



# INVESTOR R&D DAY

September 23, 2024

KODIAK

# FORWARD-LOOKING STATEMENTS

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These slides contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These forward-looking statements are not based on historical fact and include statements regarding: the progress and anticipated benefits of our ABCD platform; the prospects and anticipated milestones of the candidates in our pipeline, including tarcocimab, KSI-501, and KSI-101; the expected enhancements and benefits of a new formulation; our and Lonza's (our manufacturing counterpart) ability to successfully execute on our manufacturing development plan; the timing and success of our planned Biologics License Application ("BLA") package; the timing of anticipated topline data readouts; the potential to provide continued revenue stream starting from 2027; and our guidance on our cash runway. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "could," "expect," "plan," "believe," "intend," "pursue," and other similar expressions among others. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. The risks and uncertainties include, but are not limited to: the risk that cessation or delay of any of the on-going clinical studies and our development of tarcocimab, KSI-501 or KSI-101 may occur; the risk that ongoing clinical trial results may not provide the evidence, insights, or benefits as anticipated; the risk that safety, efficacy, and durability data observed in our product candidates in current or prior studies may not continue or persist; the risk that the results of the tarcocimab Phase 3 studies may not be sufficient to support a single BLA submission for DR, RVO and wet AMD; the risk that a BLA may not be accepted by, or receive approval from, the FDA or foreign regulatory agencies when expected, or at all; future potential regulatory milestones of tarcocimab, KSI-501 or KSI-101, including those related to current and planned clinical studies, may be insufficient to support regulatory submissions or approval; the risk that a new formulation of tarcocimab, KSI-501 or other ABC Platform derived molecules may not provide the benefits expected; our research and development efforts and our ability to advance our product candidates into later stages of development may fail; the risk that KSI-501 may not inhibit VEGF and IL-6 or have an impact on the treatment of patients as expected; any one or more of our product candidates may not be successfully developed, approved or commercialized; our manufacturing facilities may not operate as expected; adverse conditions in the general domestic and global economic markets, which may significantly impact our business and operations, including our clinical trial sites, as well as the business or operations of our manufacturers, contract research organizations or other third parties with whom we conduct business; as well as the other risks identified in our filings with the Securities and Exchange Commission. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and Kodiak undertakes no obligation to update forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements. Kodiak®, Kodiak Sciences®, ABC™, ABC Platform™, and the Kodiak logo are registered trademarks or trademarks of Kodiak Sciences Inc. in various global jurisdictions.



# WELCOME & **INTRODUCTIONS**

# KODIAK'S LEADERSHIP TEAM

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**Victor Perloth, MD**  
Chairman and CEO



**John Borgeson**  
Chief Financial Officer



**Dolly Chang, MD, MPH, PhD**  
Chief Scientific Officer



**Almas Qudrat, M.Sc**  
Chief Quality Officer



**Wayne To, M.Phil**  
Chief Technology Officer



**Pablo Velazquez-Martin, MD**  
Chief Medical Officer



**Laurent Ducry, PhD**  
Senior Vice President,  
Biologics Development and  
Manufacturing



**Hong Liang, PhD**  
Senior Vice President,  
Development



**Stephen Raillard, PhD**  
Senior Vice President,  
Chemical Development and  
Manufacturing

# MANAGEMENT ATTENDEES

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**Victor Perloth, MD**  
Chairman and CEO



**John Borgeson**  
Chief Financial  
Officer



**Dolly Chang, MD,  
MPH, PhD**  
Chief Scientific Officer



**Almas Qudrat, M.Sc**  
Chief Quality Officer



**Pablo Velazquez-  
Martin, MD**  
Chief Medical Officer

# GUEST SPEAKERS: KEY OPINION LEADERS

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**David Brown, MD**

Clinical Professor of  
Ophthalmology, Baylor  
College of Medicine

Director of Research, Retina  
Consultants of Texas

Chair, Medical Leadership  
Board, Retina Consultants  
of America



**Charles Wykoff, MD, PhD**

Clinical Professor of Ophthalmology  
Weill Cornell Medical College,  
Houston Methodist Hospital

Clinical Professor of Ophthalmology,  
Blanton Eye Institute

Director of Research, Retina  
Consultants of Texas

Deputy Chair of Ophthalmology,  
Blanton Eye Institute

# AGENDA

<b>Why Kodiak?</b>	<b>Victor Perloth, MD</b> Chairman and CEO	15 min
<b>Science of Durability</b>	<b>David Brown, MD</b>	15 min
<b>Science of the Enhanced Formulation</b>	<b>David Brown, MD</b>	15 min
Roundtable Discussion	<b>Moderator: Victor Perloth, MD</b> Chairman and CEO	10 min
Audience Q&A	All	10 min
<b>Clinical Program Overview</b>	<b>Charles Wykoff, MD, PhD</b>	15 min
<b>The Kodiak Opportunity</b>	<b>Victor Perloth, MD</b> Chairman and CEO	10 min
Roundtable Discussion	<b>Moderator: Victor Perloth, MD</b> Chairman and CEO	10 min
Audience Q&A	All	10 min
<b>ABCD Platform Preview</b>	<b>Dolly Chang, MD, PhD</b> Chief Scientific Officer	10 min
<b>Summary and Takeaways</b>	<b>Victor Perloth, MD</b> Chairman and CEO	5 min
Audience Q&A	All	15 min

# AGENDA

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# WHY KODIAK?



Victor Perloth, MD  
Chairman and CEO



# We believe Kodiak is primed for near-term and long-term success

## Agile R&D Mindset

*We have made key course corrections and implemented them into late-stage studies*

- Kodiak's late-stage ABCD pipeline activities showcase our design, manufacturing and drug development capabilities
- Our emerging ABCD Platform opens up a new generation of targeted multifunctional "poly-API" molecules
- Dual mechanism glaucoma and geographic atrophy pipeline programs are maturing

## Excellence in Execution

*Living by our "we care more" philosophy*

- **8 pivotal studies**
- **2,500+ patient years** of clinical experience with ABCDs
- 55,000+ clinical study visits
- Technical leadership and ownership is in-house across the board, enabling timely and cost-effective execution

## Diversified Late-Stage Pipeline

*3 shots on goal, each in a BLA-facing development plan, filing as early as 2026*

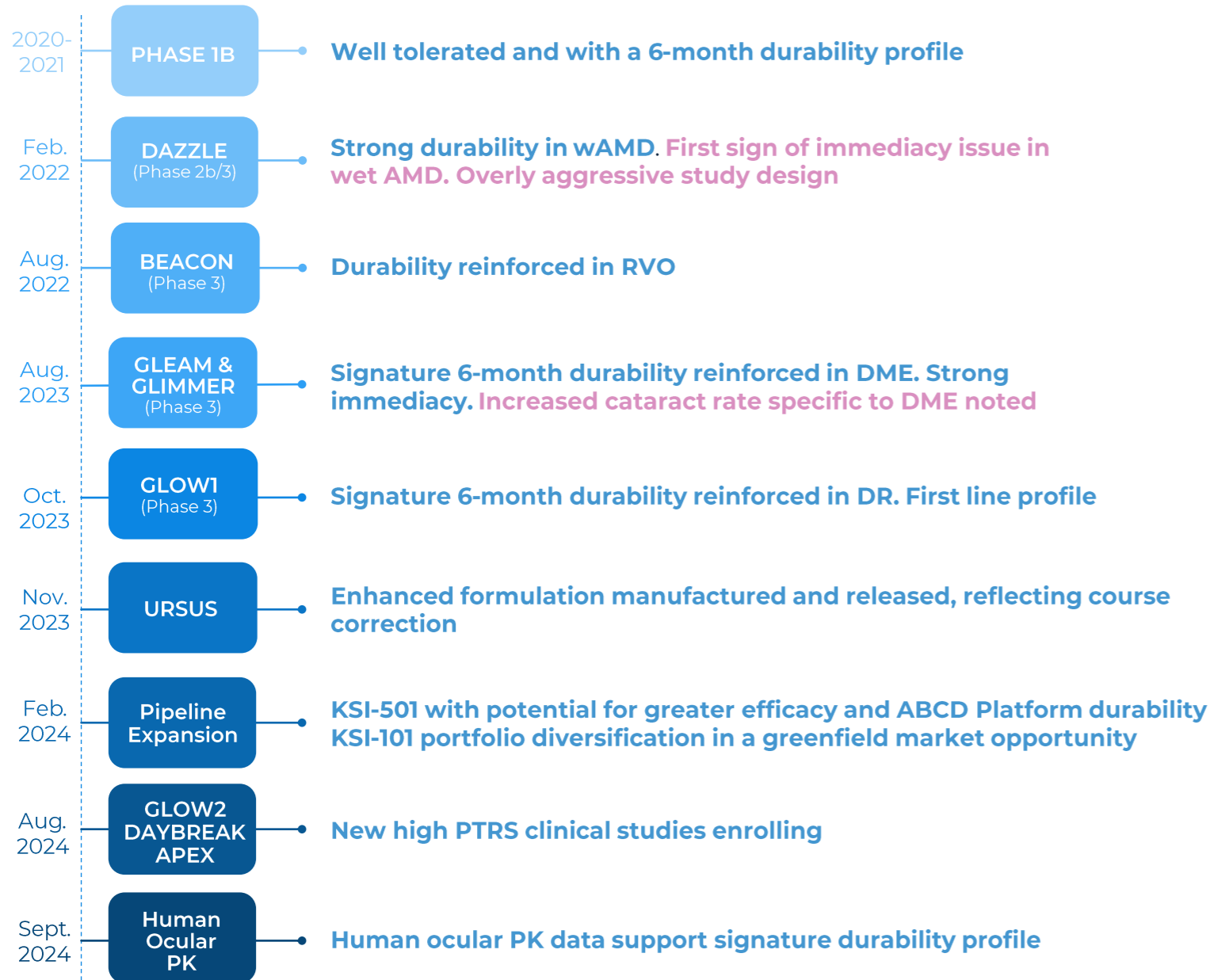
- **tarocimab tedromer:** 90% of clinical and CMC costs already incurred, enhanced formulation designed to deliver "the pulse and the durability", commercial market still poised
- **KSI-501:** Potential for combination of greater efficacy and durability
- **KSI-101:** Greenfield commercial market, near-term data, uncorrelated to ABCD platform, fast follow with dual MOA and high dose strength

## Independence

*Flexibility to make each right choice for Kodiak stakeholders*

- We own global commercial rights to all of our molecules
- We have built and completed an approved high volume commercial manufacturing facility for Kodiak ABCD's (URSUS)
- We have freedom and flexibility in how best to commercialize
- Our cash runway is expected to support operations into 2026

# Kodiak strives to be a learning organization. Through our journey, we have gathered key insights and transformed learnings into actions



## POSITIVE FINDINGS

- Tarcocimab and ABCD platform well tolerated
- Differentiated 6-month durability is real
- Ocular PK data support signature durability
- The ABCD is a true medicinal platform

## ISSUES IDENTIFIED

- Immediacy deficit in wet AMD
- Increased cataract rate specific to DME
- Overly aggressive study designs

## ACTIONS

- Enhanced formulation to course correct issues identified in wAMD and DME
- New study designs educated from prior studies anticipated to have high probability of success
- Diversified portfolio to include KSI-101: superior product in a greenfield market opportunity against sham arm

# Top 4 Questions We Hear From Investors

# Question 1: “Why is Kodiak running another wet AMD durability study for tarcocimab given the failure of the first study?”

## Why did DAZZLE not meet the primary endpoint?

- **Undertreatment** of a minority of patients, with Q12W dosing as the most frequent dosing allowed
- Compounded by a **weaker immediacy** in the loading phase

### Solving undertreatment

- **Problem:** Irrespective of the drug tested, some patients require frequent (monthly) dosing
- **Solution:** in DAYBREAK:
  1. Adding a 4th loading dose
  2. Allowing dosing as frequently as monthly
  3. Proactive treatment until dryness
  4. Detecting disease reactivations earlier

### Solving the weakness in immediacy

- **Problem:** Slow loading of the high molecular weight conjugate in some patients
- **Solution:**
  - A “Basal-Bolus” enhanced formulation combining conjugates and unconjugated free protein
  - The free protein portion alone has VEGF binding equivalent to 1.3 mg of aflibercept
  - Uncompromising durability

**The enhanced formulation should bridge the immediacy gap. Allowing dosing as frequent as monthly in our second durability study (DAYBREAK), while evaluating 6-month dosing, gives tarcocimab the best PTRS<sup>1</sup> while still allowing differentiation**

## Question 2: “Will the cataract imbalance seen in the GLEAM/GLIMMER studies impact the success of tarcocimab and KSI-501?”

### Why did GLEAM and GLIMMER not meet the primary endpoint?

- An unforeseen increase in **cataract adverse events**
- Specific to patients with advanced diabetic eye disease (DME)

### Solving the cataract issue

- **Problem:**
  - Mechanical insult to the lens capsule, which is known to be more fragile in DME patients (who have swollen lenses during hyperglycemic episodes), due to:
    - The gel-like consistency of the tarcocimab old formulation
    - High force needed to inject
    - Extended time to inject
  - Notably, cataract rate in wet AMD patients on monthly tarcocimab was lower than comparator aflibercept
- **Solution:**
  - The **enhanced formulation** of tarcocimab with less biopolymer significantly reduces injection time and force which decreases (or eliminates) any potential insult to the lens capsule in DME patients

**A problem specific to DME patients with the old formulation. In this susceptible population, the enhanced formulation is expected to bring the cataract rate back to the levels associated with all intravitreal biologics.**

### Question 3: “What is the commercial opportunity for tarcocimab and KSI-501 in an increasingly competitive landscape?”

