



KalVista
Pharmaceuticals

Corporate Presentation

March 2020



Forward-Looking Statements

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Company Highlights

- Discovery and development of small molecule protease inhibitors, with leading expertise on plasma kallikrein role in disease mechanisms
- Creating a portfolio of oral plasma kallikrein inhibitors to treat orphan disease hereditary angioedema (HAE) and diabetic macular edema (DME)
- Developing a franchise of oral treatments for HAE
 - KVD900 as on-demand therapy, Phase 2 data expected in Q2 2020
 - KVD824 for prophylaxis, Phase 2 initiation H2 2020
- KVD001 Phase 2 in patients with DME complete; next steps being evaluated
- Internal discovery and development capabilities enable high productivity and strong IP positions
- Funded into 2021, with \$80.6 million as of January 31, 2020



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"> Phase 2 data expected Q2 2020
KVD824 for Hereditary Angioedema Prophylaxis					<ul style="list-style-type: none"> Phase 2 anticipated H2 2020
KVD001 (IVT) Diabetic Macular Edema					<ul style="list-style-type: none"> Phase 2 study completed
Early Stage Programs					
Oral DME Molecules Target: Plasma Kallikrein					<ul style="list-style-type: none"> Regulatory studies ongoing
Other Proteases Target: Undisclosed					<ul style="list-style-type: none"> Lead optimization ongoing



Hereditary Angioedema (HAE)

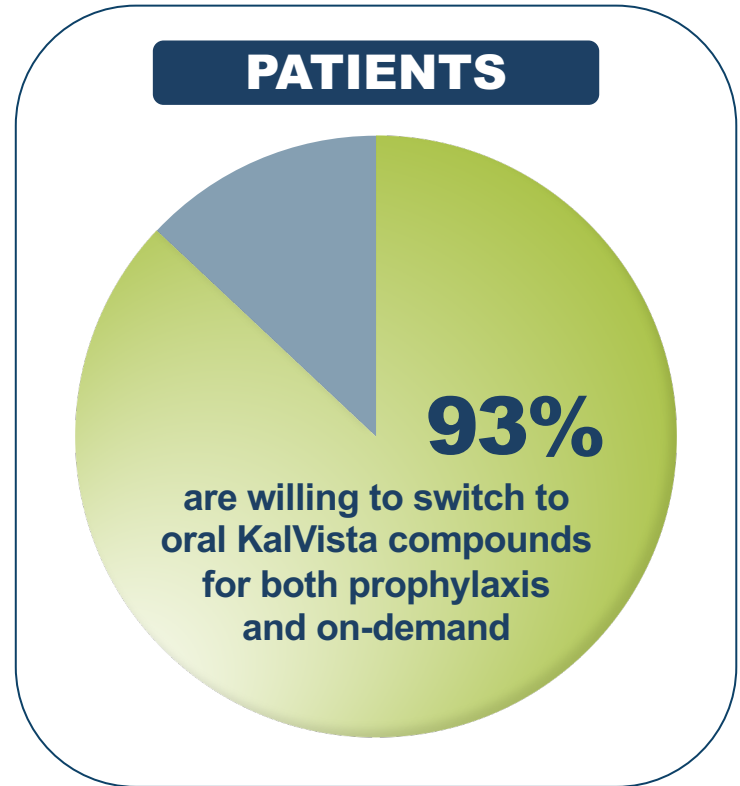
Hereditary Angioedema (HAE)

- 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 current approved therapies injected/infused - high unmet need for oral administration
- Total HAE market approximately \$2 billion annual revenues
- We are developing a franchise of HAE therapeutics, to address both on-demand and prophylactic segments



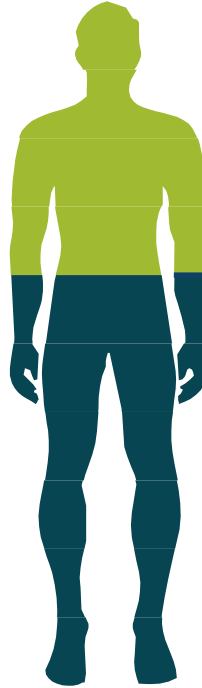
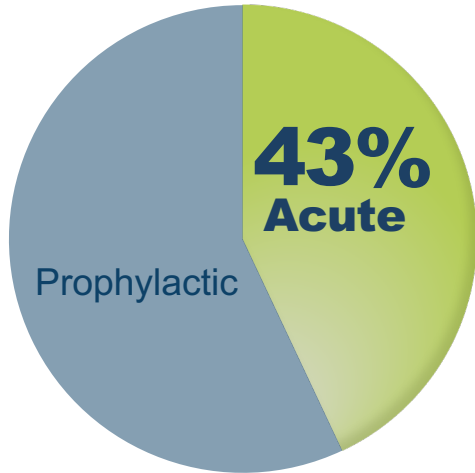
Building an Oral HAE Franchise

