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THE OPHTHALMOLOGY MEDICINES COMPANY

Corporate Presentation
June 2019

SPECIAL NOTE REGARDING

FORWARD-LOOKING STATEMENTS

These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements we make regarding the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, our ability to advance product candidates into, and successfully complete, clinical studies, and the timing or likelihood of regulatory filings and approvals are forward looking. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These statements are also subject to a number of material risks and uncertainties that are described in our most recent quarterly report on Form 10-Q, as well as our subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.



OUR MISSION

**The Ophthalmology
Medicines Company**

1 TRAILBLAZING SCIENCE

Our creative and thoughtful
foundation

2 “GO-TO” MEDICINES

Our challenge to the status quo

3 SINGULAR FOCUS IN OPHTHALMOLOGY

Our 24/7/365

STRONG

COMPANY LEADERSHIP

Management Team with Experience to Build a Leading Biotech Company

BOARD OF DIRECTORS

Deep Biotech and Governance Experience

Victor Perlroth MD
Chairman

KODIAK

Felix J Baker PhD
Director

Baker Brother
Advisors LP

Bassil I. Dahivat PhD
Director

xencor

Richard S. Levy MD
Director

Robert A. Profusek
Director

**JONES
DAY**



Victor Perlroth MD

Founder
Chief Executive Officer

Avidia **MPM** **GUZIK**



John Borgeson

Chief Financial Officer

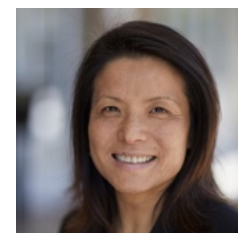
Pfizer **LABRYS BIOLOGICS** **venBio**



Jason Ehrlich MD, PhD

Chief Medical Officer
Chief Development Officer

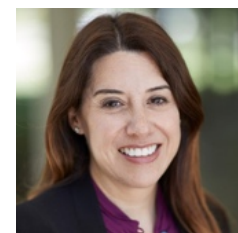
Roche **Genentech**



Hong Liang PhD

SVP Discovery Medicine

Pfizer **RINAT** **Deltagen**



Desiree Beutelspacher

VP, Clinical Operations

OPHTHOTECH **eyotech**



Joel Naor MD

VP, Clinical Science &
Development Operations

Allergan **MACUSIGHT**
STEMCELLS **QLT Inc.**



Almas Qudrat MSc

VP, Quality Operations

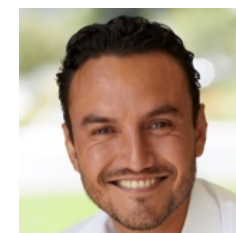
Roche **Allergan** **NEKTAR** **elan**



Stephen Raillard PhD

VP, Chemical Dev. & Mfg

XenoPort **AFFYMAX**



J. Pablo Velazquez-Martin MD

VP, Clinical Research &
Translational Medicine

BAYER



Laurent Ducry, PhD

VP, Biologics Dev. & Mfg

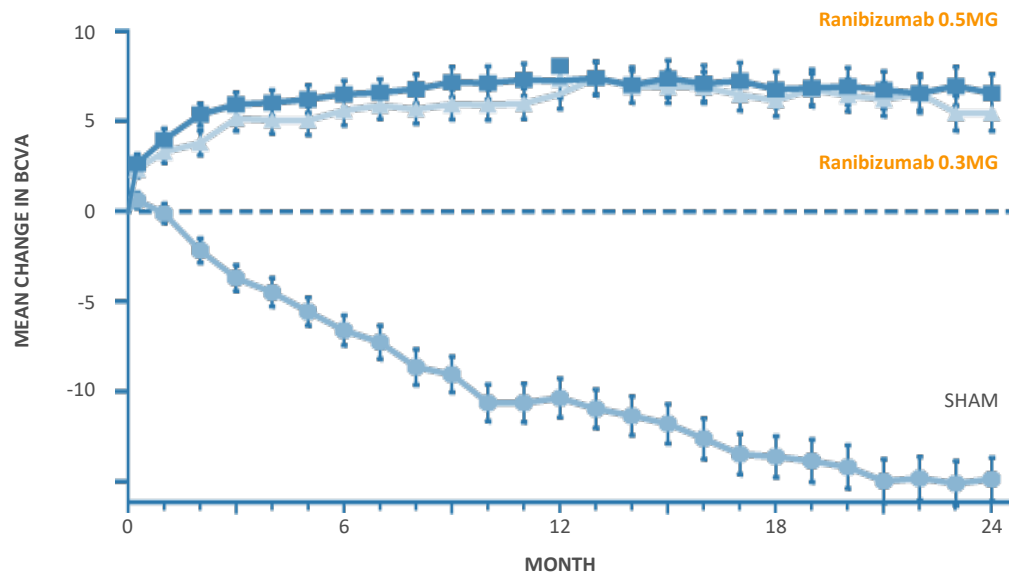
LONZA

THE WHAT

WHAT IS THE PROBLEM TO BE SOLVED?

Intravitreal agents improve & maintain vision when dosed per label...

PHASE III STUDY OF MONTHLY ANTI-VEGF¹



Recommended dosing in first year:

Ranibizumab

12

(MONTHLY)

Aflibercept

8

(BI-MONTHLY AFTER 3 MONTHLY
LOADING DOSES)

