



KalVista
Pharmaceuticals

Needham Healthcare Conference

April 10, 2019

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)
- HAE program KVD900 advanced to Phase 2 as acute therapy, with data expected in late 2019
- Collaboration with Merck in DME; lead program KVD001 Phase 2 completes H2 2019
- KVD824 filed in late 2018 as next clinical program; update to come mid-2019
- Internal discovery and development capabilities enable high productivity and strong IP positions
- Funded into 2021, with \$111.1 million as of January 31, 2019



Product Portfolio

	Route	Preclinical	Phase 1	Phase 2	Phase 3	Status
Mid Stage Programs						
KVD900 for Acute Hereditary Angioedema	Oral					<ul style="list-style-type: none"> Phase 2 data expected late 2019
KVD001* Diabetic Macular Edema	Intravitreal					<ul style="list-style-type: none"> Phase 2 complete H2 2019
Earlier Stage Programs						
KVD824 Target: Plasma Kallikrein <i>For Prophy HAE or DME</i>	Oral					<ul style="list-style-type: none"> Update mid-2019
KVDYYY Target: Plasma Kallikrein <i>For Prophy HAE or DME</i>	Oral					<ul style="list-style-type: none"> Regulatory studies
Additional Proteases Target: Undisclosed	Oral					<ul style="list-style-type: none"> Lead optimization ongoing



The background features a dark blue field with a white, abstract molecular network. This network consists of numerous interconnected nodes of varying sizes, some of which are highlighted in a lighter shade of blue. The nodes are connected by thin white lines, creating a complex, web-like structure that spans the entire frame. The overall aesthetic is clean, scientific, and modern.

Hereditary Angioedema (HAE)

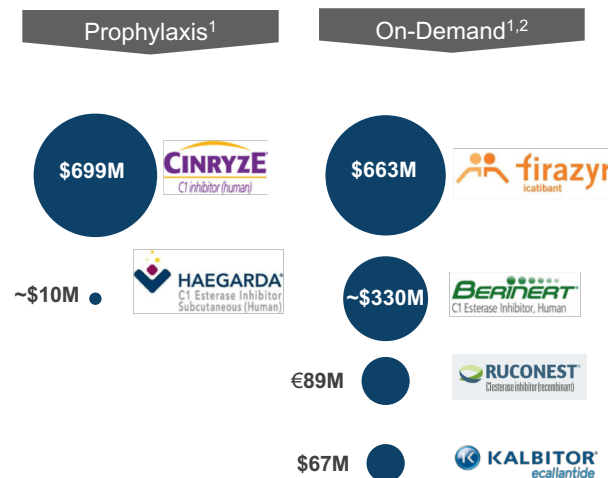
Hereditary Angioedema (HAE)

- 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
- Approved products target inhibition of plasma kallikrein
- All current approved therapies injected/infused - high unmet need for oral administration
- By 2020, total HAE market estimated to be over \$2 billion
- We intend to bring multiple candidates through Phase 1 and target both acute and prophylactic segments



Oral Acute Therapy Meets Unmet Patient Needs

1. On-demand segment is the largest market opportunity
2. Oral treatment option represents a significant advancement for patients
3. Patients on prophylaxis still require therapy for breakthrough attacks
 - WAO/EAACI 2017 revision and update for management of HAE recommends all patients carry medication for on-demand treatment of two attacks, at all times

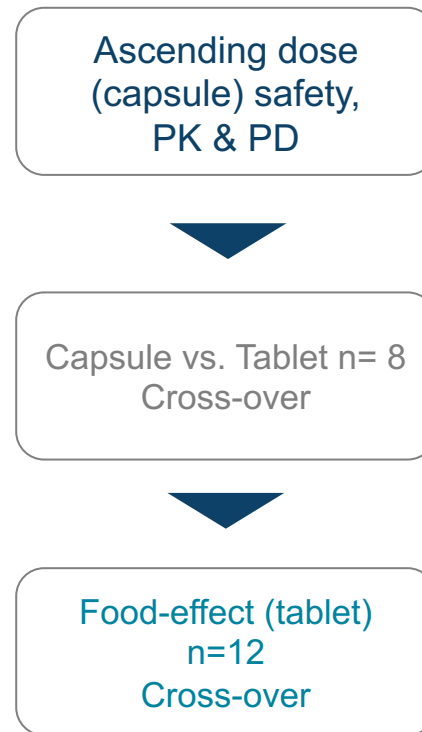


The majority of patients already manage their disease with acute therapies



KVD900 Phase 1 Overview

- Double-blind, randomized investigation of oral KVD900 recruited 84 healthy male volunteers
 - 68 received active treatment, 18 of which received 600 mg
 - Single ascending dose with crossover to tablet formulation
 - Food effect crossover using 600 mg tablet
- Safety and tolerability
 - AEs, laboratory measurements and clinical outcomes
- Pharmacokinetics
 - PK profile and PK parameters
- Pharmacodynamics
 - Ex vivo assays assessing enzyme activity and plasma kininogen substrate cleavage