- KalVista is the only company developing multiple oral therapies to treat this disease
- KVD900 and KVD824 together can meet all the needs of HAE patients
- KVD900 as on-demand therapy
 - Phase 2 data second quarter
- KVD824 for prophylaxis
 - Phase 2 initiation this year



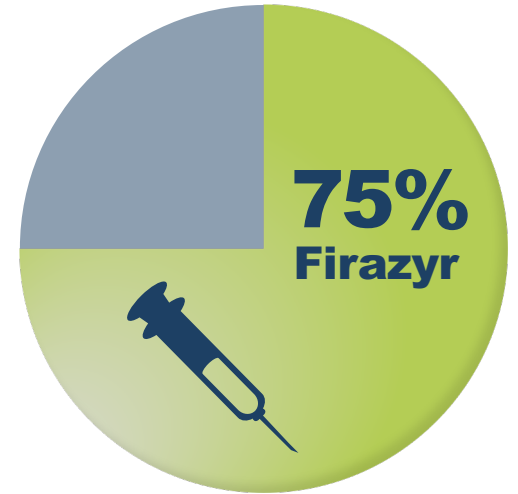
US HAE Market Landscape

Patient Distribution



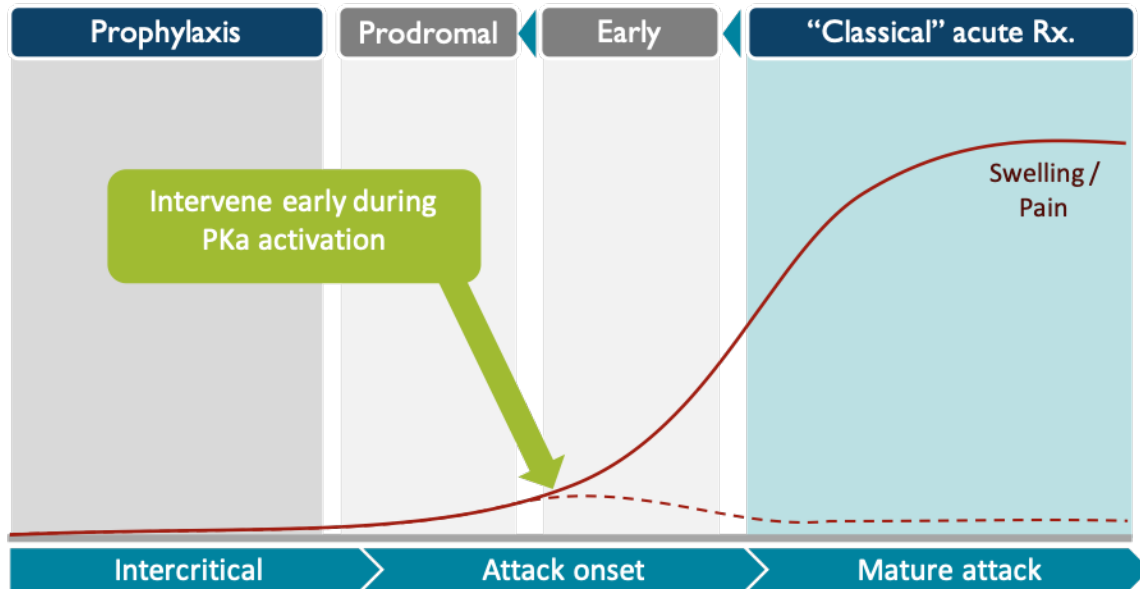
Only ~62% of
HAE patients treat
all attacks

Current Acute Treatment



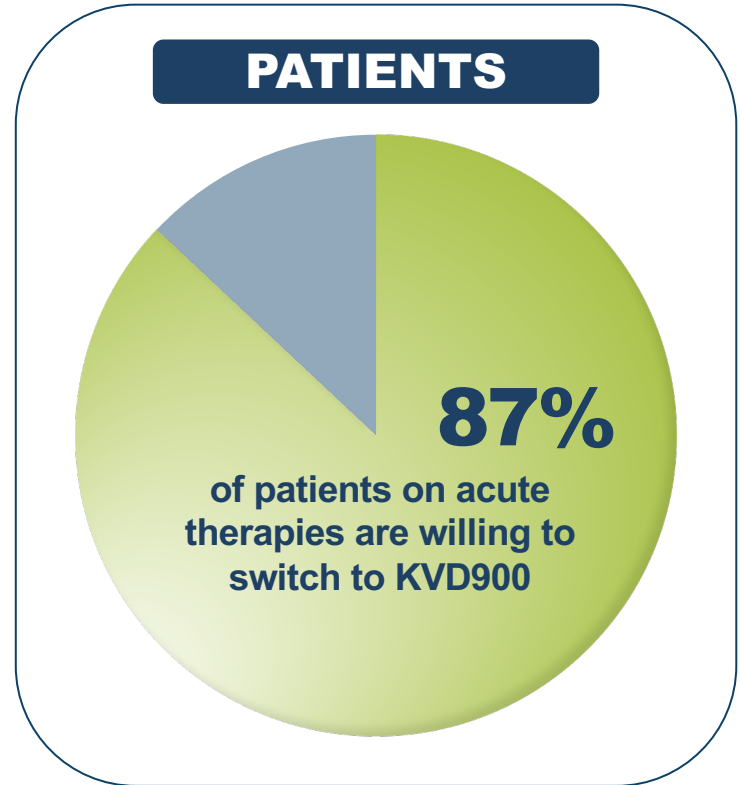
Patients Want A Safe, Efficacious, Oral Therapy

