



KalVista
Pharmaceuticals

Corporate Overview

October 2022



Forward-Looking Statements

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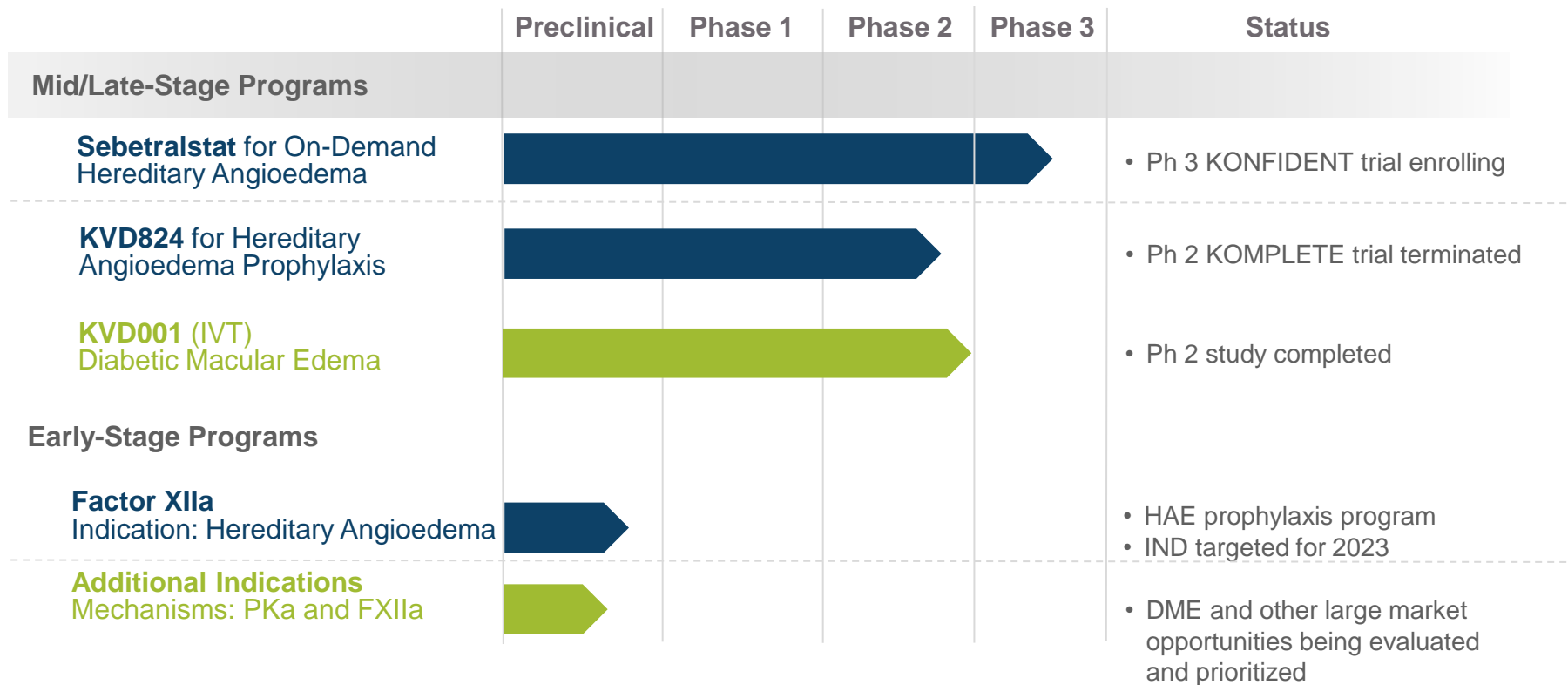
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Company Highlights

- Discovery, development, and commercialization of oral, small molecule protease inhibitors, with an initial focus on orphan disease hereditary angioedema (HAE) and large market opportunity diabetic macular edema (DME)
- Only Company developing a franchise of distinct oral treatments for HAE
 - Sebetralstat as on-demand therapy, Phase 3 KONFIDENT trial enrolling
 - Factor XIIa program as next generation oral prophylaxis therapy, IND targeted for 2023
- KVD824 Phase 2 clinical trial terminated in October 2022
 - ALT/AST elevations noted in KOMLETE trial; data to be analyzed for potential next steps
- All programs internally developed, with full rights and IP protection to at least late-2030s
- \$142 million cash as of July 31, 2022; funded to at least early 2024