1. Rosenfeld PJ et al; MARINA Study Group. N Engl J Med. 2006;355:1419-14313.

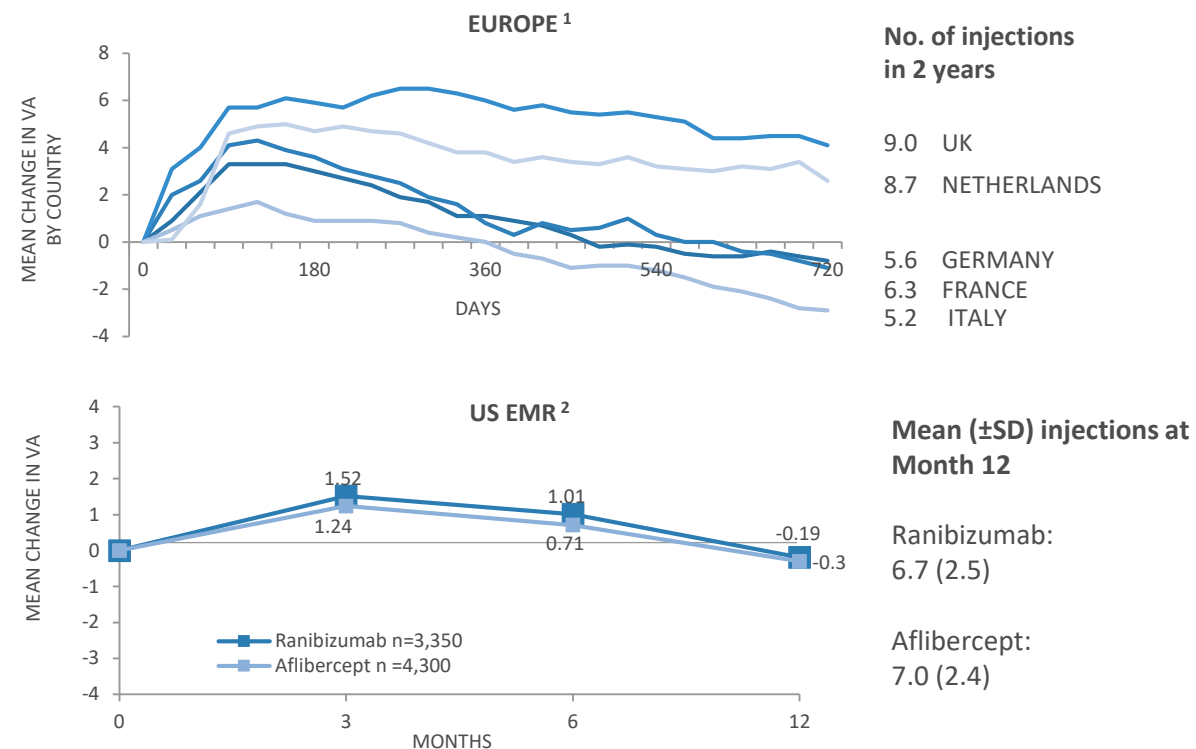
THE WHAT

WHAT IS THE PROBLEM TO BE SOLVED?

...yet minimal visual gains are achieved in real-world practice

- Without continuous high intensity treatment, vision loss can begin after only 3 months of anti-VEGF therapy
- This pattern is seen globally and with all current agents

1. The AURA Study, adapted from Holz FG et al. Br J Ophthalmol 2015; 99 (2): 220–226.
2. Adapted from Lotery A, et al. Eye (Lond). 2017 Dec;31(12):1697-1706.
EMR= Electronic Medical Records



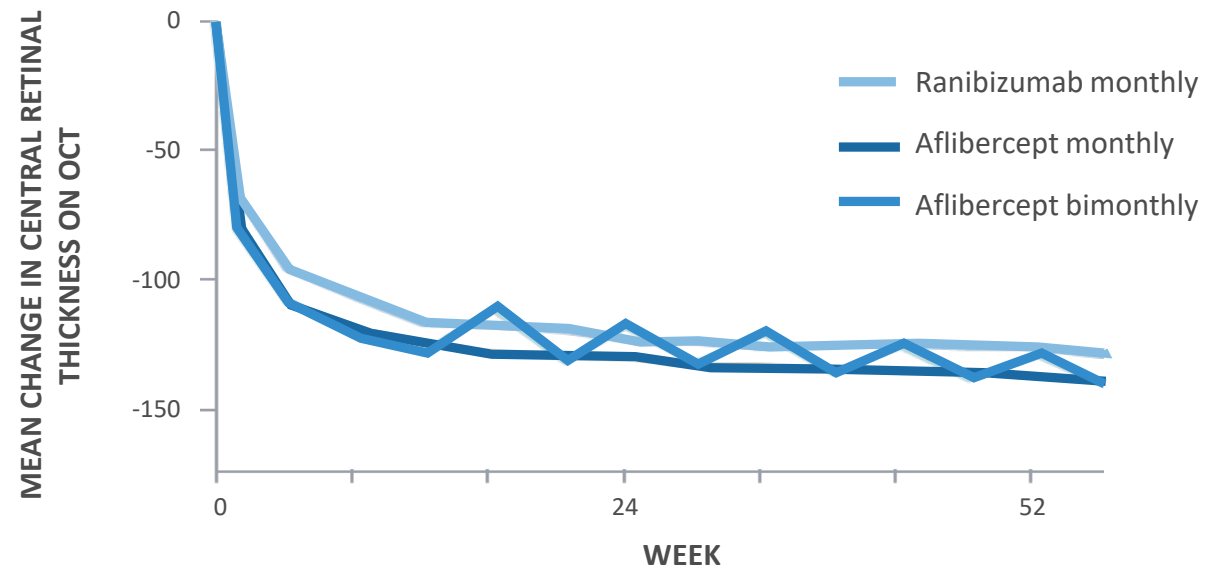
THE WHY

Current agents do not control disease for long enough between doses.

Undertreatment leads to disease progression and permanent retinal damage.

