



KalVista
Pharmaceuticals

Corporate Overview

January 2023



Forward-Looking Statements

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Company Highlights

- Discovery, development, and commercialization of oral, small molecule protease inhibitors, with an initial focus on orphan disease hereditary angioedema (HAE)
- Enrolling Phase 3 KONFIDENT trial of sebetralstat as first oral on-demand treatment for HAE
 - Data anticipated H2 2023, NDA H1 2024
- Preclinical oral Factor XIIa program represents next stage of growth
 - Initial development as next generation HAE oral prophylaxis, advancing towards IND
 - Further implicated in thrombosis and other large market indications under evaluation
- All programs internally developed, with full rights and IP protection to at least late-2030s
- Funded to 2025
 - \$122 million cash at 10/31/22 and \$58 million registered direct offering completed December 2022

Program Portfolio

Product	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Status
Sebetralstat	On-Demand HAE	KONFIDENT				• Trial enrolling
		KONFIDENT-S (Open Label Extension)				• Trial enrolling
		Orally Disintegrating Tablets				• PK profile supports advancement towards sNDA
KVD824	HAE Prophylaxis	KOMplete				• Trial terminated October '22
KVD001 (IVT)	Diabetic Macular Edema					• Trial completed
Oral Factor XIIa	HAE Prophylaxis					• IND targeted for 2023
Oral Factor XIIa	Thrombosis, inflammation					• Future opportunities under evaluation



Hereditary Angioedema (HAE)

Hereditary Angioedema (HAE)

- Genetic condition causing painful and dramatic swelling in various parts of the body
 - Primarily caused by defect in C1 inhibitor activity which leads to uncontrolled plasma kallikrein activity and excessive bradykinin release
- Orphan disease: incidence 1 in 10,000 to 1 in 50,000¹
 - Minimum of 6,500 – 8,000 patients in US; similar in EU
 - Incidence appears to be consistent worldwide; average patient has ~2 attacks/month
- Approved therapies are primarily injected/infused - high unmet need for efficacious oral administration
- Total HAE market approximately \$2 billion annual revenues in 2019; \$4 billion 2026²
 - US and Europe primary existing markets; rest of world substantially underdiagnosed and treated
 - Generics in US have reduced total on-demand market revenues, though scripts remain steady

KalVista Oral Candidates Treat the Full Spectrum of HAE

Sebetralstat: On-demand/ Breakthrough Treatment



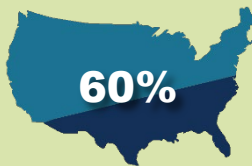
~40% of US market;
~85% in EU

Stable market share in both
US (patient preference) and
EU (limited prophylaxis use)

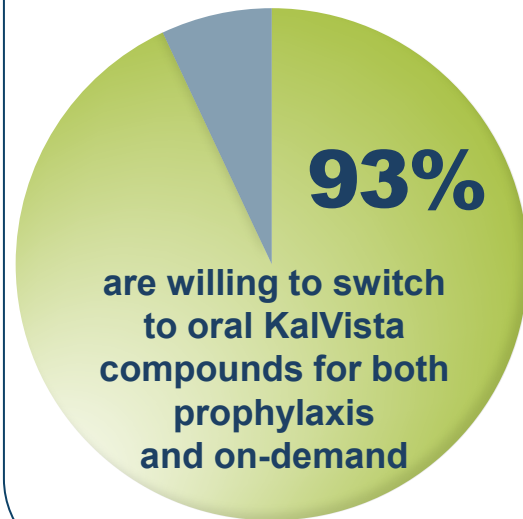
Approximately 100,000 treatable
annual attacks in US; 150,000 in
Europe

Factor XIIa inhibitor: Prophylaxis

~60% in US
~15% in EU



PATIENTS



Branded HAE Market Estimated to be \$4B Revenues by 2026

On-demand/ Breakthrough Treatment

7% CAGR

~\$800M
WW

2020

>\$1.2B
WW

E2026

Prophylaxis

15% CAGR

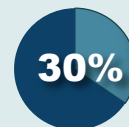
>\$1.3B
WW

2020

>\$2.8B
WW

E2026

Additional Market Growth



Untreated

Over 30% of patients do not treat every attack



Undiagnosed

30-60% globally



Normal C1 HAE
(currently **no treatments**)