Product Portfolio





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
- All but one approved therapies are 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



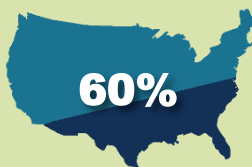
~40% of US market;
~85% in EU

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

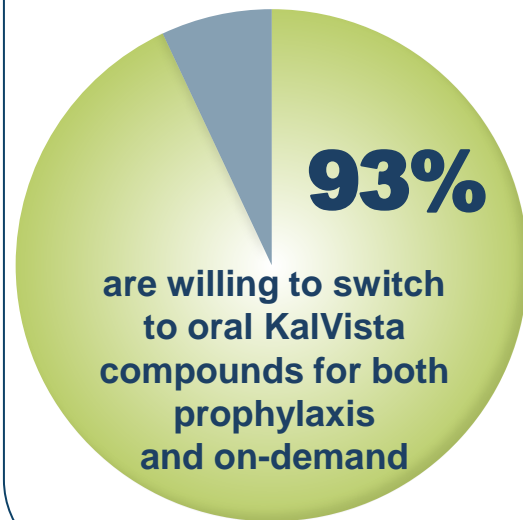
Approximately 100,000 treatable
annual attacks in US; 150,000 in
Europe

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 On-Demand Treatment

- All approved on-demand options have significant shortcomings
 - Firazyr (branded and generic) is overwhelming market leader, but SC delivery is painful and challenging under acute conditions
 - Other major therapies are IV delivery, which is even more challenging and inconvenient
- Early treatment improves outcomes but undertreatment and late treatment are common
 - In real world study of Firazyr, treatment administration within one hour of attack onset significantly reduced attack duration¹. HAE guidelines also state that early treatment of all attacks are essential to optimize attack outcomes²
 - But less than 40% of treated attacks dosed within one hour; 30% weren't treated until >5 hours
 - Patient histories showed that 45% of attacks weren't treated at all
- Sebetralstat is intended to reduce the barriers to treatment
 - Enable earliest intervention to improve treatment outcomes for patients

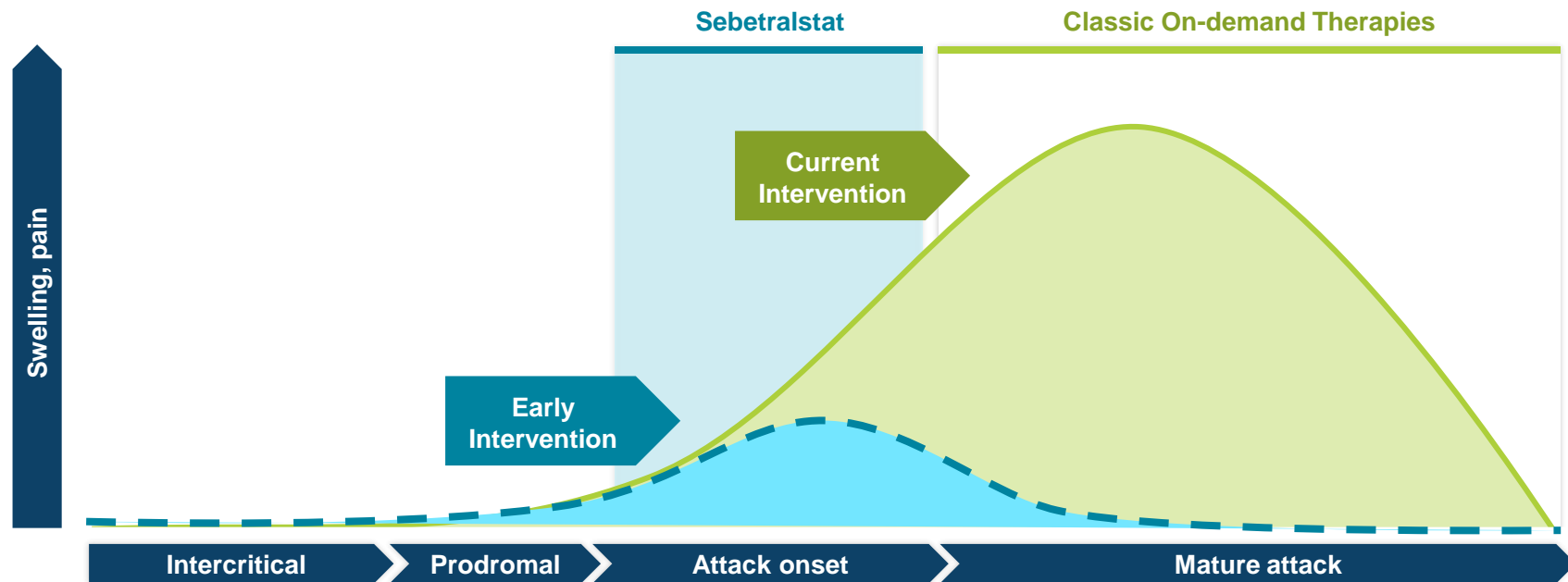
1. Maurer M, et al. Hereditary Angioedema Attacks Resolve Faster and Are Shorter after Early Icatibant Treatment. PLoS ONE. 2013;8(2):e53773.