Bimonthly anti-VEGF Therapy Results in Disease Activity between Doses due to Insufficient Durability

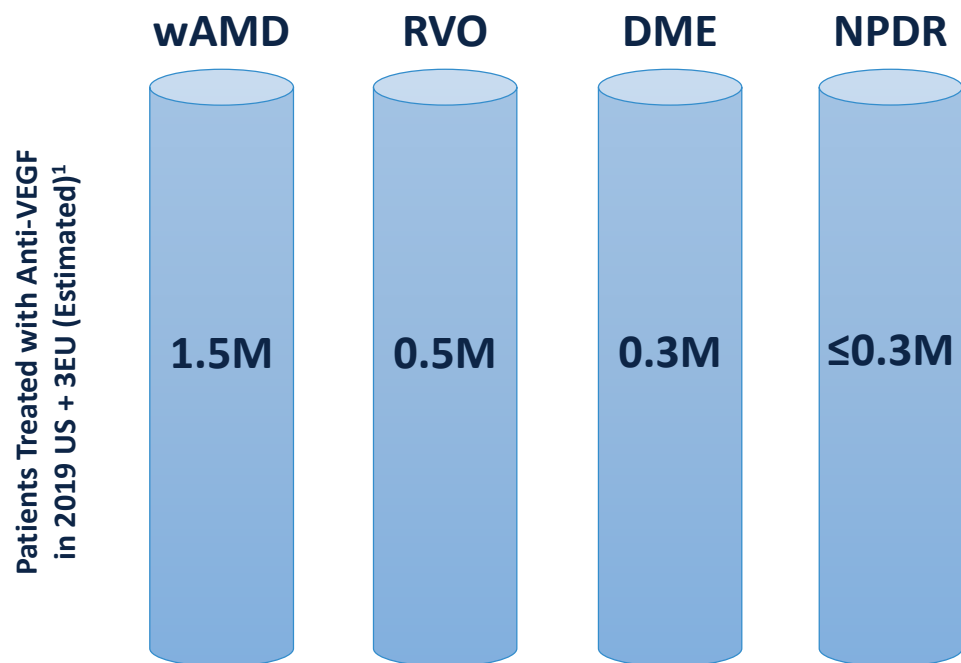
AFLIBERCEPT VIEW STUDIES ¹



THE HOW

Seamless disruption of the anti-VEGF market would be...

Four Pillars of Value
>\$10B in worldwide sales



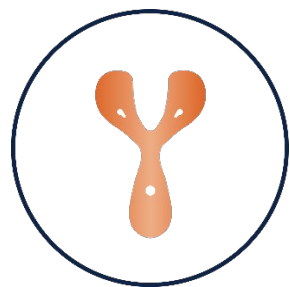
- **Fitting into the infrastructure** that supported >26 million intravitreal injections in 2018 and growing
- With **science that matches drug durability to real world dosing frequencies** – improving patient access and outcomes through meaningful differentiation in each anti-VEGF indication

Same where it matters, different where it counts

¹ United States and EU3 – France, Germany, United Kingdom
Source: Interviews and analysis of BMJ, Cowen and Journal of Ophthalmology

OUR HOW: ABC PLATFORM™

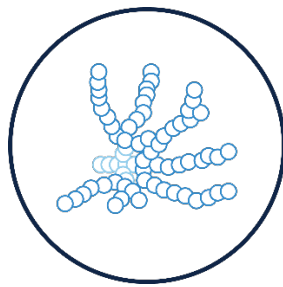
ANTIBODY BIOPOLYMER CONJUGATE



ANTIBODY
IgG1 with inert immune
effector function

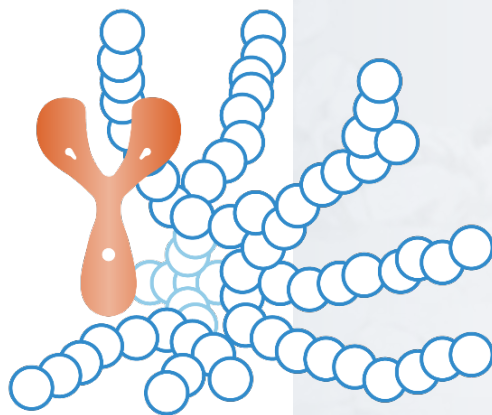
+

Stable
linkage



BIOPOLYMER
Optically clear, high molecular
weight phosphorylcholine polymer

=



**ANTIBODY BIOPOLYMER
CONJUGATE MEDICINES**
Antibody and biopolymer covalently bound
via single site-specific linkage

**KSI-301: an anti-VEGF ABC for first-line therapy
of retinal vascular diseases**

SAME WHERE IT MATTERS

- Clinically proven target
- Antibody-based biologic
- Intravitreal: safest method of administration
- Optically clear, no residues
- Fast and potent clinical responses