Sebetralstat: HAE On-Demand Therapy

Sebetralstat: Changing the Paradigm for HAE Treatment

- All current on-demand options are injectable and have significant shortcomings
 - Icatibant (Firazyr and generic) is overwhelming market leader but administration can be painful and challenging
 - Other major therapies are IV delivery which is even more challenging and inconvenient
- Early treatment improves outcomes but under-treatment and late treatment are common
 - In a real-world study with Firazyr only 40% of attacks were treated within one hour¹
 - Out of 6277 attacks recorded 53-67% remained untreated²
- In addition, most prophylaxis treatments are injectable and patients still have breakthrough attacks
 - All prophylaxis therapies are injected with one exception
- Sebetralstat is intended to reduce the barriers to on-demand treatment
 - Potential to improve treatment outcomes and increase the number of attacks treated on-demand
 - Attractive profile for both current on-demand **and** prophylaxis patients

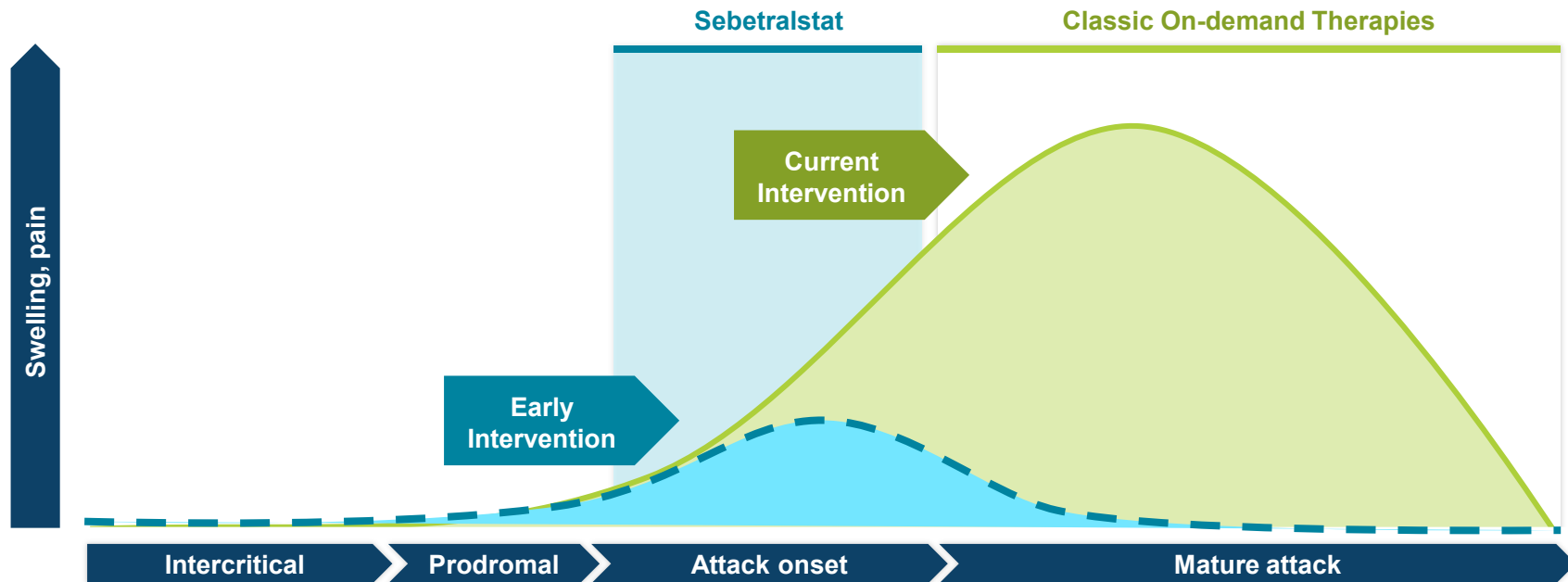
¹Maurer M, et al. Hereditary Angioedema Attacks Resolve Faster and Are Shorter after Early Icatibant Treatment. PLoS ONE. 2013;8(2):e53773.

