



KalVista
Pharmaceuticals

Corporate Presentation

July 2021



Forward-Looking Statements

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Any forward-looking statement made by us in this presentation and the accompanying oral presentation is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise. Certain information contained in this presentation may be derived from information provided by industry sources. We believe such information is accurate and that the sources from which it has been obtained are reliable. However, we cannot guarantee the accuracy of, and have not independently verified, such information.

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Company Highlights

- Discovery, development, and commercialization of 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 oral treatments for HAE:
 - KVD900 as on-demand therapy, Phase 2 trial showed statistical significance; FDA EOP2 meeting late Q3 2021
 - KVD824 for prophylaxis, Phase 2 planned with FDA response submission for clinical hold expected Q3 2021
 - Factor XIIIa program as next generation of oral therapy, IND enabling studies in 2021
- KVD001 Phase 2 in patients with DME complete; next steps being evaluated
- Internal discovery and development capabilities enable high productivity and strong IP positions
- Cash position: \$248.9 million as of April 30, 2021

Product Portfolio

	Preclinical	Phase 1	Phase 2	Phase 3	Status
Mid Stage Programs					
KVD900 for On-Demand Hereditary Angioedema					<ul style="list-style-type: none"> EOP2 meeting late Q3 2021
KVD824 for Hereditary Angioedema Prophylaxis					<ul style="list-style-type: none"> Phase 2 planned
KVD001 (IVT) Diabetic Macular Edema					<ul style="list-style-type: none"> Phase 2 study completed
Early Stage Programs					
Factor XIIa Indication: Hereditary Angioedema					<ul style="list-style-type: none"> IND enabling studies in 2021
Oral DME Molecules Target: Plasma Kallikrein					<ul style="list-style-type: none"> Regulatory studies ongoing



Hereditary Angioedema (HAE)

Hereditary Angioedema (HAE)

- Genetic condition causing painful and dramatic swelling in various parts of the body
- Orphan disease: incidence 1 in 10,000 to 1 in 50,000¹
- Primarily caused by defect in C1 inhibitor activity which leads to uncontrolled plasma kallikrein activity and excessive bradykinin release
- 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
- We are developing a franchise of oral HAE therapeutics, to address unmet patient needs in both on-demand and prophylactic segments

KalVista Oral Candidates Treat the Full Spectrum of HAE

On-demand/ Breakthrough Treatment



~40% of US market;
90+% in EU

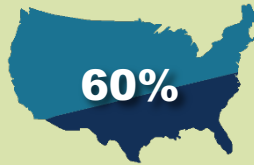
Only ~62% of HAE patients
treat all attacks



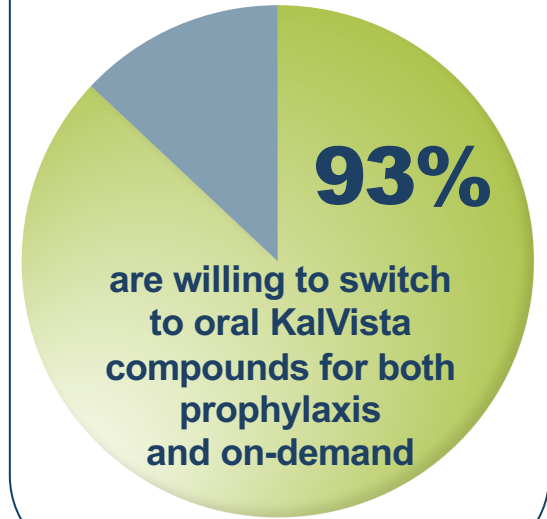
~70% of patients treat
the disease with both
prophylactic and
on-demand treatments