- On-demand therapy can meet the needs of the majority of patients
- Key requirement is rapid absorption to high exposure levels
- Even prophylactic patients need an on-demand back-up in case of breakthrough attacks



Patients Would Switch to KVD900

- Most patients are willing to switch to KVD900 even though current injectables have high efficacy
- Patients will not accept substantially lower efficacy for oral
- Pricing is not a driver for patients

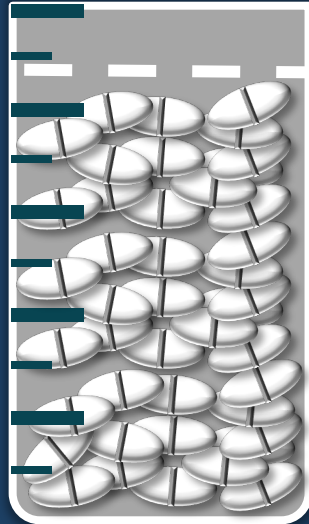


Positive Payer and Physician Reaction to KVD900

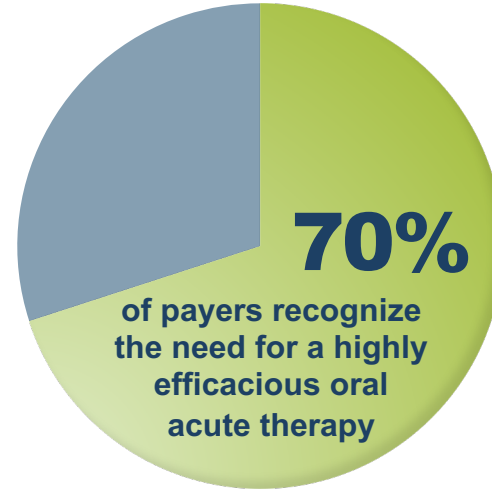
Physicians Likely to Prescribe KVD900

89%

KVD900



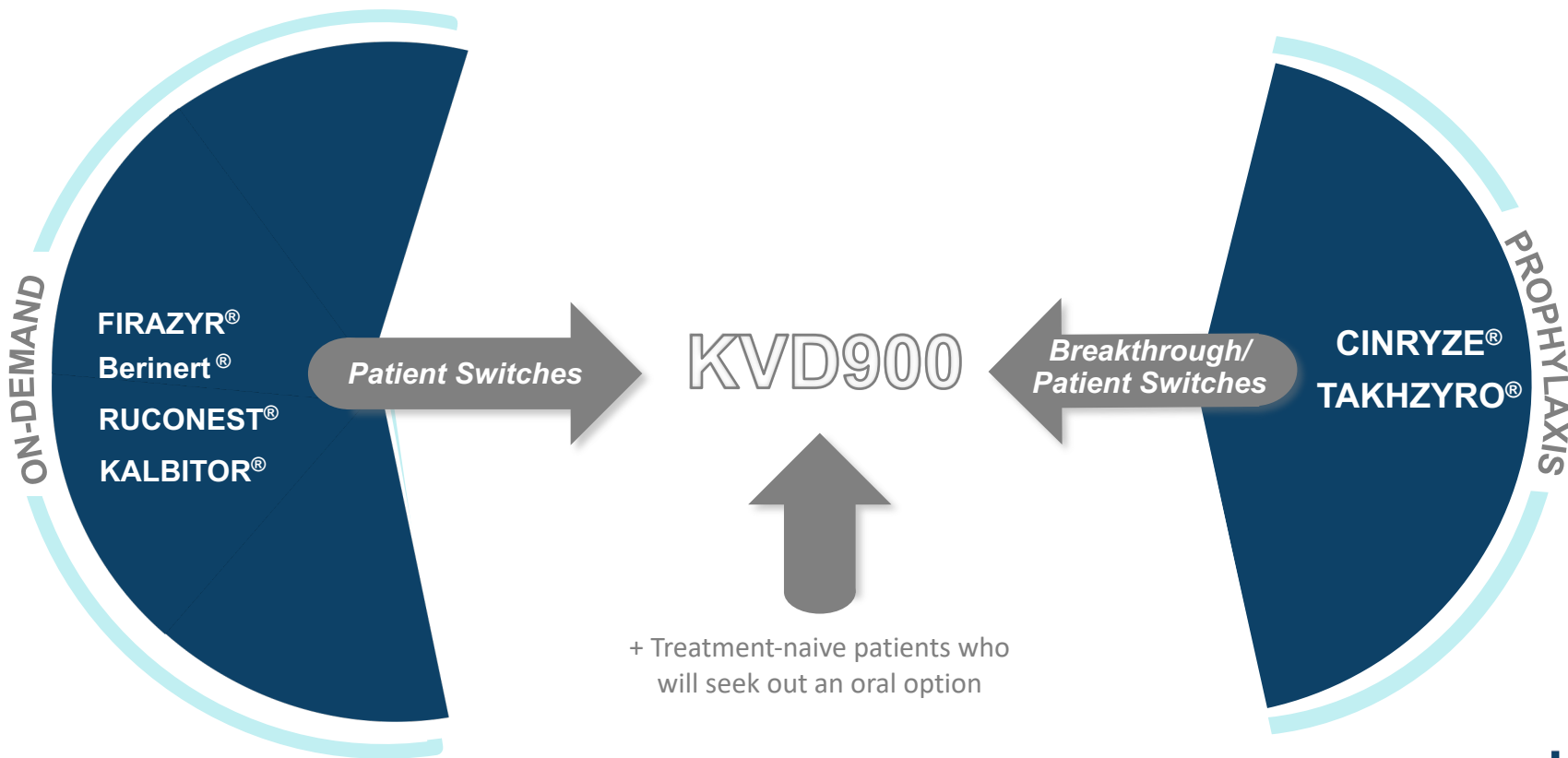
PAYERS



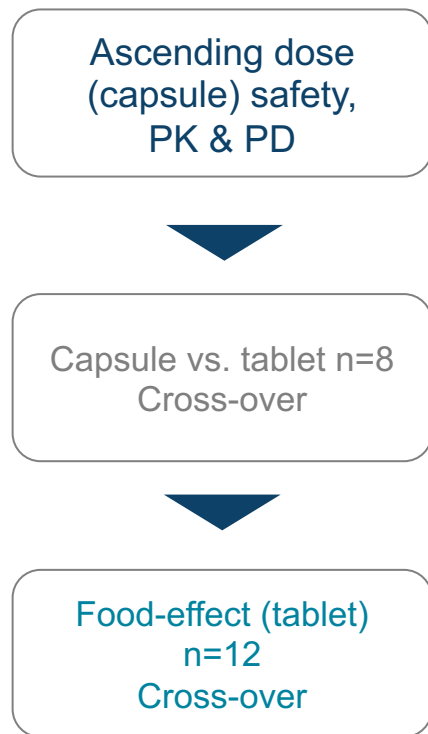
- Value proposition supports premium pricing
- Generic icatibant launch does not reduce interest in oral acute therapy