DIFFERENT WHERE IT COUNTS

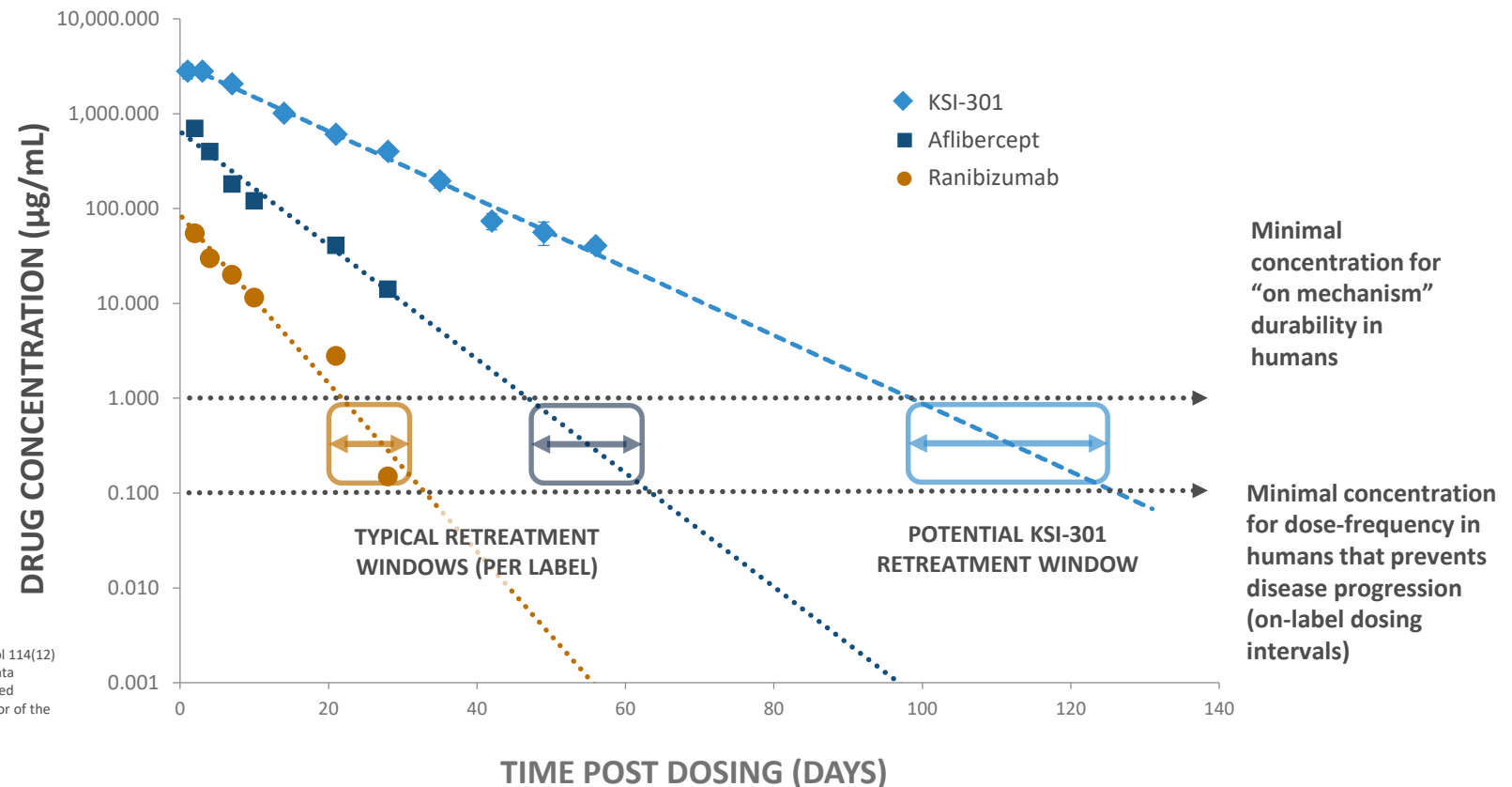
- Designed-in ocular durability
- Improved bioavailability
- Improved biocompatibility
- Improved stability
- Fast systemic clearance

KSI-301 has potential for **extended durability** and a **more flexible retreatment window** due to its larger size

- **Size extends durability**
 - 20x larger vs ranibizumab
 - 8x larger vs aflibercept
- KSI-301 has flattest (best) ocular durability curve
- This means KSI-301 has an **increasing concentration advantage over time**

Ranibizumab data: Gaudreault et al (2007) IOVS 46(2) 726 Gaudreault et al (2007) Retina 27(9) 1260 Bakri et al (2007) Ophthalmol 114(12) 2179 || Aflibercept data: EVER Congress Portoroz Slovenia (2008) Struble (Covance) Koehler-Stec (Regeneron). Aflibercept data adjusted arithmetically to reflect 2,000µg dose administered (based on rabbit in vivo dosing of 500 µg) || KSI-301 data adjusted arithmetically to reflect 5,000 µg dose administered (based on rabbit in vivo dosing of 725 µg). Error bars reflects standard error of the mean

COMPARING DURABILITY OF RANIBIZUMAB, AFLIBERCEPT & KSI-301
BASED ON DATA FROM RABBIT IN VIVO MODEL



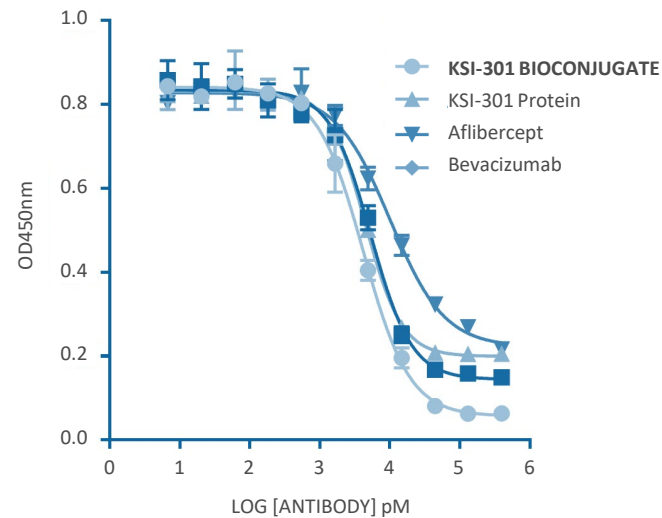
KSI-301 has shown **greater potency in vitro** than unconjugated anti-VEGFs

In vitro assays demonstrate KSI-301 has a **deeper potency** compared to ranibizumab, aflibercept and bevacizumab because of the special nature of its phosphorylcholine biopolymer

- KSI-301 has **high binding affinity** to VEGF (K_D 6.75 pM)
- KSI-301 bioconjugate has a **deeper potency** than its unconjugated starting protein, suggesting an **additive effect of the biopolymer**