²Longhurst H J et al. Real-world outcomes in hereditary angioedema: first experience from the Icatibant Outcome Survey in the United Kingdom Allergy, Asthma & Clinical Immunology volume 14, Article number: 28 (2018)

The Sebetralstat Treatment Vision

- Enable treatment of all attacks according to current guidelines
- Patients take sebetralstat at first symptoms of an attack
 - Act while symptoms are mild and swelling has not yet progressed significantly
- Attack development is halted in its earliest stages
- Sebetralstat dosing is straightforward and simple
 - Expected to be 1 or 2, 300 mg tablets, contained in an easy-to-access, individual package
 - Final formulation, including color and coating, already developed and patient-friendly
 - Easy to store, easy to carry, easy to take – dramatically different from icatibant or other injectables
- Oral disintegrating tablet (ODT) further enhances treatment options
 - Particularly valuable for younger patients or those with difficulty swallowing – 15 second dissolution
 - Phase 1 data announced October 2022, regulatory plan under development

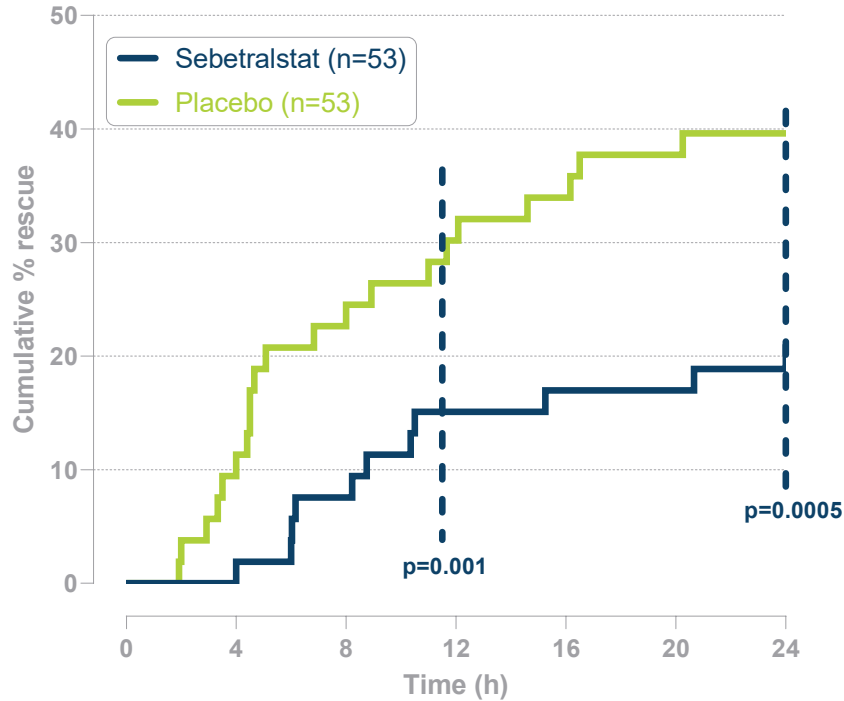
“Flattening the Curve” of HAE Attack Progression With Early Initiation of On-demand Therapy



Positive Sebetralstat Phase 2 Clinical Trial Results

- Sebetralstat met all primary and secondary endpoints
 - Including endpoint being used as primary in ongoing KONFIDENT Phase 3 study
- Sebetralstat enables early intervention and maximises 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 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

