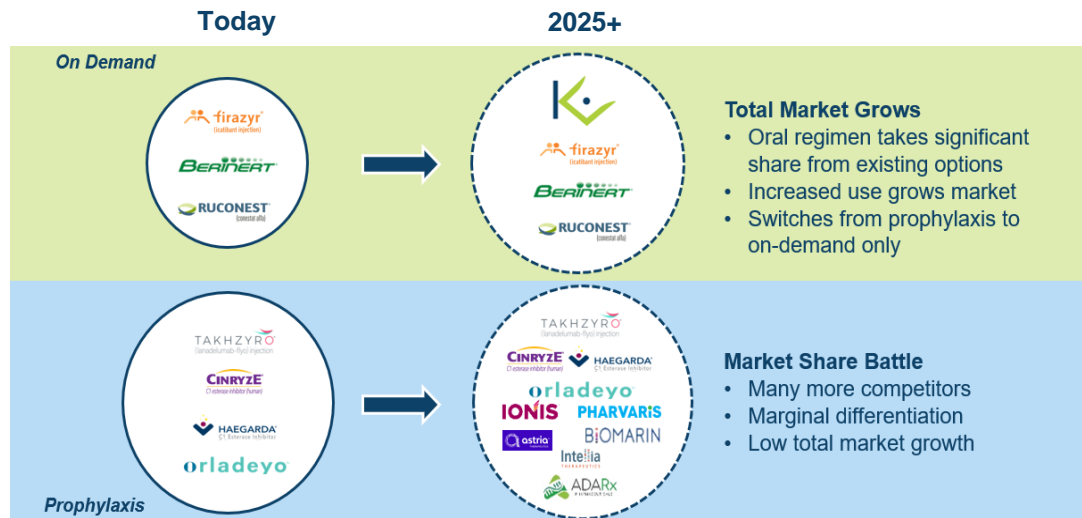
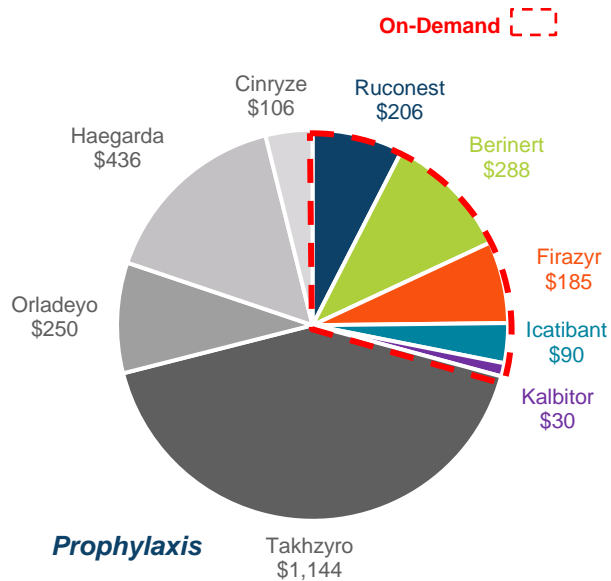
- Genetic condition causing painful and pronounced swelling in various parts of the body
  - Primarily caused by defect in C1 inhibitor activity, which leads to uncontrolled plasma kallikrein activity and bradykinin release
- Orphan disease: incidence 1 in 10,000 to 1 in 50,000<sup>1</sup>
  - Minimum of 6,500 – 8,000 patients in US; similar in EU
  - Incidence consistent worldwide; average patient has ~2 attacks/month
- Approved therapies are primarily injected / infused - high unmet need for efficacious oral administration

<sup>1</sup>[www.haei.org](http://www.haei.org)

# On Demand is a Significant Portion of Market, With Opportunities for Growth

**On Demand is 1/3 Total Revenues**

**On Demand has Greater Growth Potential**



(1) As per Evaluate Pharma and public filings.