#### Is there space for new treatments in retinal vascular diseases?

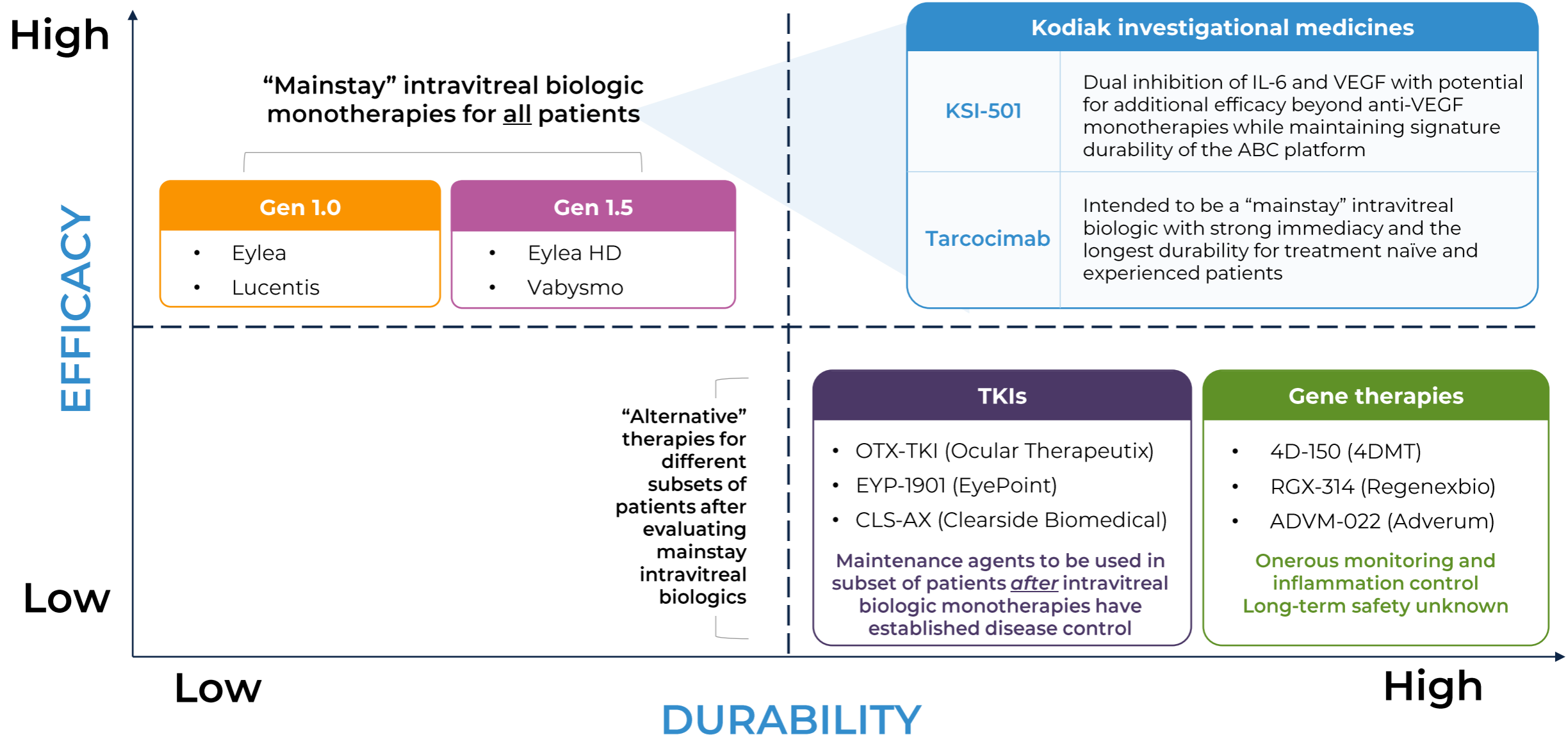
- Intravitreal anti-VEGF biologics are the mainstay of therapy for patients
- Despite limited differentiation, “Gen 1.5” biologics Vabysmo & Eylea HD have significant market uptake
- They have high efficacy but limited true durability
- **There remains a high interest for a mainstay biologic with high efficacy and high durability**

#### Tarcocimab and KSI-501 have the potential to be meaningful products in the marketplace

- The science of our ABC Platform and of our enhanced formulation delivers the immediacy and the durability
- Tarcocimab and KSI-501 are being developed as mainstay biologic monotherapies for all patients (treatment naïve, treatment experienced, mild patients, severe patients)
- Pivotal studies support a wide range of dosing, from monthly to 6-month dosing
- If successful, the initial BLA package for tarcocimab could provide approval for 3 indications: DR, RVO and wAMD
- Kodiak has complete flexibility in its approach to commercialization

**With a differentiated clinical profile, along with creative and thoughtful commercial strategies in a \$14B+ marketplace, tarcocimab and KSI-501 have a meaningful commercial opportunity if approved**

Tarcocimab and KSI-501 are being developed as “mainstay” intravitreal biologic monotherapies that provide *high efficacy and high durability and a flexible 1-month through 6-month label*





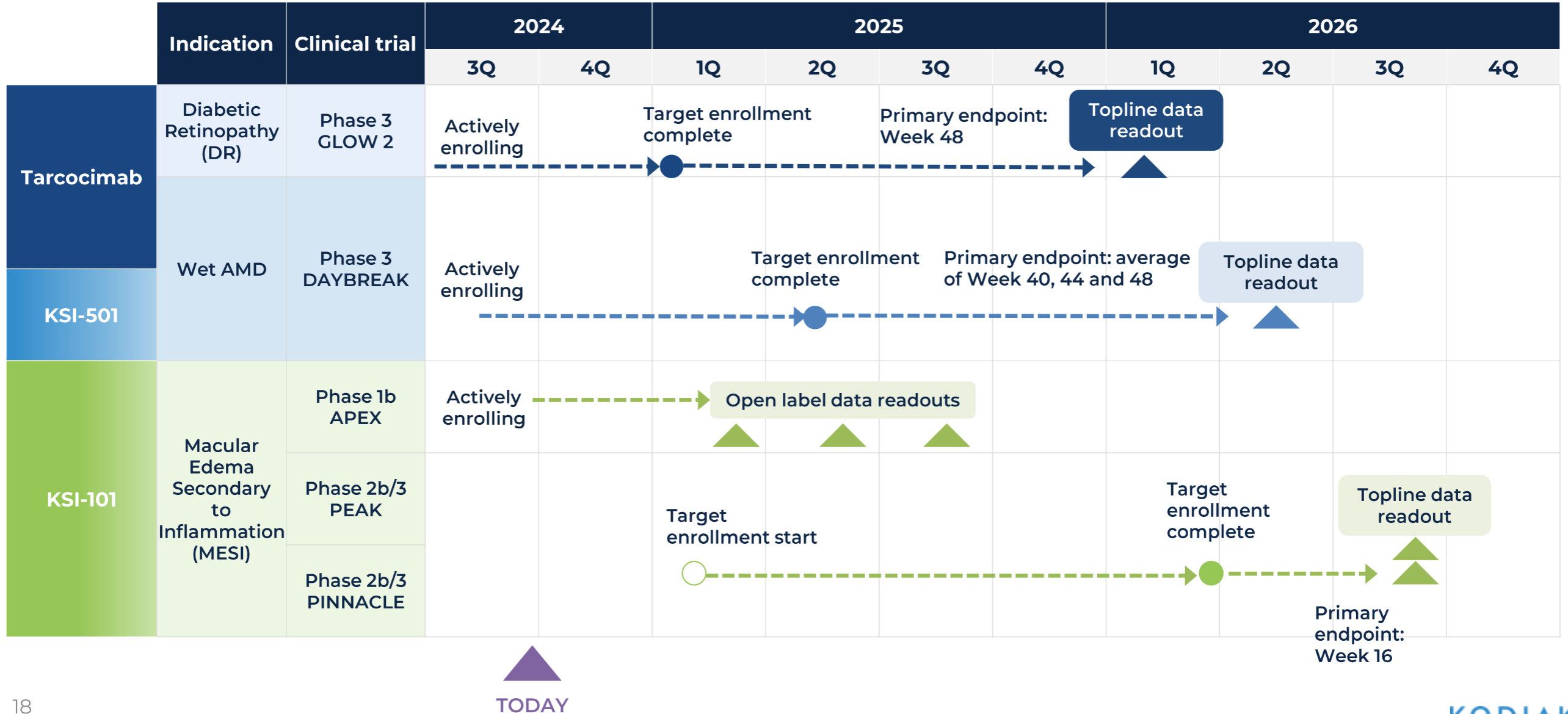
## Question 4: “Will Kodiak’s cash runway last through topline read-outs of ongoing clinical trials?”

### Kodiak has always been thoughtful in its approach to spending and raising funds

- **Our cash runway is expected to support operations into 2026**
- **We believe we have increased our probability of success utilizing historical learnings and corrections.**
  - **Tarcocimab:**
    - GLOW2 has an additional dose compared to the unequivocal GLOW1 (29x benefit over sham).
    - DAYBREAK optimizes treatment for each patient and incorporates our enhanced formulations. These address our two key insights: undertreatment and immediacy deficit.
  - **KSI-501:** intensive and optimized dosing up to monthly, with enhanced formulation.
  - **KSI-101:** uncorrelated profile to the ABC platform, registrational studies with sham as a comparator.
- **Our studies are run fully in house without a CRO.** This increases efficiencies and reduces cash requirements.
- **We own commercial rights to all our molecules, both US and ex-US.** We can decide to act on the option to partner, and retina is an area of high partnering interest.

**We anticipate approximately \$200 million in cash & equivalents at the end of 3Q24. We remain committed to raising capital at the right times and in the right ways to enable cash runway through critical milestones while maximally preserving value for existing shareholders**

# Summary of clinical programs and timeline of anticipated milestones



# With 3 clinical programs leveraging our 15-year history, Kodiak is at a decisive moment and represents an exciting investment opportunity

## Antibody Biopolymer Conjugate Drugs (“ABCD”s) for Retinal Vascular Diseases

### UPCOMING MILESTONES

**TARCOCIMAB** Phase 3  
**TEDROMER**  
Enhanced anti-VEGF “ABCD”

Tracking to a registration package in DR, RVO and wAMD, a \$14B market. Biologic drug for patients of all disease severity. Enhanced formulation “primes” the patient *and* delivers 1-month through 6-month durability

Topline Phase 3 data 1H26 for GLOW2 and DAYBREAK

**KSI-501** Phase 3  
Enhanced anti-IL-6 and VEGF trap bispecific “ABCD”

Potential for the best combination of greater efficacy and differentiated durability

Topline Phase 3 data 1H26 for DAYBREAK

## Unconjugated protein for Inflammatory Retinal Diseases

**KSI-101** Phase 1b  
High-strength anti-IL-6 and VEGF trap bispecific protein

Greenfield commercial space (macular edema secondary to inflammation) with risks uncorrelated to Kodiak’s ABCD Platform molecules

Phase 1b APEX study clinical data 1H25

Phase 3 initiation 1H25

## Our Vision for 2026

**KSI-101**  
Topline data readouts from twin pivotal studies in MESI & BLA preparation

**Tarcocimab**  
BLA filing in DR, RVO and wAMD supported by 5 successful studies

**KSI-501**  
Exploring the potential for better efficacy, 1 study away from registration

**Cash Equivalents**  
~\$200 expected 3Q24 supporting operations into 2026

**Reimagining Drug Development  
with the ABCD Platform, an  
Evolution of our ABC Platform**

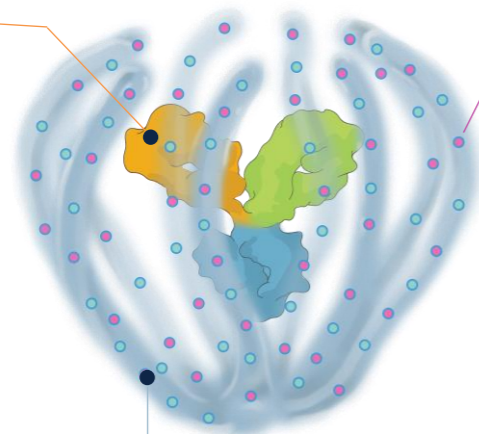
# Our ABCD Platform builds in modular fashion from our ABC Platform development and is maturing rapidly

## Antibody Biopolymer Conjugate Drug (“ABCD”):

Designed to embed small molecules and other **Active Pharmaceutical Ingredients (“API”)** such as oligonucleotides and peptides into the biopolymer backbone for release over a designed-in time period

### Antibody or other Biologic

Engineered to exhibit high binding affinity and specificity. Any biologic can be conjugated to the biopolymer



### Drug Cargo

Diverse APIs of varying biophysical properties including small molecules, macrocycles, peptides and oligonucleotides are embedded in the biopolymer and released over a designed-in time

### Biopolymer

Combines multiple APIs and can be tailored to meet a specific therapeutic goal. It is optically clear and made of phosphorylcholine, the primary hydrophilic component of human cell membranes

**Conjugates of diverse APIs +/- a biologic**  
Target both intracellular and extracellular pathways

**High Drug Antibody Ratio (“DAR”) medicines**  
Can include APIs with DAR of 10 up to >250

**Tailored release of APIs**  
Release of API payloads enabled by pH modulation or enzymatic cleavage of linkers

**Proven safety record of the ABC Platform**  
>2,500 patient years of experience in patients

**A new combination of targeting, high drug loading, mixed API formats and tailored drug release – with applications in ophthalmic and systemic diseases**

Targeting one IND per year starting in 2025

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# SCIENCE OF **DURABILITY**



David Brown, MD

# Extended Duration and Higher Dose Anti-VEGF agents

“Is 12 Weeks the New Norm?”



Retina  
Consultants  
of Texas  
RESEARCH CENTERS

David M Brown, MD



RETINA  
Consultants of America



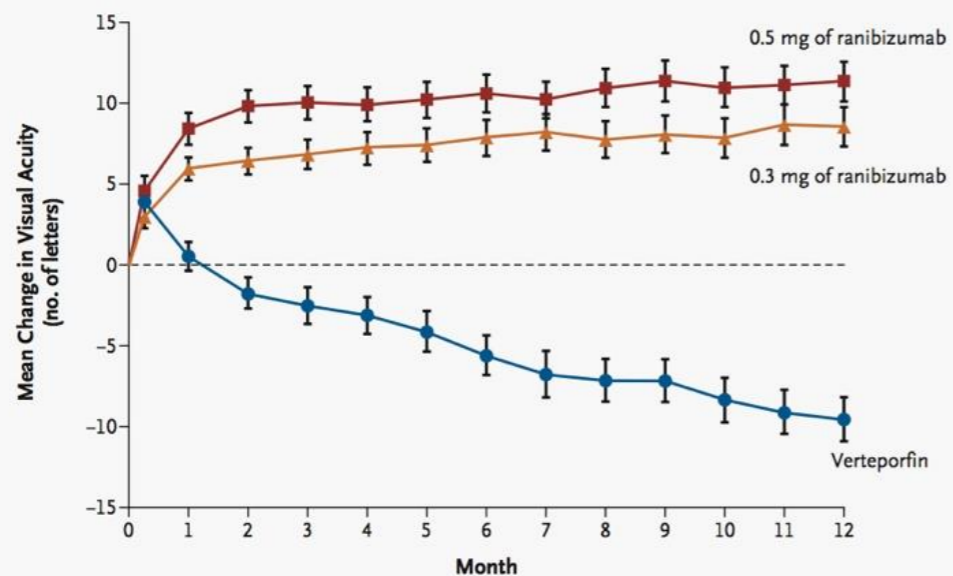
# David M Brown MD Disclosures

Aerie (RG,C), Alcon/Novartis (RG,C), Alexion (C), Allegro (RG,C), Allergan (RG,E,C), Annexon (RG,C), Apellis (RG,C), Astellas (RG), Adverum (RG,E,C), Boehringer- Ingelheim (RG,C), Carl Zeiss Meditec (C), Celltrion (RG, C), Clearside Biomedical (RG,E,C), Coda Therapeutics (C), Envisia (C), 4D Molecular Therapeutics (C), Gemini Therapeutics (RG,C), Google/ Verily (C), Genentech/ Hoffman-La Roche (RG,C), Graybug (RG,C), Heidelberg Engineering (RG,C), Iconic (C), iRenix (E,C), IvericBio (RG,C), Janssen (C), Johnson & Johnson (C), Kanghong Pharma (RG,C), Kodiak Science (RG,C), Merck (C), NEI/NIH (RG), Nicox (C), Notal Vision (RG,C), Ohr (RG,C), Ophthotech, OPTOS/Nikon (RG,C), Optovue (RG,C), Pfizer (RG,C), PRN (C), Regeneron/Bayer (RG,C), RegenXbio (RG,C), Samsung Bioepis (RG,C), Santen (RG,C), SciFlour Life Sciences (C), Second Sight (RG,C), Senju Pharmaceuticals (RG,C), Spark Bio (RG,C), Stealth Biotherapeutics (RG,C), Thrombogenics/Oxurion (RG,C), Tyrogenix (RG,C), Wyle / NASA (C)

RG- Research Grant to Institution E= Equity/ Options C: Consultant / Scientific Advisory Board