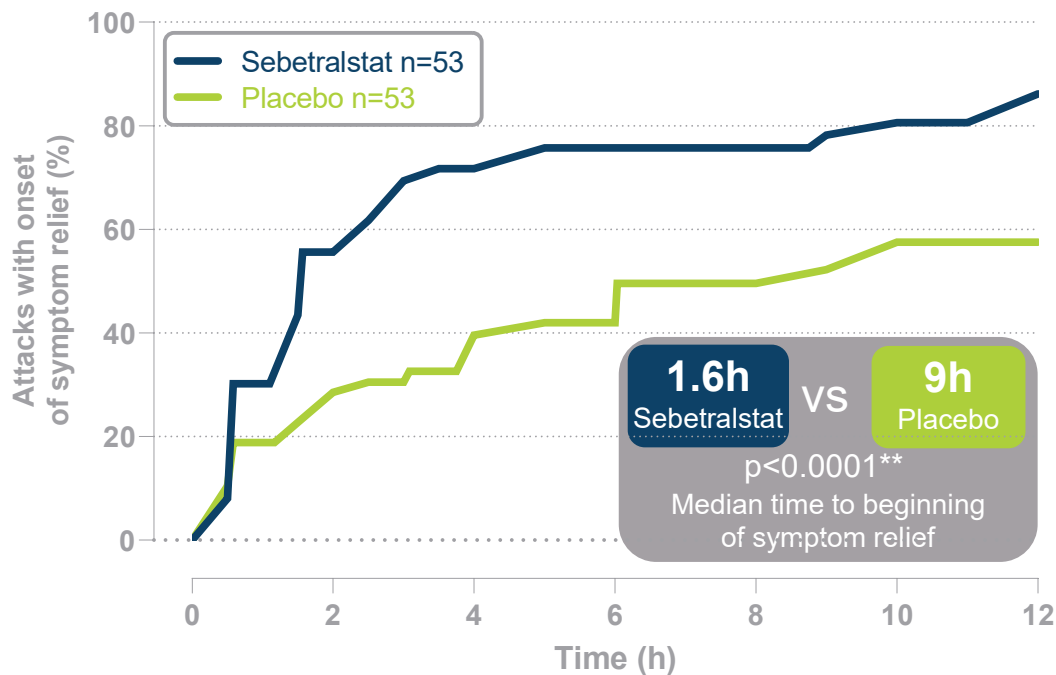


- Sebetralstat significantly increased time to rescue within 12 hours: $p=0.001^*$
 - Placebo 30.2%
 - Sebetralstat 15.1%
- Efficacy maintained at 24 hours
 - $p=0.0005^*$

*Gehan's Generalized Wilcoxon Test

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**

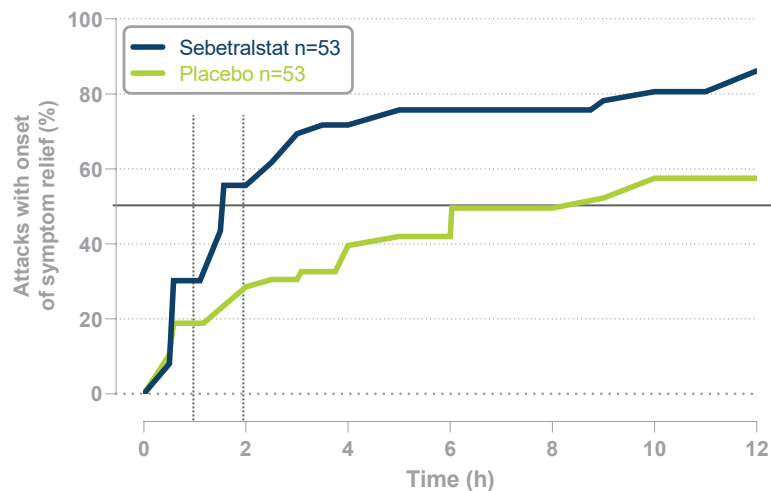


****Gehan's Generalized Wilcoxon Test Full analysis set**
Censoring occurs where HAE attack was not rated "a little better" or higher or conventional attack treatment was used within 12h
Data on File. KalVista Pharmaceuticals, Inc.