2. Busse P, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema

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

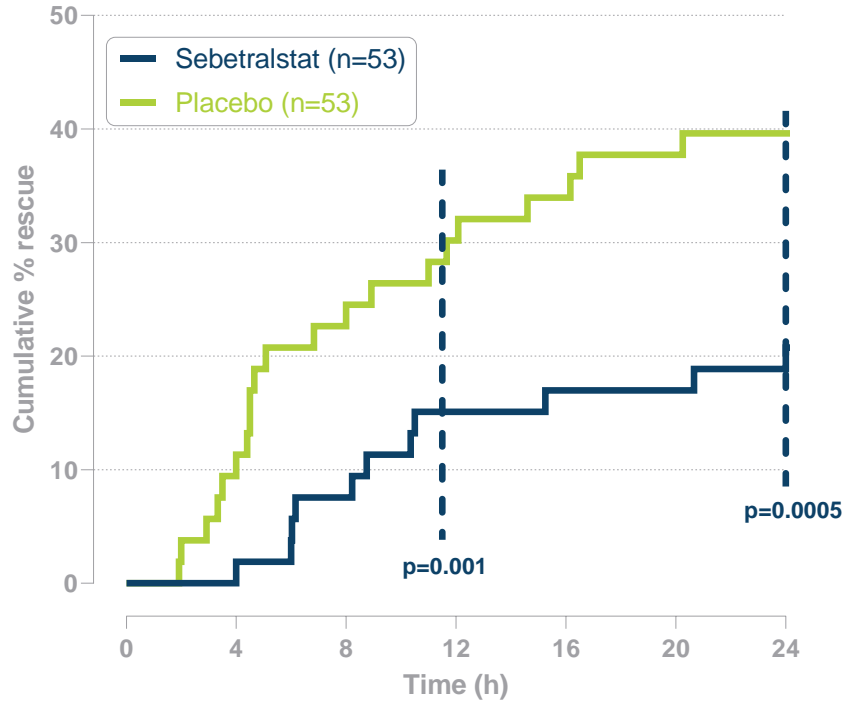
“Flattening the Curve” of HAE Attack Progression With Early Initiation of On-demand Therapy



Positive Sebetralstat Phase 2 Clinical Trial Results

- Primary endpoint statistically significant $p=0.001$
 - Reduced rescue use over 12 and 24 hours
- 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 Endpoint

