



KalVista  
Pharmaceuticals

# Corporate Presentation

February 2020



# Forward-Looking Statements

This presentation and the accompanying oral presentation contain “forward-looking” statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as: “anticipate,” “intend,” “plan,” “goal,” “seek,” “believe,” “project,” “estimate,” “expect,” “strategy,” “future,” “likely,” “may,” “should,” “will” and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding our future financial performance, business plans and objectives, timing and success of our clinical trials, our ability to obtain regulatory approval or the timing of regulatory filings, the potential therapeutic benefits and economic value of our lead product candidates, financing plans, competitive position, industry environment and potential market opportunities.

Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, the following: those related to our future financial performance, our ability to raise additional funding when needed, our ability to develop and maintain partnerships, our ability to identify and develop new products in a timely manner, the outcome, cost and timing of our product development activities and clinical trials, market size and acceptance of our products, our ability to maintain, protect and enhance our brand and intellectual property, our ability to continue to stay in compliance with applicable laws and regulations, our ability to scale our business and make key hires and such other factors as discussed under the section titled “Risk Factors” and elsewhere in our Annual Report on Form 10-K, definitive proxy statement and quarterly reports on Form 10-Q that we file with the Securities and Exchange Commission (“SEC”) as well as our other filings and the documents incorporated by reference therein, with the SEC.

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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 \$93.5 million as of October 31, 2019



# Product Portfolio

	Preclinical	Phase 1	Phase 2	Phase 3	Status
<b>Mid Stage Programs</b>					
<b>KVD900</b> for On-Demand Hereditary Angioedema					<ul style="list-style-type: none"> <li>• Phase 2 data expected Q2 2020</li> </ul>
<b>KVD824</b> for Hereditary Angioedema Prophylaxis					<ul style="list-style-type: none"> <li>• Phase 2 anticipated H2 2020</li> </ul>
<b>KVD001</b> (IVT) Diabetic Macular Edema					<ul style="list-style-type: none"> <li>• Phase 2 study completed</li> </ul>
<b>Early Stage Programs</b>					
<b>Oral DME Molecules</b> Target: Plasma Kallikrein					<ul style="list-style-type: none"> <li>• Regulatory studies ongoing</li> </ul>
<b>Other Proteases</b> Target: Undisclosed					<ul style="list-style-type: none"> <li>• Lead optimization ongoing</li> </ul>





# Hereditary Angioedema (HAE)

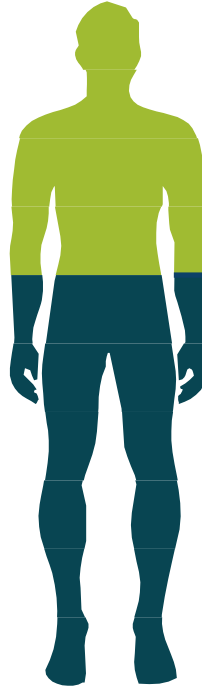
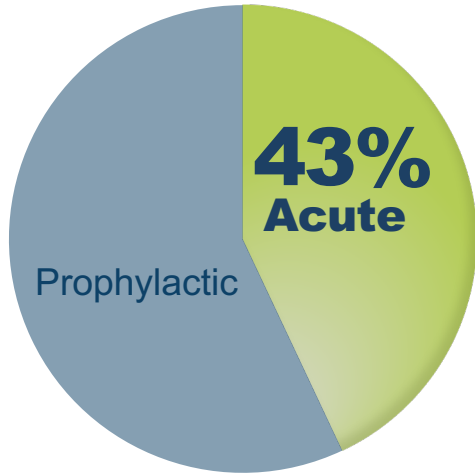
# Hereditary Angioedema (HAE)

- Genetic condition causing painful and dramatic swelling in various parts of the body
- Orphan disease: incidence 1 in 10,000 to 1 in 50,000<sup>1</sup>
- 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



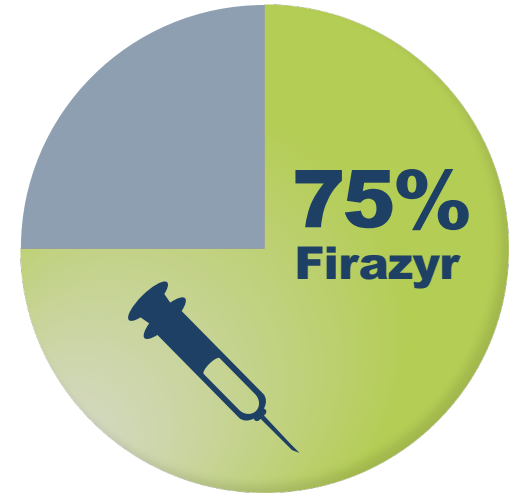
# US HAE Market Landscape

## Patient Distribution



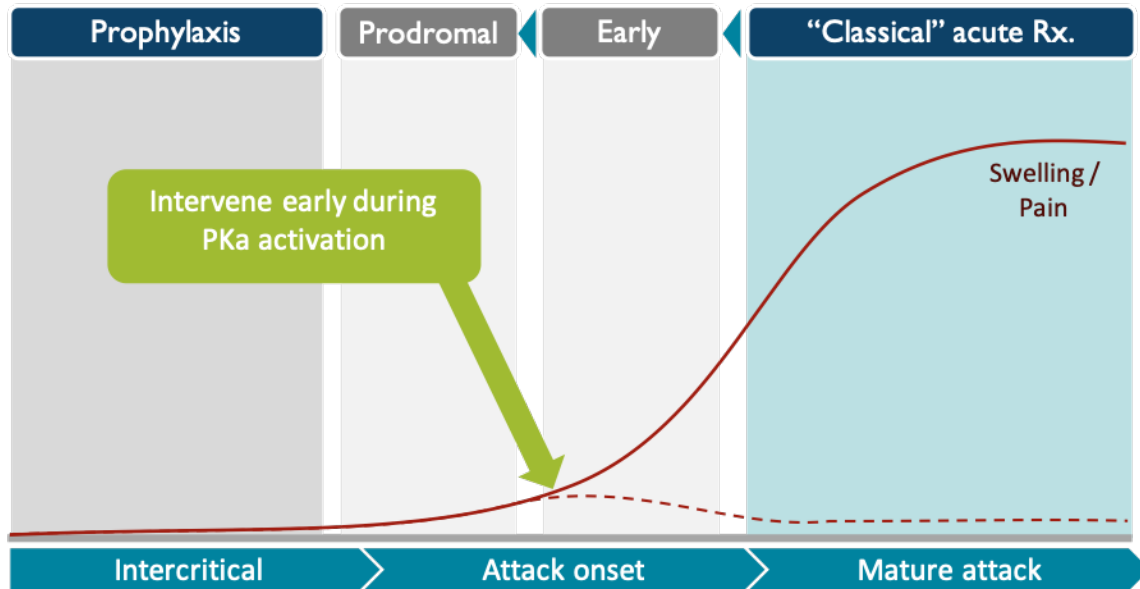
Only ~62% of  
HAE patients treat  
all attacks