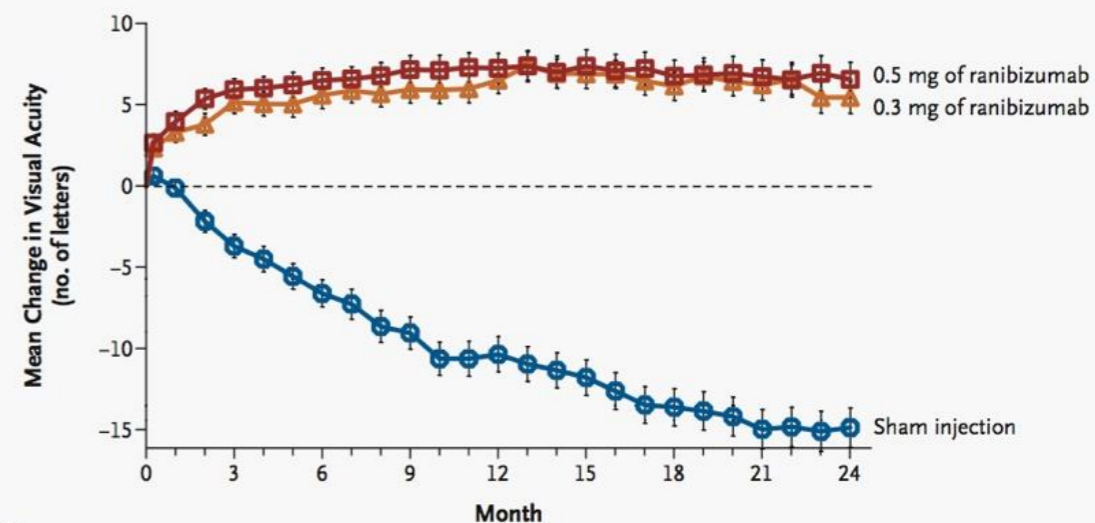
Intellectual Property: Co-patent holder OPTOS “dewarping” algorithms  
Inventor: Sub-retinal Injector Micro-kit for Gene Therapy/ Stem Cell Application

# Goal = Gold Standard Vision Gain



Mean Change from Baseline	(day 7)
0.5 mg of ranibizumab	+4.6 +8.4 +9.8 +10.0 +9.9 +10.2 +10.6 +10.2 +10.9 +11.4 +10.9 +11.1 +11.3
0.3 mg of ranibizumab	+2.9 +5.9 +6.4 +6.8 +7.2 +7.4 +7.9 +8.2 +7.7 +8.1 +7.8 +8.6 +8.5
Verteporfin	+3.9 +0.5 -1.8 -2.5 -3.1 -4.1 -5.6 -6.8 -7.1 -7.1 -8.3 -9.1 -9.5

A



Mean Change from Baseline	(day 7)
0.5 mg of ranibizumab	+2.6 +5.9 +6.5 +7.2 +7.2 +7.4 +6.8 +6.7 +6.6
0.3 mg of ranibizumab	+2.3 +5.1 +5.6 +5.9 +6.5 +6.9 +6.1 +6.2 +5.4
Sham injection	+0.6 -3.7 -6.6 -9.1 -10.4 -11.8 -13.6 -15.0 -14.9

# Routine Quarterly Ranibizumab Dosing = Vision Loss

## Loss

### Randomized, Double-Masked, Sham-Controlled Trial of Ranibizumab for Neovascular Age-related Macular Degeneration: PIER Study Year 1

CARL D. REGILLO, DAVID M. BROWN, PREMA ABRAHAM, HUIBIN YUE, TSONTCHO IANCHULEV, SUSAN SCHNEIDER, AND NAVEED SHAMS, ON BEHALF OF THE PIER STUDY GROUP

• **PURPOSE:** To evaluate the efficacy and safety of ranibizumab administered monthly for three months and then quarterly in patients with subfoveal choroidal neovascularization (CNV) secondary to age-related macular degeneration (AMD).

• **DESIGN:** Phase IIIb, multicenter, randomized, double-masked, sham injection-controlled trial in patients with predominantly or minimally classic or occult with no classic CNV lesions.

• **METHODS:** Patients were randomized 1:1:1 to 0.3 mg ranibizumab (n = 60), 0.5 mg ranibizumab (n = 61), or sham (n = 63) treatment groups. The primary efficacy endpoint was mean change from baseline visual acuity (VA) at month 12.

• **RESULTS:** Mean changes from baseline VA at 12 months were -16.3, -1.6, and -0.2 letters for the sham, 0.3 mg, and 0.5 mg groups, respectively ( $P \leq .0001$ , each ranibizumab dose vs sham). Ranibizumab arrested CNV growth and reduced leakage from CNV. However, the treatment effect declined in the ranibizumab groups during quarterly dosing (e.g., at three months the mean changes from baseline VA had been gains of 2.9 and 4.3 letters for the 0.3 mg and 0.5 mg doses, respectively). Results of subgroup analyses of mean change from baseline VA at 12 months by baseline age, VA, and lesion characteristics were consistent with the overall results. Few serious ocular or nonocular adverse events occurred in any group.

• **CONCLUSIONS:** Ranibizumab administered monthly for three months and then quarterly provided significant VA benefit to patients with AMD-related subfoveal CNV and was well tolerated. The incidence of serious ocular or nonocular adverse events was low. (Am J Ophthalmol 2008;145:239-248. © 2008 by Elsevier Inc. All rights reserved.)

AJO.com Supplemental Material available at AJO.com. Accepted for publication Oct 5, 2007.

From the Retina Service, Wills Eye Institute, Philadelphia, Pennsylvania (C.D.R.); Vitreoretinal Consultants, The Methodist Hospital, Houston, Texas (D.M.B.); BH Regional Eye Institute, Rapid City, South Dakota (P.A.); and Genentech, Inc, South San Francisco, California (H.Y., T.I., S.S., N.S.).

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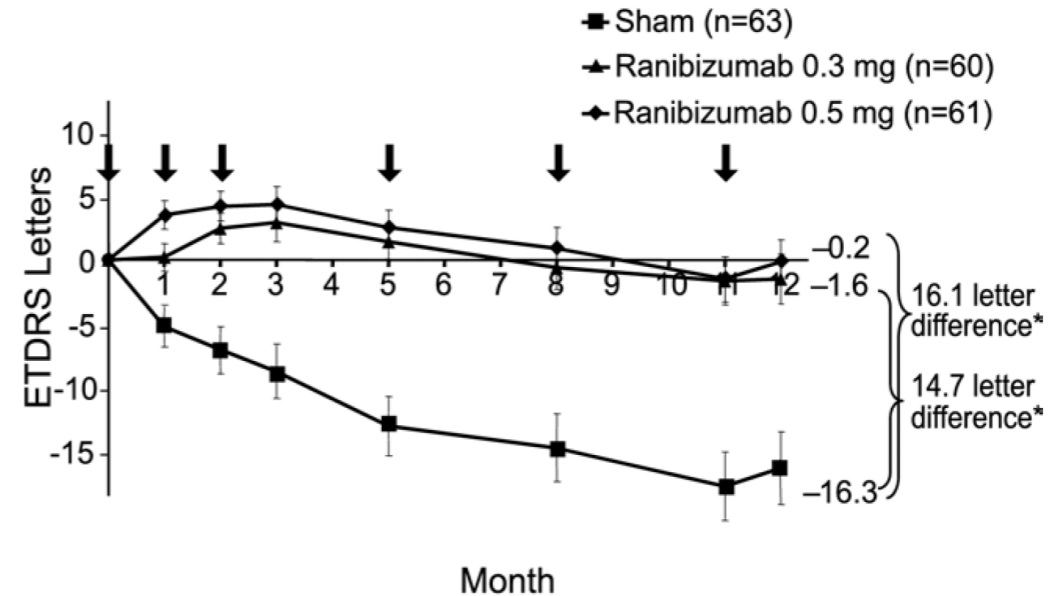
**R**ANIBIZUMAB (LUCENTIS; GENENTECH, INC, SOUTH SAN FRANCISCO, CALIFORNIA, USA) is an intravitreally administered recombinant, humanized, monoclonal antibody antigen-binding fragment (Fab) that neutralizes all known active forms of vascular endothelial growth factor-A (VEGF-A). It is the first treatment shown to not only prevent loss of visual acuity (VA) but also improve VA on average in patients with subfoveal choroidal neovascularization (CNV) secondary to age-related macular degeneration (AMD). In the two pivotal phase III trials—the MARINA Study in patients with minimally classic or occult with no classic CNV<sup>1</sup> and the ANCHOR Study in patients with predominantly classic CNV<sup>2</sup>—ranibizumab was injected monthly.

The phase IIIb PIER Study was designed to determine whether a less frequent ranibizumab dosing schedule (monthly for three months and then once every three months) would also prevent loss of VA in patients with AMD-related subfoveal CNV with or without a classic component, and to provide additional safety information. This alternative dosing regimen was selected for testing based on evidence from phase I and II studies indicating that the pharmacodynamic activity of ranibizumab (0.3 and 0.5 mg) administered intravitreally monthly for three doses may last 90 days.<sup>3,4</sup>

#### METHODS

PIER IS A TWO-YEAR, PHASE IIIb, MULTICENTER, RANDOMIZED, DOUBLE-MASKED, SHAM INJECTION-CONTROLLED STUDY OF THE EFFICACY AND SAFETY OF RANIBIZUMAB IN PATIENTS WITH AMD-RELATED SUBFOVEAL CNV, WITH OR WITHOUT CLASSIC CNV. After providing written informed consent, patients entered a screening period ( $\leq 28$  days), with eligibility determined by the investigator. A central reading center (University of Wisconsin Fundus Photograph Reading Center, Madison, Wisconsin) later re-assessed the CNV types based on fluorescein angiograms, but this did not affect patients' eligibility. See Supplemental Table A (available at AJO.com) for full eligibility criteria.

Only patients  $\geq 50$  years old were eligible. One eye per subject (the "study eye") received study treatment. If both eyes were eligible, the one with better VA was selected



\* $P < .0001$



# Anti-VEGF Agents in the Treatment of Neovascular Age-related Macular Degeneration: Applying Clinical Trial Results to the Treatment of Everyday Patients

DAVID M. BROWN AND CARL D. REGILLO

• **PURPOSE:** The vision gains reported with monthly intravitreal ranibizumab in the MARINA and ANCHOR trials led to an immediate paradigm shift in the treatment of neovascular AMD with retina physicians universally switching to the pan-VEGF blocking agents ranibizumab and bevacizumab, and patients expecting visual improvement. As these agents are primarily used on a pro re nata (PRN) dosing schedule (because neither patients nor physicians want monthly injections), the factors involved in making the treatment and retreatment decisions are very important in any attempt to maximize vision gain.

• **DESIGN:** Analysis of literature, ongoing clinical trials, and the clinical assessments that can aid clinicians in treatment and retreatment decisions.

• **METHODS:** Literature review and perspective.

• **RESULTS:** If a monthly injection protocol is not used, clinicians should use both functional and anatomic criteria to attempt to guide treatment and retreatment decisions. Qualitative optical coherence tomography (OCT) appears to be the most sensitive and practical assessment tool to determine anatomic response to treatment but should be used in conjunction with clinical examination.

• **CONCLUSIONS:** If monthly intravitreal injections are not performed, a combination of clinical examination (looking for new hemorrhage) and qualitative OCT (to assess response to treatment and early signs of recurrent leakage) can be used to guide anti-vascular endothelial growth factor (anti-VEGF), treatments with the goal of maintaining a "normal" retinal anatomy in an attempt to maximize the benefit (visual acuity gains) to risk (number of injections required) ratio. (Am J Ophthalmol 2007;144:627-637. © 2007 by Elsevier Inc. All rights reserved.)

**T**REATMENTS FOR NEOVASCULAR AGE-RELATED MACULAR degeneration (AMD) have improved dramatically since 1999 when the only treatment clinically available was Macular Photocoagulation Study (MPS)-style laser photocoagulation.<sup>1</sup> For subfoveal choroidal neovascularization (CNV), MPS guided laser photocoagulation leads to an

immediate, permanent loss of central vision with its aim to limit the spread of the uncontrollable disease analogous to surgical amputation in general surgery. Photodynamic therapy with verteporfin (vPDT) became available in 2000. Unlike laser photocoagulation, vPDT involves relatively selective photochemical damage to CNV, with less damage to the associated choroid and retina. vPDT decreased the rate of moderate and severe vision loss, demonstrated improved vision (a gain of  $\approx 15$  letters on the Early Treatment of Diabetic Retinopathy Study (ETDRS) chart in up to 6% of patients with subfoveal CNV secondary to AMD) (Table).<sup>2,3</sup> However, 30% to 40% of vPDT-treated patients still lost at least 15 letters from the pretreatment baseline visual acuity (VA). Furthermore, although PDT clinical trials showed consistent benefit when treating patients with subfoveal predominantly classic CNV, other CNV subtypes appeared to benefit only if the lesion was relatively small in size.<sup>2,3,7</sup> Combining vPDT treatment with intravitreal (ITV) injection of a corticosteroid was popularized by Spaide and associates.<sup>8</sup> This combination approach appeared to decrease the number of required vPDT treatments to achieve a nonleaking CNV, but has yet to demonstrate definitive, clinically significant, added visual benefit compared with vPDT alone.

## THE SEARCH FOR A MORE TARGETED TREATMENT

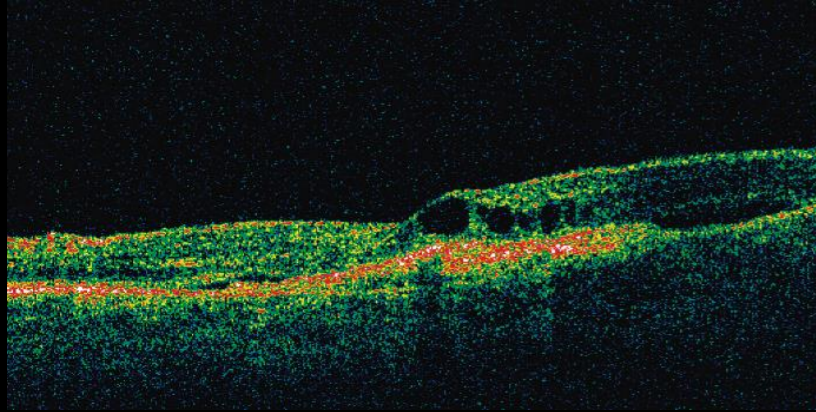
NEOVASCULAR AMD IS ASSOCIATED WITH INCREASED VASCULAR permeability as well as CNV infiltration. This increase in vascular permeability leads to abnormal fluid collection within or below the retina that causes visual dysfunction when it involves the center of the macula. For the past 50 years, researchers have attempted to determine the underlying mechanism of neovascularization and vascular leakage in the eye. In 1983, Senger and associates identified a "tumor vascular permeability factor" (VPF) that could induce vascular leakage.<sup>9</sup> In 1989, Ferrara and Henzel reported the isolation and sequencing of an endothelial cell mitogen dubbed vascular endothelial growth factor (VEGF),<sup>10</sup> which was later determined to be the same molecule as VPF. VEGF-A (also referred to as simply VEGF) is a vascular endothelial cell-specific growth factor

Accepted for publication Jun 20, 2007.  
From the Vitreoretinal Consultants, Houston, Texas (D.M.B.); and the Wills Eye Institute, Philadelphia, Pennsylvania (C.D.R.).  
Inquiries to David M. Brown, Vitreoretinal Consultants, Texas Medical Center Office, Scurlock Tower, 6560 Fannin, Suite 750, Houston, TX 77030; e-mail: dmbend@houstonretina.com.