Prophylaxis

~60% in US
<10% 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

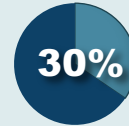
>\$1.3B
WW

2020

>\$2.8B
WW

E2026

Additional Market Growth



Untreated

Over 30% of patients do not treat every attack



Undiagnosed

30-60% globally

C1

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



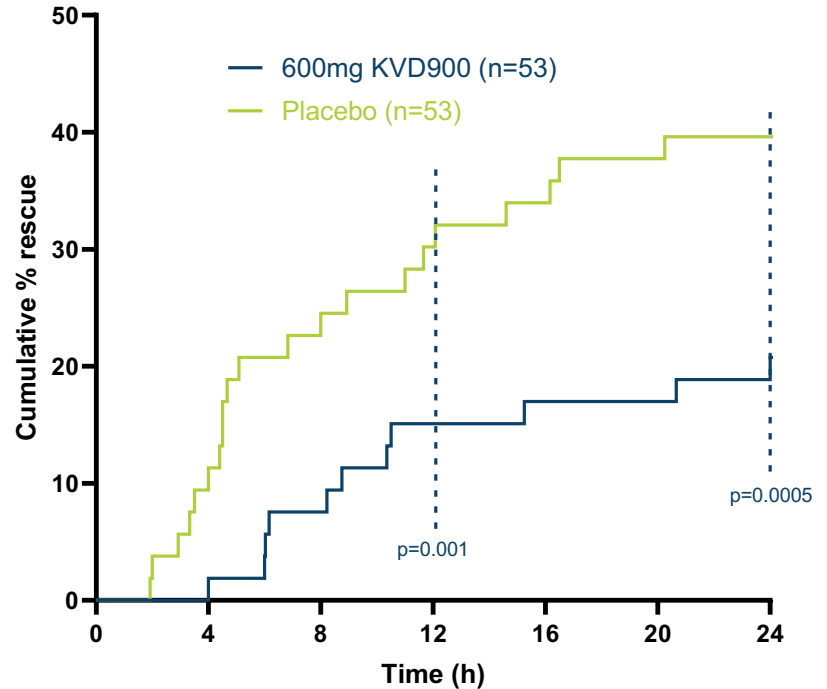
KVD900: HAE On-demand Therapy

Positive KVD900 Phase 2 Clinical Trial Results

- Primary endpoint was statistically significant $p=0.001$
 - Secondary endpoints all $p<0.0001$
- KVD900 rapidly suppresses circulating plasma kallikrein, halts attack progression, reduces symptoms and improves patient well-being
- KVD900 enables early intervention and improved treatment outcomes
 - Efficacy profile is fast and comparable with current injectable products
 - Patients feel better and symptoms resolve quickly with KVD900
- KVD900 is generally safe and well tolerated

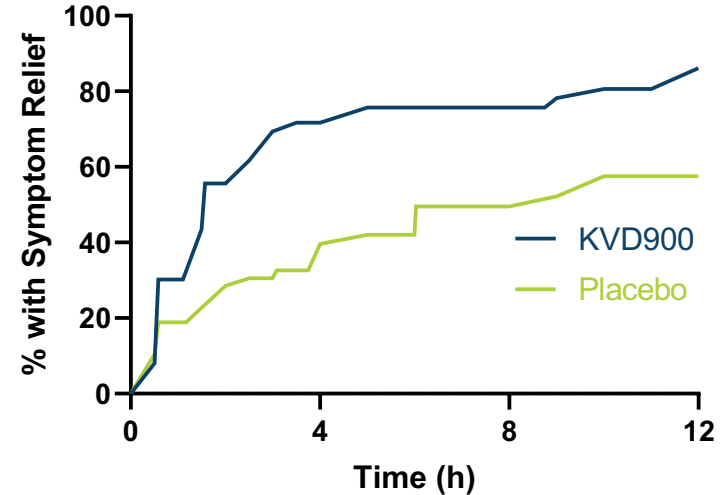
KVD900 Met its Primary Endpoint

- KVD900 significantly reduced use of rescue within 12 hours: $p=0.001^*$
 - Placebo 30.2%
 - KVD900 15.1%
- Efficacy maintained at 24 hours
 - $p=0.0005^*$



KVD900 Speeds Symptom Relief: Impression of Change

- KVD900 treated attacks achieved symptom relief more quickly: $p < 0.0001^*$
 - Patient Global Impression of Change (PGI-C)
 - Primary endpoint Ruconest phase 3
- Median time to symptom relief
 - KVD900 1.6 hours
 - Placebo 9 hours



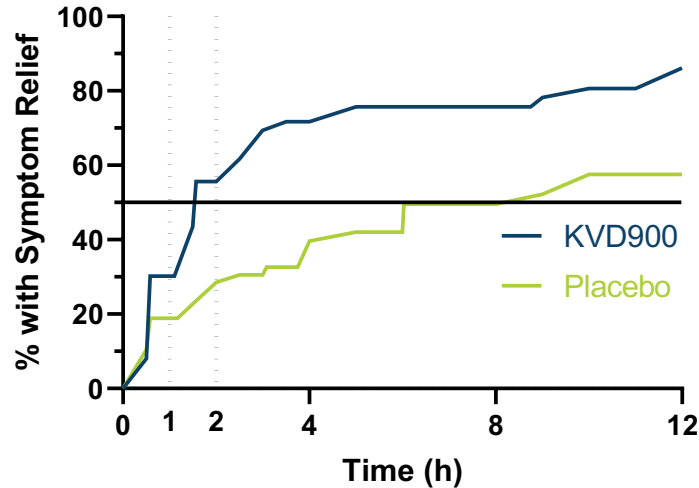
Symptom relief defined as attack rated a little better or higher for 2 consecutive time points

KVD900 Symptom Relief Time Similar to IV Injected Ruconest (rC1-INH)

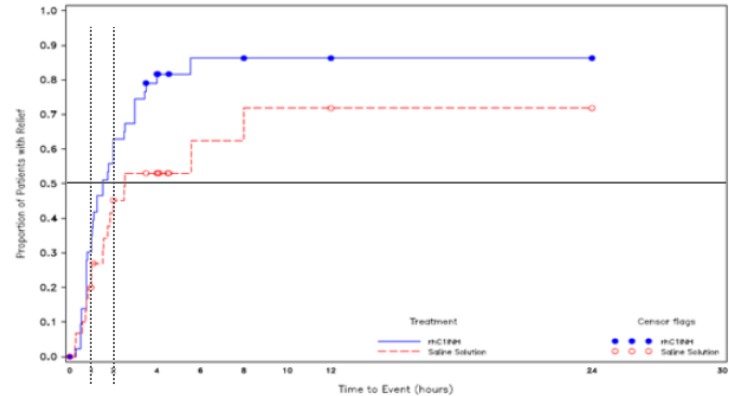
KVD900 1.6 hours

Ruconest 1.5 hours

Survival PGI-C (up%)