## Current Acute Treatment



# Patients Want A Safe, Efficacious, Oral Therapy

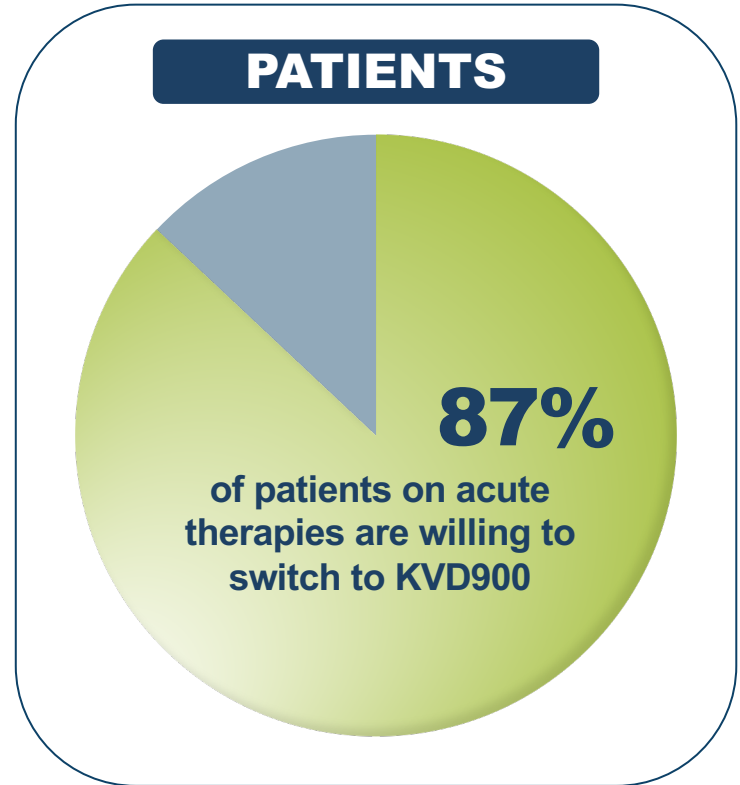
- On-demand therapy can meet the needs of the majority of patients
- Key requirement is rapid absorption to high exposure levels
- Even prophylactic patients need an on-demand back-up in case of breakthrough attacks