# Sebetralstat Can Become the Dominant HAE Therapy

## Market Share



- ✓ Leading share of existing on-demand market
- ✓ Branded prices

## Increased Treatment



- ✓ Only ~50% of attacks are treated, including for prophylaxis patients
- ✓ More attacks will ultimately be treated for both prophylaxis and on-demand patients

## Prophy Switch to Acute



- ✓ Patients may switch from prophylaxis solutions to acute, seeking an efficacious and safe oral option
- ✓ More cost effective for many prophylaxis patients

## Future Indications



- ✓ Normal C1-INH HAE
- ✓ Short-term prophylaxis
- ✓ Pediatrics 2-12





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## Sebetralstat: HAE On-Demand Therapy

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# Level Of Unmet Need In HAE Therapy Is Underappreciated

The goal of treatment is to minimize compromises in lifestyle, but attacks still cause anxiety and impact quality of life



Anxiety and depression are common in people living with HAE



Even people taking prophylaxis continue to experience HAE attacks



96% of people living with HAE on prophylaxis feel they must change their plans for the day when an attack occurs<sup>3</sup>



People living with HAE prefer to treat at home to avoid treating attacks in public



People try to “save” doses and some studies show 50% or more of attacks aren’t treated at all<sup>1,2</sup>

<sup>1</sup>Maurer M, et al. Hereditary Angioedema Attacks Resolve Faster and Are Shorter after Early Icatibant Treatment. *PLoS ONE*. 2013;8(2):e53773. <sup>2</sup>Longhurst H J et al. Real-world outcomes in hereditary angioedema: first experience from the Icatibant Outcome Survey in the United Kingdom *Allergy Asthma Clin Immunol*. 2018;14: 28. <sup>3</sup>Remaining Burden of Hereditary Angioedema (HAE) Attacks Despite Modern Long-term Prophylaxis Stephen Betschel, Sally van Kooten, Markus Heckmann, Sherry Danese, Ledia Goga, Teresa Caballero; EAACI 2023 Hybrid Congress

# Prophylaxis Users Still Make Compromises To Avoid Triggers

Despite being on prophylaxis therapy, the need for on-demand treatment has impacted aspects of respondents' lives:



Choice of career



Where they travel



Social activities



Day-to-day work



School

# The Sebetralstat Treatment Vision Is Much Better



- Patients treat at **first recognition** of attack
- Halt attack at **earliest stages**