Sebetralstat Symptom Relief Time Similar to IV Injected Ruconest (rC1-INH)

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

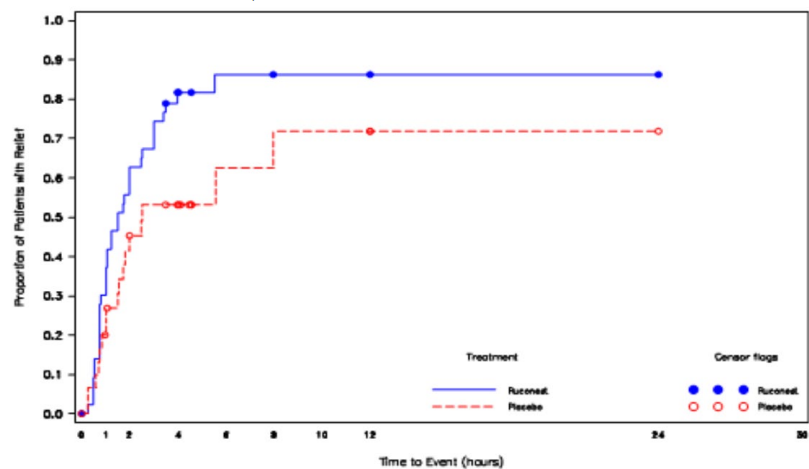
Patient Global Impression of Change (PGI-C)



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

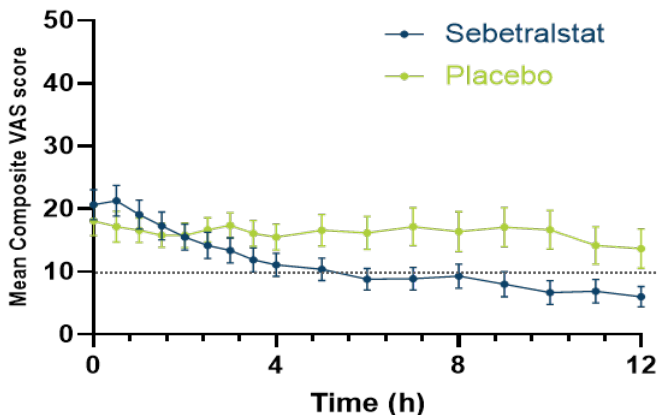
Ruconest data from Charles M. Maplethorpe, MD, PhD. Clinical Reviewer. Summary Basis of Approval, Recombinant C1 Esterase Inhibitor, STN: 125495/0.

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 VAS Reduction and Firazyr (icatibant)

Although VAS is not recommended by FDA it was previously used in phase 3 trials

- Early treatment with sebetralstat
 - Consistent with HAE treatment recommendations
 - Minimizes symptom scores
- Delayed treatment with icatibant
 - Delayed treatment leads to increased symptom scores before and after treatment



Firazyr data from Lumry et al., Ann Allergy Asthma Immunol. 2011;107:529–537. The results of the trials for sebetralstat and Firazyr may not be directly comparable, as they are not from a single head-to-head clinical trial

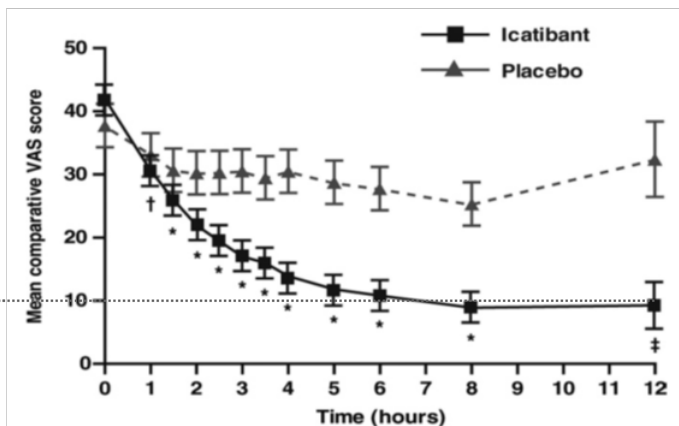
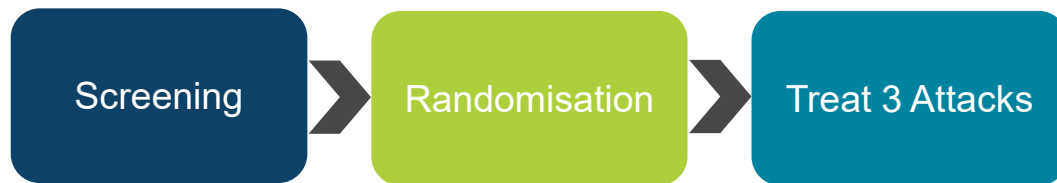