KVD900 Phase 1 Safety Profile

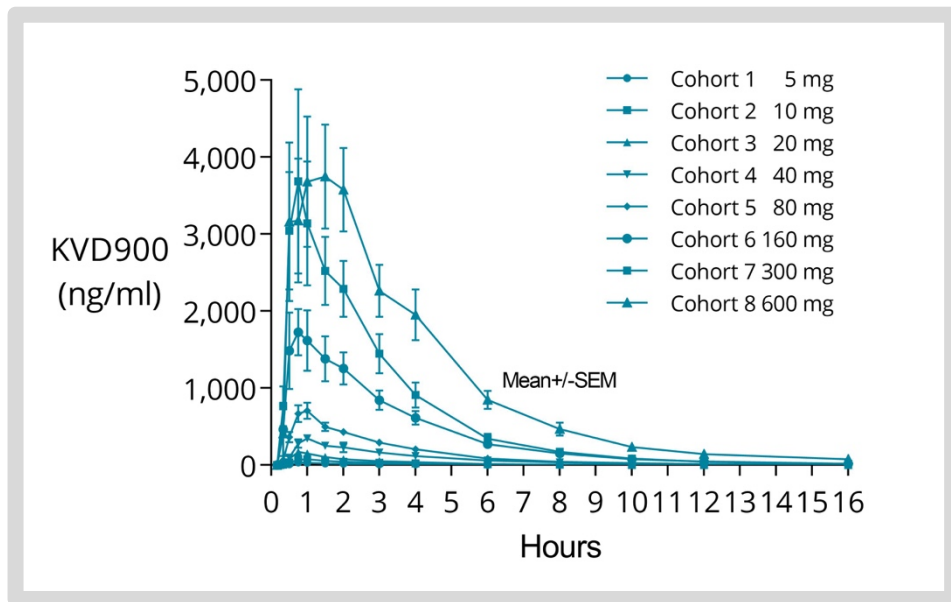
- No SAEs reported
- 44/45 AEs were mild
 - One moderate (headache at 10 mg)
 - No GI AEs considered related to KVD900
- No clinically significant changes in vital signs, ECG, safety labs
- No subjects withdrew

	Placebo	KVD900 5-160mg	KVD900 300mg	KVD900 600mg	KVD900 600mg	
	<i>Exposures / subjects</i>				Fed	Fasted
	16 / 16	52 / 44	6 / 6	6 / 6	12 / 12	12 / 12
Vomiting*					1	
Fatigue					3	
Folliculitis						1
Nasopharyngitis		2				
Oral herpes	1	1				
Upper respiratory tract infection		1				
Arthropod bite					1	
Back pain	1	2				
Myalgia		1				
Dizziness		1			5	3
Headache		1			3	2
Lethargy					1	1
Syncope					1	
Cough		1				
Oropharyngeal pain	1	1				
Eczema						1

*3 days post-dose



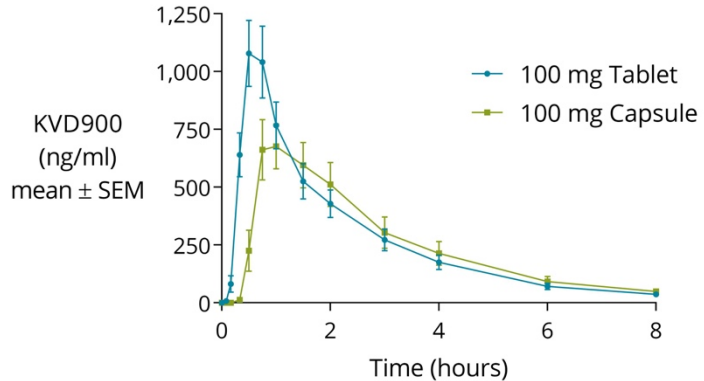
KVD900 Rapidly and Highly Absorbed at All Doses



- Capsule formulation
- Mean T_{max} around 1 hour
- Mean C_{max} up to 3,500 ng/ml

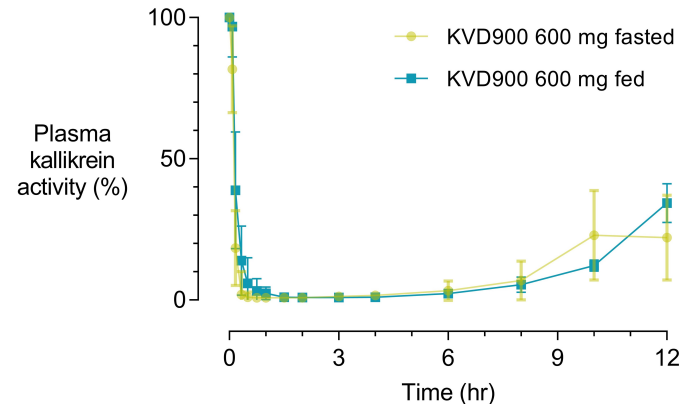


KVD900 Phase 1 Trial – Tablet Formulation and Food Effect



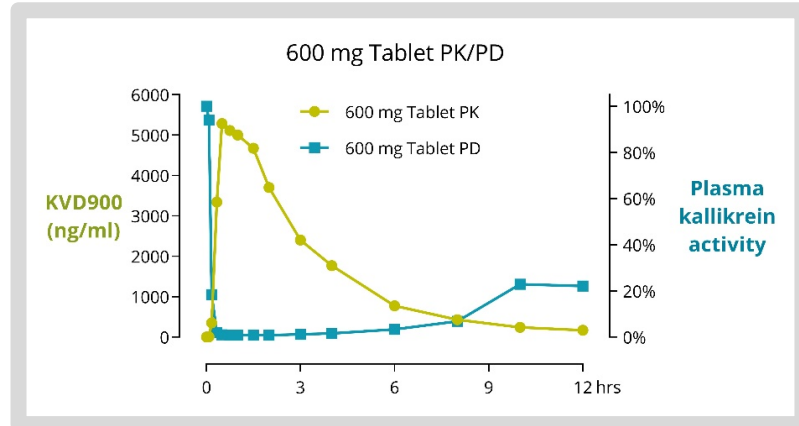
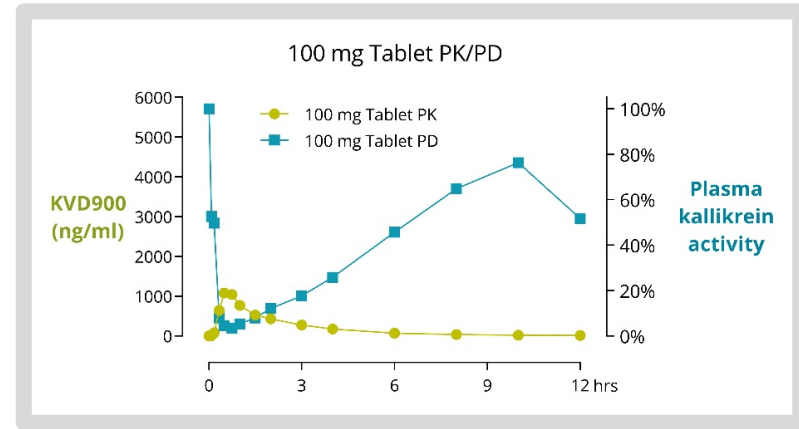
- Fed state has little impact on the PD profile of KVD900 tablets delivering 95% inhibition within 30 minutes