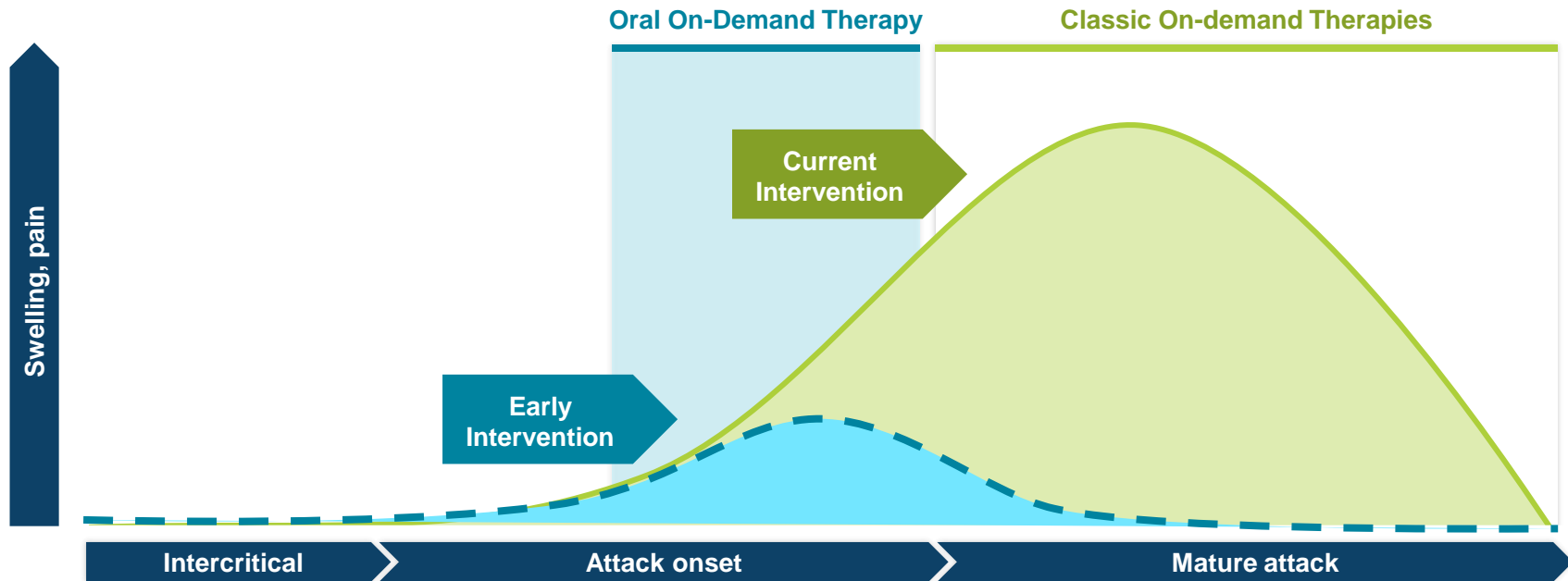


- Patients **treat all attacks**, since it is impossible to predict which ones will **escalate in severity**
- Current **barriers** to treatment are **removed**



- Sebetralstat dosing is **simple** with easy-to-take **tablets**
- Patients can **easily carry, store and access** when needed
- **Oral disintegrating tablet** a potential future benefit for **pediatrics** and other patients

# “Flattening the Curve” Of HAE Attack Progression



# Oral On-Demand Is A Meaningful Improvement For Patients

Patients say an on-demand oral treatment would simplify the treatment decision and change how and when they treat attacks

**95%**

*Proportion of time patients would carry treatment<sup>1</sup>*

**94%**

*Proportion of attacks patient would treat<sup>2</sup>*

**93%**

*Proportion of patients who would treat earlier<sup>3</sup>*

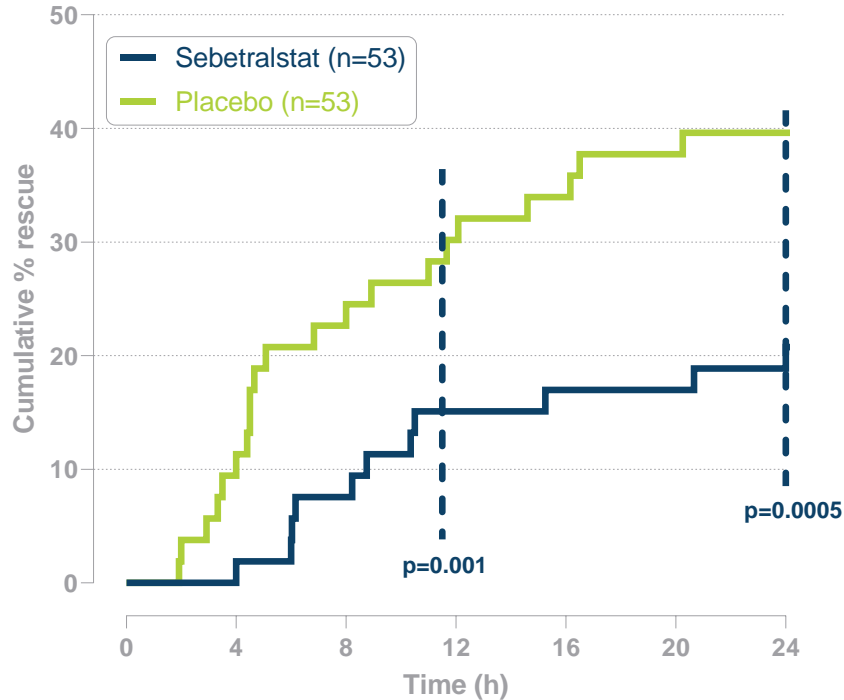
1. Percent of time patients would carry an effective oral on-demand treatment with them outside the home.
2. What percentage of attacks would you treat with an HAE on-demand pill/tablet?
3. Would you treat your attacks faster/earlier with an HAE on-demand pill/tablet?