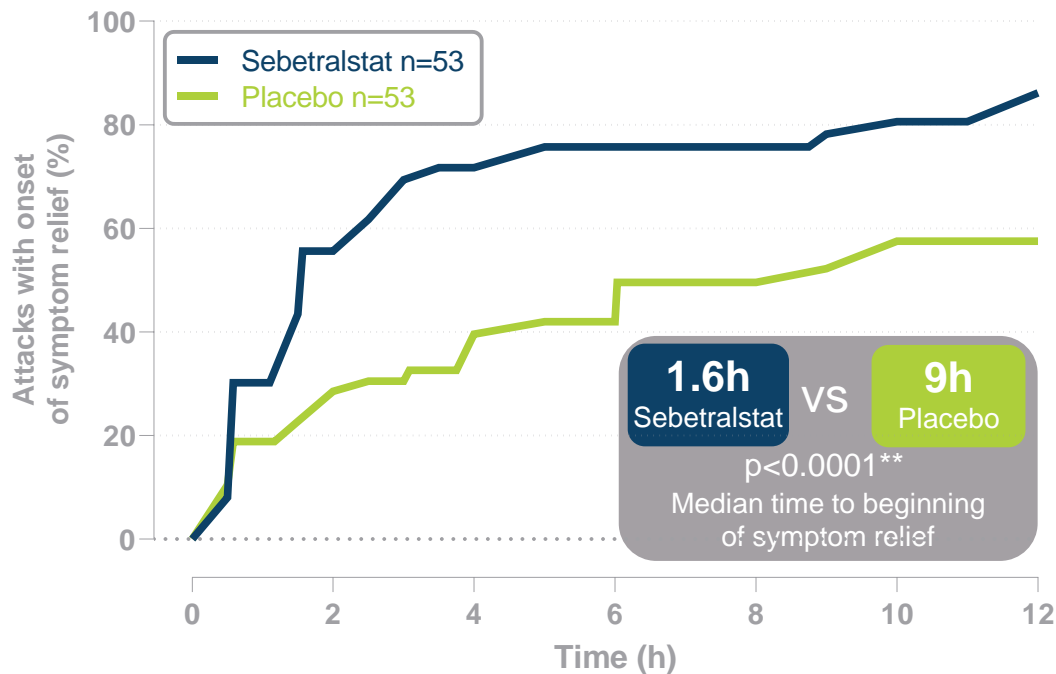


- Sebetralstat significantly reduced time to rescue within 12 hours: $p=0.001^*$
 - Placebo 30.2%
 - Sebetralstat 15.1%
- Efficacy maintained at 24 hours
 - $p=0.0005^*$

*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**

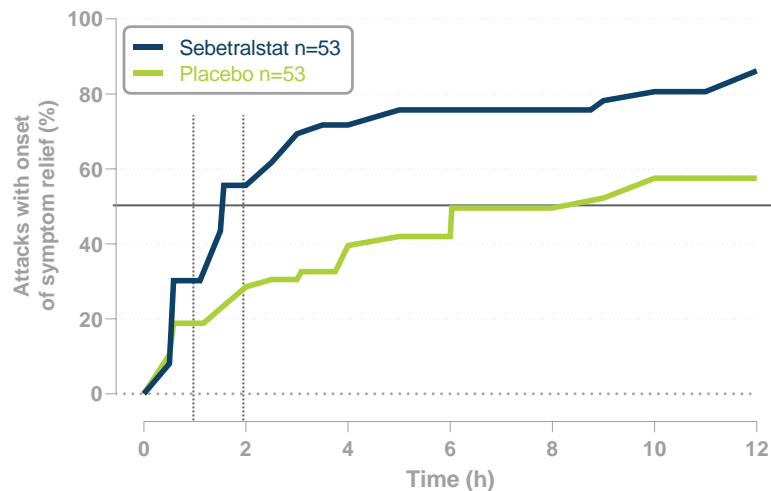


****Gehan's Generalized Wilcoxon Test Full analysis set**
Censoring occurs where HAE attack was not rated "a little better" or higher or conventional attack treatment was used within 12h
Data on File. KalVista Pharmaceuticals, Inc.