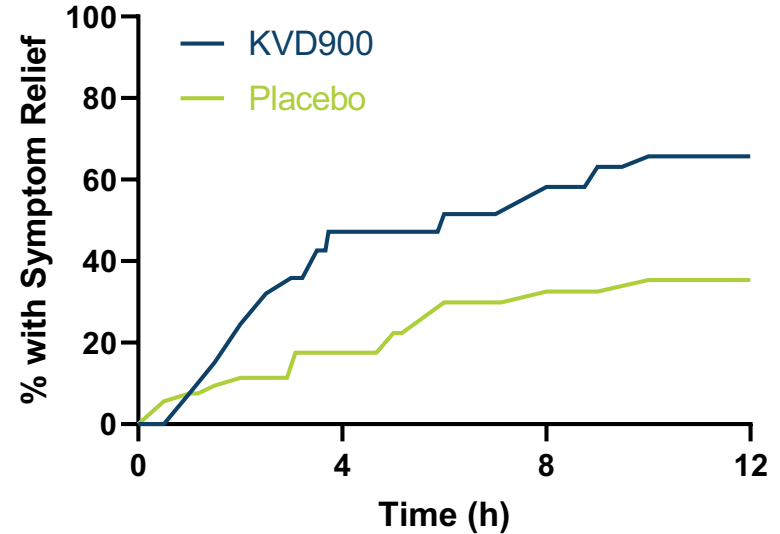


Study 1310: Kaplan-Meier Plot of Time to Beginning of Relief of Symptoms with Persistence (Based on Questions 1 and 2 of the TEQ, with Persistence) in the RCT Phase: RCT ITT Analysis Set



KVD900 Speeds Symptom Relief: Composite VAS

- KVD900 treated attacks achieved symptom relief more quickly: $p < 0.0001^*$
 - Composite VAS (abdominal pain, skin pain and skin swelling)
- Median time to onset of symptom relief
 - KVD900 6 hours
 - Placebo >12 hours**



Symptom relief defined as 50% reduction in composite VAS score for three consecutive time points

KVD900 VAS Reduction and Firazyr (icatibant)

- KVD900 enables patients to treat early
 - Key benefit of oral therapy
 - Consistent with HAE treatment recommendations
 - Minimises symptoms at time of treatment and overall symptoms experienced
- Delayed treatment means symptoms progress
 - Baseline severity moderate/severe in icatibant trial
 - Reflective of patient experience with injectable therapies
 - Increases overall symptoms experienced

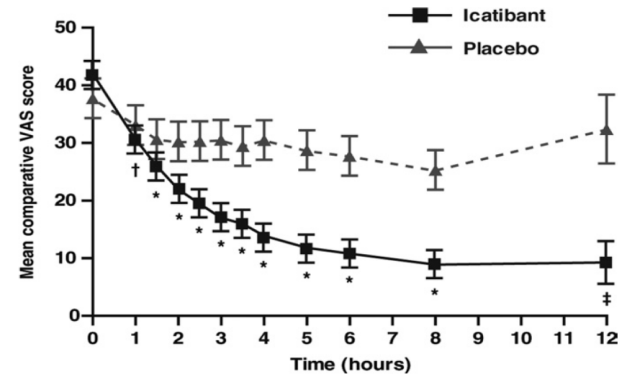
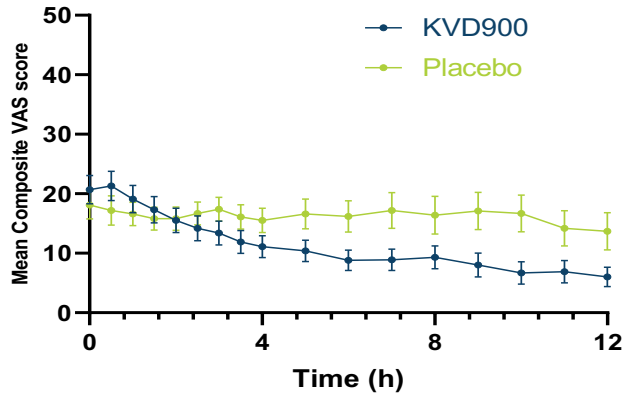


Figure 3. Mean composite VAS-3 score for the first 12 hours after treatment (nonlaryngeal ITT population). * $P \leq .001$; † $P = .003$; ‡ $P = .041$, vs placebo. Sixteen subjects (icatibant $n = 5$; placebo $n = 11$) who had not achieved relief by hour 8 had nonmissing data for hour 12.