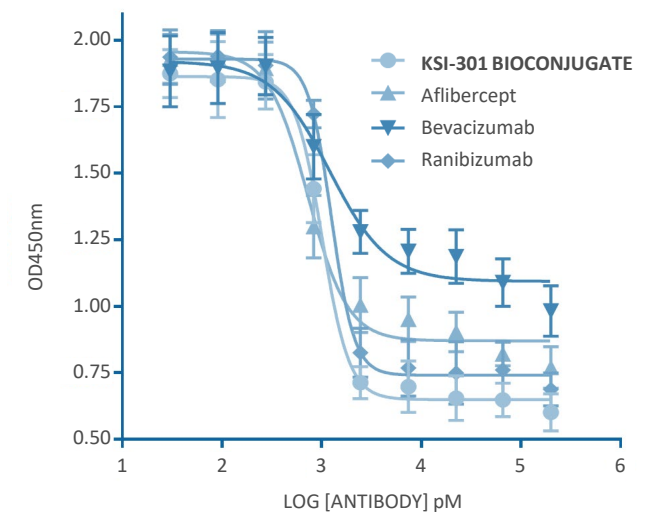
BIOCHEMICAL ASSAY

Anti-VEGF Inhibition of
VEGF: VEGFR binding



PRIMARY HUMAN RETINAL CELL-BASED ASSAY

Anti-VEGF Inhibition of
HRMVEC Proliferation

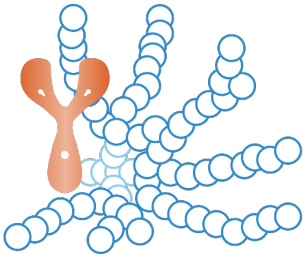


KSI-301 optimizes size & formulation strength to improve durability

Drug/Candidate:	BROLUCIZUMAB	RANIBIZUMAB	AFLIBERCEPT
Molecule type	Single-chain antibody fragment	Antibody fragment	Recombinant fusion protein
Molecular structure			
Molecular weight	26 kDa	48 kDa	115 kDa
Clinical dose	6 mg	0.3-0.5 mg	2 mg
Equivalent molar dose	22	1	2
Equivalent ocular PK	<1	1	1.5
Equivalent ocular concentration at 3 months	10	1	1,000

KSI-301

Antibody Biopolymer Conjugate (ABC)



950 kDa

5 mg (by weight of antibody)

7

4

1,000,000

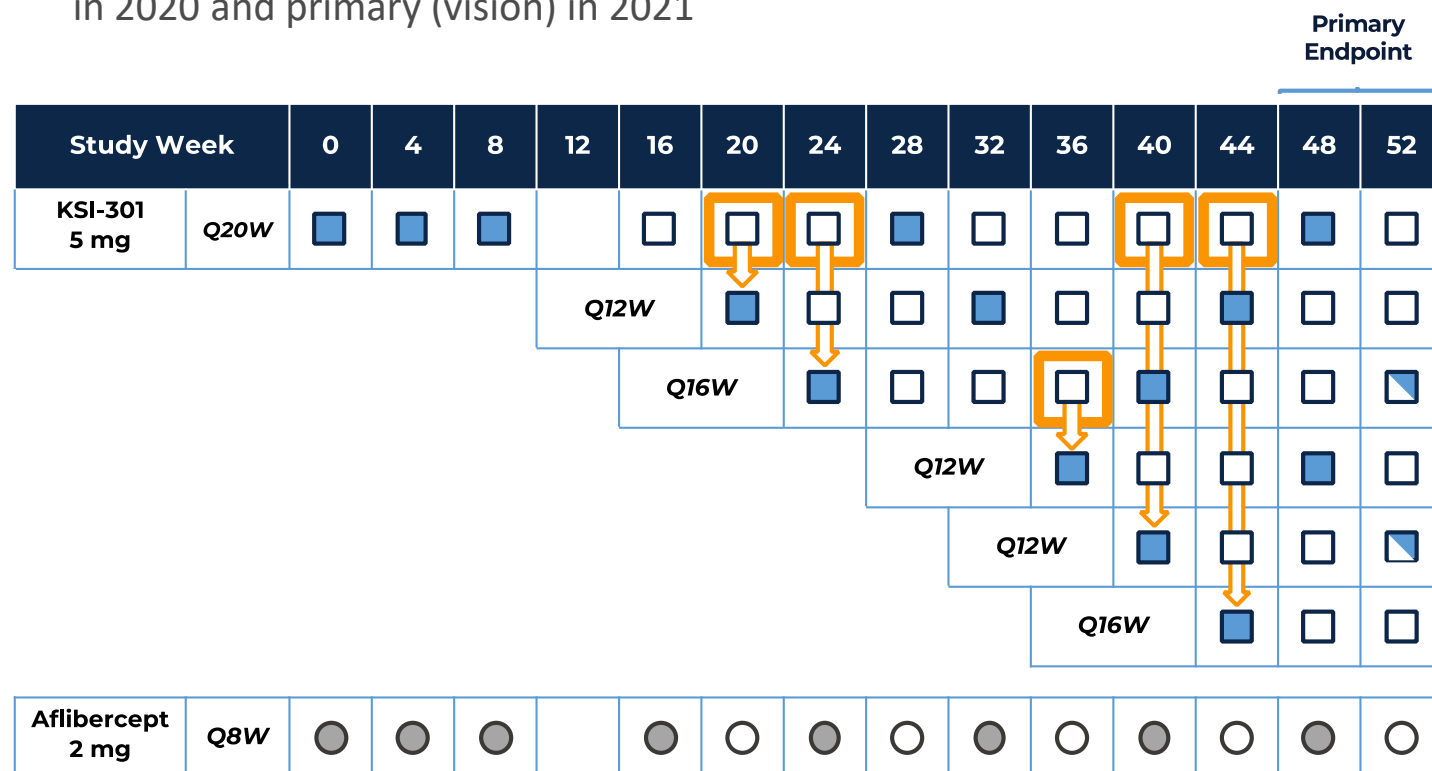
PHASE 2/3 TRIAL

DAZZLE STUDY IN WET AMD

Pivotal study design, head-to-head
against standard of care aflibercept

US & EU study centers

- All patients $\geq$ Q12W with KSI-301
- As infrequent as Q20W dosing with KSI-301
- Non-inferiority pivotal design study
- Estimated 400 patients (US/EU)
- On track to begin enrolling in 2H 2019, with interim (durability) in 2020 and primary (vision) in 2021



■ KSI-301 injection

▣ KSI-301 individualized treatment/sham

● Aflibercept injection

○ Sham injection

□ Disease Activity Assessment Visit

↓ Disease Activity Dosing Adjustment

Retina Specialists and Payers find KSI-301 attractive due to its potential to solve the real world problem with extended dosing and durability

Based on an independent survey of retina specialists and payers in the US, EU and China

Retina Specialists

“This product is really what we need. It keeps the safety and effectiveness of anti-VEGFs, and increases the time between injections...”