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

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

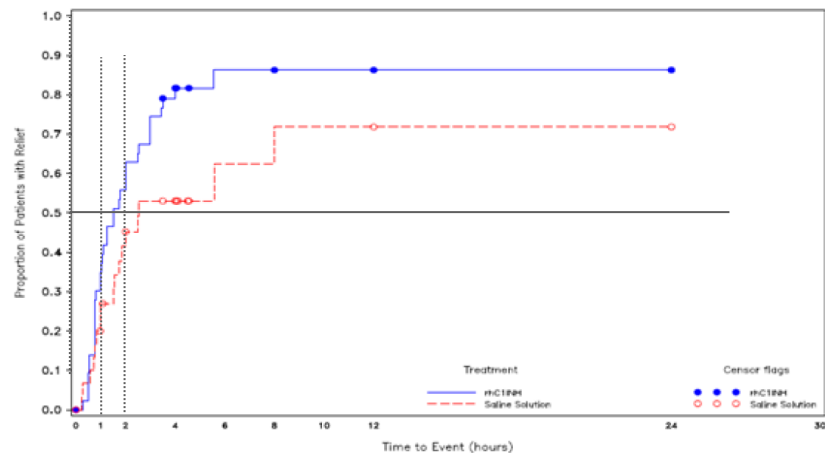
Patient Global Impression of Change (PGI-C)



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.

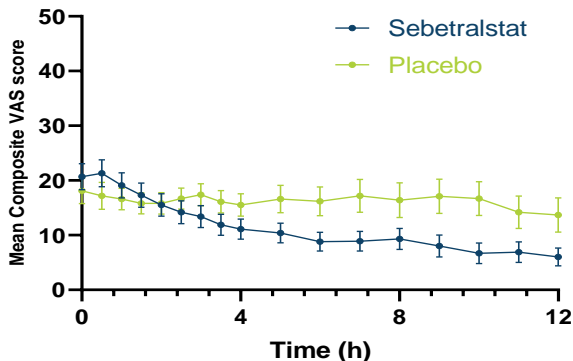
The results of the trials for sebetralstat and Ruconest may not be directly comparable, as they are not from a single head-to-head clinical trial

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

- Key benefit of oral therapy
- Consistent with HAE treatment recommendations
- Minimizes overall symptoms experienced



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

- Delayed treatment with icatibant

- Phase 3 data reflects requirement for attacks to progress significantly prior to treatment – undesirable in real world
- Even outside of clinical trial, injections are often delayed
- Delay is known to increase overall attack symptoms