Summary of Topline Outcomes

	KVD900	Placebo	p value
Rescue			
Use of rescue within 12h*	15.1%	30.2%	0.001
Use of rescue within 24h*	20.8%	39.6%	0.0005
PGI-S			
Time to Worsening or rescue within 12h*	>12h***	3.0h	<0.0001
Cumulative Symptom Relief over 12h**			0.0024
Cumulative Symptom Relief over 24h**			0.0036
PGI-C			
Time to Symptom Relief within 12h*	1.6h	9.0h	<0.0001
Cumulative Symptom Relief over 12h**			0.005
Cumulative Symptom Relief over 24h**			0.0036
VAS			
Time to Symptom Relief within 12h*	6.0h	>12h***	<0.0001
Cumulative Symptom Relief over 12h**			0.0008
Cumulative Symptom Relief over 24h**			0.0005

*Gehan's Generalized Wilcoxon Test; **ANOVA with fixed effects of treatment, sequence and HAE Attack (1st or 2nd) and subject nested within sequence as a random effect; ***Data censored at 12 hours

Related Treatment Emergent Adverse Events*

	Part 1 KVD900 N=68	Part 2 KVD900 N=58	Part 2 Placebo N=55
Total (events/patients)	8 / 5 (7.4%)	3 / 3 (5.2%)	2 / 2 (3.6%)
Gastrointestinal Disorders	1 / 1 (1.5%)	1 / 1 (1.7%)	1 / 1 (1.8%)
Abdominal Pain Upper	-	1 / 1 (1.7%)	-
Anal Incontinence	-	-	1 / 1 (1.8%)
Nausea	1 / 1 (1.5%)	-	-
General Disorders	1 / 1 (1.5%)	-	-
Malaise	1 / 1 (1.5%)	-	-
Musculoskeletal Disorders	1 / 1 (1.5%)	1 / 1 (1.7%)	-
Back Pain	1 / 1 (1.5%)	1 / 1 (1.7%)	-
Nervous System Disorders	3 / 3 (4.4%)	1 / 1 (1.7%)	1 / 1 (1.8%)
Dizziness	1 / 1 (1.5%)	-	-
Headache	2 / 2 (2.9%)	1 / 1 (1.7%)	1 / 1 (1.8%)
Vascular Disorders	2 / 2 (2.9%)	-	-
Flushing	2 / 2 (2.9%)	-	-

KVD900 Next Steps

- FDA End-of-Phase 2 meeting scheduled for late Q3 2021
- Phase 3 trial initiation expected quickly thereafter
 - Anticipated to be similar number of patients and endpoints to Phase 2
 - All sites identified and qualified worldwide
 - Commercial formulation finalized and Phase 3 drug supply in hand
- KVD900 data represents a positive read through for our work on KVD824 as an oral prophylactic HAE treatment

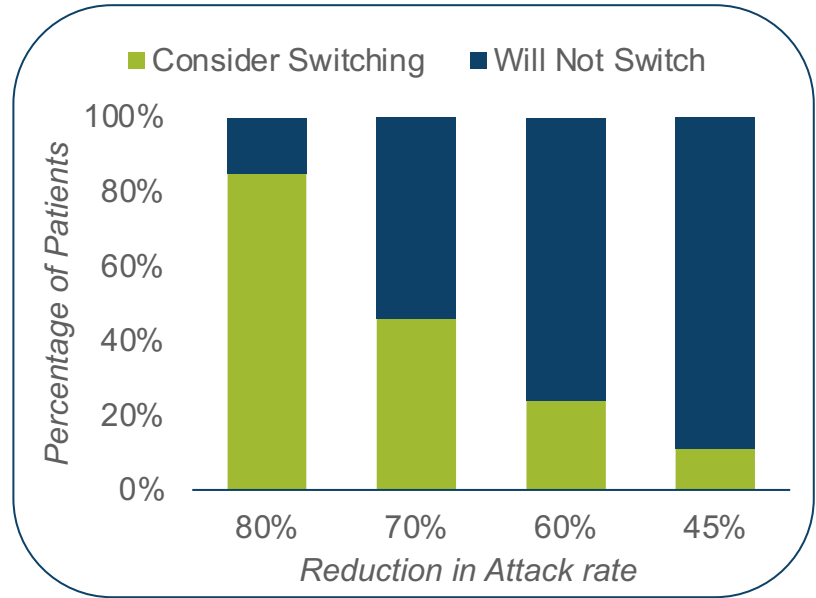
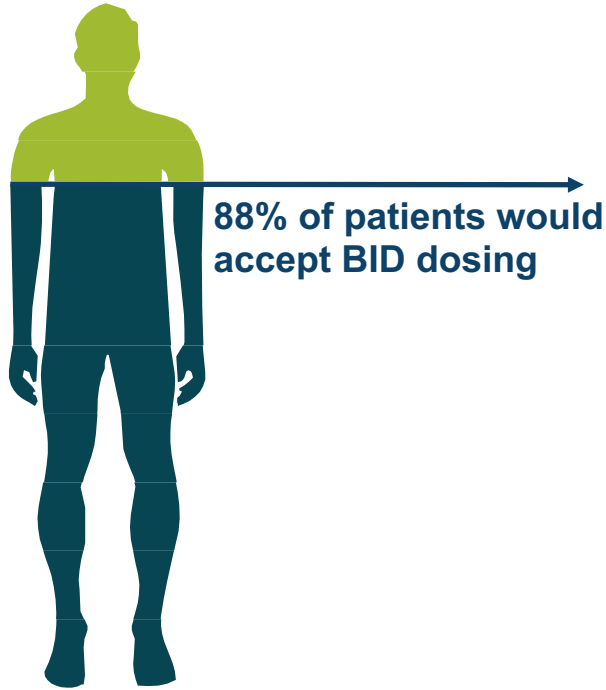