“This begs the question of whether it’s still ethical to treat with Avastin when there is a novel therapeutic that can be extended beyond 3 months...”

Payers

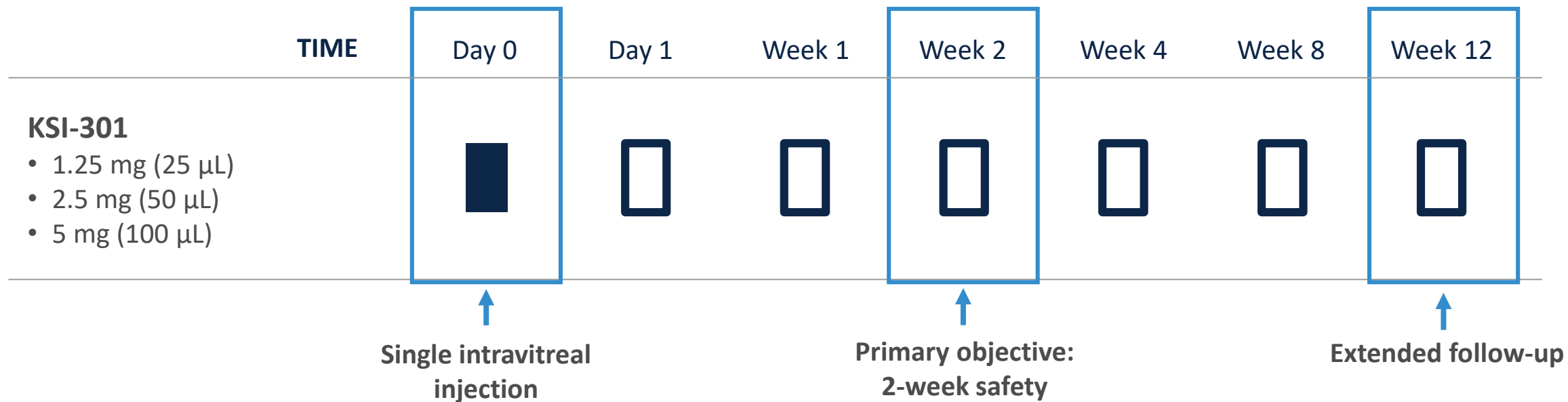
“I can imagine a possible scenario where this is given preferential access over Eylea. If efficacy, safety, and annual cost are roughly equal, why wouldn’t we promote use of something that extends intervals...”

“Absolutely would cover this based on the non-inferior efficacy and safety and improved dosing intervals. Why would we not cover this?”

KSI-301
PHASE 1
CLINICAL STUDY

KSI-301 PHASE 1 CLINICAL STUDY

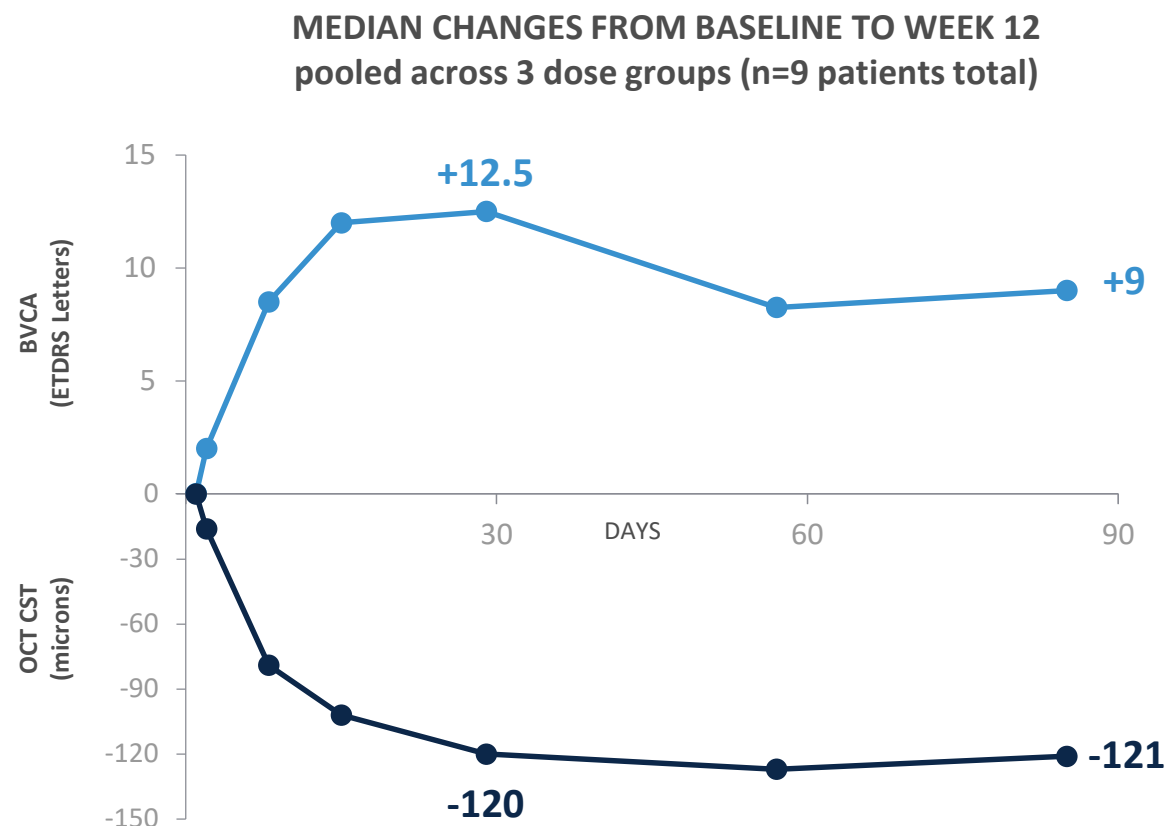
Single Ascending Dose Study in Diabetic Macular Edema Patients