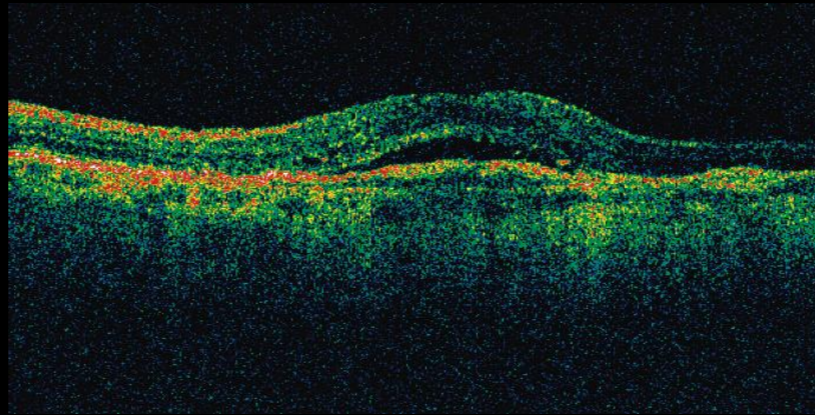
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doi:10.1016/j.ajo.2007.06.039

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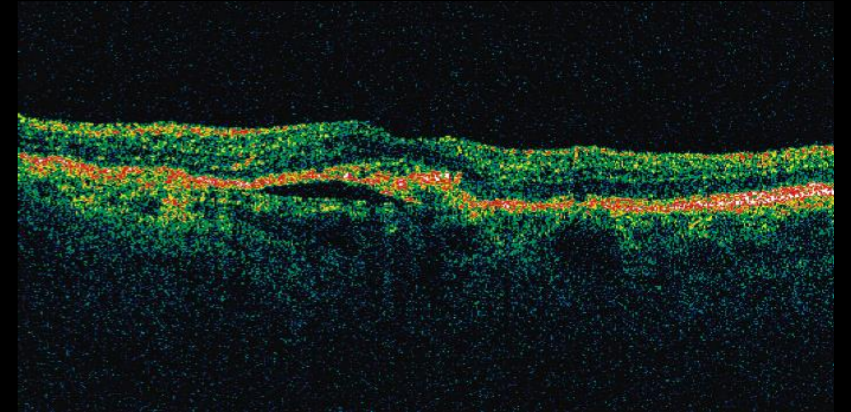
627



Intraretinal Fluid



Subretinal Fluid

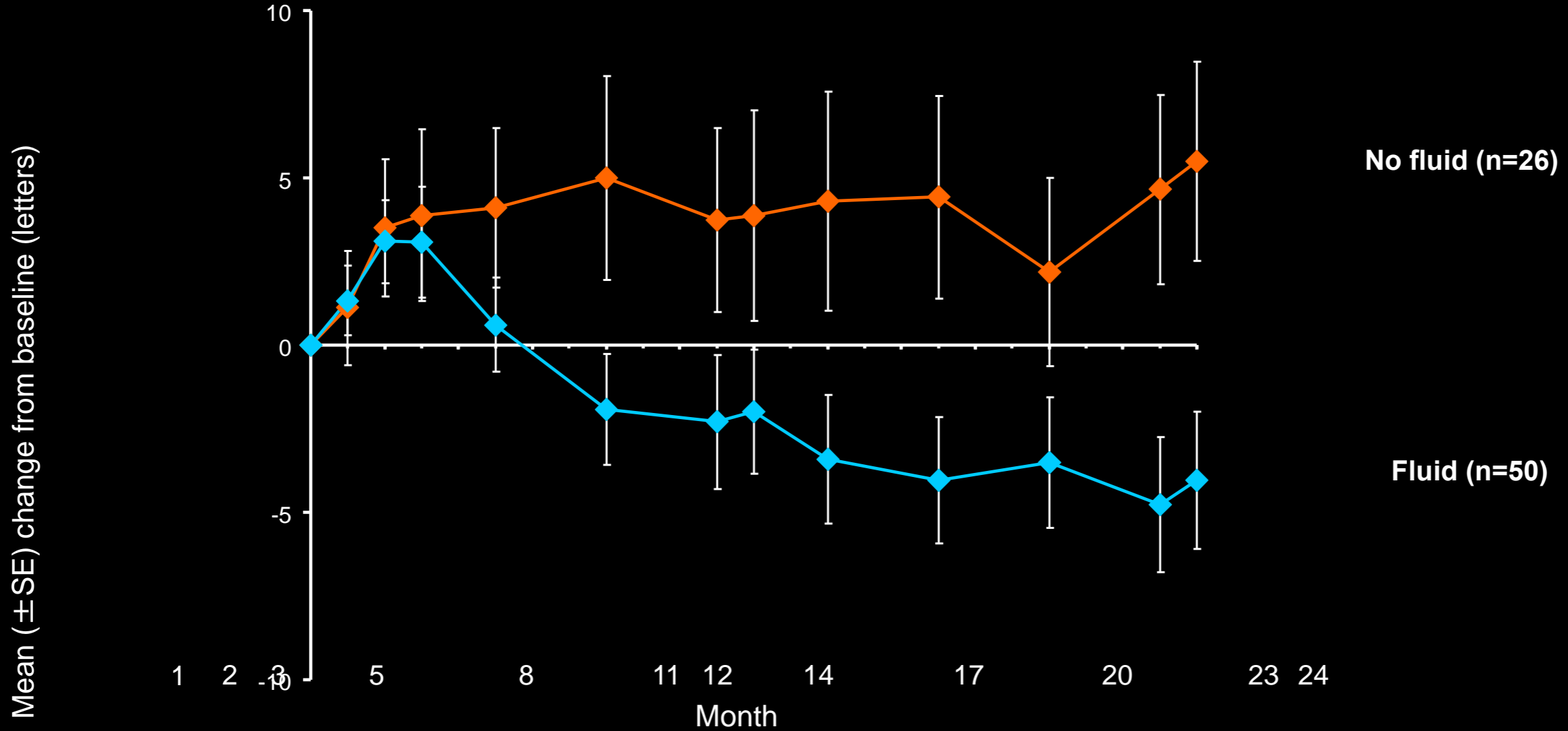


Sub-RPE Fluid

FIGURE 2. Examples of optical coherence therapy (OCT) images from different patients being treated with ranibizumab for neovascular age-related macular degeneration (AMD) demonstrating various patterns of recurrent choroidal neovascularization (CNV) leakage such as (Top row) diffuse edema; (Second row) intraretinal cysts; (Third row) subretinal fluid; or (Bottom row)



# Mean Change in VA by Retinal Fluid (DISS\*) at Month 8



Data from both 0.3 and 0.5 mg ranibizumab groups were pooled. LOCF was used for missing VA outcomes.

\*DISS: Diffuse edema, Intraretinal cysts, Subretinal fluid, and/or SubRPE fluid (PED).

# Absence of OCT Fluid Correlates with Vision Gain

## ANATOMICAL MEASURES AS PREDICTORS OF VISUAL OUTCOMES IN RANIBIZUMAB-TREATED EYES WITH NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

DAVID M. BROWN, MD, FACS,\* LISA TUOMI, PHARM.D,† HOWARD SHAPIRO, PH.D,‡ FOR THE PIER STUDY GROUP

**Purpose:** To investigate if anatomical characteristics of eyes undergoing ranibizumab therapy were predictive of best-corrected visual acuity (BCVA) outcomes over 2 years.

**Methods:** Post hoc analyses of patients with age-related macular degeneration from PIER studies, defined by fundus fluorescein angiography, quantitative optical coherence tomography (OCT), and qualitative OCT, were performed to determine if associations with BCVA outcomes could be found.

**Results:** Ranibizumab-treated subgroups defined by baseline fundus fluorescein angiography lesion size and composition did not differ in BCVA outcomes at Month 24 ( $P = 0.13-1.0$ ). Inactivity on fundus fluorescein angiography at Month 3 was associated with a 12-letter gain by Month 12 ( $P < 0.01$ ), whereas inactivity on Month 3 qualitative OCT was not ( $P > 0.05$ ). Qualitative OCT inactivity at Month 5 and separately at Month 8 was associated with greater BCVA gains by Month 24 (7.1 and 9.5 letters, respectively;  $P \leq 0.045$ ) versus eyes with OCT activity.

**Conclusion:** When assessed separately, eyes with qualitative OCT (Months 5 and 8) or fundus fluorescein angiography (Months 3 and 5) inactivity maintained vision gain from baseline at Month 24, while those with leakage not only lost initial vision gains achieved by intraocular ranibizumab but also had net vision losses from baseline at Month 24. The PIER infrequent dosing regimen likely exaggerated and accelerated the deleterious effects of retinal fluid on BCVA, and it is not known whether these findings are applicable to treatment regimens that use more frequent monitoring and dosing of ranibizumab.

RETINA 33:23-34, 2013

Neovascular age-related macular degeneration (AMD) is characterized by new vessel growth and leakage in the choroidal vascular network beneath

From the \*Retina Consultants of Houston, The Methodist Hospital, Houston, Texas; and †Genentech, Inc, South San Francisco, California. Portions of this work were presented at the 31st Annual Meeting of The Macular Society, Palm Beach, FL, March 26-29, 2008 and the 2008 American Academy of Ophthalmology Annual Meeting, Atlanta, GA, November 8-11, 2008.

D. M. Brown is a consultant for Genentech Inc. and Carl Zeiss Meditec. L. Tuomi and H. Shapiro are employees of Genentech Inc. L. Tuomi has stock options with F. Hoffman-La Roche Ltd.

Genentech, Inc, participated in study design, data collection, data management, data analysis, data interpretation, and manuscript preparation.

The authors have no proprietary or conflicts of interest.

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Bruch membrane. Although the pathologic events that precede choroidal neovascularization (CNV) are not clearly understood, disrupting activity of vascular endothelial growth factor A (VEGF-A), a diffusible cytokine that promotes angiogenesis and vascular permeability, is an effective strategy for treating CNV secondary to AMD. Ranibizumab (Lucentis; Genentech, Inc, South San Francisco, CA) is a humanized, affinity-matured, anti-VEGF antigen-binding fragment (Fab) that binds to and neutralizes all isoforms of VEGF-A and their biologically active degradation products. In two pivotal Phase III trials—Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular Age-Related Macular Degeneration (MARINA)<sup>1</sup> and Anti-Vascular Endothelial Growth

# Gain

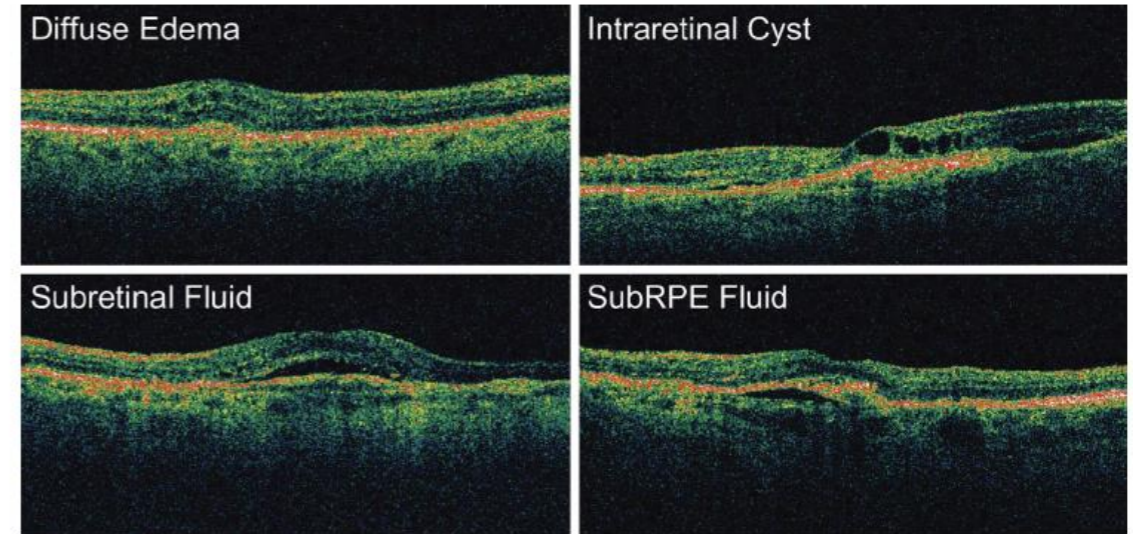
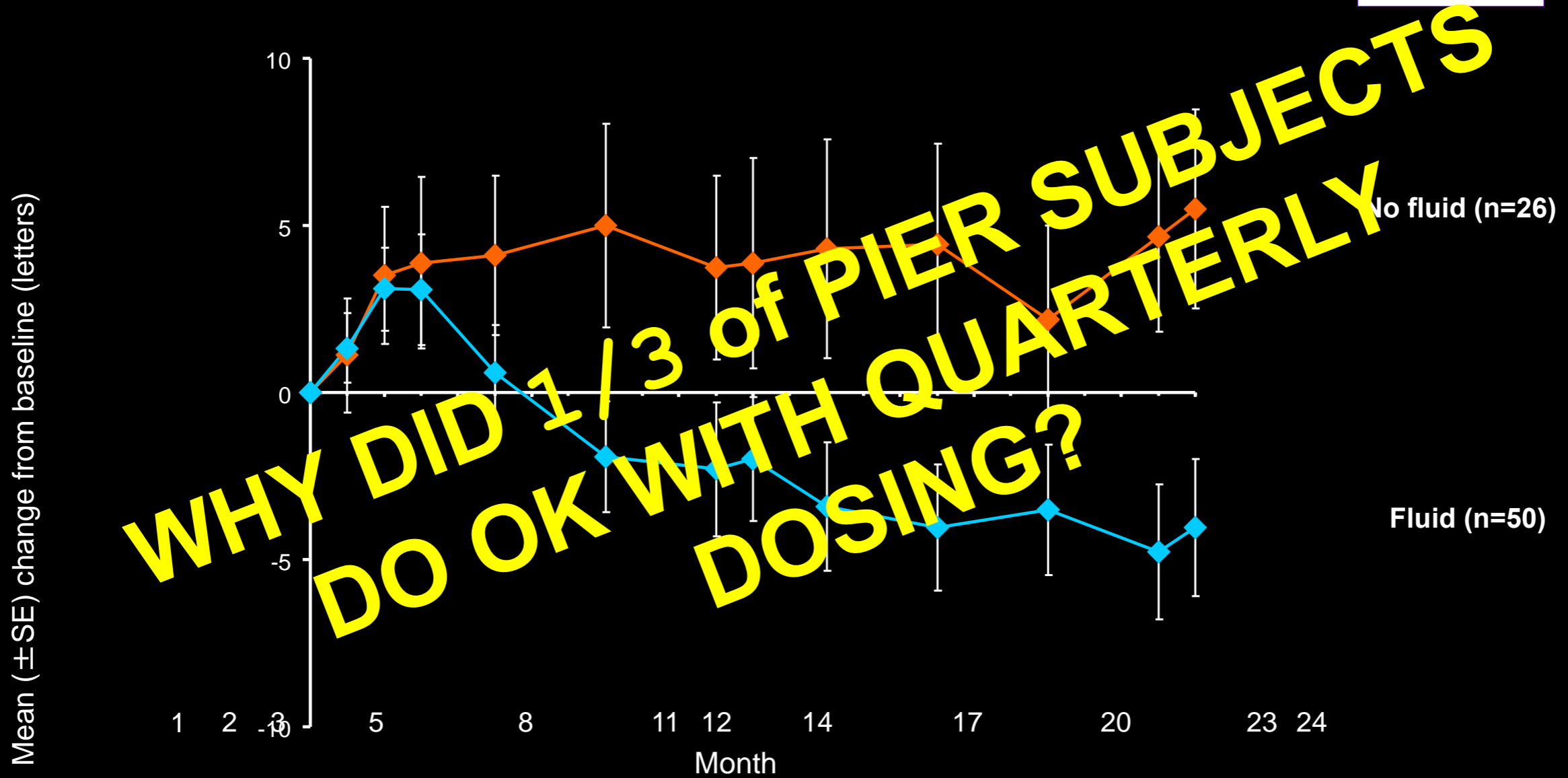


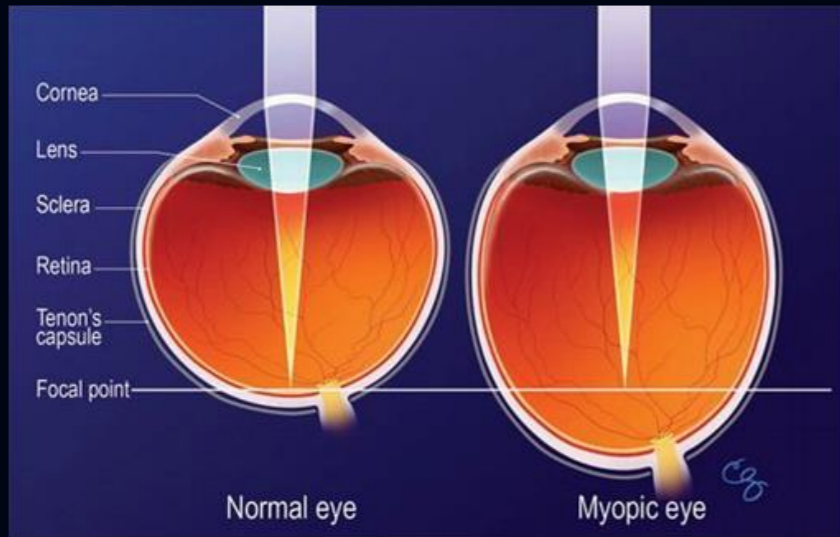
Fig. 2. Optical computed tomography images of fluid components. The images exemplify the qualitative measures of fluid, including diffuse edema, intraretinal cysts, subretinal fluid, and sub-RPE fluid.