KVD824: HAE Prophylactic Therapy

KVD824 for Prophylaxis: Efficacy Is Key Driver for Patients

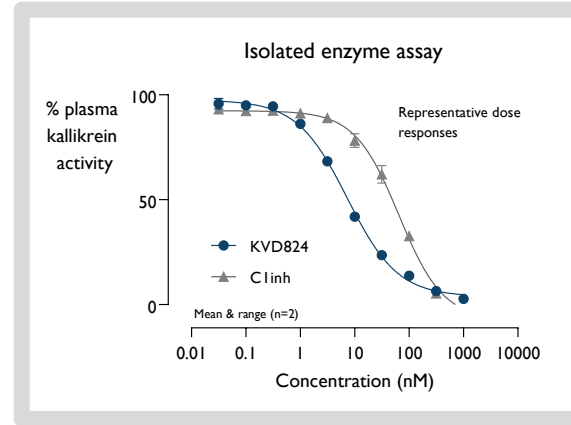
Dosing regimen is secondary to efficacy in importance

Patients will not trade lower efficacy for oral dosing



KVD824: Potent, Competitive Inhibitor of Plasma Kallikrein

- Isolated enzyme assay
 - Isolated enzyme $IC_{50} = 8$ nM



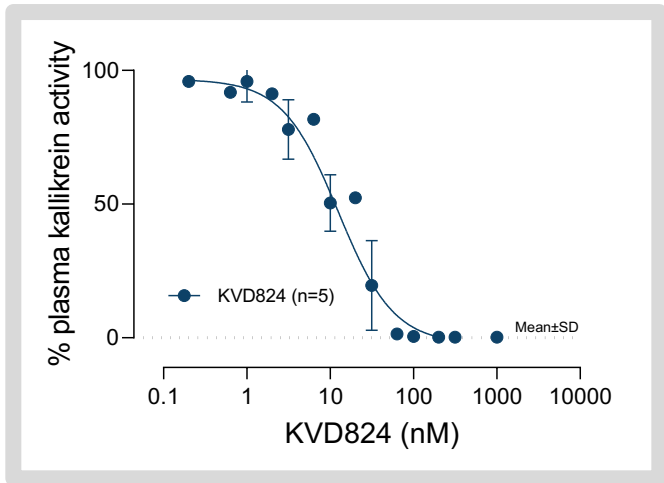
- Selective against a range of serine proteases including tissue kallikrein

Target	Fold Selectivity
Tissue Kallikrein	>1000
Plasmin	>1000
Thrombin	>1000
Matriptase	>1000
Trypsin	>1000
Factors VIIa, X, XIa, XIIa	>1000

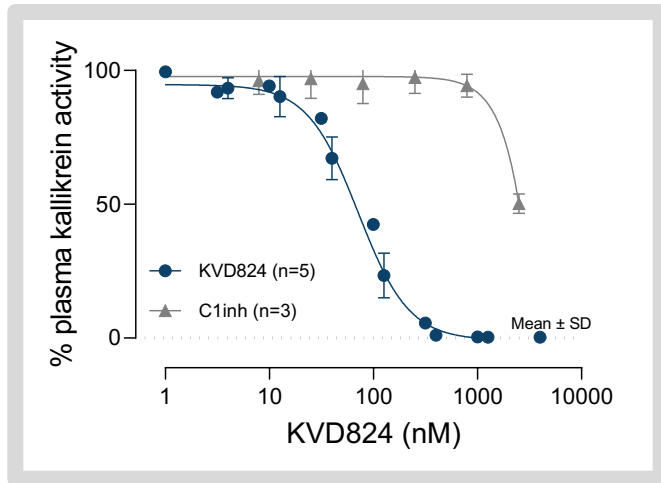
KVD824: Plasma Based Assays

- KVD824 inhibits plasma kallikrein enzyme activity in activated whole plasma
- KVD824 inhibits bradykinin release by protecting kininogen from cleavage by plasma kallikrein

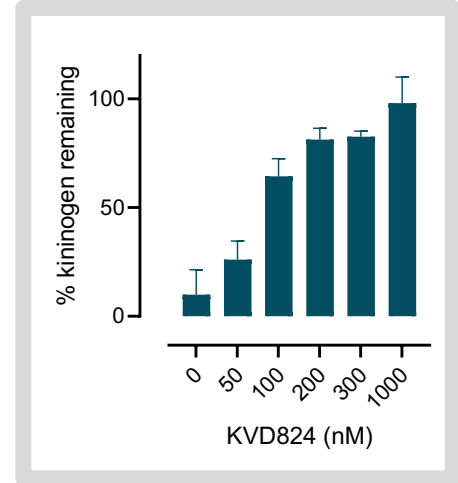
Diluted plasma enzyme assay
KVD824 IC₅₀ = 11 nM