Figure 3. Mean composite VAS-3 score for the first 12 hours after treatment (nonlaryngeal ITT population). * $P \leq .001$; $^{\dagger}P = .003$; $^{\ddagger}P = .041$, vs placebo. Sixteen subjects (icatibant $n = 5$; placebo $n = 11$) who had not achieved relief by hour 8 had nonmissing data for hour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

Sebetralstat Phase 3 Trial Design



- Double-blind, 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 re-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:

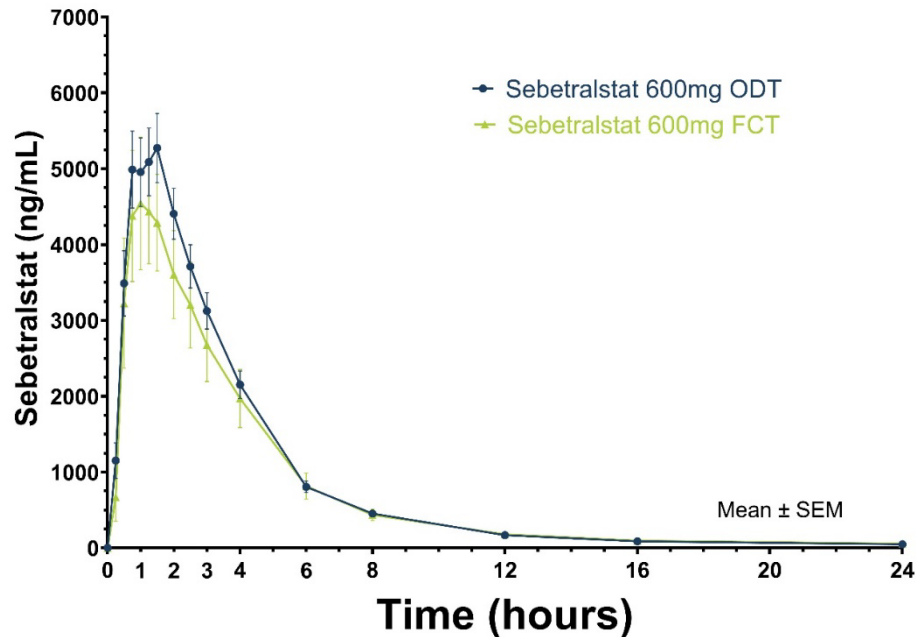
- Time to improvement (PGI-S)
- Time to resolution (PGI-S)

Sebetralstat Phase 3 Trial Design

- The KONFIDENT trial will complete at least 84 patients
 - 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 endpoint
- At least 90% power to detect the phase 2 treatment effect
- First patient recruited March 2022; Data anticipated H2 2023, NDA filing H1 2024

Orally Disintegrating Tablet 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)
- Regulatory interactions initiated to determine approval pathway & timing
- Expected to be lifecycle extension in US & EU; potentially launch formulation in other geographies