# Positive Sebetralstat Phase 2 Clinical Trial Results

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- Sebetralstat met all primary and secondary endpoints
  - Including endpoint being used as primary in ongoing KONFIDENT phase 3 study
- Sebetralstat enabled early intervention to maximize treatment success
  - Median time to treatment was 30 minutes
- Significantly improved patient-reported outcomes of treatment effect and attack severity
  - Reduced time to beginning of symptom relief, time to improved attack severity, and attack resolution
- Sebetralstat was generally safe and well tolerated
  - No serious adverse events reported, and no patients withdrew due to adverse events

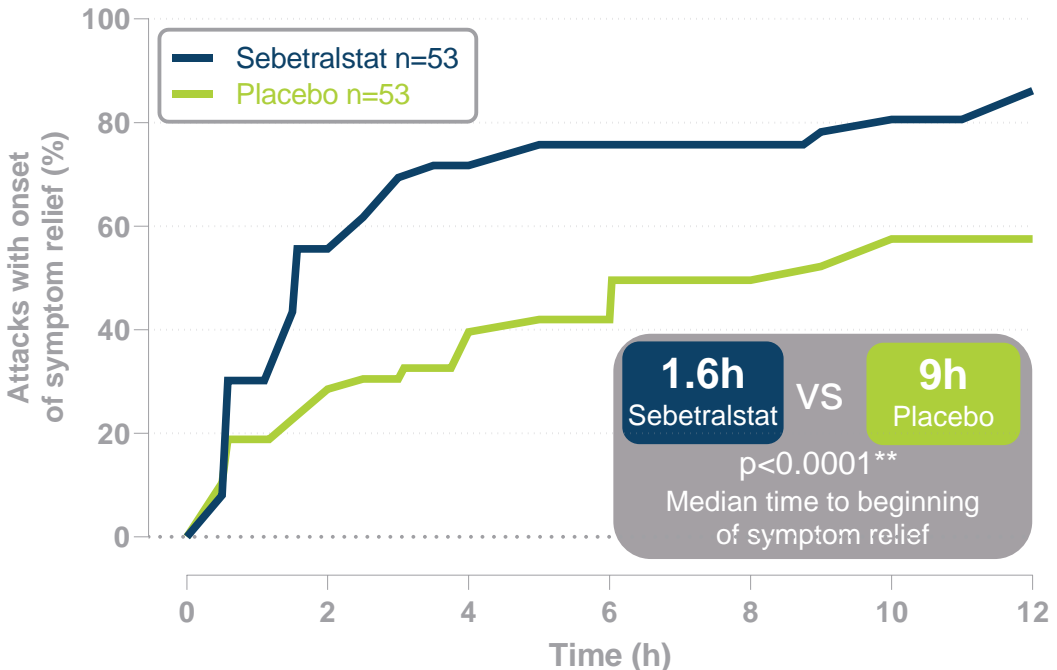
# Sebetralstat Met Primary Phase 2 Endpoint



- Sebetralstat significantly increased time to rescue within 12 hours:  $p=0.001^*$ 
  - Placebo 30.2%
  - Sebetralstat 15.1%
- Efficacy maintained at 24 hours
  - $p=0.0005^*$