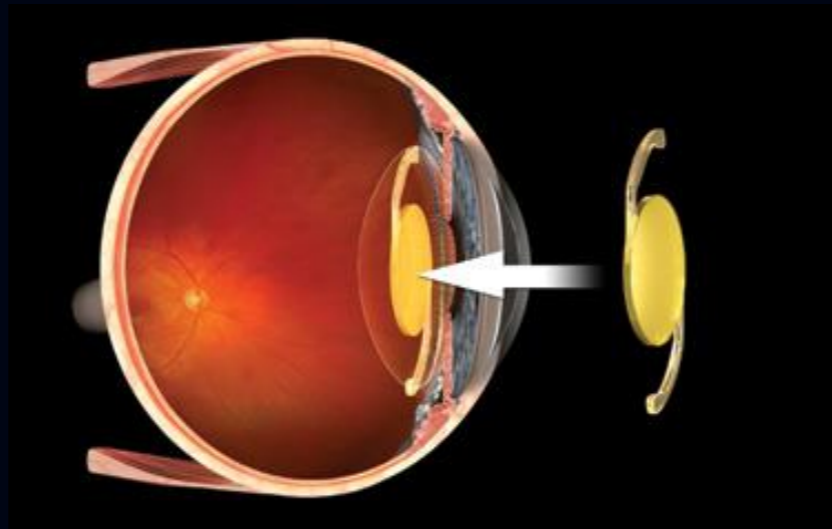
Data from both 0.3 and 0.5 mg ranibizumab groups were pooled. LOCF was used for missing VA outcomes.  
\*DISS: Diffuse edema, Intraretinal cysts, Subretinal fluid, and/or SubRPE fluid (PED).



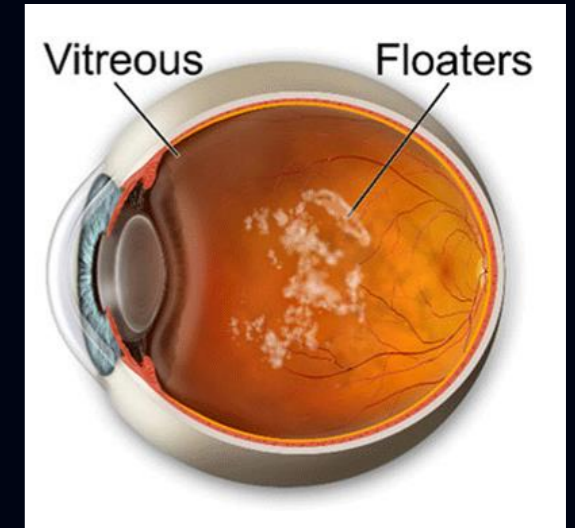
# What Determines Drug Clearance?



**Axial Eye Length**

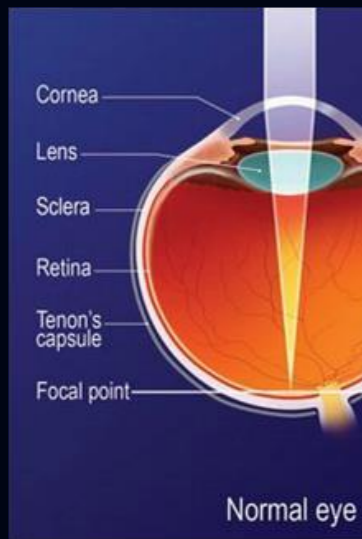


**Pseudophakia**

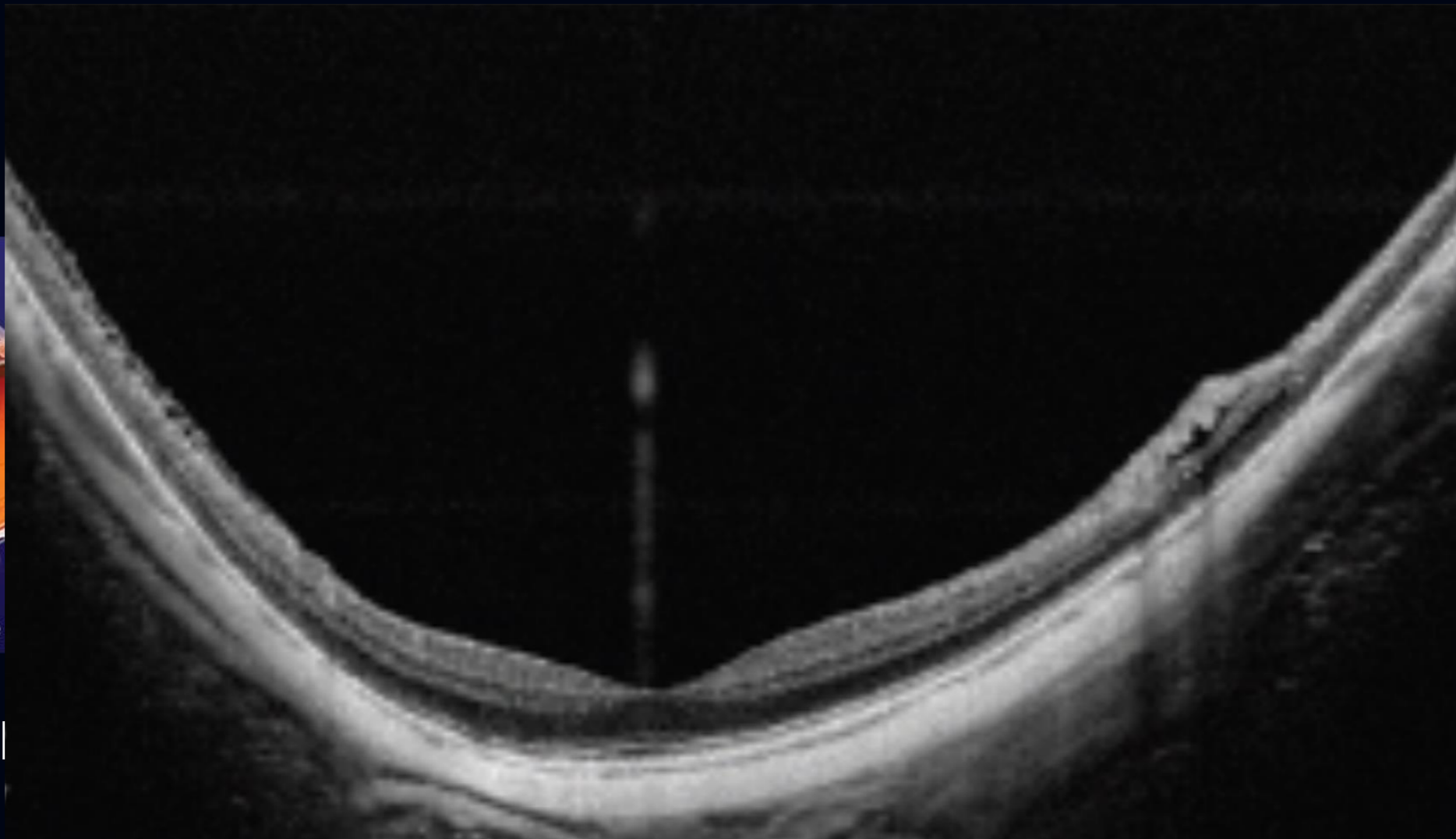


**Vitreous Syneresis**

# What Determines Drug Clearance?



**Axial**



**Syneresis**

# Anti-Drug Antibodies = Increase Drug Clearance

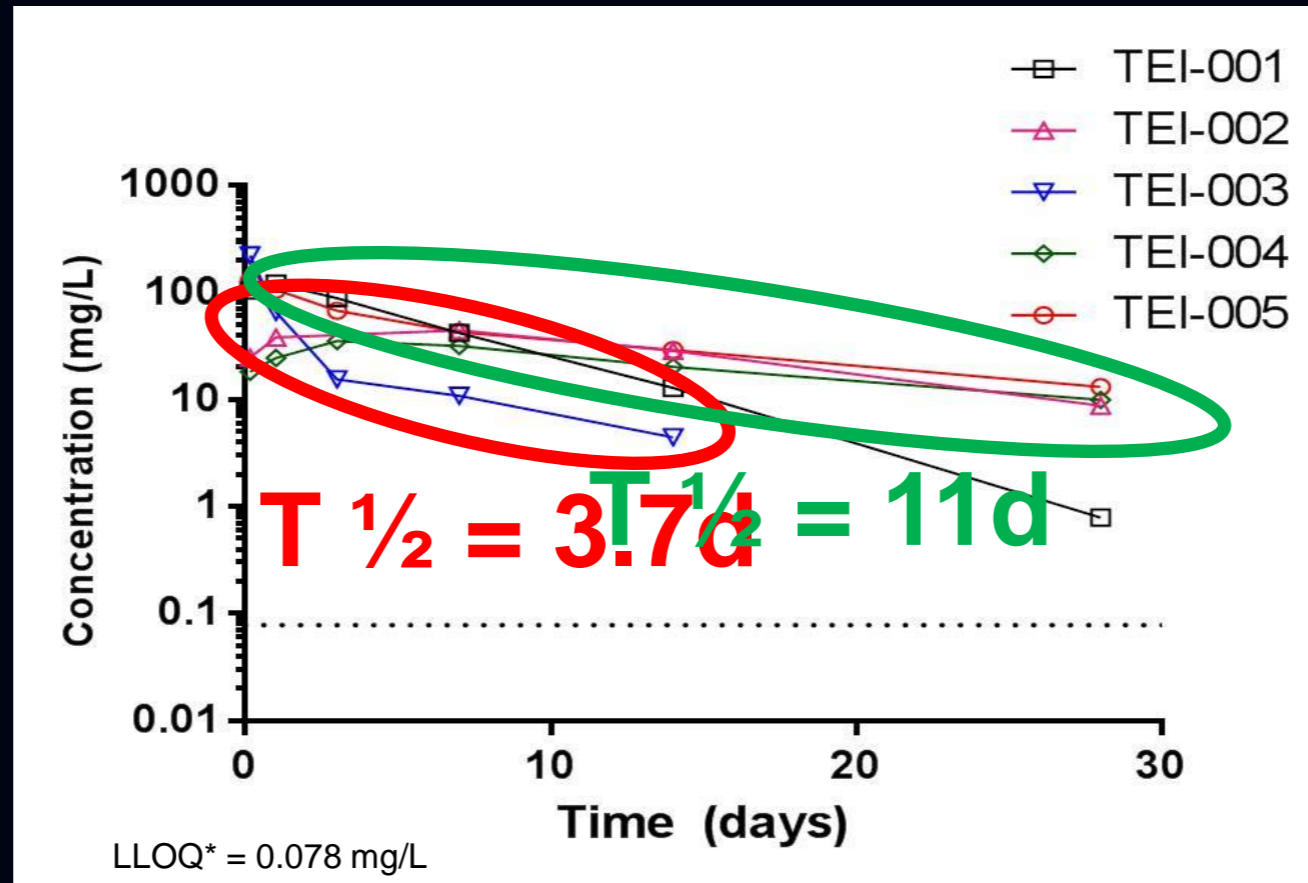
**Table 29. Logistic regression final model of Q8W dosing regimen (Arms A of Phase III nAMD studies)**

Parameter	Coefficient	SE	RSE	95% CI	p-value	Group
Intercept	1.234	0.4613	37.39	0.3295;2.138	0.007	Q8W
VH half-life	-0.4365	0.06166	14.13	-0.5573;-0.3156	<0.0005	
PEDT	0.00305	0.00053	17.38	0.002011;0.004089	<0.0005	
ADA = Yes	-1.008	0.3514	34.86	-1.697;-0.3194	0.004	

Source: PK and ER of Faricimab, Report # 1105763, Page 97, Table 30.