- Tablet formulation shows even faster absorption than capsule
- This is the intended commercial formulation



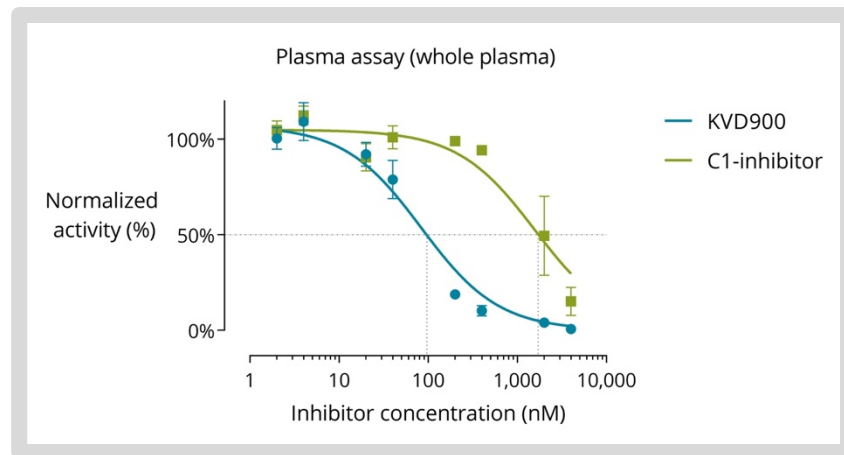
KVD900 Phase 1 Trial – Single Dose PK/PD of Tablets

- Strong inhibition of plasma kallikrein activity following tablet administration
 - 100 mg and 600 mg shown
- Plasma activated by the addition of dextran sulfate
 - Plasma kallikrein activity monitored using a fluorescent substrate
- Rapid onset of inhibition
 - KVD900 exposure delivers rapid and potent inhibition of plasma kallikrein
 - 98% inhibition at 20 minutes



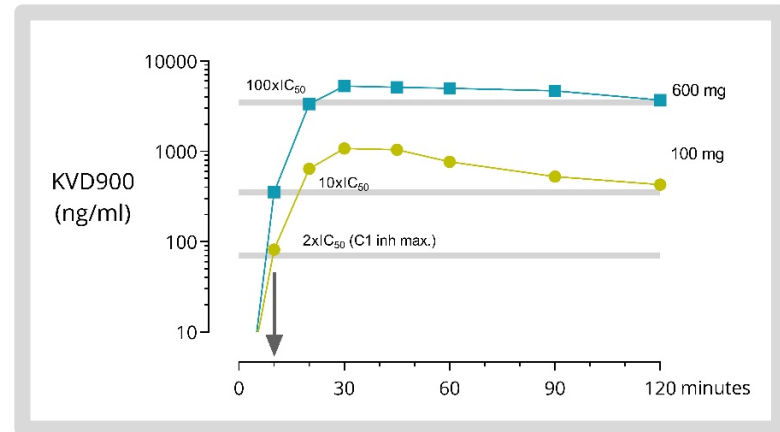
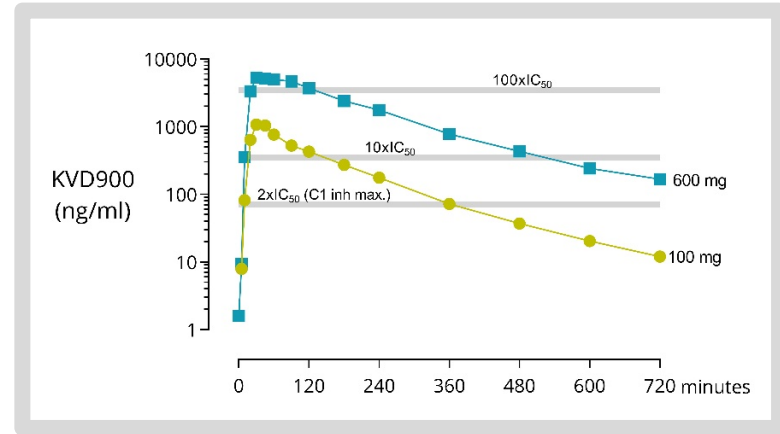
KVD900 Potency Compares Favorably to Berinert

- Comparing to approved, acute C1 inhibitor treatments demonstrates the level of plasma kallikrein inhibition that delivers clinical efficacy
- C1 inhibitor potency
 - IC_{50} in whole plasma is 1700 nM
 - KVD900 is 90 nM
- Berinert
 - Following administration of the approved dose of 20 IU/kg
 - C_{max} » 3,000 nM (0.32 mg/ml) reached within 48 minutes of dosing
 - Maximal concentration is $\approx 2x IC_{50}$