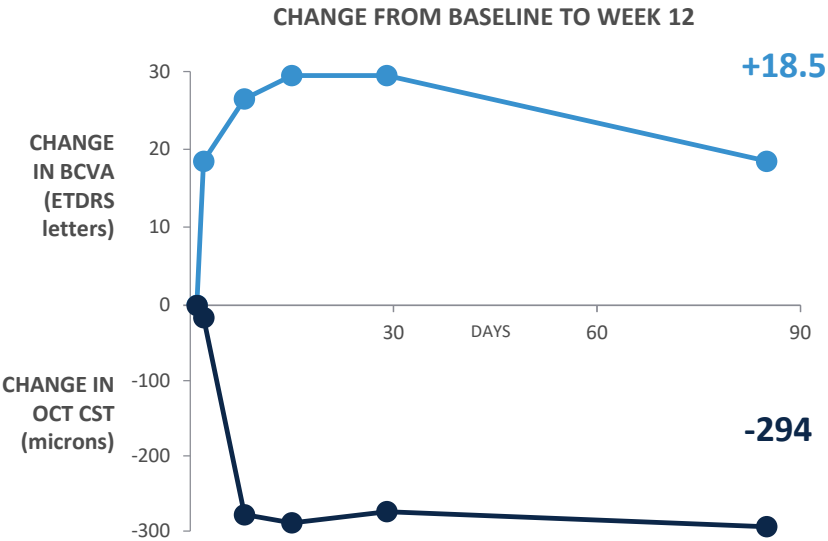
- 9 subjects – 3 per dosing cohort, 7-day safety review between each cohort
- Conducted at 5 US sites
- Single dose with observation to 12 weeks (no retreatment)

Improvements in vision and retinal thickness after single-dose KSI-301 maintained through 12 weeks

- Rapid, high magnitude responses as early as 1 week after dosing
- Durable improvements out to 12 weeks



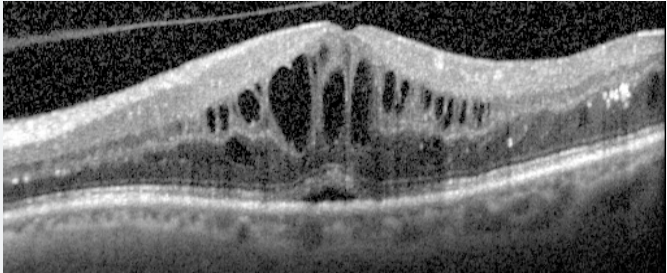
CASE EXAMPLE 1



CLINICAL HISTORY SUMMARY (SITE REPORTED):

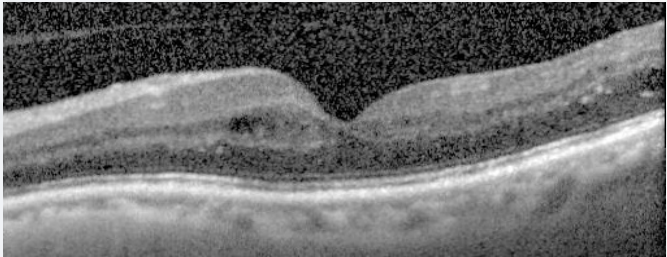
	Date	Treatment	VA Snellen	CST
Retrospective	1/2018		20/40	-
	4/2018	Bevacizumab	20/40	431
	6/2018	Bevacizumab	20/60	655
	8/2018	KSI-301	20/160	636

Resolution of macular edema sustained through 12 weeks in patient with prior suboptimal response

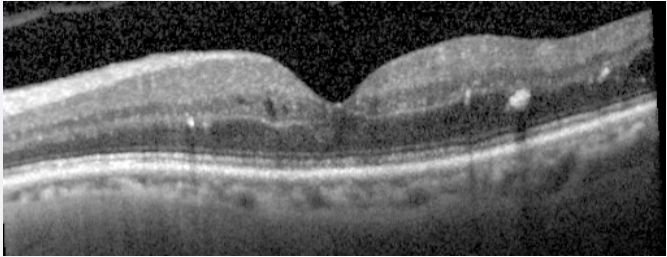


BASELINE

Single dose
KSI-301 (5 mg)



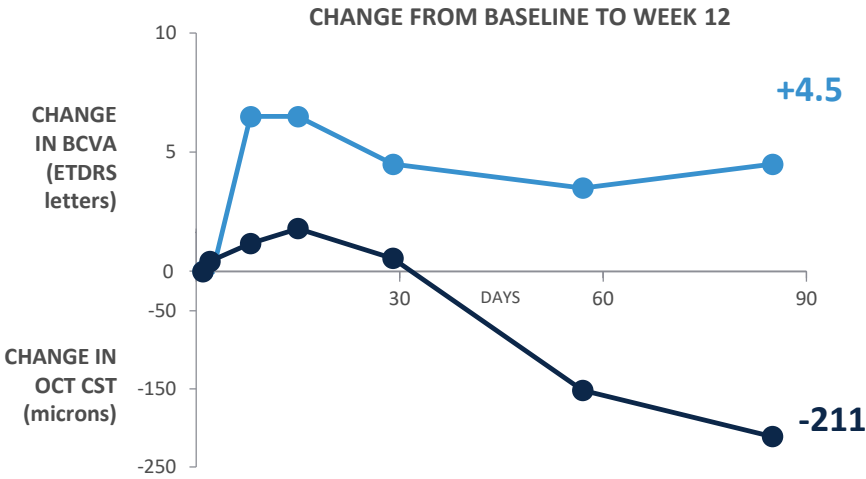
WEEK 4



WEEK 12

First post-study treatment **155 days (22 weeks)** following KSI-301 5 mg injection