# Sebetralstat Reduced Time To Beginning Of Symptom Relief



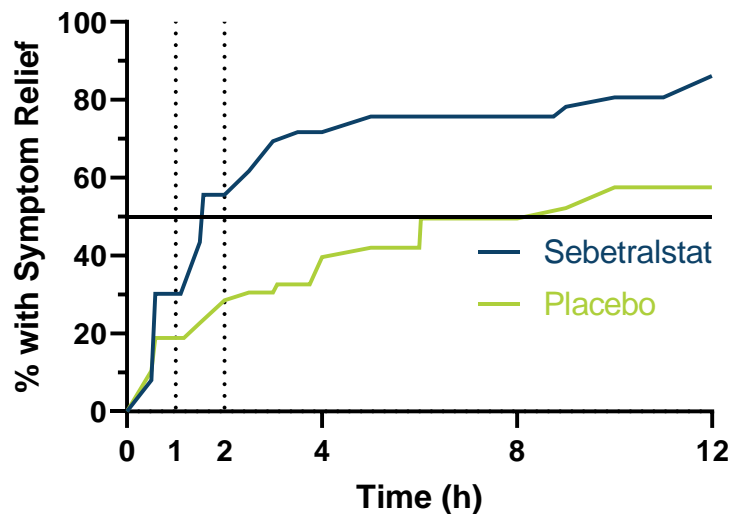
- Assessed using Patient Global Impression of Change (PGI-C)
- Highly significant treatment effect compared to placebo
- **Phase 3 primary endpoint**

\*\*Gehan's Generalized Wilcoxon Test Full analysis set / KalVista Phase 2 Sebetralstat Data Published in the Lancet, Feb 2023  
Censoring occurs where HAE attack was not rated "a little better" or higher or conventional attack treatment was used within 12h.

# Sebetralstat Similar To IV-Injected Ruconest (rC1-INH)

Sebetralstat 1.6 hours; Placebo 9 hours  
 $p < 0.0001^*$

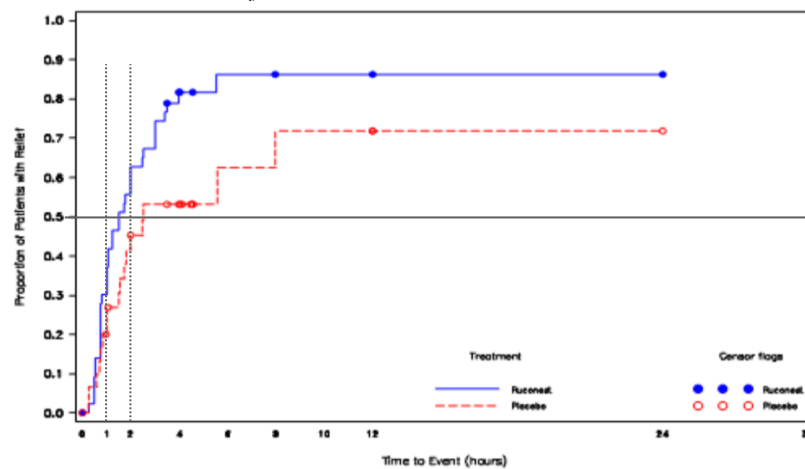
*Patient Global Impression of Change (PGI-C)*



Ruconest 1.5 hours; placebo 2.5 hours  
 $p = 0.031$

*Primary endpoint Ruconest Phase 3*

Study 1310: Kaplan-Meier Plot of Time to Beginning of Relief of Symptoms with Persistence (Based on Questions 1 and 2 of the TEQ, with Persistence) in the RCT Phase: RCT ITT Analysis Set



\*Gehan's Generalized Wilcoxon Test / KalVista Phase 2 Sebetralstat Data Published in the Lancet, Feb 2023

Ruconest data from Charles M. Maplethorpe, MD, PhD. Clinical Reviewer. Summary Basis of Approval, Recombinant C1 Esterase Inhibitor, STN: 125495/0. The results of the trials for sebetralstat and Ruconest may not be directly comparable, as they are not from a single head-to-head clinical trial