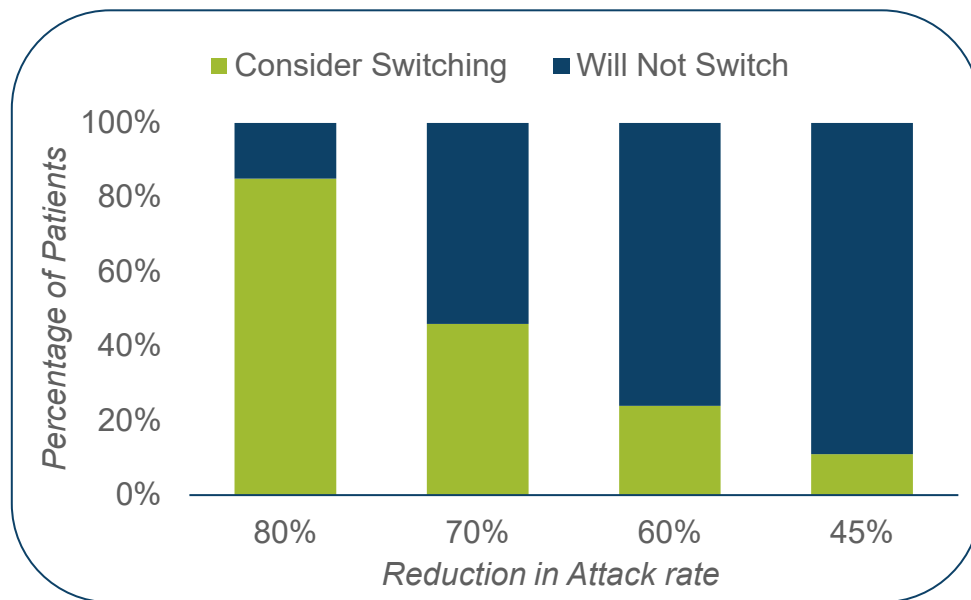




Factor XIIa

Oral Factor XIIa Designed to Meet Unmet Need in HAE Prophylaxis

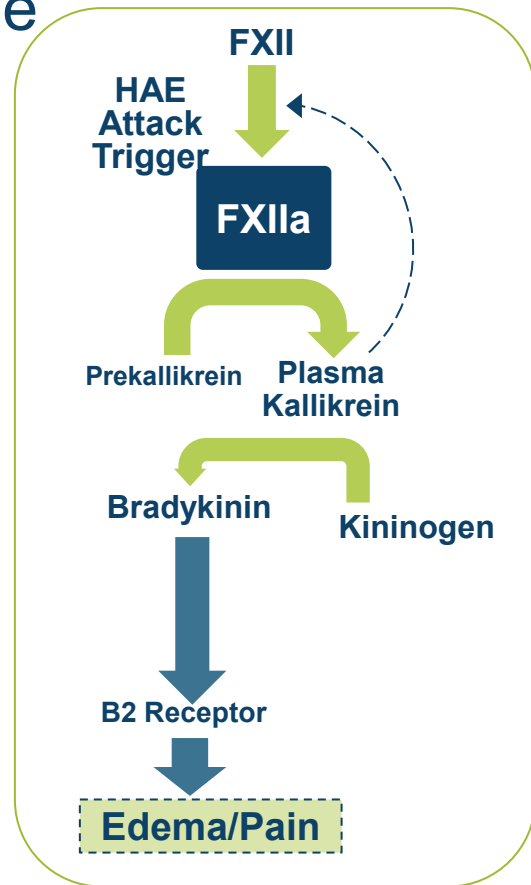
Patients will not trade lower efficacy for oral dosing



Our goal is to achieve an oral treatment with an efficacy profile similar to injectable treatments

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
- Bradykinin generated by the plasma kallikrein kinin system causes edema and pain in HAE attacks
 - 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
- Factor XIIa likely plays a role in other diseases