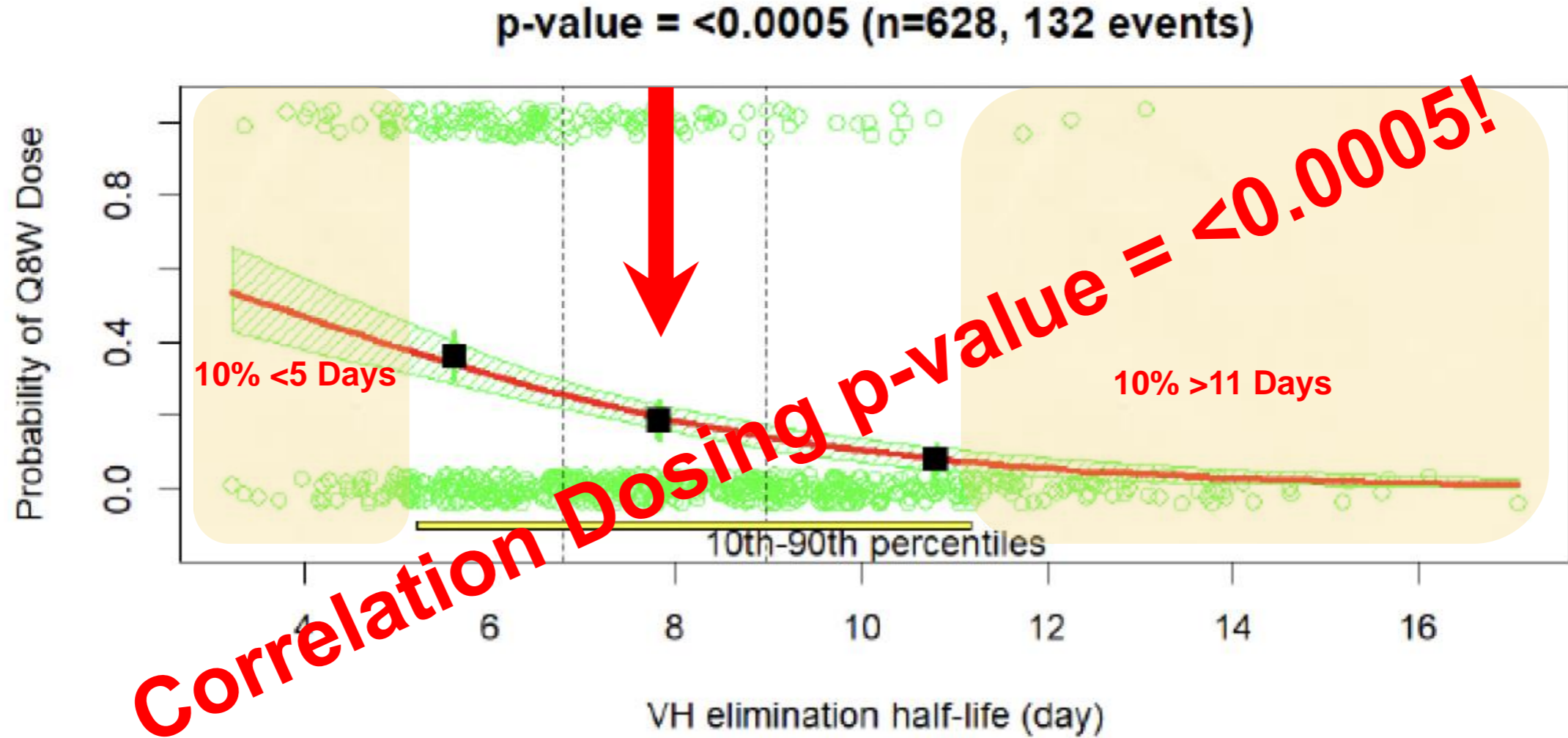
# Aqueous and Plasma Concentrations Vary Among Patients

## Aqueous- Free Aflibercept Concentrations by Patient



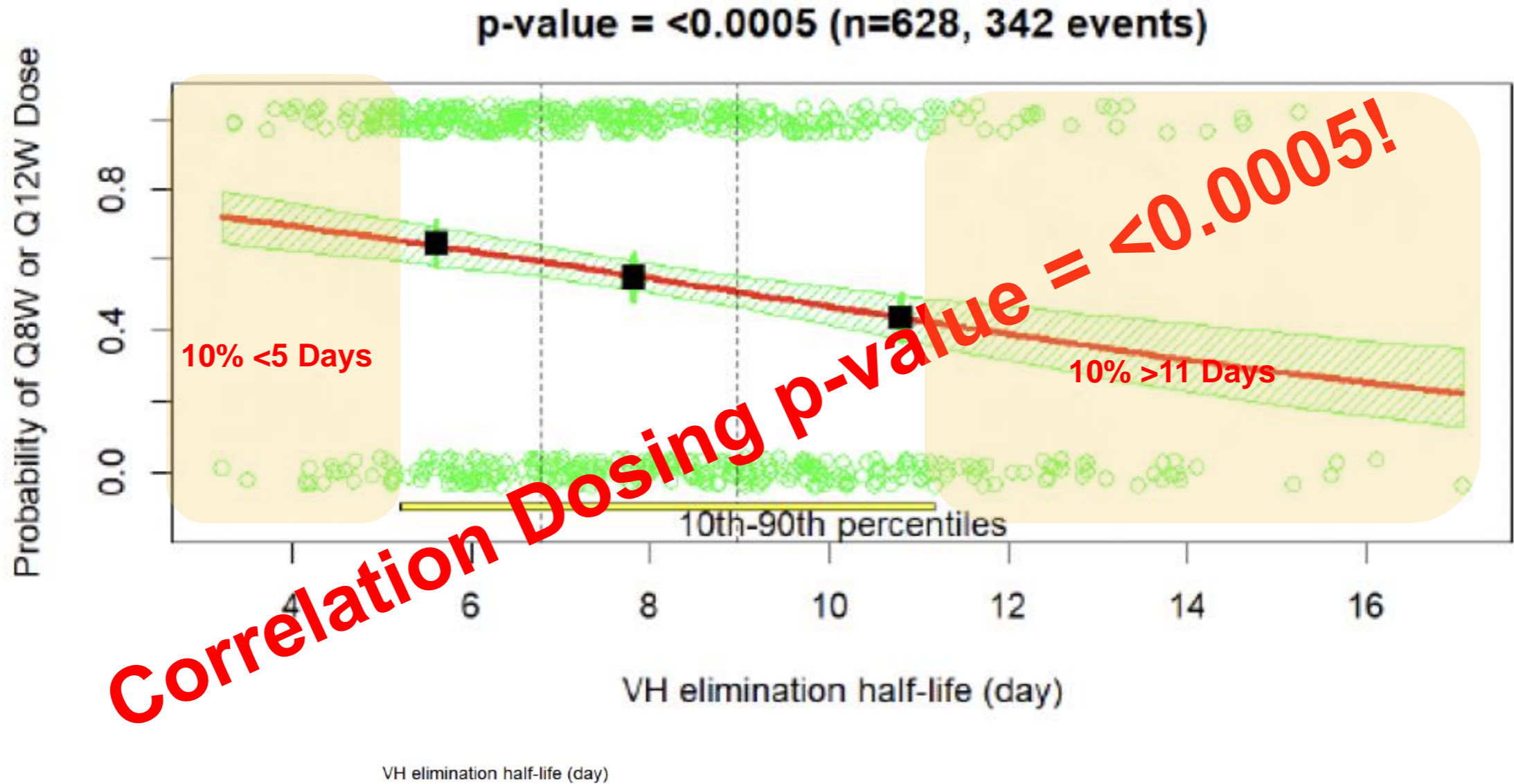
\*LLOQ: Lower Limit Of Quantification  
Do, D. Retina 00:1-5, 2019

Figure 42. Logistic regression for probability of requiring a Q8W dosing for nAMD studies GR40306 and GR40844 (Arms A).



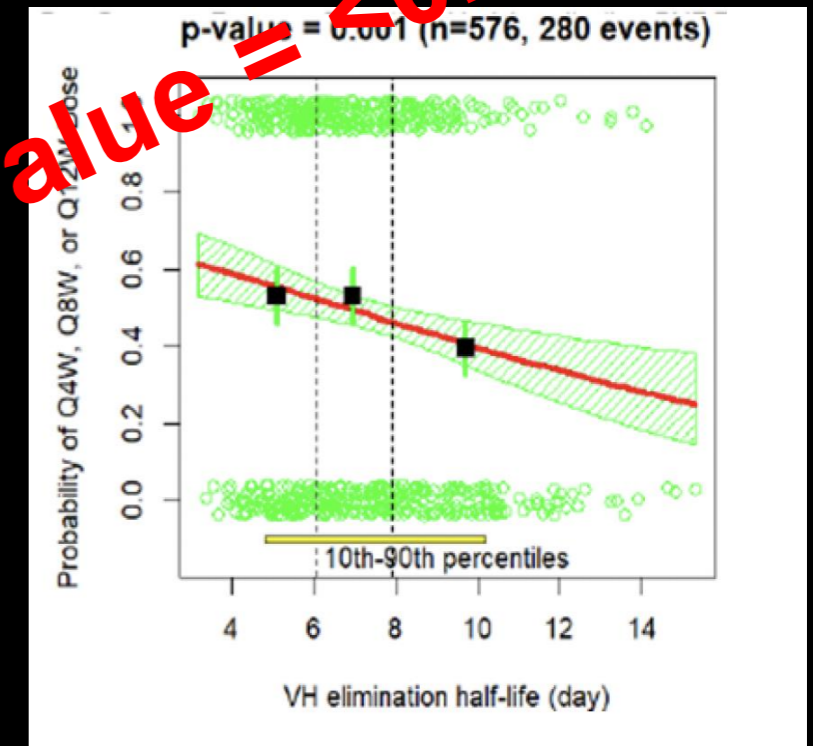
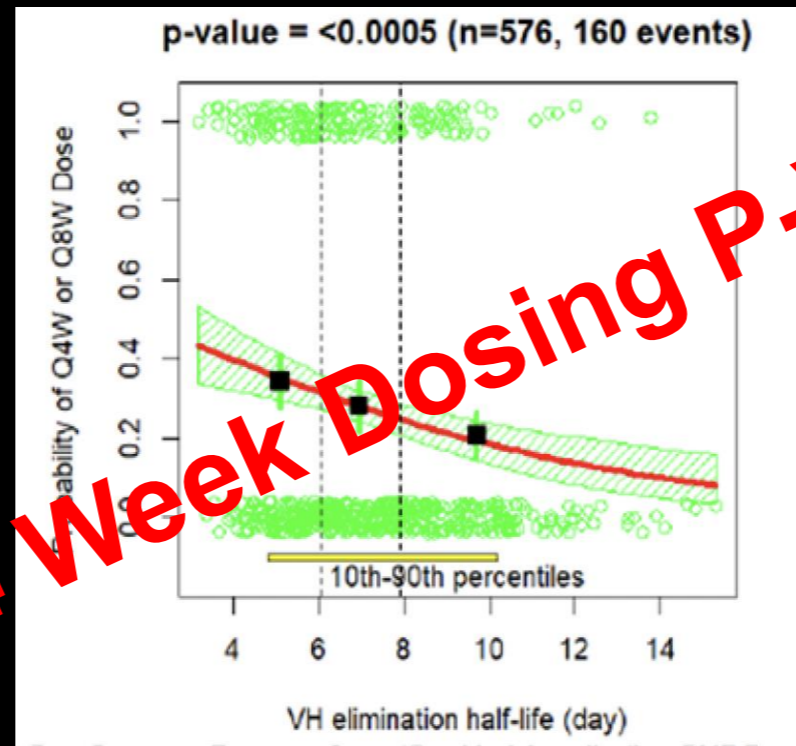
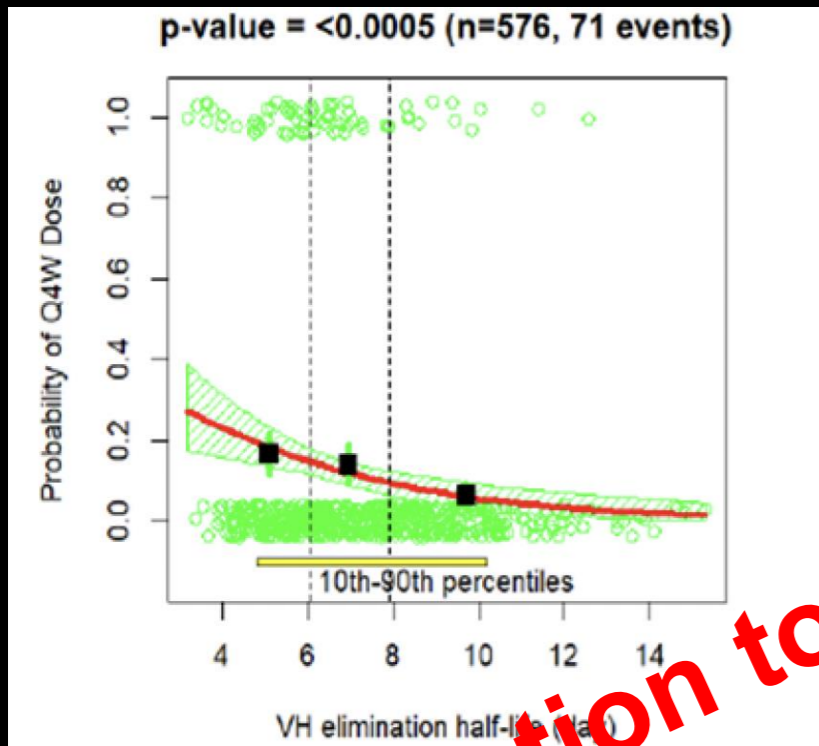
Source: PK and ER of Faricimab, Report # 1105763, Page 269, Figure 173.

Figure 43. Logistic regression for probability of requiring a Q8W or Q12W dosing for nAMD studies GR40306 and GR40844 (Arms A)



Source: PK and ER of Faricimab, Report # 1105763, Page 270, Figure 174.

**Figure 45. Logistic regression for probability of dropout, Q4W regimen, Q4W or Q8W regimen, Q4W, Q8W or Q12W regimen at Week 52 for DME studies GR40349 and GR40398 (Arms B)**



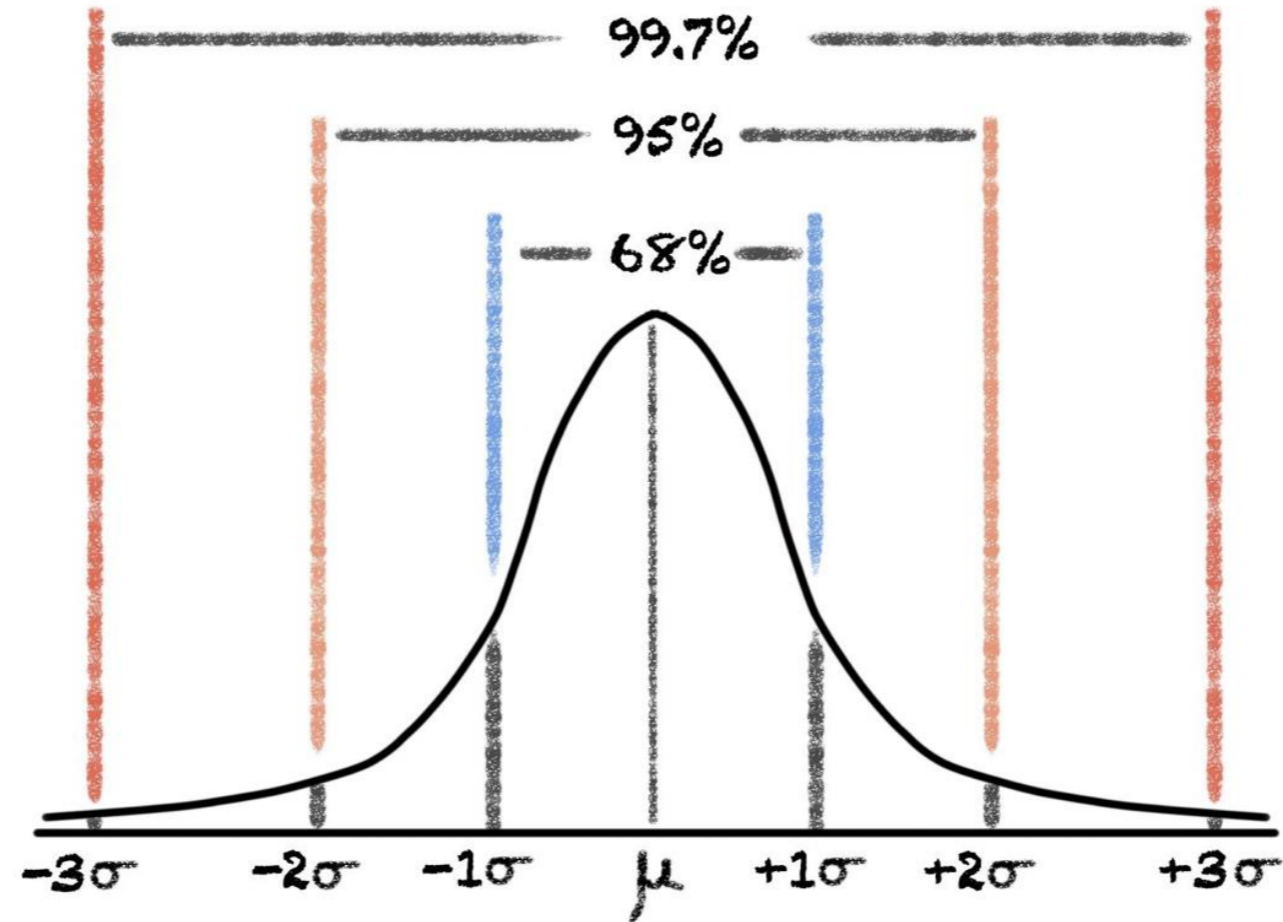
**Correlation to 4 Week Dosing P-value = <math><0.0005!</math>**

Source: PK and ER of Faricimab, Report # 1105763, Page 320-323, Figure 224-227.