# Sebetralstat Phase 3 Trial Design

- Double blind, event-driven, crossover trial assessing 300 mg and 600 mg sebetralstat versus placebo
- Each patient treats 3 attacks at home
  - One with each treatment in a randomized, blinded sequence
  - Patients can take an additional dose if symptoms warrant, no statistical impact on primary or secondary endpoints



## Primary endpoint:

- Time to beginning of symptom relief (PGI-C)

## Key secondary endpoints:

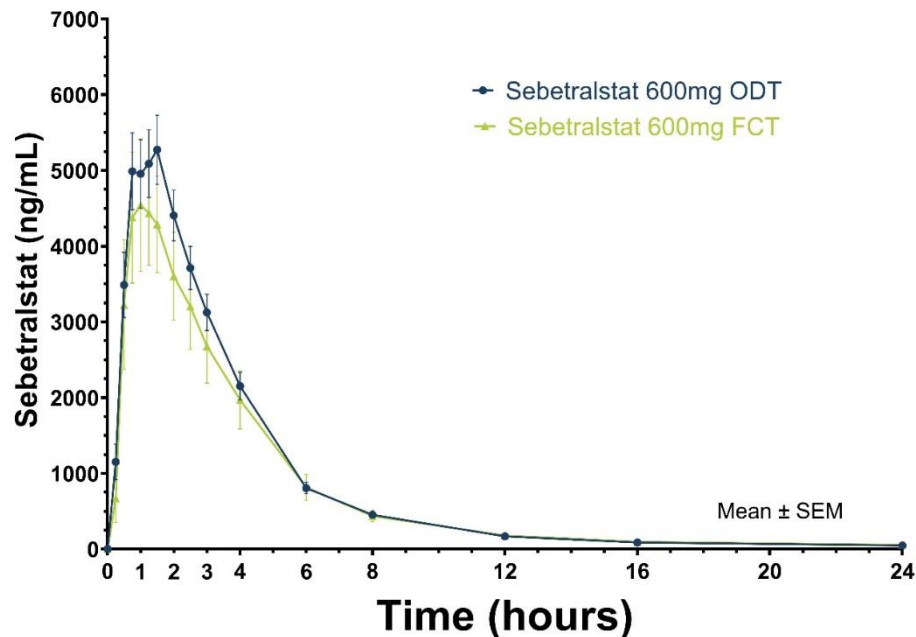
- Time to improvement (PGI-S)
- Time to resolution (PGI-S)

# Sebetralstat Phase 3 Trial Design And Timing

- KONFIDENT will end when approximately 84 patients have completed three attacks
  - HAE type 1 and 2, including adults, adolescents and patients with ongoing prophylaxis
  - All attack locations eligible, including laryngeal attacks
- FDA-agreed primary endpoint: time to beginning of symptom relief using PGI-C
  - *A priori* secondary endpoint in phase 2 trial
  - Expected to be sufficient to file NDA
  - FDA does not recommend the use of VAS to support the primary or key secondary endpoints
- At least 90% power to detect treatment differences vs placebo
- Achieved targeted number of on-treatment attacks to complete Sebetralstat phase 3 KONFIDENT trial; data expected early 2024, NDA H1 2024

# Orally Disintegrating Tablet (ODT) Further Enhances Options For Patients

- ODT increases ease of dosing for younger patients or those with difficulty swallowing
- Phase 1 data shows similar pharmacokinetics to current film-coated tablets (FCT)
- Expected to be lifecycle extension in US and EU; potentially launch formulation in other geographies