Opportunity to Capture Market Share and Growth



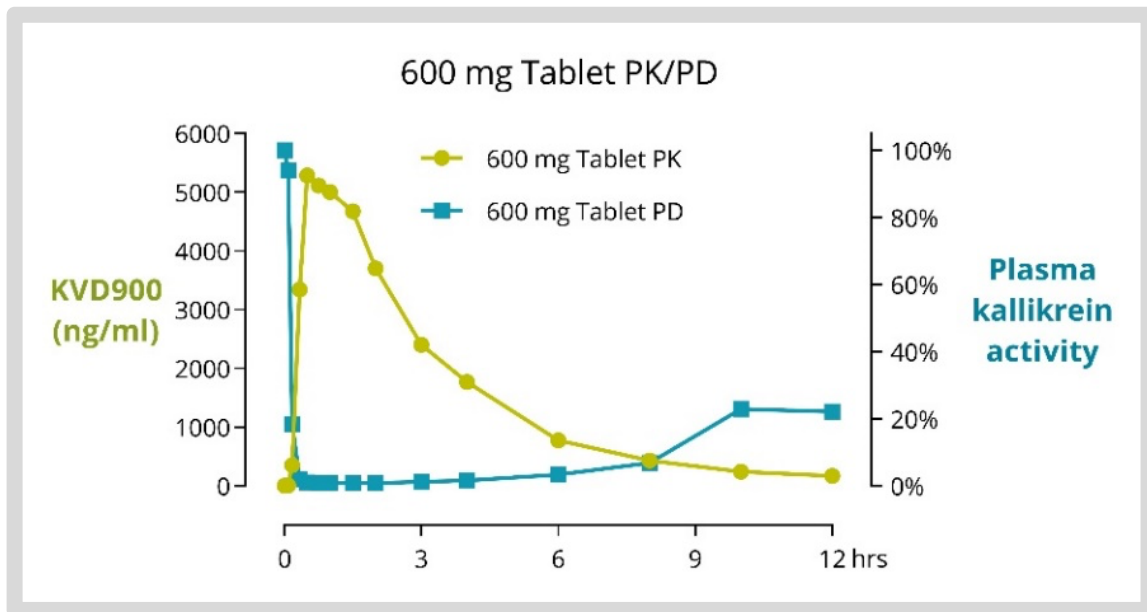
KVD900 Phase 1 Overview



- 68 subjects received active treatment
- No severe adverse events (SAEs) reported
- 22/23 treatment emergent adverse events (TEAEs) on active were mild
 - One moderate (headache at 10 mg)
 - Only one GI AE, and unrelated to KVD900
- No clinically significant changes in vital signs, ECG, safety labs
- No subjects withdrew

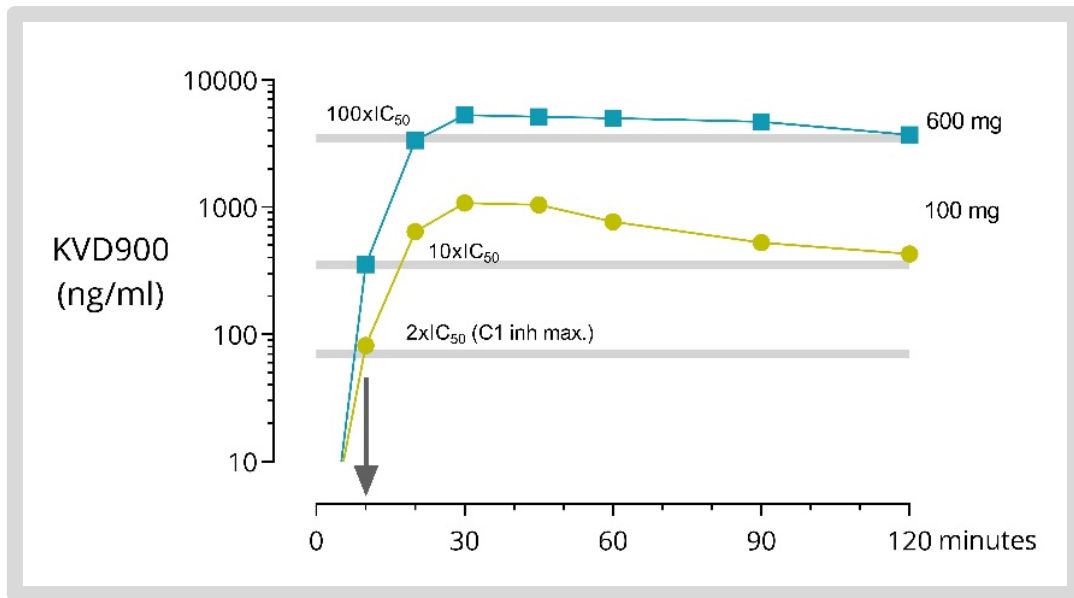
Rapid and Complete Inhibition of Plasma Kallikrein

- Plasma kallikrein assay using whole plasma