KVD900 Achieves 50-100x IC₅₀

- Multiple dose levels achieve sufficient plasma kallikrein inhibition
 - Based on clinically efficacious doses of C1-INH
 - 600 mg tablet – exceeds 100x IC₅₀
 - 100 mg tablet – exceeds 50x IC₅₀
-
- Rapid exposure is important for acute efficacy
 - 2x IC₅₀ reached around 10 minutes
 - At least as quickly as C1-INH injection
 - 100x IC₅₀ before 30 minutes

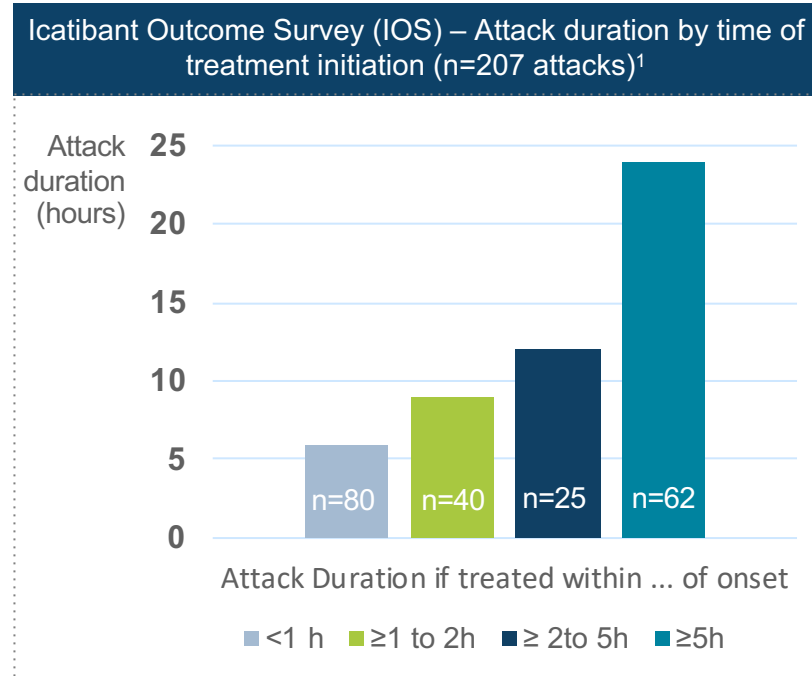


KVD900: On-Demand Treatment of HAE Attacks

- Data shows what we believe is an ideal profile for acute oral therapy
 - Tablet formulation rapidly and highly absorbed driving very fast onset of effect
 - Effective concentrations maintained for at least 10 hours
 - No safety or tolerability signals to date
 - No GI effects
 - Short residence time to minimize any tolerability findings or impact on other medications
- KVD900 has the potential to be a patient-friendly treatment which offers the opportunity to intervene early resulting in higher efficacy
 - Efficacy of acute injectable treatments is often undermined by late dosing
 - Early treatment has been shown to be key in maximizing treatment outcomes
 - Potential label extension for treatment on prodromal symptoms → episodic prophylaxis



Early Treatment Significantly Reduces Attack Duration...



Delaying treatment dramatically extends attack duration



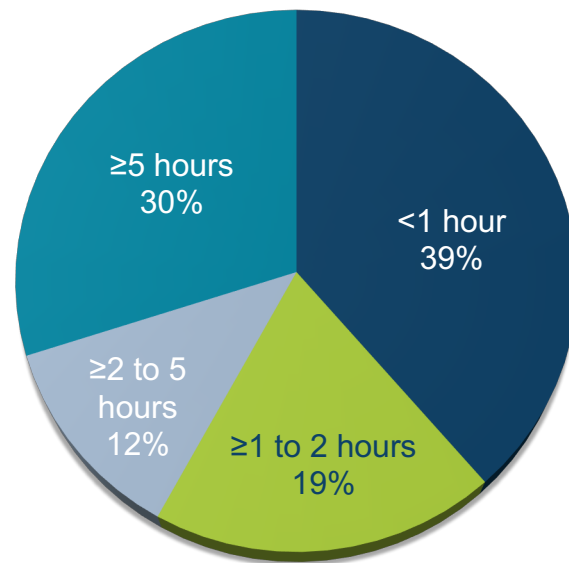
...But Majority of Patients Do Not Treat Early Enough

>60% of patients administer their therapy more than one hour after the beginning of an attack, per IOS

We believe there are several reasons why treatment is delayed:

1. Inconvenient – many therapies require medical professional training
2. Painful – both during and after administration
3. Hope – rather than treat, patients frequently will just hope for a less severe attack

Time to Treatment (n=207)