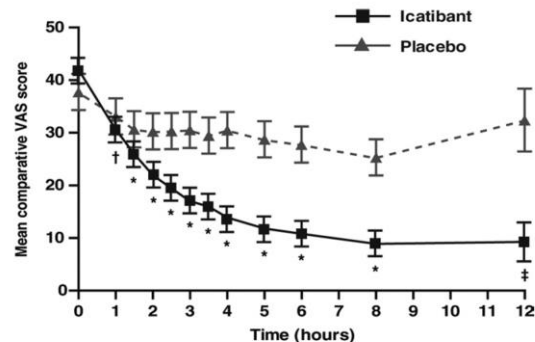


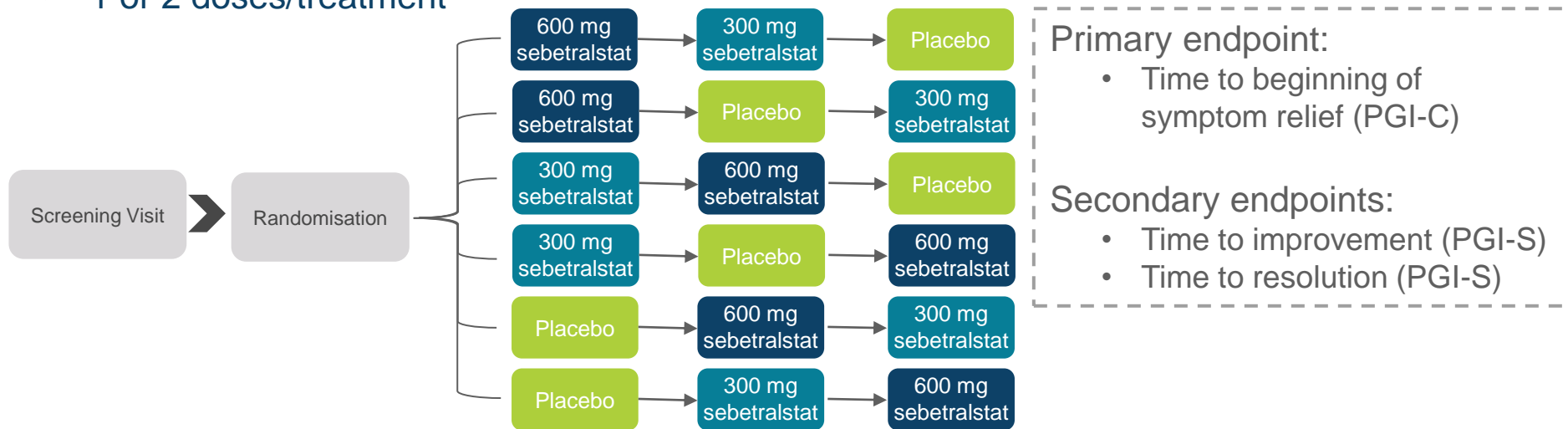
Figure 3. Mean composite VAS-3 score for the first 12 hours after treatment (nonlaryngeal ITT population). * $P \leq .001$; [†] $P = .003$; [‡] $P = .041$, vs placebo. Sixteen subjects (icatibant $n = 5$; placebo $n = 11$) who had not achieved relief by hour 8 had nonmissing data for hour 12.

Sebetralstat Phase 3 KONFIDENT Trial Underway

- Complete at least 84 patients
 - Double-blind, 3-way crossover trial assessing 300 mg, 600 mg and placebo
 - Supporting broad label including adolescents, prophylaxis patients and laryngeal attacks
- Worldwide recruitment in approximately 60 sites in 20 countries
- FDA agreed primary endpoint: time to beginning of symptom relief using PGI-C
 - FDA does not recommend use of VAS as primary endpoint
 - Patients allowed to re-dose if symptoms warrant, with no statistical impact
 - Expected to be sufficient to file NDA
- At least 90% powered to detect the phase 2 treatment effect
- Anticipating data H2 2023, NDA H1 2024

Sebetralstat Phase 3 Trial Design

- N = 84
- Six sequences
- 1 or 2 doses/treatment



KONFIDENT will be conducted at approximately 60 sites in 20 countries



KVD824: Summary

KVD824 and Phase 2 KOMplete Trial

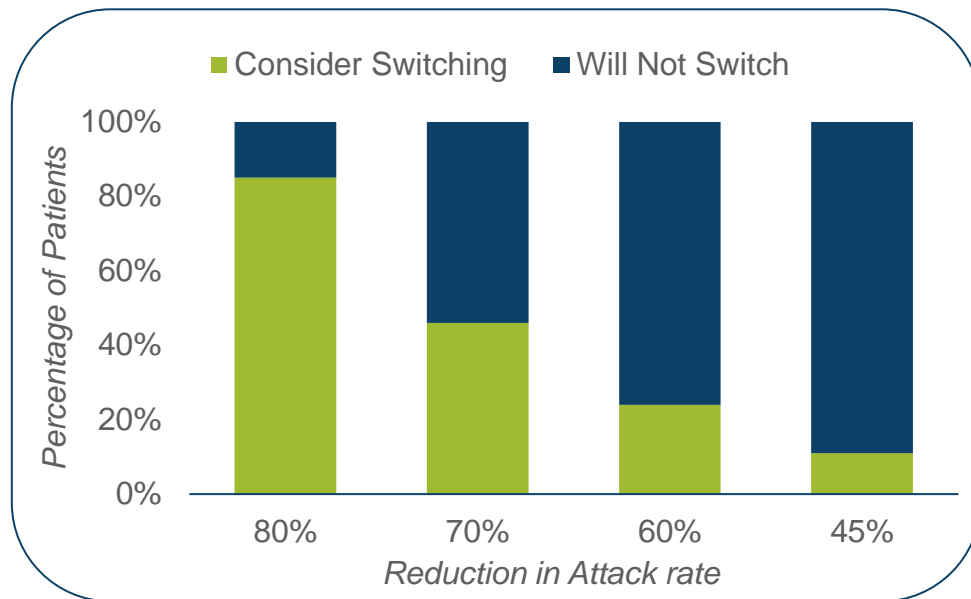
- KOMplete trial was terminated based on the observation of elevations of liver enzymes (ALT/AST) across multiple patients in all treatment groups of the study
 - 33 patients enrolled in study: 7 experienced either Grade 3 or Grade 4 elevations of liver enzymes at timeframes ranging from two to twelve weeks
 - No patients had concomitant elevation of bilirubin levels and all were asymptomatic
- Current formulation did not meet our requirements for a best-in-class oral prophylactic HAE therapy
- KalVista will finalize the database of the study and assess the unblinded data for efficacy and safety to determine the potential for any further development
- No impact on sebetralstat development; KVD824 is a distinct molecule