# 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

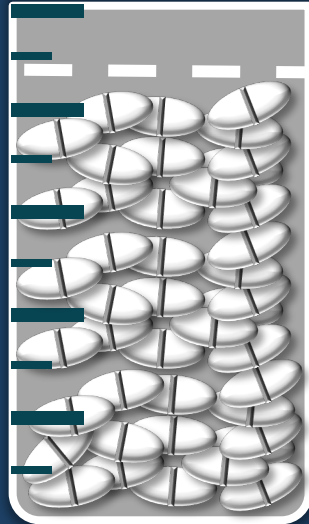


# Positive Payer and Physician Reaction to KVD900

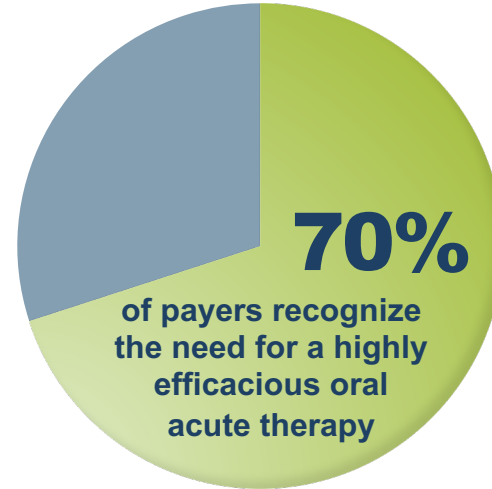
*Physicians Likely to Prescribe KVD900*

**89%**

KVD900



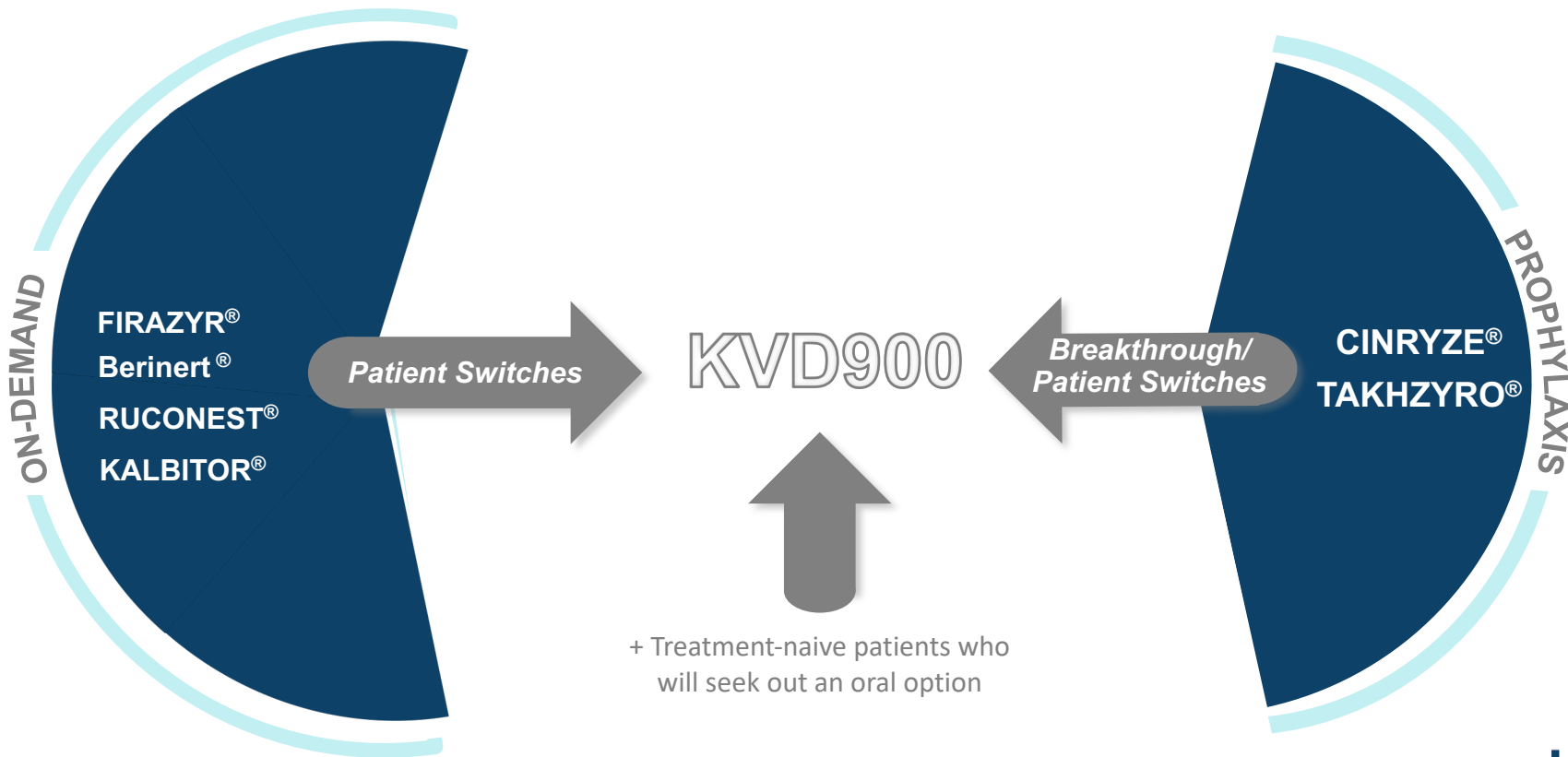
**PAYERS**



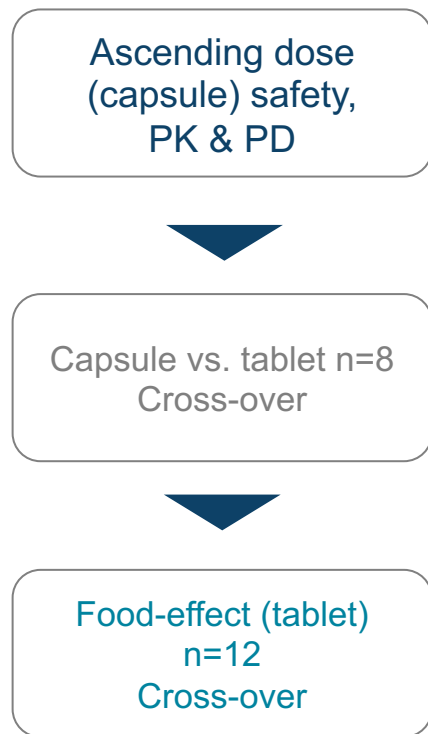
- Value proposition supports premium pricing
- Generic icatibant launch does not reduce interest in oral acute therapy