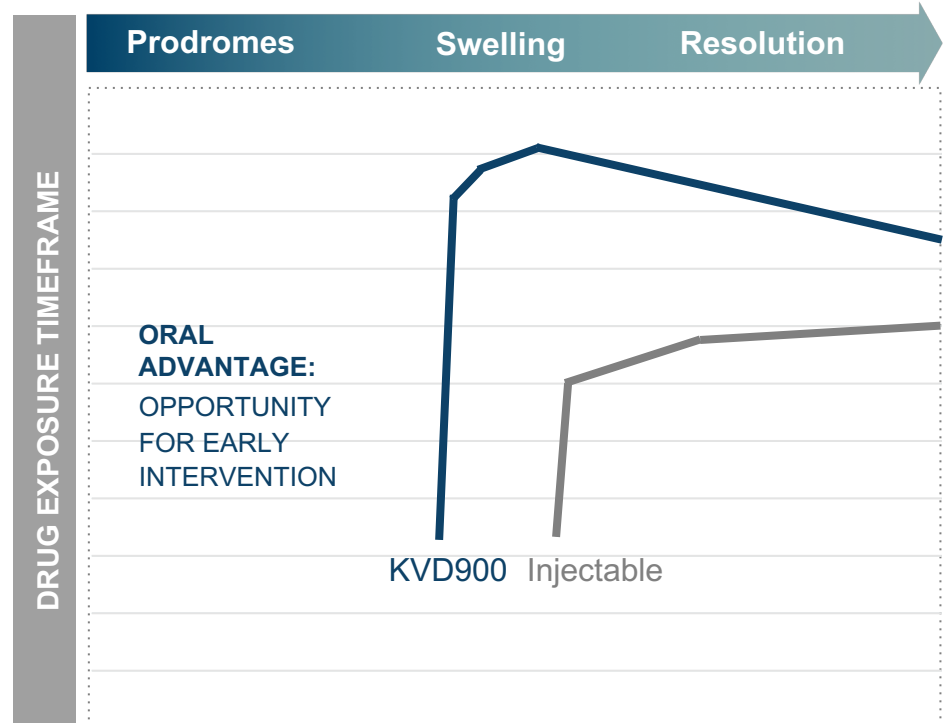


■ <1 hour ■ ≥1 to 2 hours ■ ≥2 to 5 hours ■ ≥5 hours

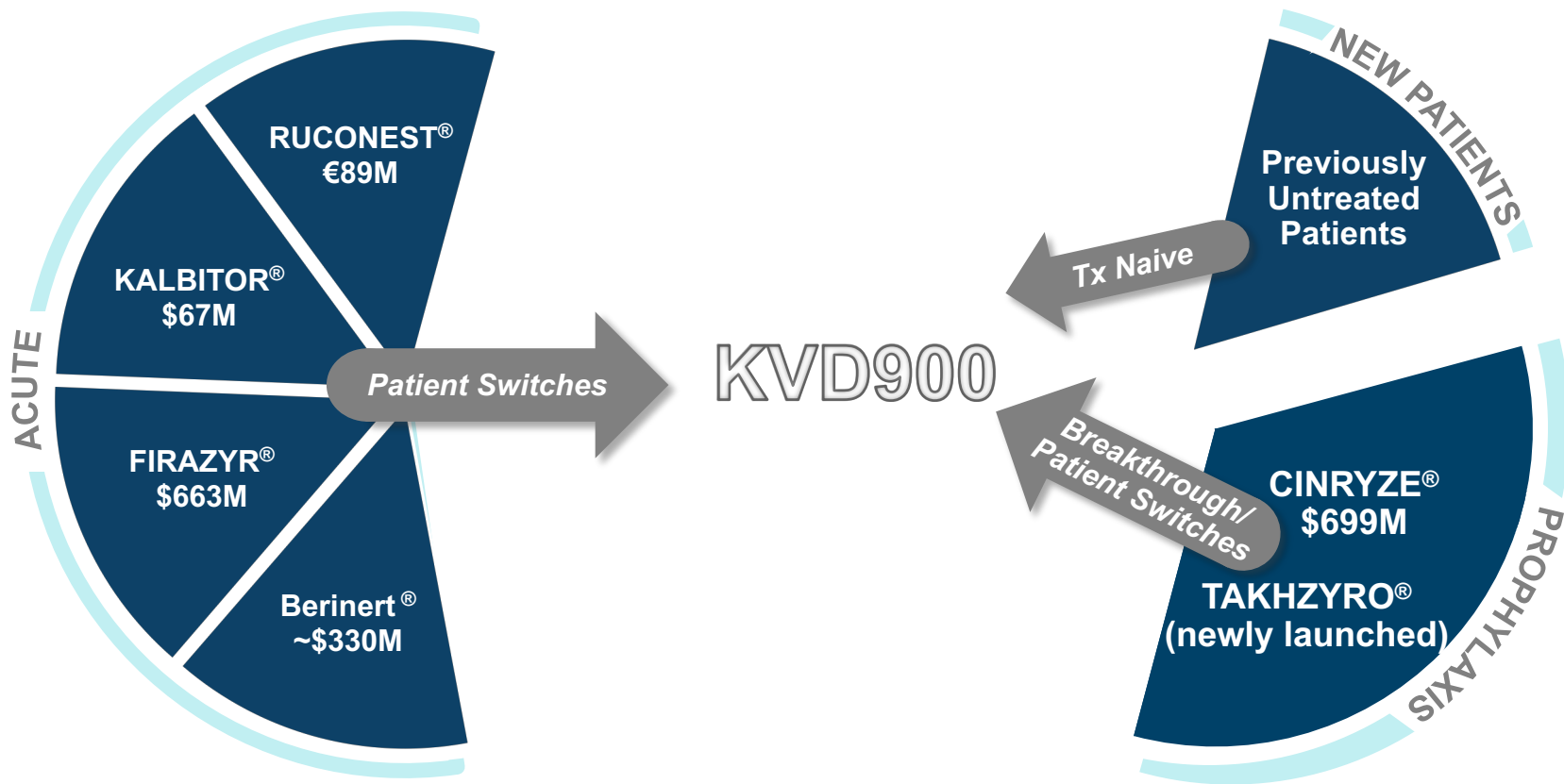


KVD900 Supports Earlier Treatment and Faster Attack Resolution

- Convenience and tolerability of KVD900 compared to other therapies may encourage earlier dosing
- Rapid absorption of KVD900 yields high exposures which compare favorably to injectable therapies
- Combination of these attributes may lead to shorter and less severe attacks and better treatment outcomes
- **Offers the potential to dramatically improve patient quality of life by providing better disease control**