Factor XIIa

Factor XIIa Designed to Meet Unmet Need in Oral Prophylaxis

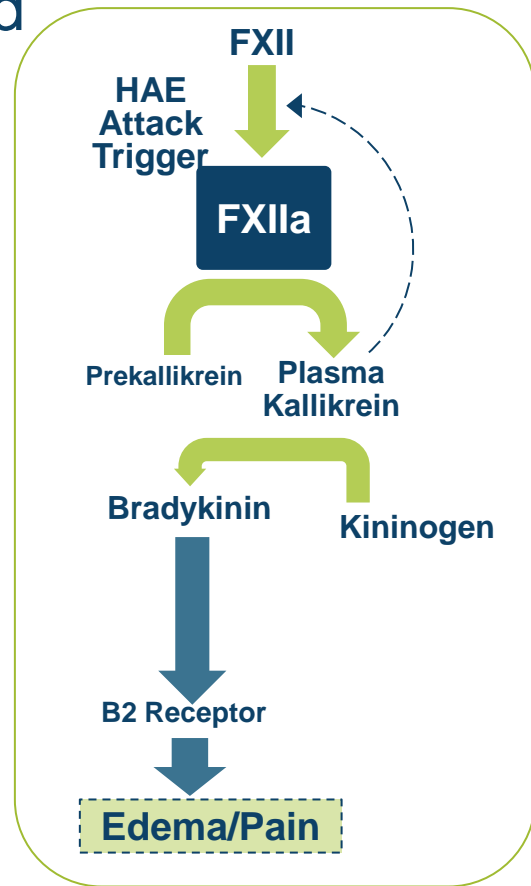
Patients will not trade lower efficacy for oral dosing



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

Future of the Oral HAE Franchise and Beyond

- Factor XIIa (FXIIa) sits at the top of the contact system
 - Activates plasma kallikrein leading to uncontrolled bradykinin release in HAE
- Bradykinin generated by the contact system causes edema and pain in HAE attacks
 - FXIIa and plasma kallikrein inhibitors are selective for contact system bradykinin, unlike bradykinin antagonists
- Clinical studies of Factor XIIa antibodies reduce HAE attack frequency
 - At least as efficacious as approved therapies
 - No known chronic safety implications
- Factor XIIa likely plays a role in other diseases