# Opportunity to Capture Market Share and Growth



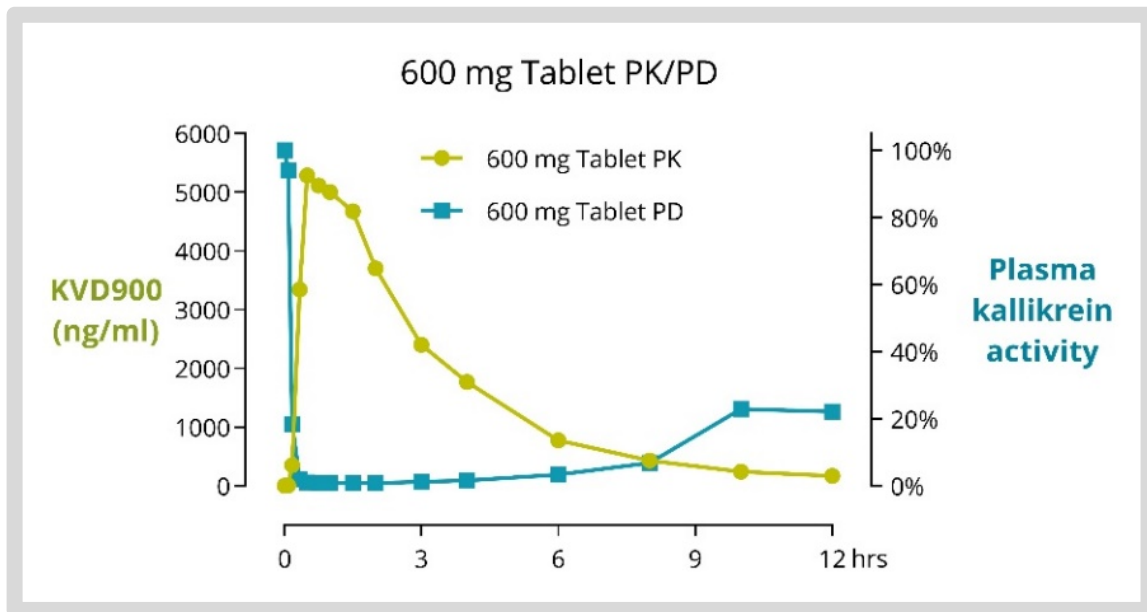
# KVD900 Phase 1 Overview



- 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

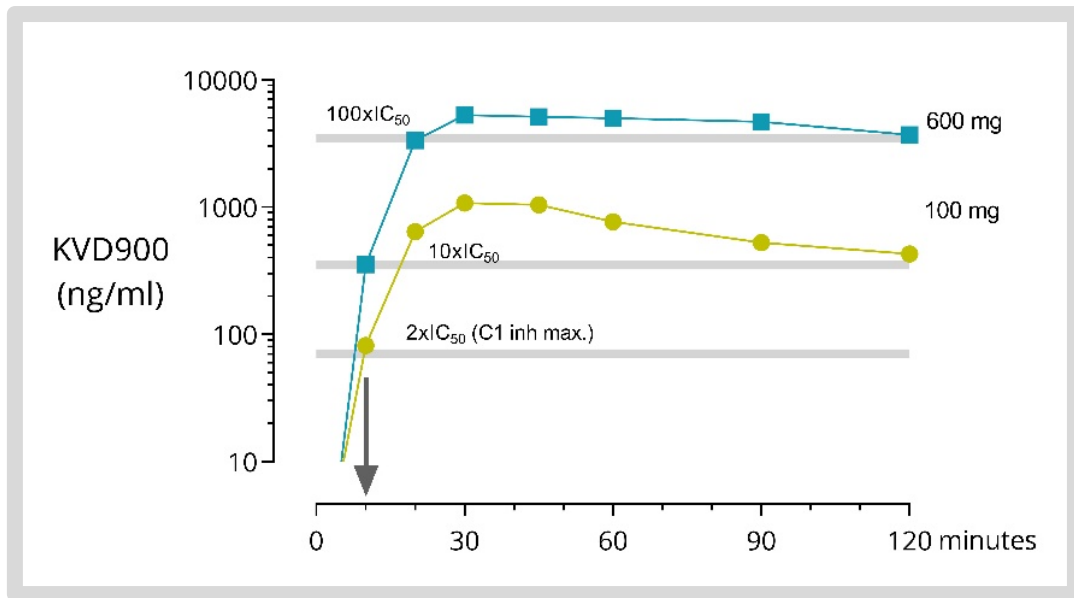
- Plasma kallikrein assay using whole plasma
- Rapid onset of inhibition
  - 98% inhibition at 20 minutes
  - Inhibition through 12 hours
  - Food has no meaningful impact on PD profile of KVD900 tablets
- Phase 2 study and commercial use will be tablet formulation





# KVD900 Achieves 100x IC<sub>50</sub>

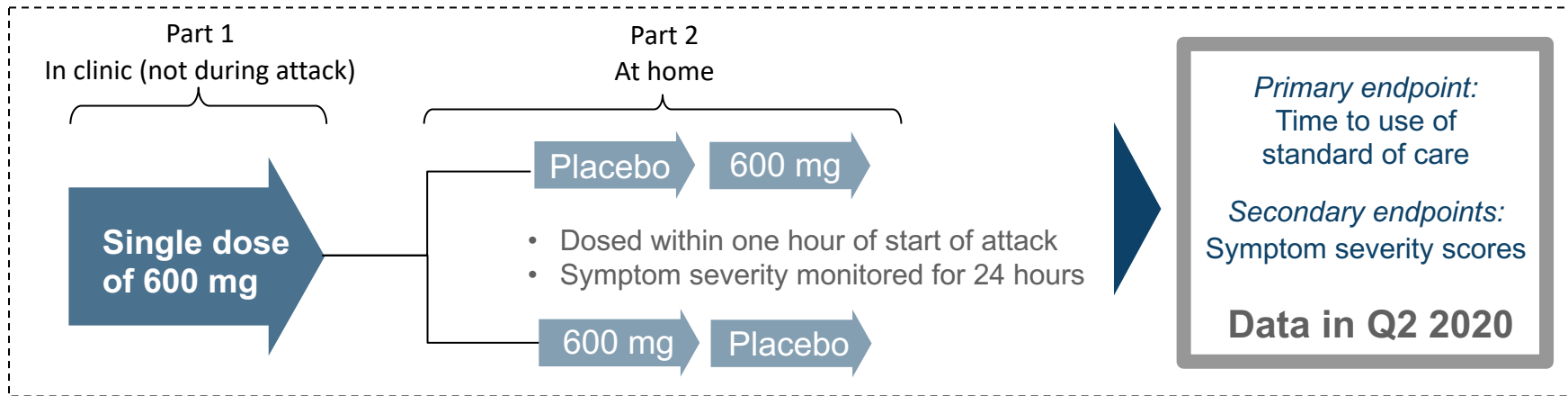
- Multiple dose levels achieve sufficient plasma kallikrein inhibition
  - Based on clinically efficacious doses of C1-INH<sup>1</sup>
- Rapid exposure important for on-demand efficacy
- 2x IC<sub>50</sub> reached around 10 minutes
  - At least as quickly as C1-INH injection
- 100x IC<sub>50</sub> before 30 minutes



<sup>1</sup>IC<sub>50</sub> 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<sub>max</sub> is »3,000 (0.32 mg/ml) reached within 48 minutes of dosing. Maximal concentration is ≈ 2x IC<sub>50</sub>.