- Rapid onset of inhibition
 - 98% inhibition at 20 minutes
 - Inhibition through 12 hours
 - Food has no meaningful impact on PD profile of KVD900 tablets
- Phase 2 study and commercial use will be tablet formulation



KVD900 Achieves 100x IC₅₀

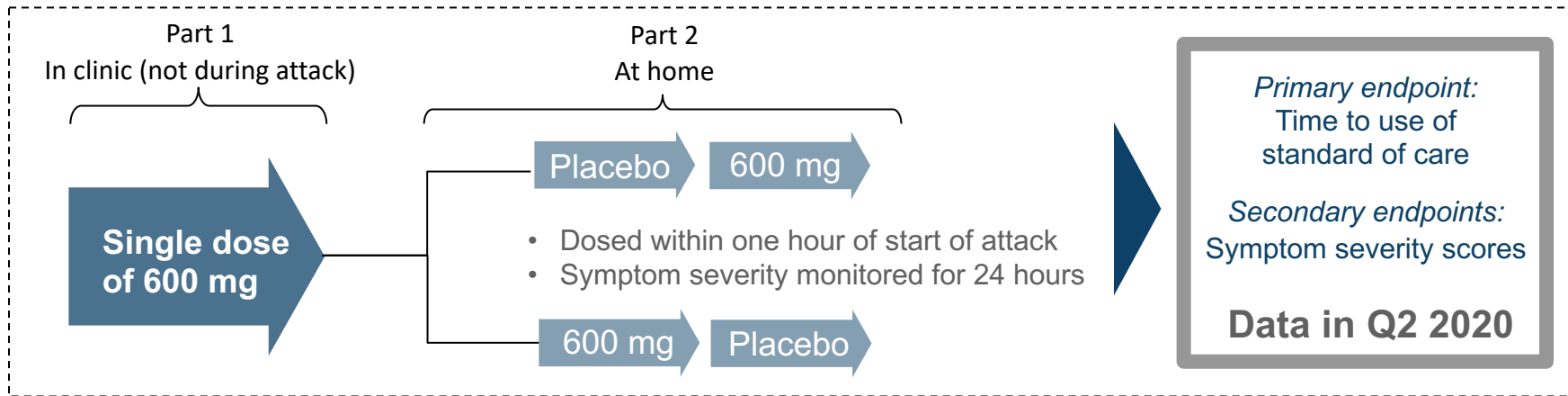
- Multiple dose levels achieve sufficient plasma kallikrein inhibition
 - Based on clinically efficacious doses of C1-INH¹
- Rapid exposure important for on-demand efficacy
- 2x IC₅₀ reached around 10 minutes
 - At least as quickly as C1-INH injection
- 100x IC₅₀ before 30 minutes