Whole plasma enzyme assay
KVD824 IC₅₀ = 62 nM



Whole plasma HK cleavage assay



KVD824: First-in-Human Clinical Trial

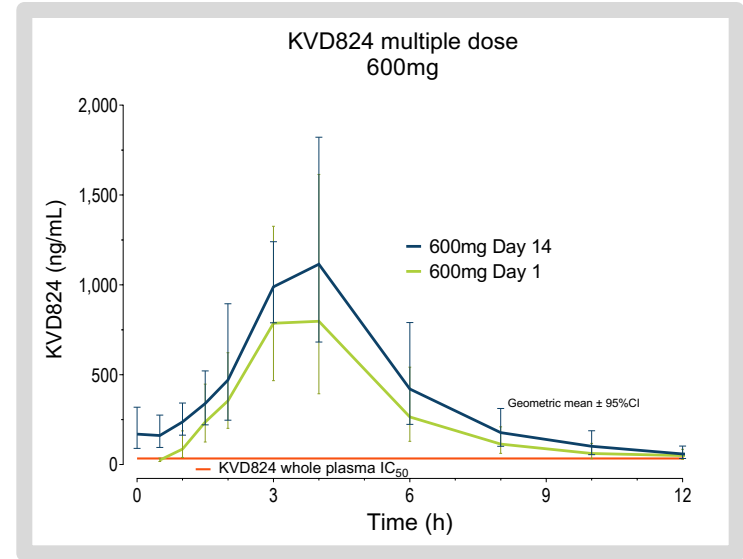
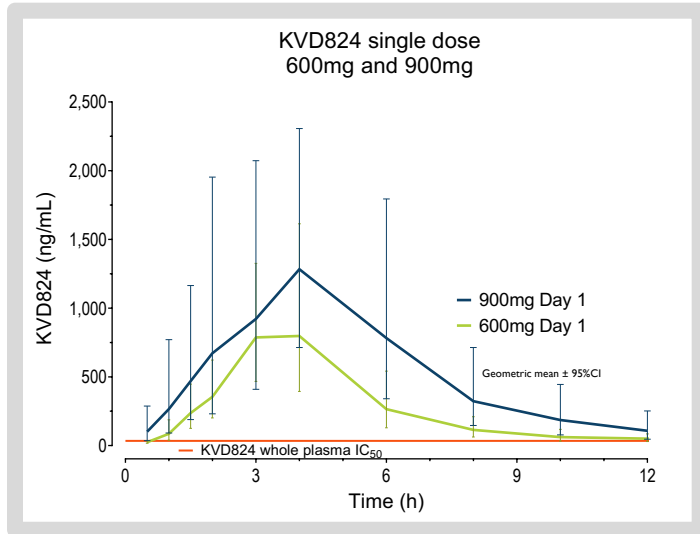
- KVD824 was rapidly absorbed with a mean half-life 3-5 hours on repeat dosing
 - Steady state achieved by day 3
 - Food lengthened absorption phase and increased exposure ~30%
- Overall safety
 - No subjects withdrew from the study
 - 17.9% active-treated versus 25% placebo-treated subjects reported treatment-emergent adverse events
- Multiple dose safety
 - 25% subjects on both active and placebo reported treatment-emergent adverse events
 - All events were mild and resolved without treatment
 - 1 adverse event (headache) at 160 mg dose level considered possibly related to treatment (doses up to 640 mg administered)

KVD824: Formulation Study

- Single and multiple dose formulation study
- Optimization of exposure profile to maintain concentrations of KVD824 in a twice-daily dosing regimen
- Cross-over, single dose phase
 - 6 formulations of 600 to 900 mg assessed in 16 healthy male and female subjects
- Multiple dose phase
 - 14 days, twice daily up to 900 mg in 9 subjects per dose formulation (2 placebo, 7 active)
- Pharmacokinetic profiles
 - 12 hour profiles collected on Day 1 and Day 14 following final dose
 - Trough concentrations (pre-dose) collected on all days