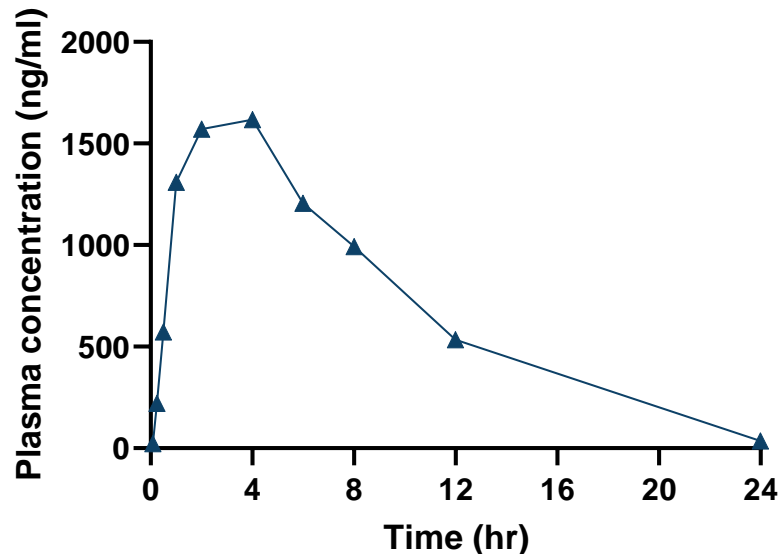


KalVista is Building a Portfolio of Potent, Oral FXIIa Inhibitors

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

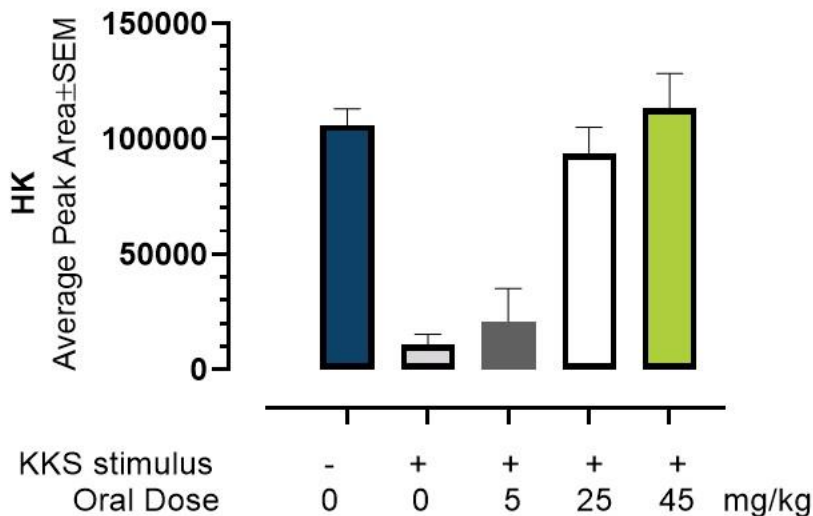
Plasma exposure following oral dosing in rats



- 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

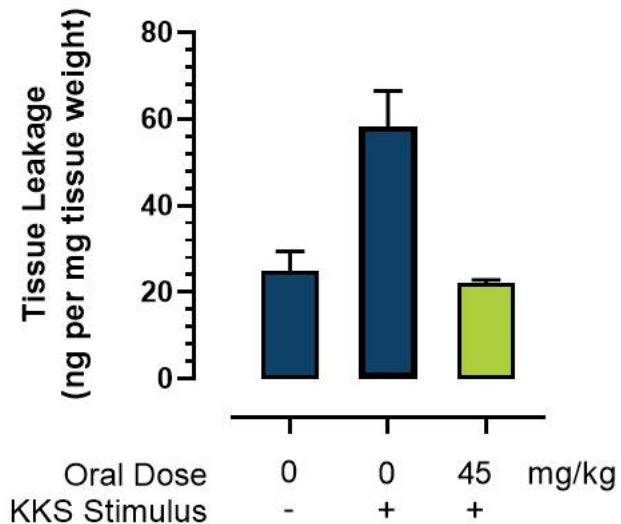
Orally delivered Factor Xlla Inhibitor blocks Kallikrein-Kinin System effects in mouse models of angioedema

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 cascade
 - Inhibitors block the activation of plasma kallikrein and thereby the generation of bradykinin
- KalVista is advancing the first oral FXIIa inhibitors for HAE – no other known competitors in oral therapy
- Oral Factor XIIa inhibitors have additional potential commercial opportunities
- 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
 - Factor XIIa prophylaxis program the next generation of oral HAE prophylaxis: IND 2023
- Factor XIIa also has potential in large market opportunities in inflammation and thrombosis
- Funded to at least early 2024



NASDAQ: KALV