¹IC₅₀ of C1-INH in whole plasma is 1700 nM, compared to KVD900 which is 90 nM. Following administration of approved dose of 20 IU/kg of Berinert, C_{max} is »3,000 (0.32 mg/ml) reached within 48 minutes of dosing. Maximal concentration is ≈ 2x IC₅₀.

KVD900 Phase 2 Efficacy Study Ongoing

- ~50 HAE patients at approximately 20 sites in Europe and US
- Part 1: All patients receive a single dose of KVD900 in clinic for PK/PD assessment
- Part 2: All patients then randomized to treat the first attack with either KVD900 or placebo and then treat a second attack with the alternative treatment



KVD824 as Oral Prophylactic

- Prophylactic treatment of HAE requires strong inhibition of plasma kallikrein maintained over the dosing period
 - Previous studies have shown that as the concentration of inhibitor drops, efficacy is rapidly lost
 - Breakthrough attack frequency increases late in dosing cycles
- Level of inhibition is determined by potency and concentration of drug
 - Appropriate assessment of potency is key to define the concentration that needs to be maintained
- Maintaining suitable concentrations of drug is challenging
 - Antibody drugs have inherent long half-life, but given by injection
 - Exposure profile of oral drugs is difficult to deliver along with other characteristics e.g. potency, tolerability
 - Effective suppression of attacks requires high level of inhibition



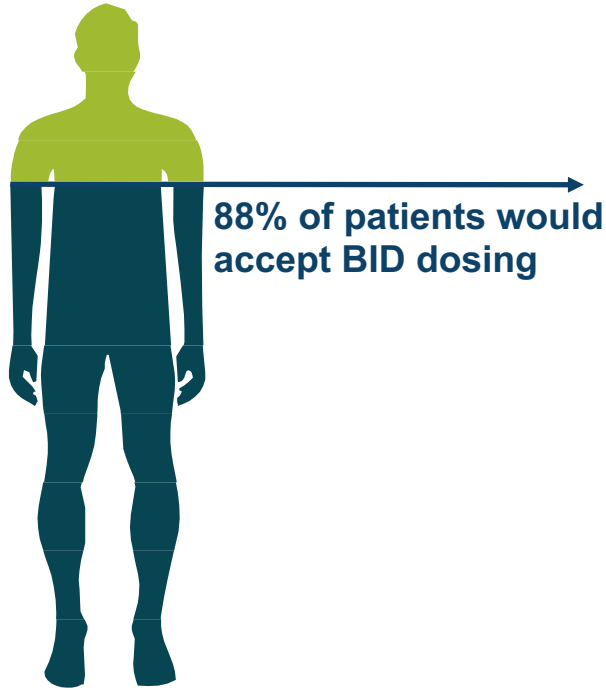
KVD824 as Oral Prophylactic

- KVD824 offers the opportunity to tailor an exposure profile which delivers the required strong and sustained inhibition of plasma kallikrein
 - KVD824 is potent inhibitor of plasma kallikrein in vitro ($<10\text{nM}$) and in whole human plasma assays ($<80\text{nM}$)
 - The first in human study showed very high exposures and essentially complete suppression of plasma kallikrein activity
 - Tolerability was good following single and multiple dosing
- The properties of KVD824 facilitate optimization of the exposure profile through investigation of formulation
- 89% of current prophylaxis patients surveyed expressed interest in switching to oral medication
- The initial development plan is focused on twice daily dosing
 - Ensures trough concentrations are maintained well above target required to maximize efficacy
 - Patient surveys indicate this schedule causes no reduction in attractiveness of oral therapy