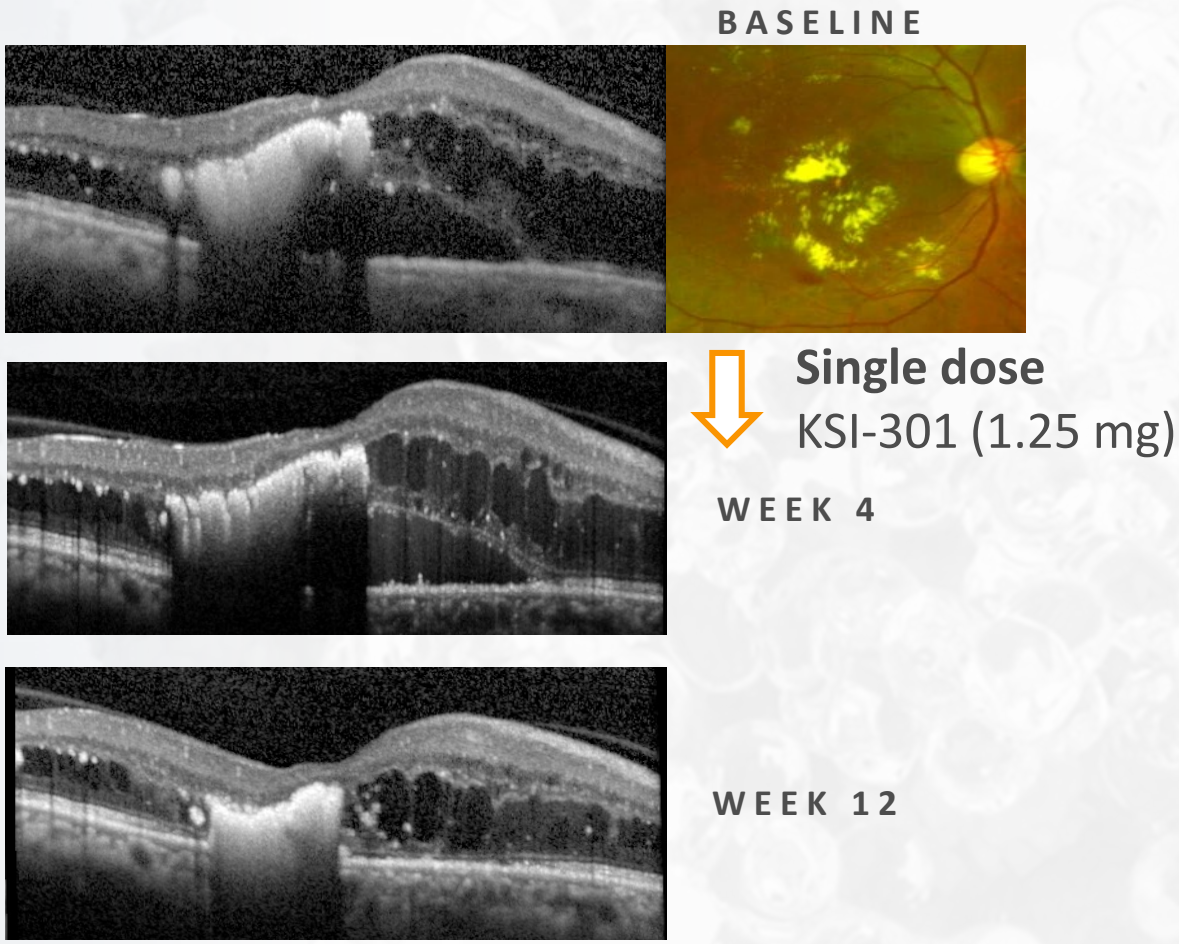
CASE EXAMPLE 2



CLINICAL HISTORY SUMMARY (SITE REPORTED):

	Date	Treatment	VA Snellen
Retrospective	1/2018	Bevacizumab	20/60
	3/2018	Bevacizumab	20/100
	4/2018	Bevacizumab	20/150
	5/2018		20/350
	7/2018	KSI-301	20/80

Resolution of subretinal fluid through 12 weeks in patient with extensive foveal lipid exudates



First post-study treatment **146 days (21 weeks)** following KSI-301 1.25 mg injection

PHASE 1B

OPEN LABEL STUDY

Wet AMD, DME, RVO
NCT03790852

- Open-label study to explore KSI-301 safety, bioactivity, durability
- Actively enrolling, goal ~90 patients (increased from 50)
- Anti-VEGF **treatment naïve** patients only
- **3 loading doses** in every patient
- **7-month follow-up** to explore durability (vision, retinal thickness)
- Initial data presentations in 2H19 at ASRS (July) and AAO (October)

Week		0	4	8	12	16	20	24	28	32	36	Primary Endpoint
KSI-301 5 or 2.5 mg	wAMD											
	DME											
	RVO											

 KSI-301 injection

 Dosing as needed (PRN)

 Retreatment criteria assessment

Expanded recruitment into phase 1b multiple-dose study in patients with wet AMD, DME, and RVO

Announce KSI-301 clinical and regulatory strategy based on Phase 1b data

Initiate next set of global pivotal phase 2/3 studies

On-going phase 1b data presentations

Present expanded 1b data at AAO

Present initial 1b data at ASRS

2019

2020

Held successful China Pre-IND meeting

R&D Day

Submit China INDs

Initiate China pivotal dual-use clinical studies

Start global pivotal phase 2/3 head-to-head study against aflibercept in wet AMD

Interim phase 2/3 durability data from global wet AMD

K S I - 3 0 1 P O T E N T I A L

CATALYSTS

KSI-301

KEY TAKEAWAYS



A novel **Antibody Biopolymer Conjugate** inhibiting VEGF

- Same where it matters, different where it counts



Phase 1a single ascending dose study results

- Well-tolerated at all dose levels
- **Rapid-onset, high-magnitude responses sustained to 12 weeks**



Executing on a comprehensive clinical strategy in retinal vascular diseases

- **Meaningful differentiation** in each indication
- Phase 1b data in 2019 (ASRS, AAO)
- Initiating multiple global pivotal studies



Objective

- Develop a **first-line therapy**, meeting all treatment needs for VEGF-mediated retinal vascular diseases

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