# KVD900 Phase 2 Efficacy Study Ongoing

- ~50 HAE patients at 10-15 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



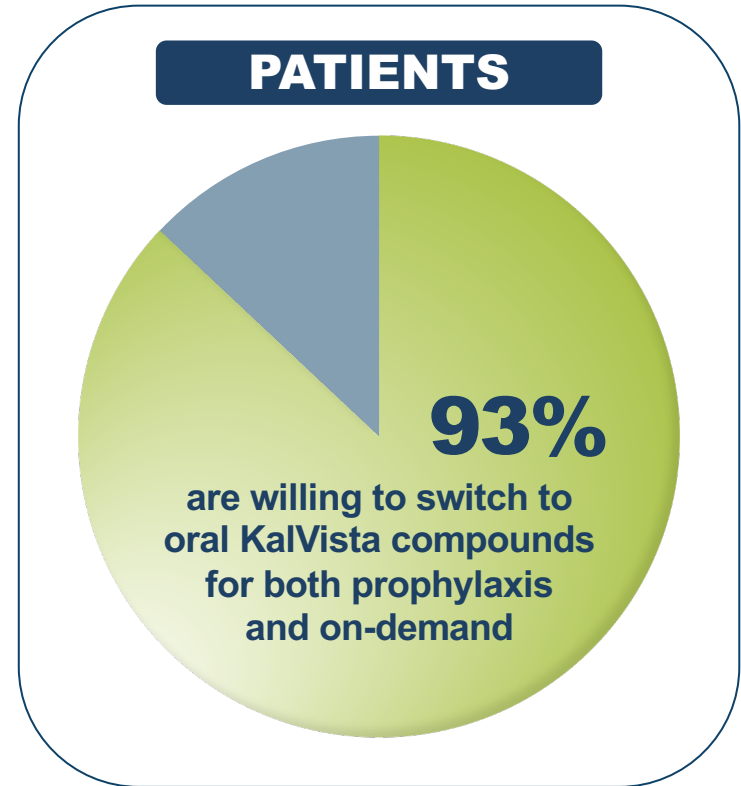
# KVD824 as Oral Prophylactic

- 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
- 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



# KVD824 as Oral Prophylactic

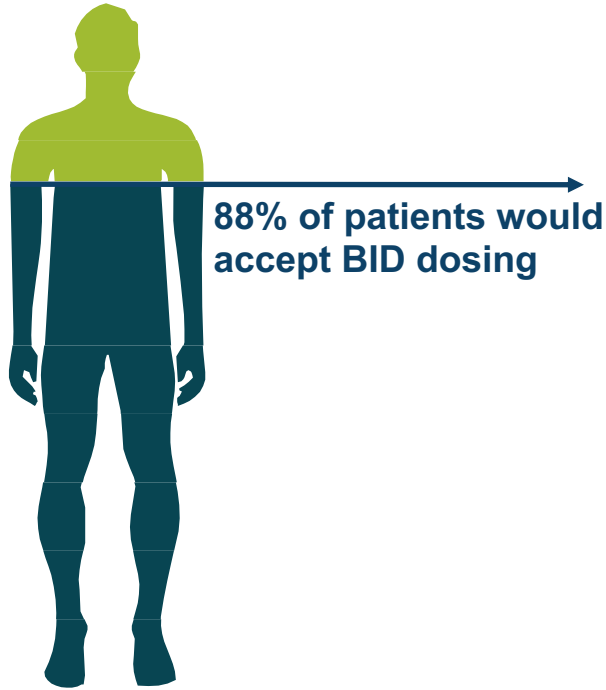
- KVD824 is moving forward as a twice-daily prophylactic therapy
- 89% of current prophylaxis patients surveyed expressed interest in switching to oral medication
  - Number of current attacks or level of control of attacks not a factor
  - Improve their quality of life
  - Physical and psychological issues still exist with injections



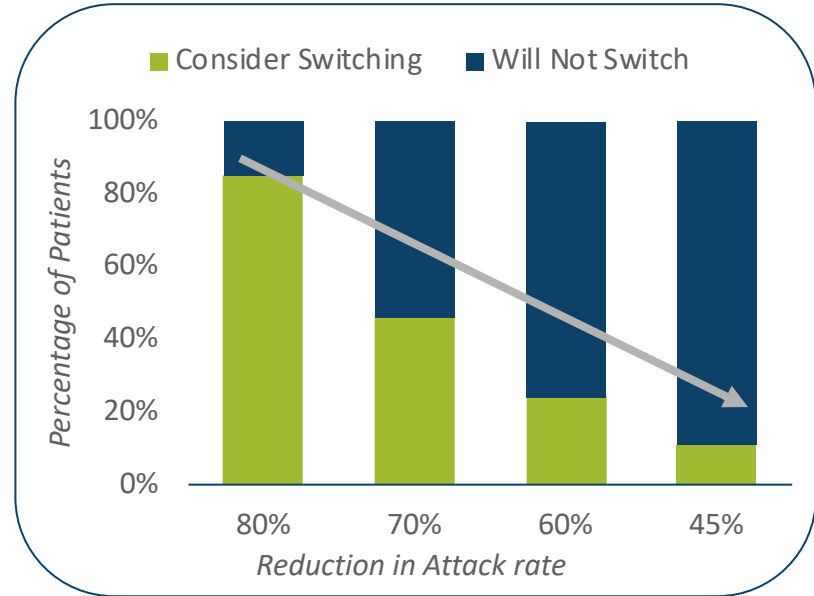


# Efficacy Is Key Driver of Willingness to Switch to Oral

Dosing regimen is secondary to efficacy in importance



Patients will not trade lower efficacy for oral dosing



The background of the slide features a close-up photograph of tall, thin, golden-brown grasses. A semi-transparent green overlay covers the entire image, with a darker green triangular shape in the top-left corner.