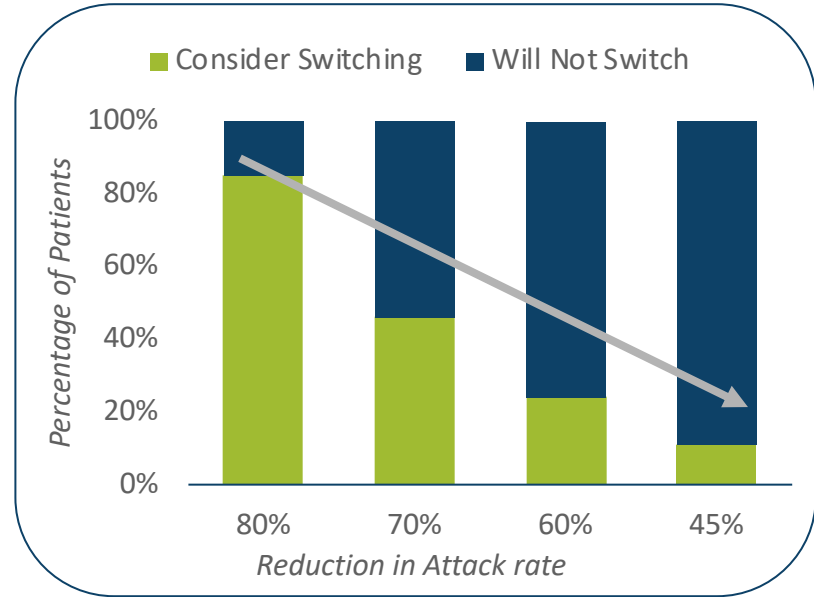


Efficacy Is Key Driver of Willingness to Switch to Oral

Dosing regimen is secondary to efficacy in importance



Patients will not trade lower efficacy for oral dosing

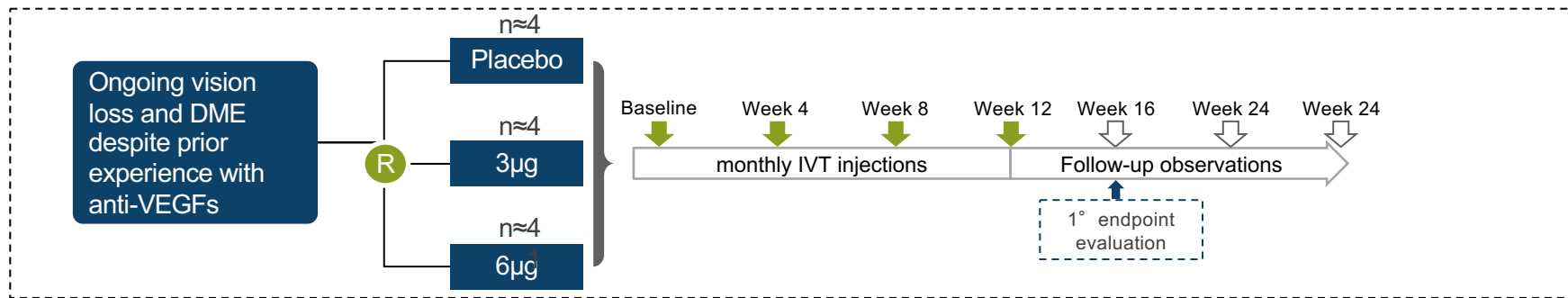


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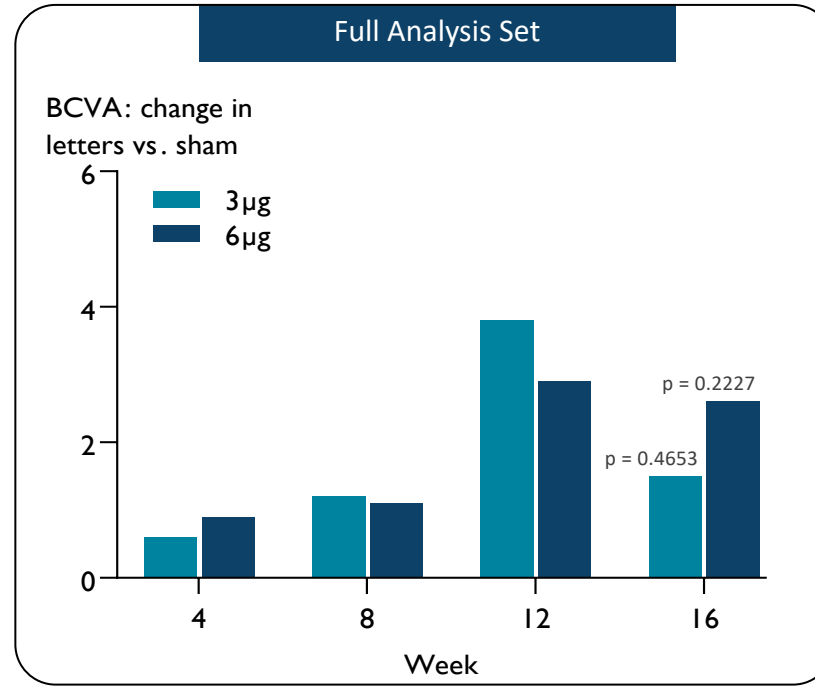
Diabetic Macular Edema (DME)