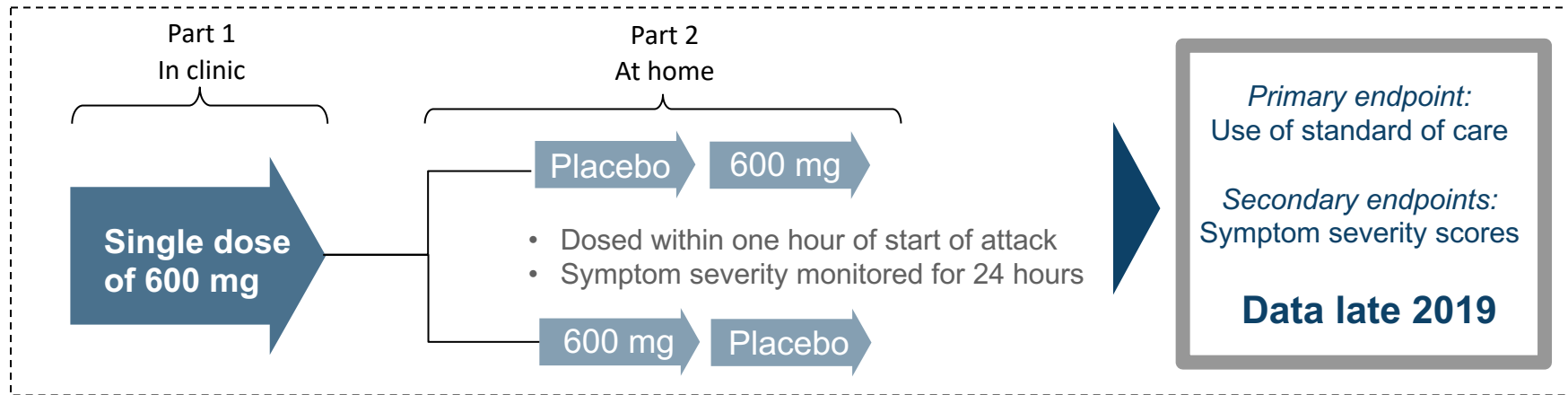


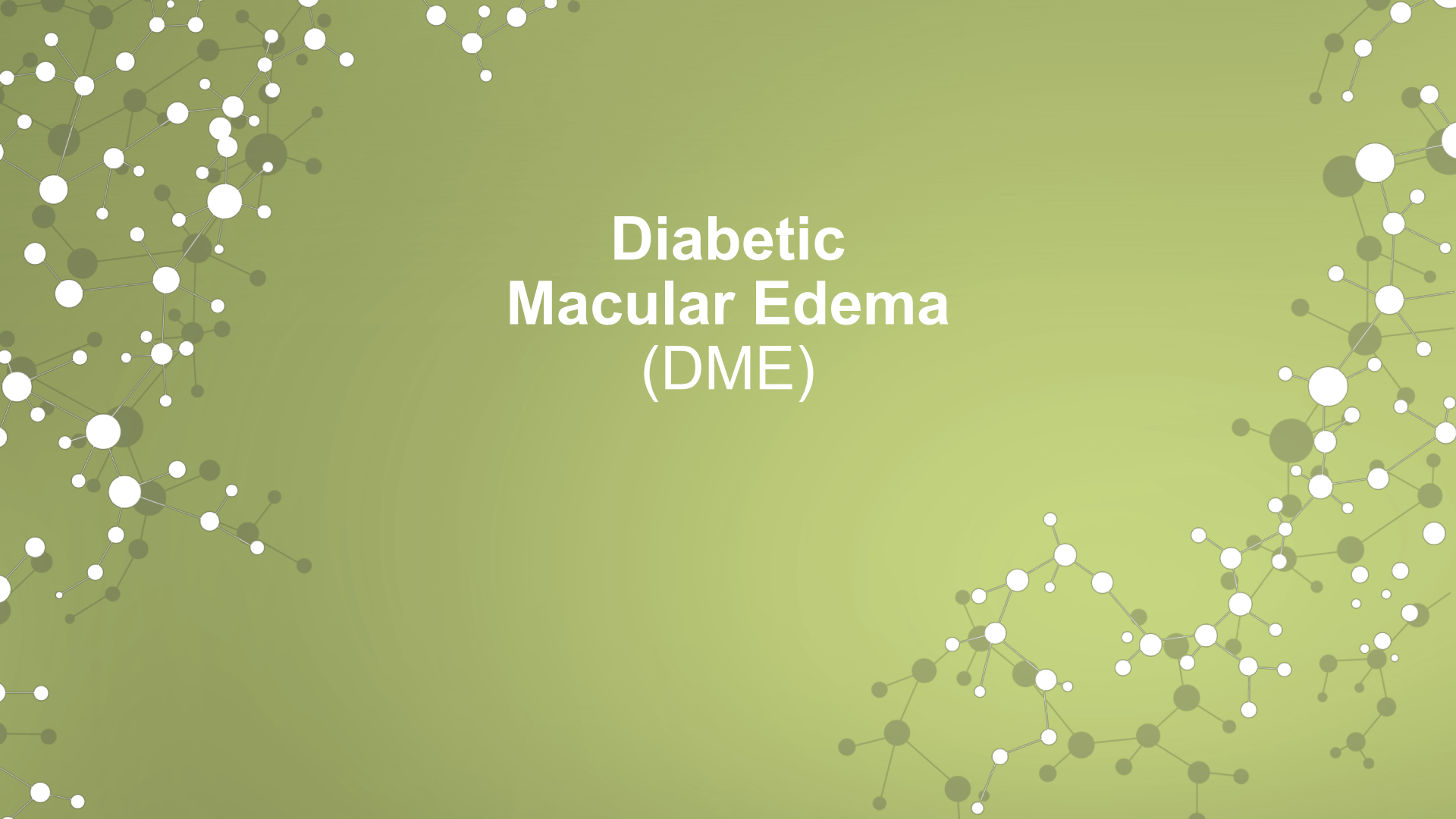
Opportunity: Capture Market Share and Growth of \$2B Market