KVD824: Phase 1 Formulation Study

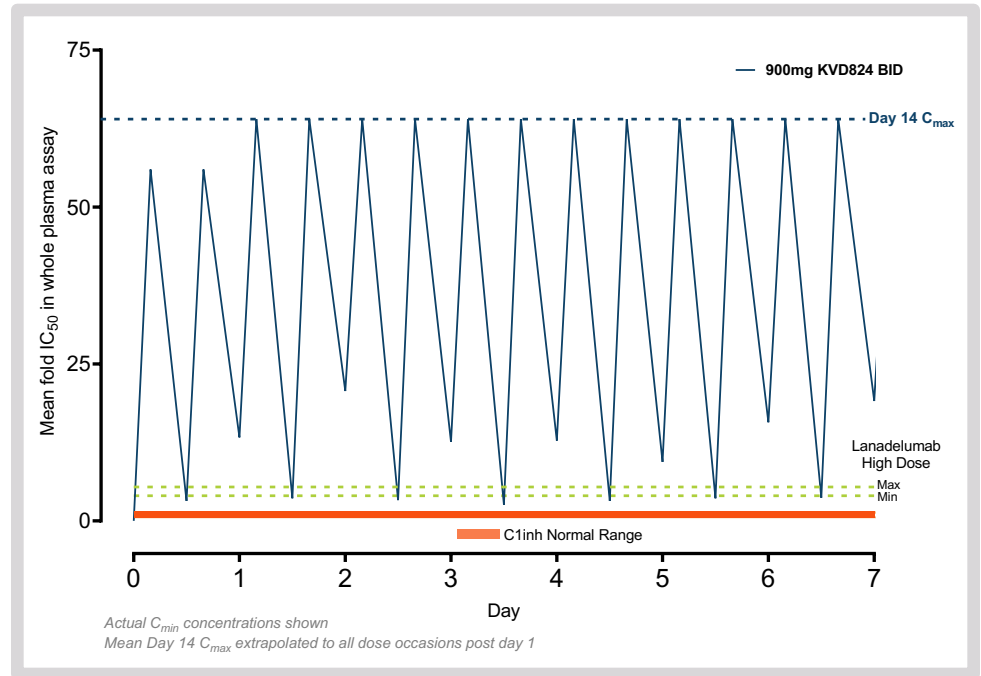
- Modified release formulation
 - Consistent pharmacokinetic profile over repeat dosing
 - No impact of multiple doses on rates of absorption or elimination
 - Reduces potential for drug-drug interactions



- Dose of 900mg increases exposure without affecting profile of exposure

KVD824: Restores Control of Plasma Kallikrein

- KVD824 concentrations maintained at levels well above functional concentrations of endogenous C1inhibitor and lanadelumab
- Predicted inhibition of plasma kallikrein should be sufficient to maximise clinical efficacy



KVD824: Formulation Study Safety and Tolerability

- Single dose phase
 - 16 subjects received 6 doses of 600-900 mg
 - 5 possibly related to treatment, all mild and resolved without treatment
 - 2 x headache, fatigue, dizziness, decreased appetite
- Multiple dosing for 14 days
 - 21 subjects received KVD824 at doses of 600 to 900mg, 6 subjects received placebo
 - Five adverse events reported by 4 subjects considered possibly related to treatment with KVD824
 - All were mild and resolved without treatment
 - Pruritus, joint stiffness, joint swelling, muscle spasm, elevated transaminases
 - Two adverse events reported by 1 subject considered related to treatment with placebo
 - 2 x nausea

KVD824 Next Steps: FDA Response Submission in Q3

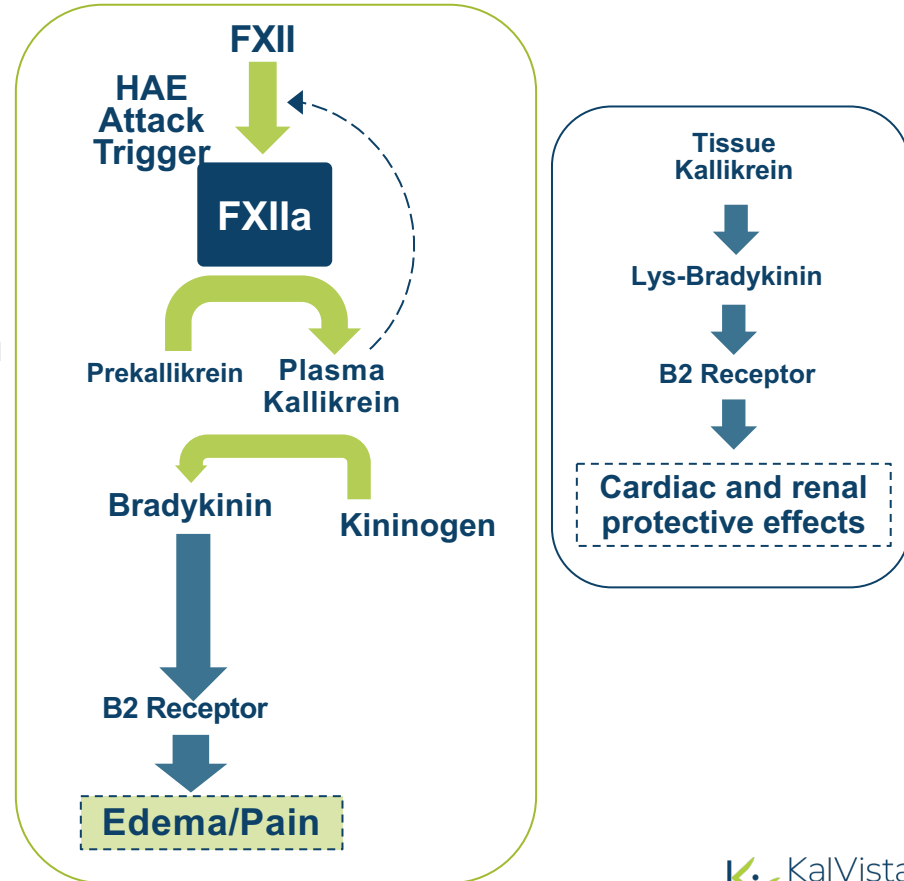
- FIH and formulation study performed in the UK
- Phase 2 trial submitted to FDA as the IND opening study
- Placed on clinical hold
 - Questions related to certain preclinical studies and refinements to Phase 2 protocol
 - No new data was requested to initiate the Phase 2 trial
- FDA letter related only to KVD824 and does not impact our activities or expectations for KVD900
- Regulatory filings underway in other countries