KVD001 Phase 2 Clinical Trial Design

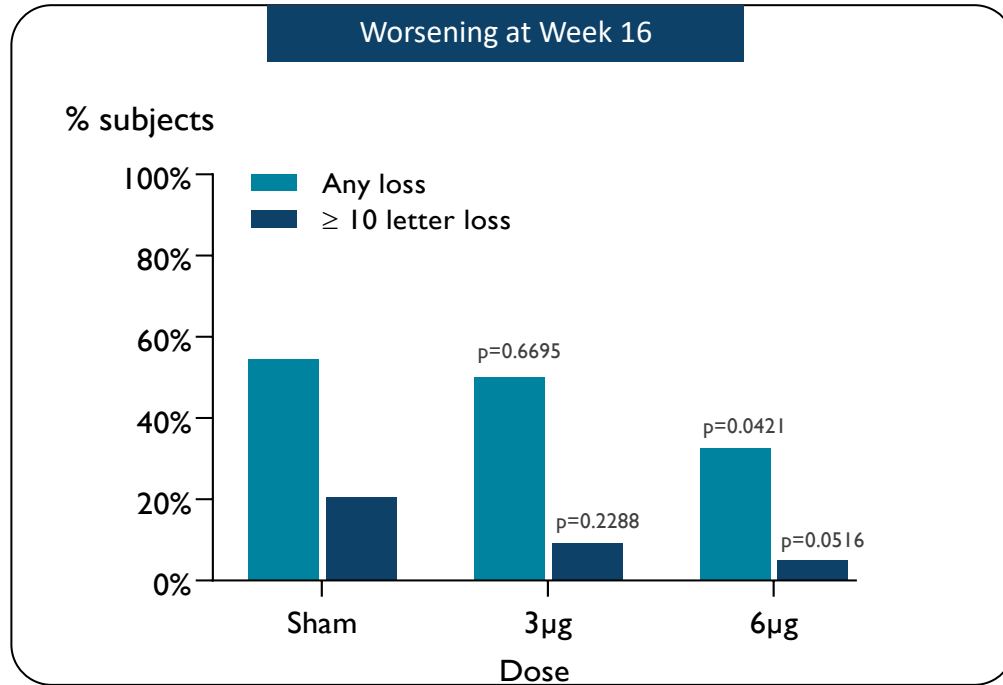
- Adult male or female subjects with confirmed DM (type I or II)
- Presence of ciDME (F: > 305 μ m; M: > 320 μ m)
- Ongoing vision loss (20/40 or worse) despite prior anti-VEGF treatment
- Conducted at 38 US Sites
- Primary endpoint: change from baseline BCVA letter count at Week 16



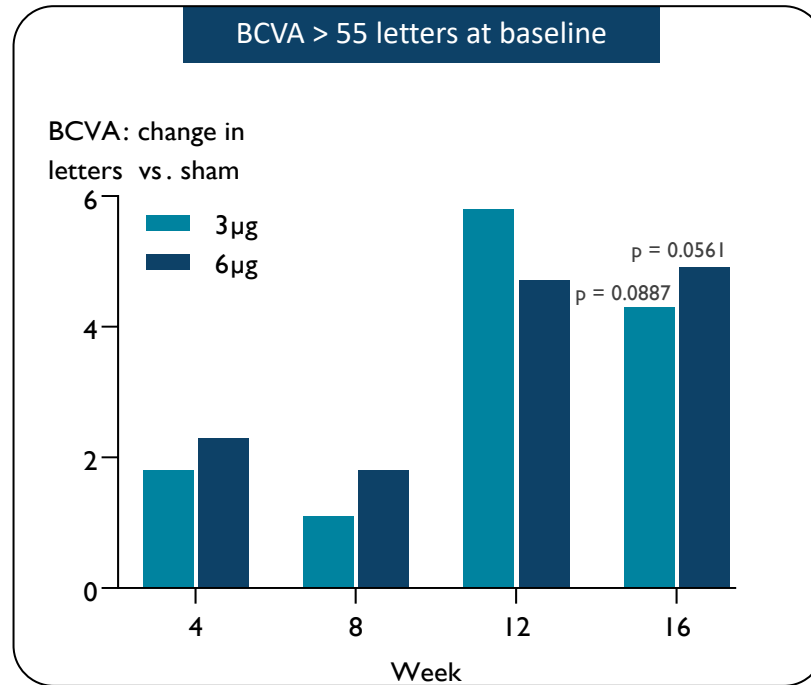
Study Did Not Meet the Primary BCVA Endpoint



Vision Loss Protected In a Dose Responsive Manner



More Robust Response in Subjects with Baseline Vision of >55 Letters



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





NASDAQ: KALV