# **Diabetic Macular Edema (DME)**

# KVD001 Phase 2 Clinical Trial Design

## Subjects

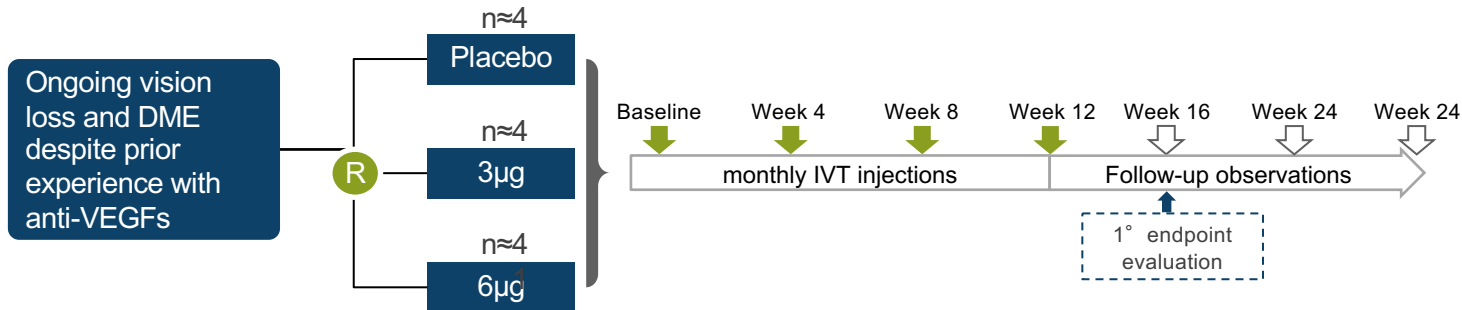
- Adult male or female subjects with confirmed DM (type I or II)
- Presence of ciDME (F: > 305 $\mu$ m; M: > 320  $\mu$ m)
- Ongoing vision loss (20/40 or worse) despite prior anti-VEGF treatment (within 36 months of Day 1)

## Setup

- 38 US sites
- Double-masked, parallel group, 1:1:1 randomization, stratified for BCVA, CST at baseline
- 4 monthly injections with safety follow-up

## Stats

- N=41 per arm, power 80%, with change in  $5 \pm 7.5$  letters between active and sham,  $\alpha=0.05$
- Primary analysis: ANCOVA, LSmeans change in BCVA at week 16 from baseline, active vs. sham, adj. for BCVA at baseline, last-observation carried forward



# KVD001 Phase 2 Clinical Trial Endpoints

## 1° efficacy endpoint

- Change from baseline BCVA letter count via ETDRS at Week 16

## 2° efficacy endpoints

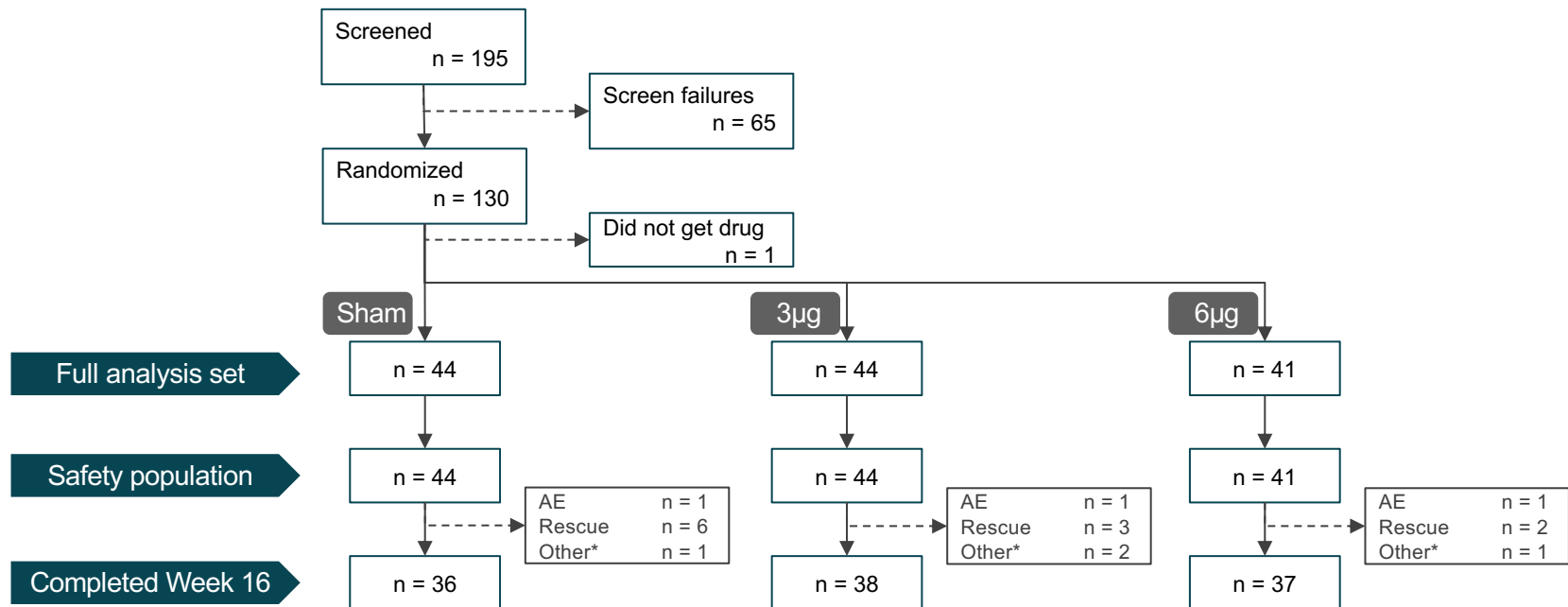
- Change from baseline CST via SD-OCT
- Proportion of eyes w/  $\geq 2$  step DRSS improvement from baseline
- Change from baseline BCVA via ETDRS at wk 4, 8, 12, 20 and 24
- Proportion of eyes with  $\geq 5$ ,  $\geq 10$  and  $\geq 15$  BCVA letter change from baseline (gain and loss)

## Safety endpoints

- Adverse events
- Ophthalmic exam and physical exam findings
- Laboratory test results
- Vital signs