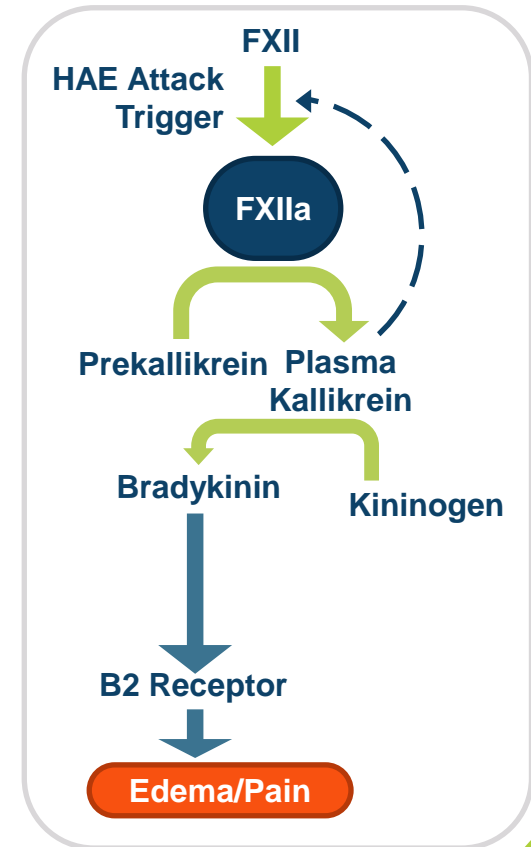
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# Factor XIIa

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# Factor XIIa Sits At Top Of HAE Attack Cascade

- Factor XIIa (FXIIa) activates the kallikrein kinin system
  - Generates plasma kallikrein, leading to uncontrolled bradykinin release in HAE
  - FXIIa and plasma kallikrein inhibitors selectively block bradykinin generated by the plasma kallikrein kinin system, unlike bradykinin receptor antagonists
- FXIIa inhibitory antibody has been shown clinically to reduce HAE attack frequency\*
  - At least as efficacious as approved therapies against other targets
  - No known chronic safety implications



\*1Banerji et al JAMA 2018, 2Craig et al Lancet 2023

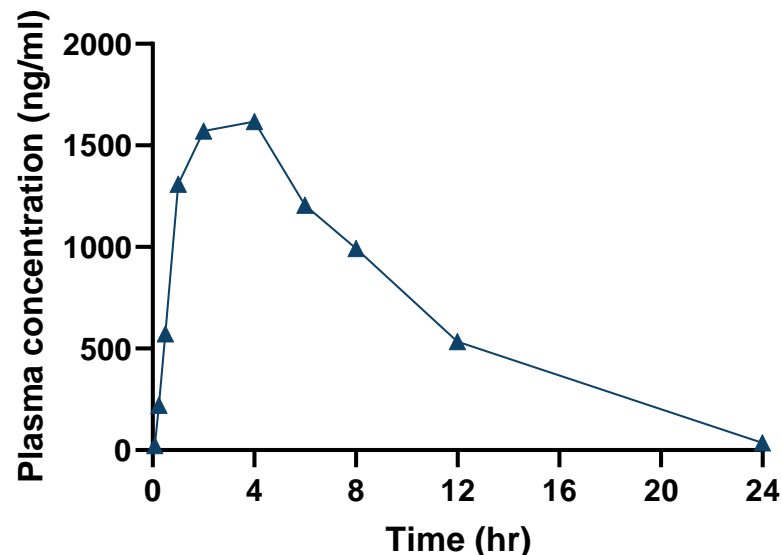
# KalVista Is Building A Portfolio Of Potent, Oral FXIIa Inhibitors

## High potency for FXIIa in multiple series

Compound	FXIIa IC <sub>50</sub> (nM)	Series
1	10	A
2	9.7	A
3	12	B
4	1.9	B
5	7.8	C
6	7.5	C
7	3.5	C
8	2.7	C

- High potency and >1000-fold selectivity against other proteases
- Oral profiles consistent with once-daily dosing in humans
- Multiple distinct series reduce risk, yield broader IP and support development for multiple indications