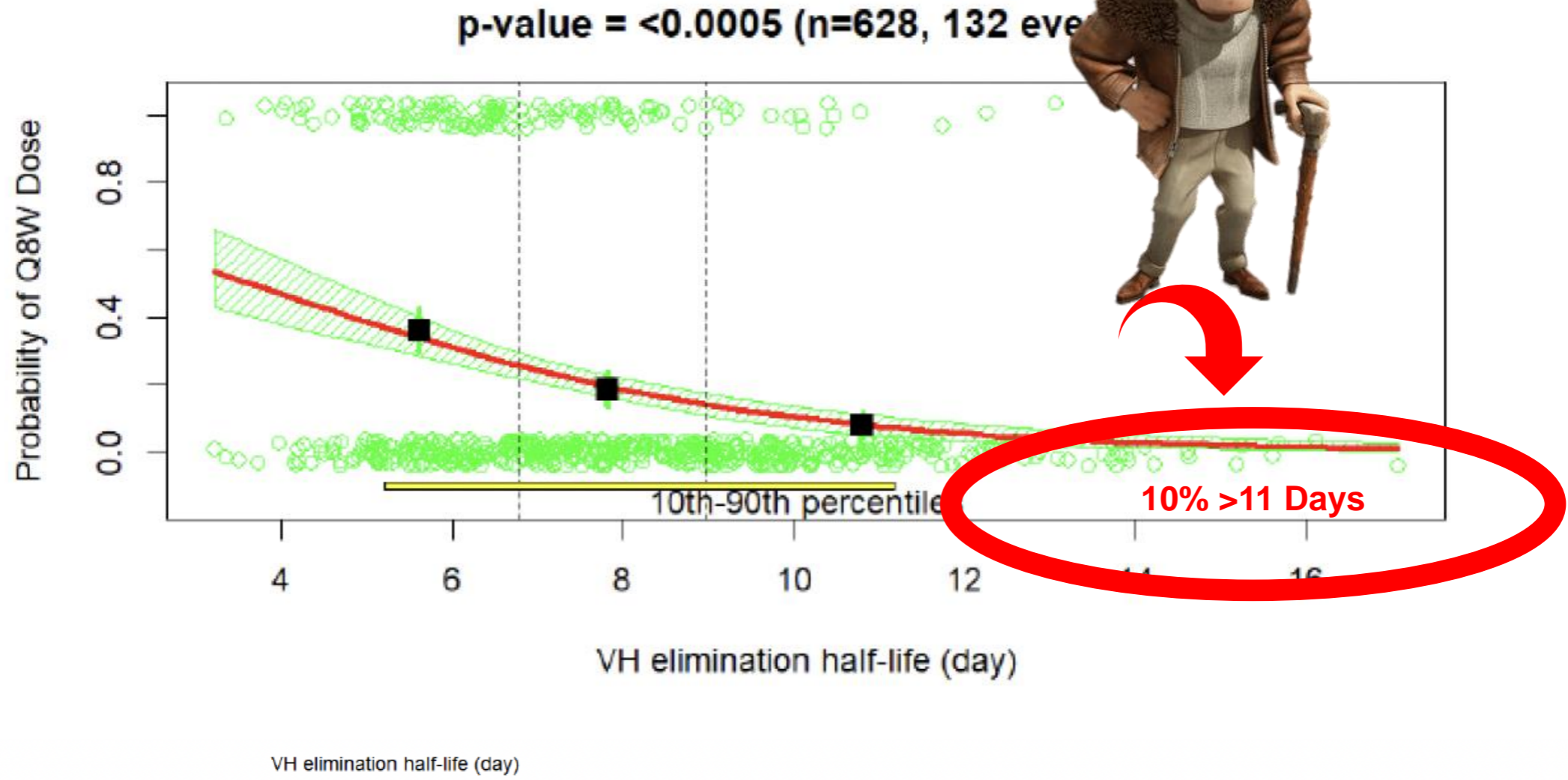
# Normal Distribution



$\mu$  = mean

$\sigma$  = std. dev

Figure 42. Logistic regression for probability of requiring a Q8W dosing for nAMD studies GR40306 and GR40844 (Arms A).



Source: PK and ER of Faricimab, Report # 1105763, Page 269, Figure 173.

**"Three and Done"  
Exit the Clinic**

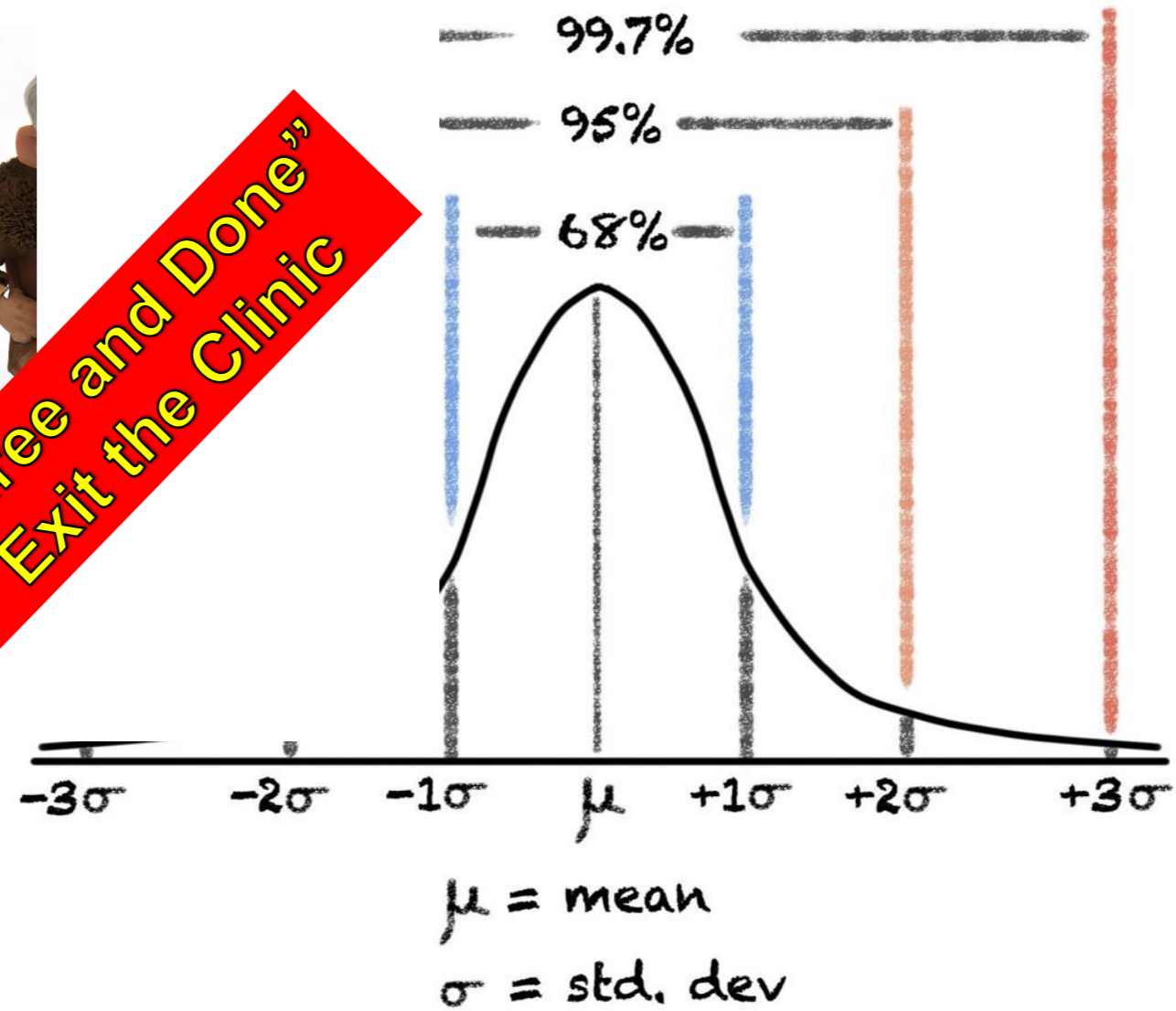
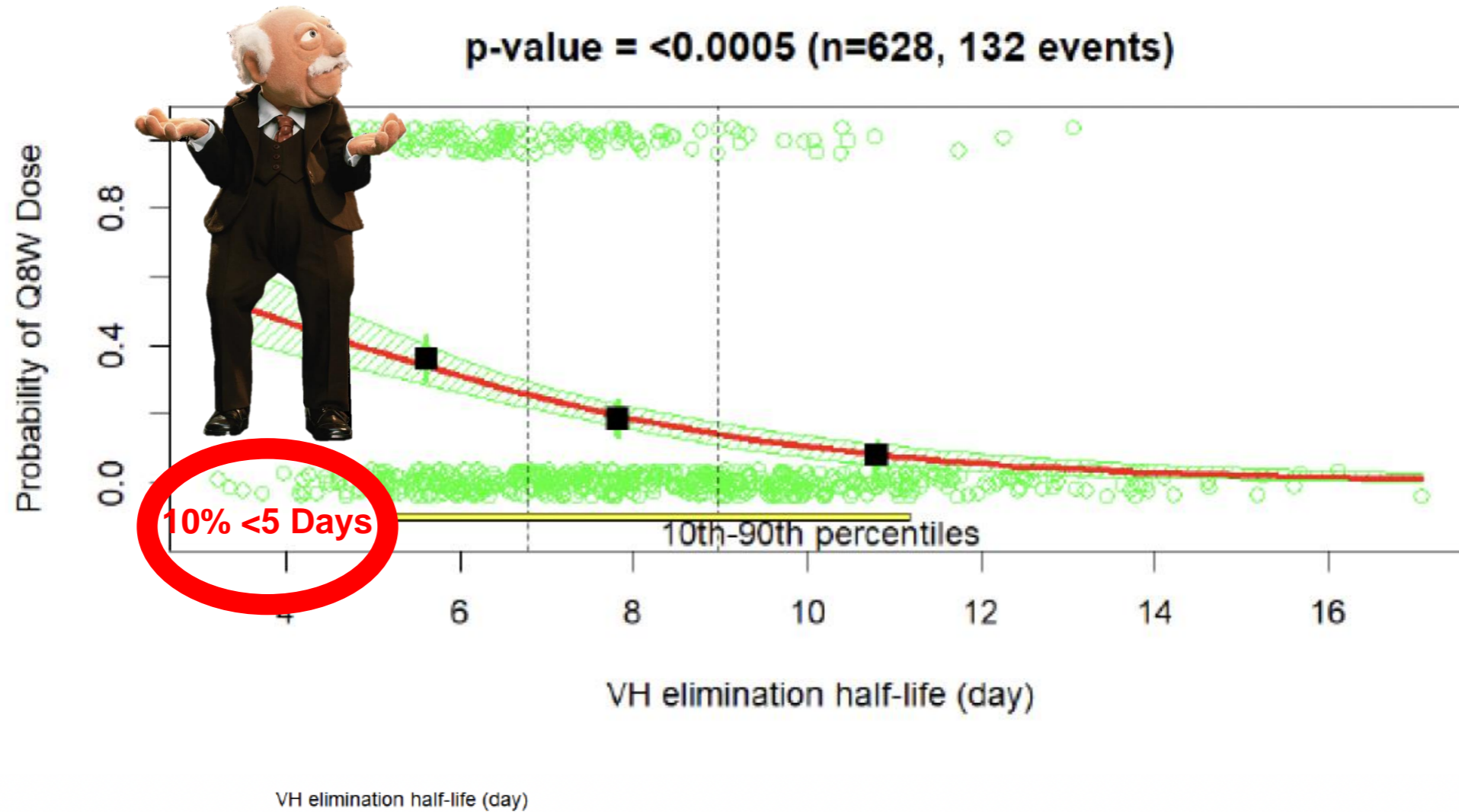
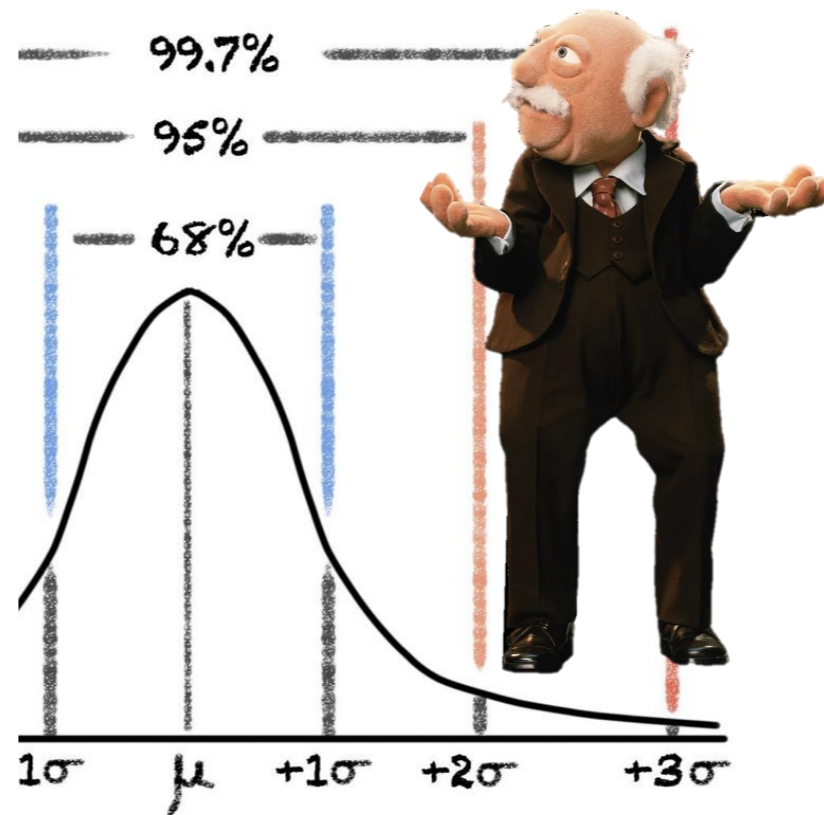


Figure 42. Logistic regression for probability of requiring a Q8W dosing for nAMD studies GR40306 and GR40844 (Arms A).



Source: PK and ER of Faricimab, Report # 1105763, Page 269, Figure 173.