# CONSORT Diagram & Analysis Populations





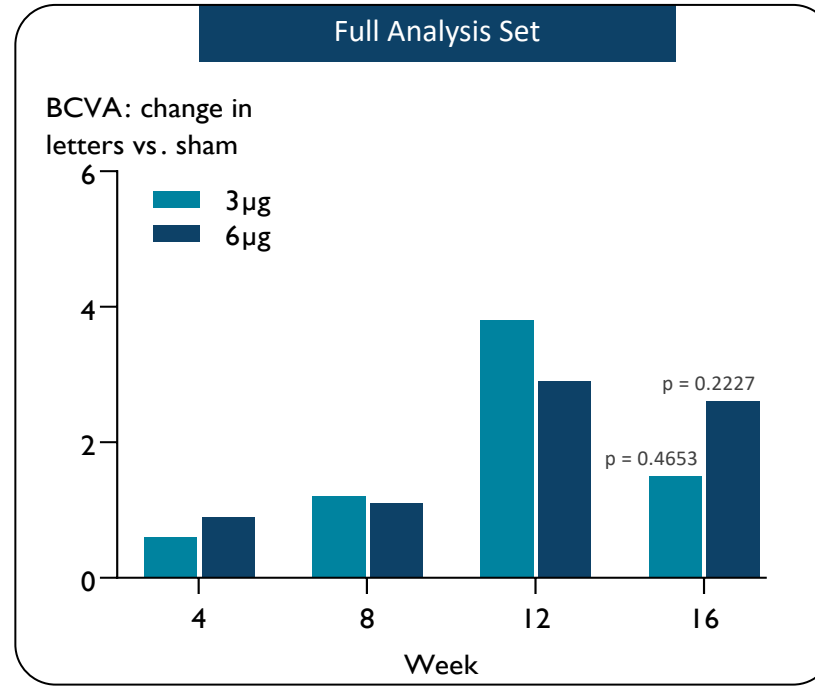
# Baseline Population Characteristics

Variable		Sham n = 44		KVD001 3μg n= 44		KVD001 6μg n= 41		Total n = 129	
Age	mean (SD)	64.6	(8.6)	61.1	(10.7)	63.2	( 9.6)	63.0	(9.7)
Sex	female / male n (%)	23/21	(52.3/47.7)	20/24	(45.5/54.5)	15/26	(36.6/63.4)	58/71	(45.0/55.0)
Race	white n (%)	37	(84.1)	37	(84.1)	37	(90.2)	111	(86.0)
	black n (%)	3	(6.8)	5	(11.4)	4	(9.8)	12	(9.3)
	other n (%)	4	(9.1)	2	(4.6)	0	(0)	6	(4.7)
BMI	mean (SD)	31.6	(7.0)	33.0	(7.7)	31.7	(5.4)	32.1	(6.8)
HbA1c	mean (SD)	7.5	(1.2)	7.6	(1.3)	8.0	(1.5)	—	—
Duration of DME (yrs)	mean (SD)	1.4	(1.3)	1.0	(0.9 )	1.0	(1.2)	1.1	(1.1)
Type 2 DM	n (%)	44	(100)	40	(90.9)	40	(97.6)	124	(96.1)

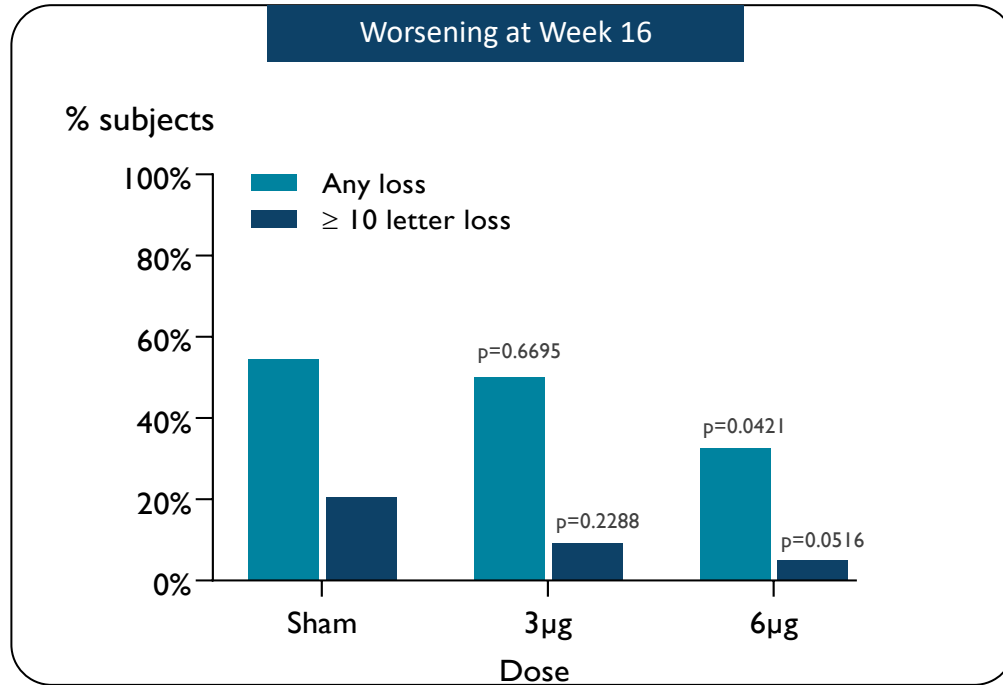
# Baseline Ocular Characteristics

Variable		Sham n = 44		KVD001 3μg n= 44		KVD001 6μg n= 41		Total n = 129	
BCVA (letters)	mean (SD)	60.7	(7.4)	58.8	(12.5)	58.0	(12.8)	59.2	(11.1)
BCVA > 55	n (%)	33	(75.0)	31	(70.5 )	30	(73.2)	94	(72.9)
CST (μm)	mean (SD)	500	(131)	540	(166)	512	(134)	517	(145)
CST ≤ 450 μm	n (%)	17	(38.6)	17	(38.6)	15	(36.6)	49	(38.0 )
Prior IVT anti-VEGF Tx	mean (SD)	8.0	(4.0)	7.4	(4.1)	5.9	(3.0)	7.1	(3.8)
Prior IVT steroid	n (%)	13	(29.5)	12	(27.3)	10	(24.4)	35	(27.1)