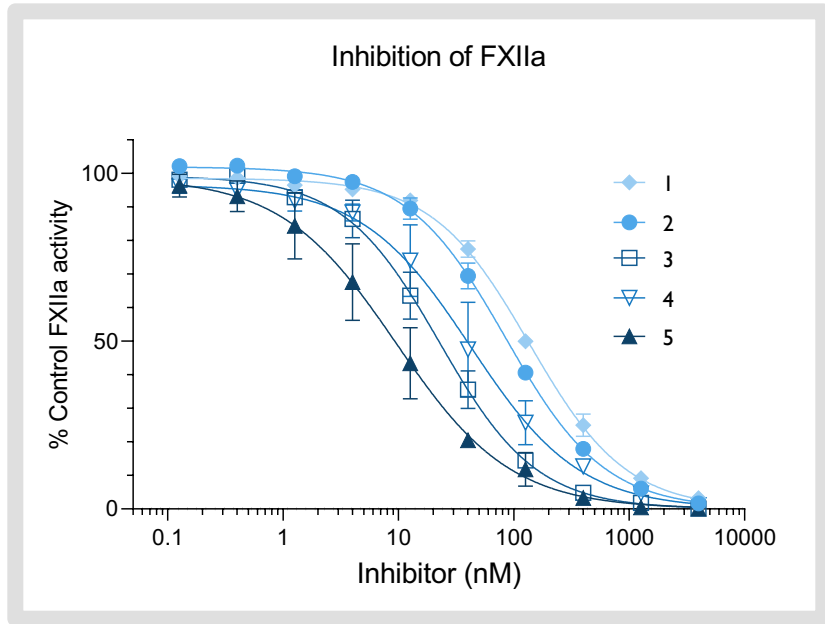
Factor XIIa

Future of the Oral HAE Franchise: FXIIa Inhibitor Program

- Factor XIIa (FXIIa) is the serine protease that drives generation of plasma kallikrein (PKa) and bradykinin during contact system activation and HAE attacks
- Genetic mutations that enhance FXII activation is a cause of HAE in people with normal C1-INH¹
- Clinical studies of Factor XIIa antibodies have shown ability to reduce attacks on par with approved therapies, and there are no known long-term safety implications of Factor XIIa inhibition
- Contact system-generated bradykinin is responsible for edema in HAE, not tissue kallikrein



KalVista has Potent, Selective, and Oral FXIIa Inhibitors



COMPOUND	FXIIa IC ₅₀ (nM)	PKa IC ₅₀ (nM)
1	103	16,932
2	86	>20,000
3	20	3,321
4	47	5,650
5	12	4,889

- ✓ Discovery of low nM FXIIa inhibitors – selective, established oral availability
- ✓ Lead series identified – program in lead optimization
- ✓ Multiple Patents submitted – robust IP protection

Factor XIIa Program is Advancing Toward IND Enabling Studies

- Strong scientific rationale and positive clinical evidence for FXIIa inhibition in HAE prophylaxis
 - Blocking the most upstream mechanism of the contact system (FXIIa) is the next generation of HAE therapeutics
 - Factor XIIa inhibition blocks the uncontrolled generation of both plasma kallikrein and bradykinin and thereby has the potential for the most complete attack protection of all HAE prophylactic therapeutic options
- KalVista has deep expertise in oral therapies for HAE, and is advancing the first oral FXIIa inhibitors for HAE
- Oral Factor XIIa inhibitors have additional potential commercial opportunities
- IND enabling studies anticipated in 2021

The background features a field of tall, thin, golden-brown grasses. A bright green diagonal shape is in the top-left corner, and a solid green horizontal bar is at the bottom. The text is centered in white.

Diabetic Macular Edema (DME)

KVD001 Phase 2 and Status

- The study did not meet the primary or secondary efficacy endpoints of changes in BCVA, CST, or DRSS
- The trial population had shown poor BCVA response to prior anti-VEGF
- KVD001 showed dose responsive protection from vision loss
- Patients with less severe vision loss experienced more robust treatment benefit
 - This represents >70% of the total trial population
- KVD001 was generally safe and well tolerated
- The results support further study of KVD001 as a treatment for DME
 - Higher doses and combination with anti-VEGF already enabled
- Potential for orally delivered molecules to deliver differentiated treatment option
- Merck options on KVD001 and future oral DME options expired; next steps under evaluation

KalVista Value Proposition

- The only Company developing oral treatments for the full spectrum of HAE disease management
 - KVD900: on-demand entering Phase 3
 - KVD824: prophylaxis entering Phase 2
- Factor XIIa program is the next generation of oral HAE therapy
 - Multiple potential candidates being advanced through to IND enabling studies in 2021
- Additional future opportunities include DME and other indications for Factor XIIa
- Funded to KVD900 NDA



KalVista
Pharmaceuticals

NASDAQ: KALV