KVD900 Phase 2 Efficacy Study

- ~50 HAE patients at 10-15 sites in UK, Germany and several other European countries
 - Patients required to have at least 3 attacks in previous 90 days
- 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



The background of the slide is a solid olive green color. It is decorated with a complex, abstract network of white and dark grey nodes connected by thin lines, resembling a molecular or biological structure. The nodes vary in size, and the lines are thin and light grey. The network is distributed across the slide, with a higher density of nodes and lines in the corners and along the sides, leaving the central area where the text is located relatively clear.

Diabetic Macular Edema (DME)

Diabetic Macular Edema: Over \$1 Billion Market

- Retinal swelling due to leaky blood vessels in the macula – a leading cause of blindness
- Approximately 900,000 patients in the United States have active DME and are at serious risk of vision loss
- Standard of care is anti-VEGF injected into the eye – currently there are no oral treatments for DME
- Over 40% of patients do not adequately respond and continue to have impaired visual function and macular edema – significant unmet clinical need
- Plasma kallikrein has been identified as a potential VEGF-independent mediator of DME
- KalVista developed KVD001 as an IVT therapy and is also working to develop an orally delivered plasma kallikrein inhibitor therapy for DME
 - The basis of Merck collaboration announced in October 2017

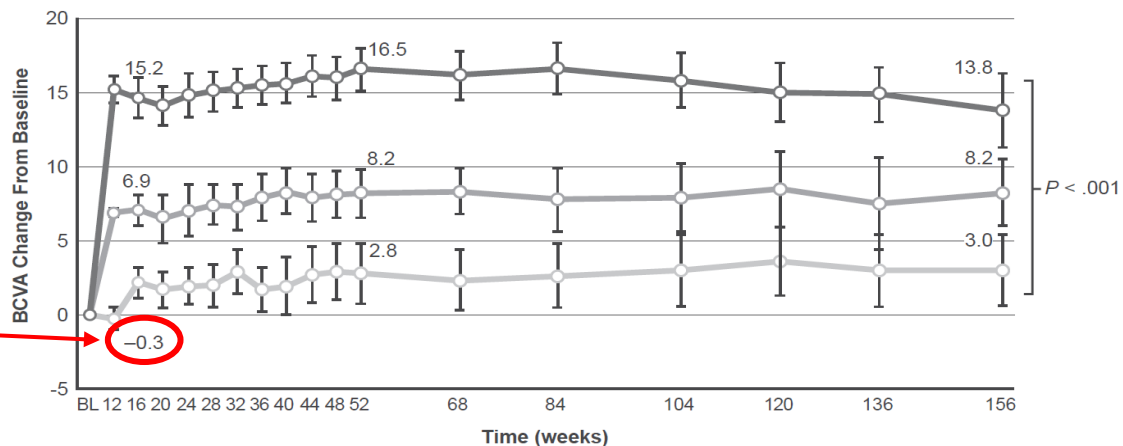


Over 40% of anti-VEGF Patients are Not Adequately Treated

- Large well controlled trial (DRCR Protocol I) of anti-VEGF treatment in DME patients evaluated 854 eyes
- 40% of eyes showed -0.3 letters of improvement in mean BCVA after 3 injections

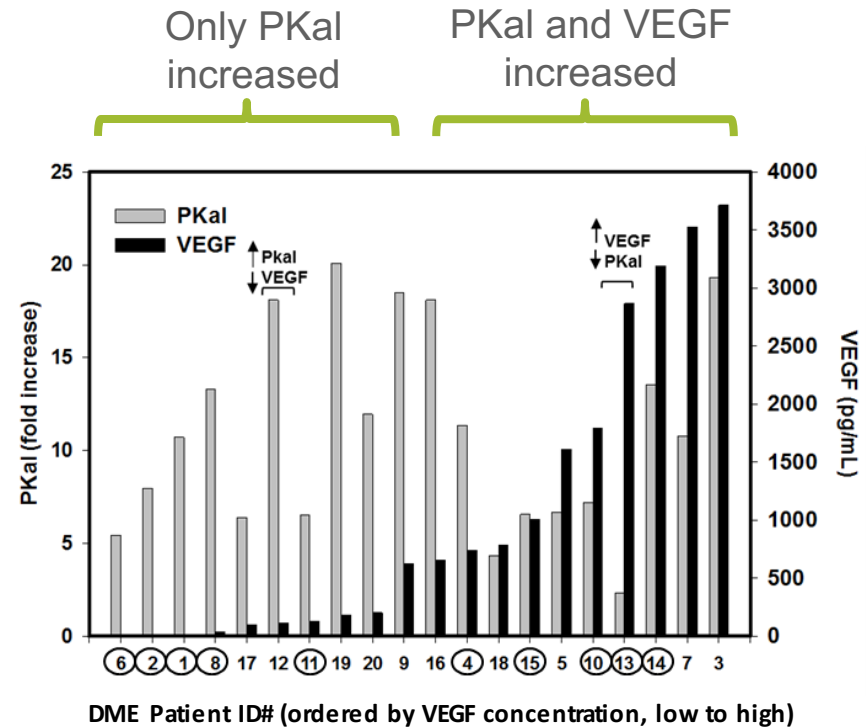
Protocol I analysis of ranibizumab treated eyes (n=340 at 12 wks)