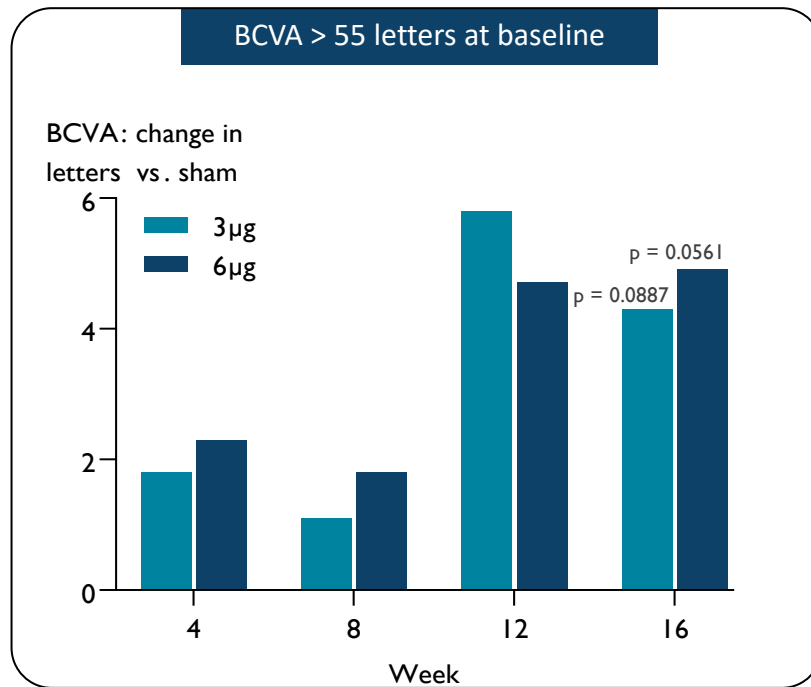
# Study Did Not Meet the Primary BCVA Endpoint



# Vision Loss Protected In a Dose Responsive Manner

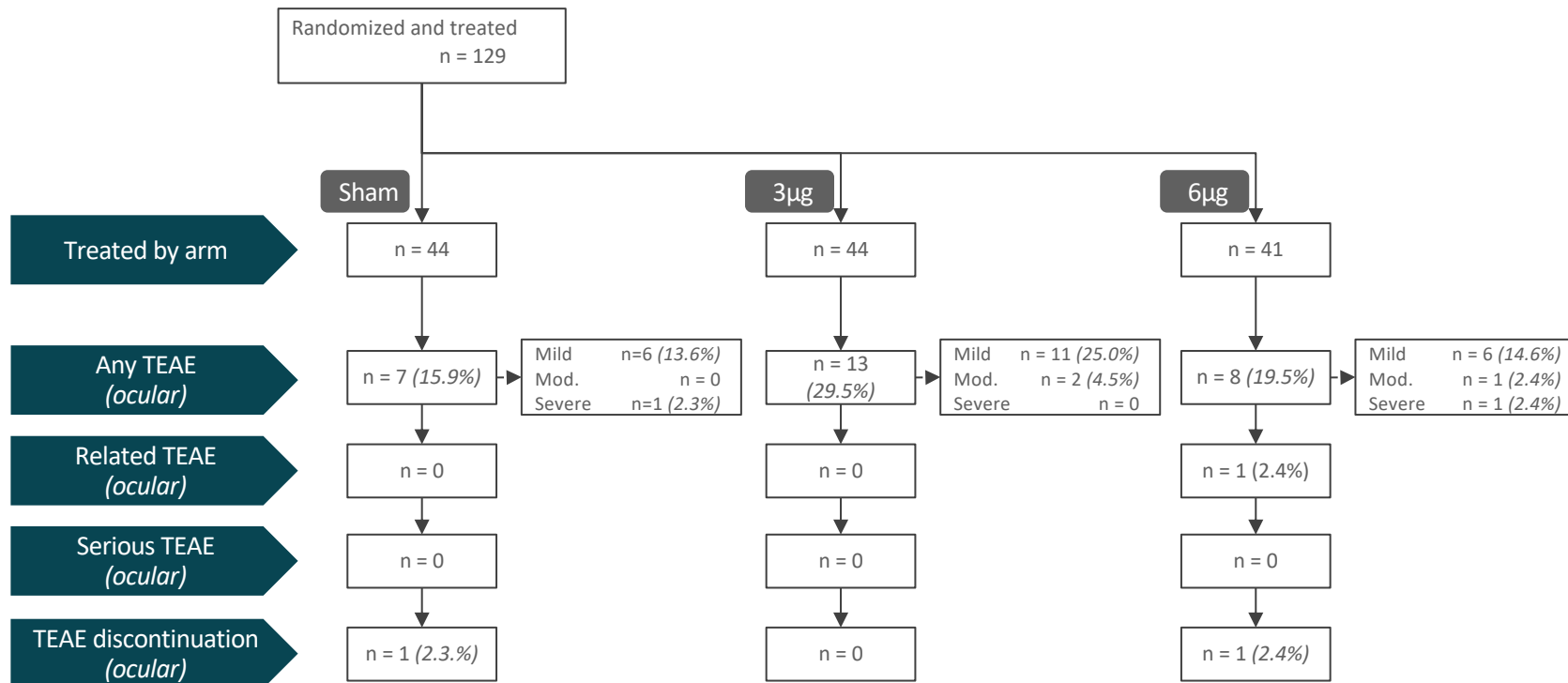


# More Robust Response in Subjects with Baseline Vision of >55 Letters





# KVD001: Generally Safe and Well Tolerated



# 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**