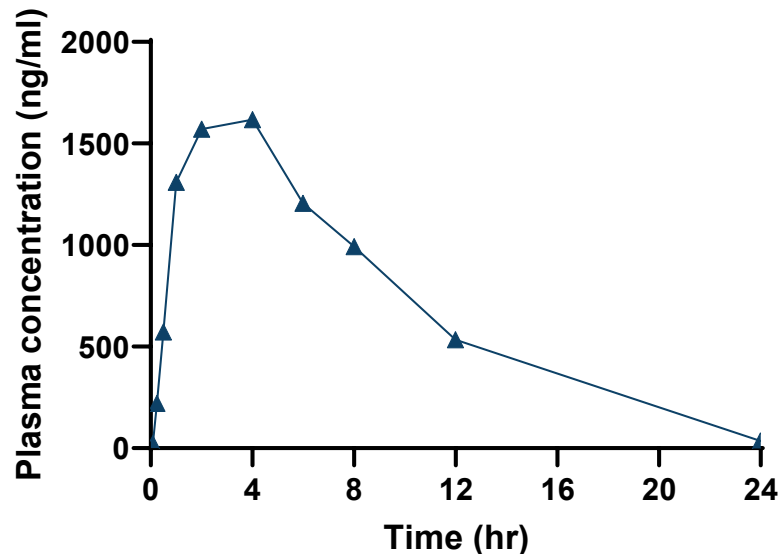


KalVista is Building a Portfolio of Potent, Oral FXIIa Inhibitors

High potency for FXIIa in multiple series

Compound	FXIIa IC ₅₀ (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

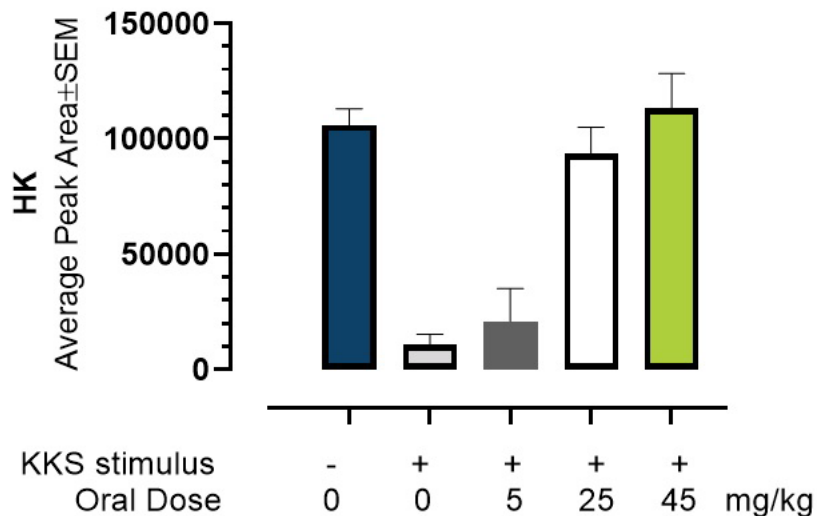
Plasma exposure following oral dosing in rats



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

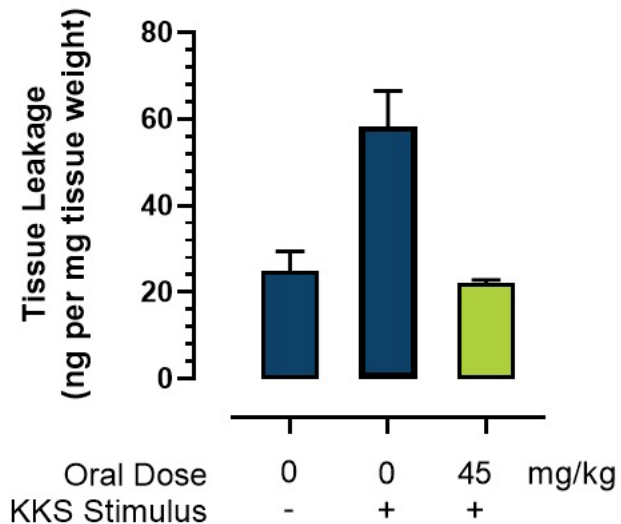
Orally delivered Factor Xlla Inhibitor blocks Kallikrein-Kinin System effects in mouse models of angioedema

Blocks cleavage of kininogen and release of bradykinin



Carrageenan-stimulated paw edema model

Prevents angioedema in HAE-related tissues



Angiotensin converting enzyme inhibitor angioedema model

Factor XIIa Inhibitor Program is Advancing Towards IND

- Strong scientific rationale and positive clinical evidence for FXIIa inhibition in HAE prophylaxis
 - Factor XIIa is at the top of the kallikrein-kinin system
 - Inhibitors block the activation of plasma kallikrein and thereby the generation of bradykinin
- KalVista is advancing the first oral FXIIa inhibitors towards the clinic – no known competitors in oral therapy
- Factor XIIa implicated in other indications that may represent large future opportunities, including thrombosis and inflammation
- IND targeted for 2023

KalVista Value Proposition

- The only company developing distinct oral treatments for the full spectrum of HAE disease management
- Sebetralstat: on-demand Phase 3 KONFIDENT clinical trial enrolling
 - Data expected H2 2023, NDA H1 2024
- Oral Factor XIIa inhibitor program the next substantial growth opportunity
 - Initial development in HAE prophylaxis, based on clinical validation of target and high unmet need
 - Factor XIIa also has potential in large market opportunities in inflammation and thrombosis
- Funded to 2025



NASDAQ: KALV