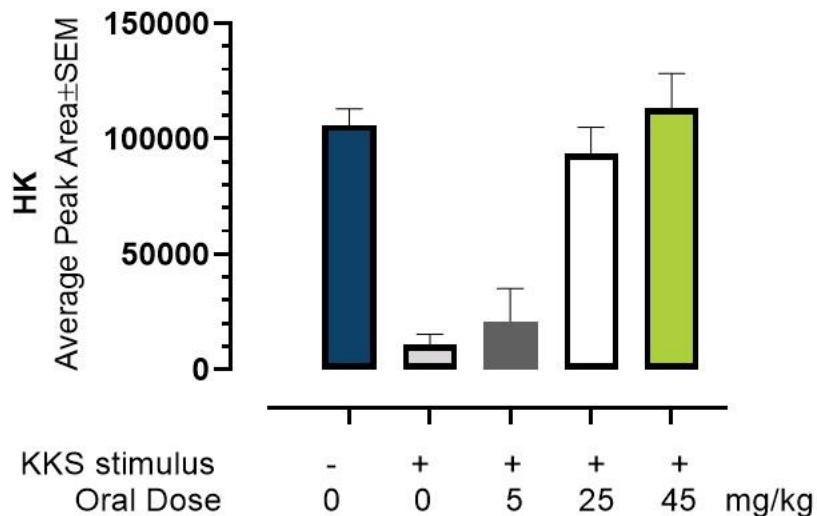
## Plasma exposure following oral dosing in rats





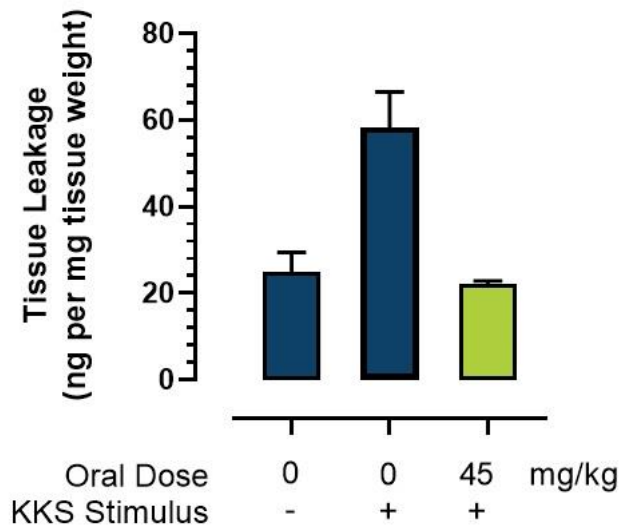
# Orally Delivered FXIIa Inhibitor Blocks Kallikrein-Kinin System Effects In Mouse Models Of Angioedema

**Blocks cleavage of kininogen and release of bradykinin<sup>1</sup>**



Carrageenan-stimulated paw edema model

**Prevents angioedema in HAE-related tissues<sup>2</sup>**



Angiotensin-converting enzyme inhibitor angioedema model

# Factor XIIa Inhibitor Program Is Advancing

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- Strong scientific rationale and positive clinical evidence for FXIIa inhibition in HAE prophylaxis
- KalVista is advancing the first oral FXIIa inhibitors towards the clinic – no known competitors in oral therapy
- FXIIa implicated in other indications that may represent large future opportunities, including thrombosis and inflammation
- Program IND timing adjusted in July 2023 due to compound-specific potential for drug-drug interaction challenges identified with lead candidates
  - Newer compounds have been developed that avoid this liability, optimization now ongoing

# KalVista Value Proposition

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- The only company developing distinct oral treatments for the full spectrum of HAE disease management
- Sebetralstat on-demand phase 3 KONFIDENT data expected early 2024, NDA H1 2024
- Sebetralstat would be the first oral on-demand therapy and has market transformation potential
- Oral FXIIa inhibitor program future growth opportunity
  - Initial development in HAE prophylaxis, based on clinical validation of target and high unmet need
  - FXIIa also has potential in large market opportunities in other therapeutic areas, including inflammation and thrombosis
- Funded into 2025



**NASDAQ: KALV**

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