Mean Change: 12 weeks	Eyes
15.2 letters	37% (126 of 340)
6.9 letters	23% (79 of 340)
-0.3 letters	40% (135 of 340)



Plasma Kallikrein (Pkal) Elevated in DME Vitreous

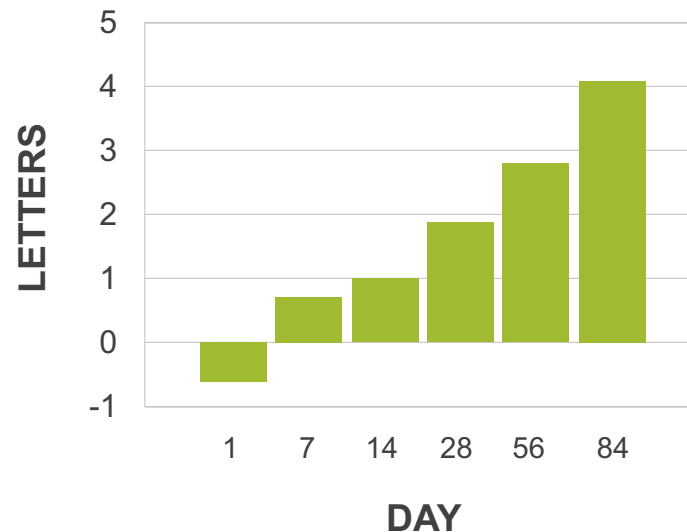
- Vitreous samples from patients with DME show increased Pkal levels
- Significant population has elevated Pkal and low VEGF
 - Patients who may respond well to Pkal inhibition and poorly to anti-VEGF treatment
 - Clear medical need
- Presence of Pkal in addition to VEGF suggests potential utility in broader population



Phase 1 Trial Results

- KVD001: IVT first-in-class plasma kallikrein inhibitor for DME
- Open label, single ascending dose Phase 1 trial in 14 DME patients complete
 - All patients had previously received anti-VEGF treatment
 - Well tolerated
 - Signal of improved visual acuity following single dose
- Duration of animal exposure consistent with signal of improvement

Best Corrected Visual Acuity Change



Mean change in visual acuity following a single dose of KVD001
N=14



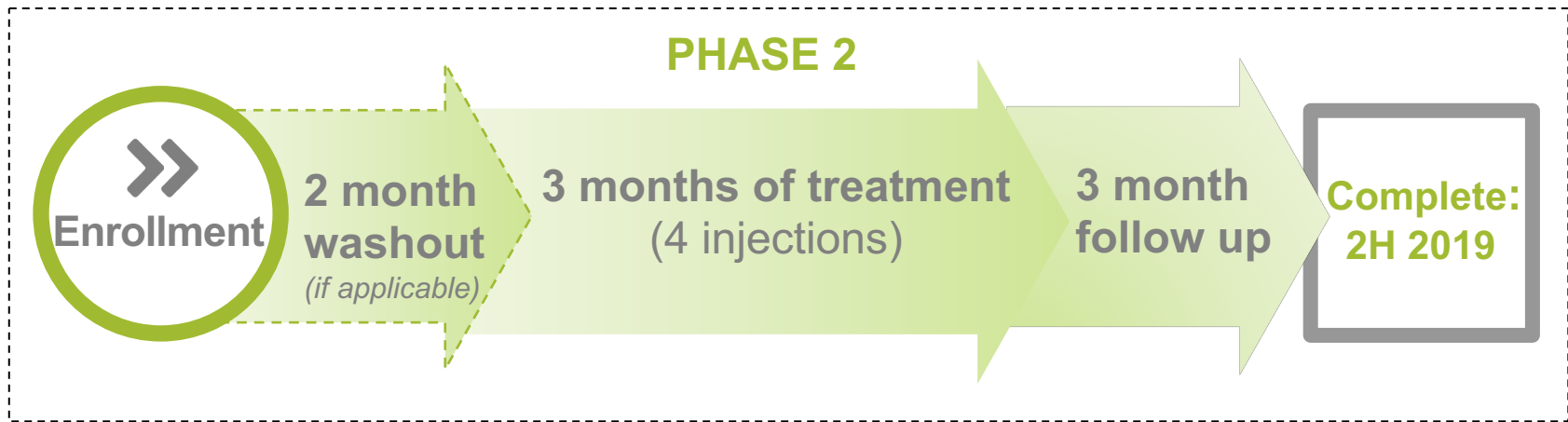
Option Agreement With Merck on DME Programs

- In October 2017, KalVista and Merck announced a collaboration for KVD001, KalVista's intravitreal DME program, as well as future orally-delivered plasma kallikrein inhibitors for DME developed by KalVista
- Merck has two options, to acquire KVD001 and/or oral DME assets until a specified time following certain data on each
- Until the options are exercised, KalVista retains full ownership and control of the assets
 - KalVista to execute and fund the Phase 2 KVD001 trial and other activities
 - Merck pays all costs post-exercise
- \$37 million upfront payment to KalVista
- \$715 million in potential additional milestone payments
- Tiered sales royalties on global net sales
- Merck acquired a 9.9% stake in KalVista in a concurrent PIPE



KVD001 Phase 2 Enrollment on Track

- Approximately 123 patients who have discontinued treatment with anti-VEGF therapy and who still have significant edema and reduced visual acuity
- Sham-controlled, double-masked clinical trial will evaluate two doses
- Efficacy endpoints include best corrected visual acuity (BCVA), central subfield thickness (CST), and the diabetic retinopathy severity scale (DRSS)



2019 Milestones

KVD824 update

Mid-year

KVD001 Phase 2 complete

H2 2019

KVD900 Phase 2 data

Late 2019

KVD900 Orphan Drug application

2019





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NASDAQ: KALV