$\mu$  = mean

$\sigma$  = std. dev

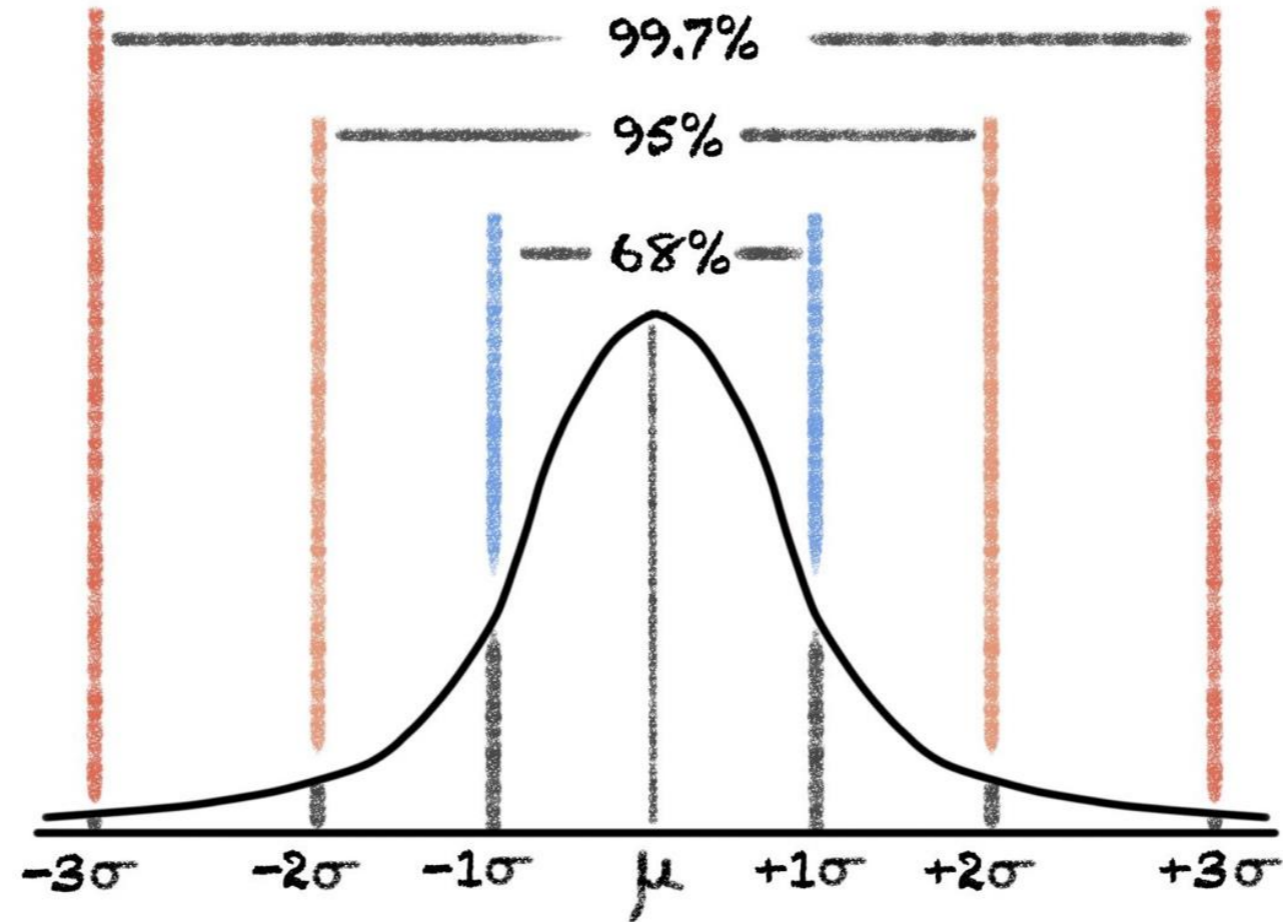
$\sigma$  = std. dev



## Anti-VEGF Molar Equivalency

Aflibercept 2.0 mg	Ranibizumab 0.5 mg	Faricimab 6.0 mg	Aflibercept 8.0 mg	Brolucizumab 6.0 mg
1.0	0.6	2.3	4.0	>10

# Normal Distribution

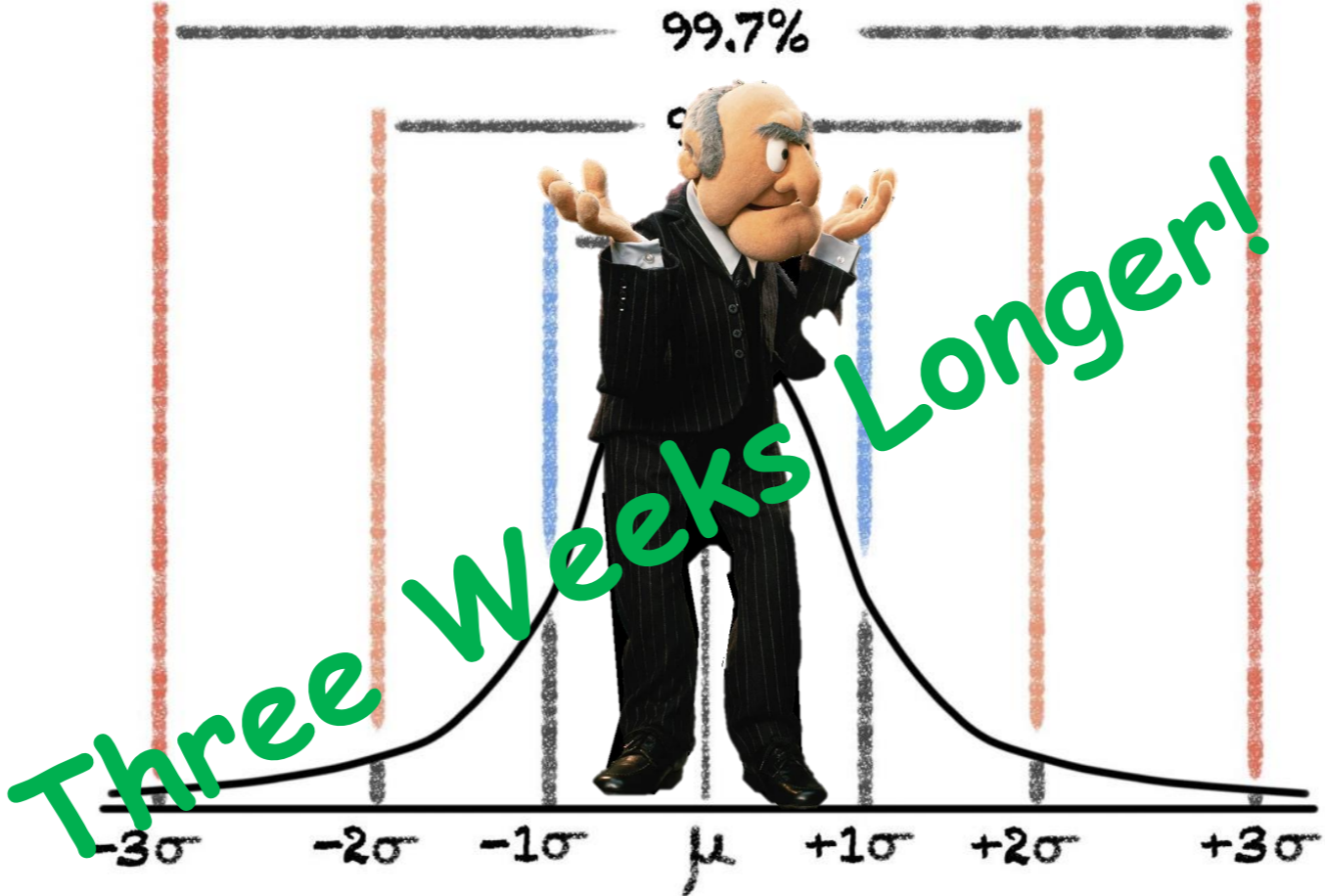


$\mu$  = mean

$\sigma$  = std. dev

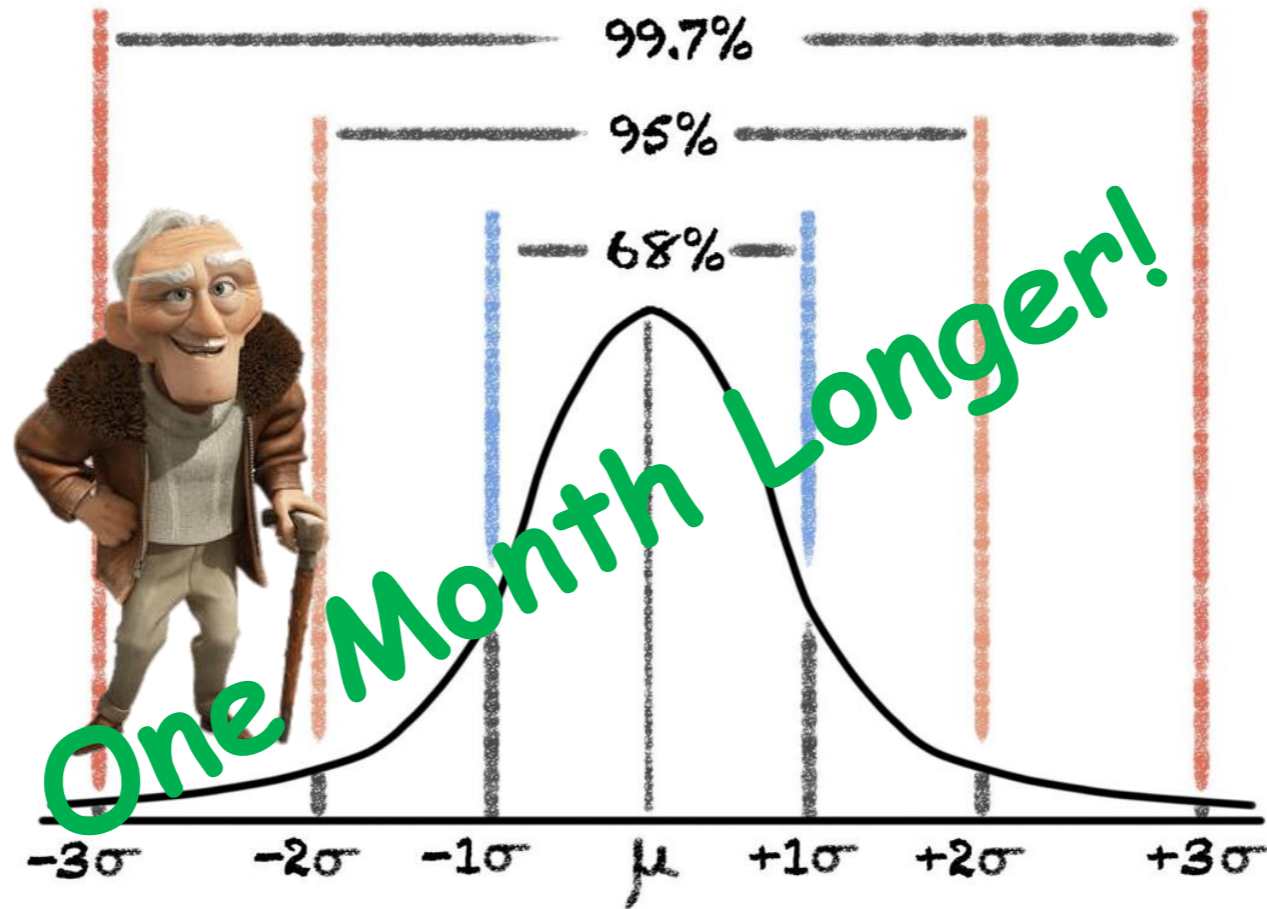


Average Eye (t1/2= 10 days)



$\mu$  = mean  
 $\sigma$  = std. dev

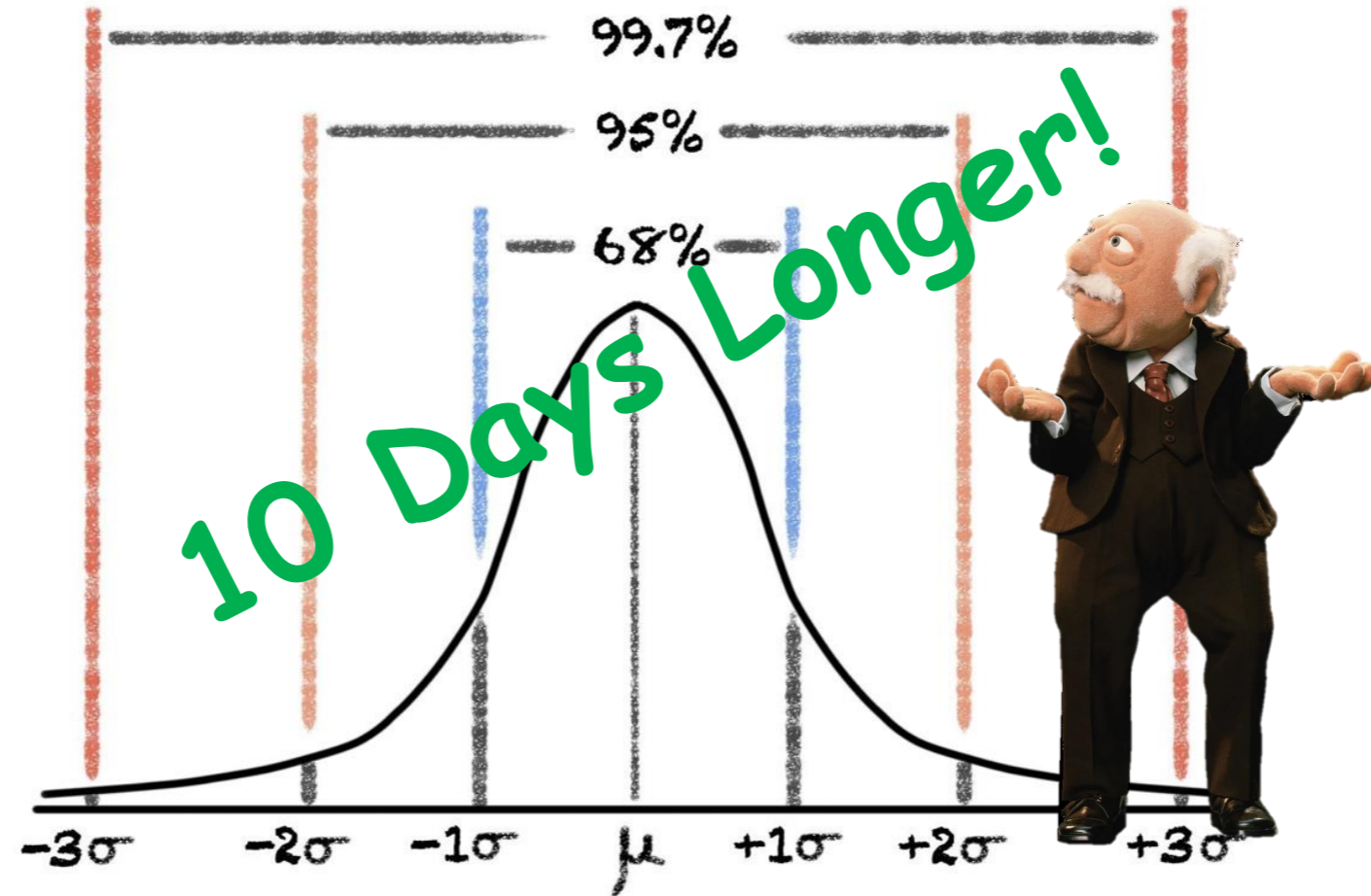
# Slow Clearance Eyes (+1/2 = 14 days)



$\mu$  = mean

$\sigma$  = std. dev

# Fast Clearance Eyes ( $t_{1/2} = 5$ days)



$\mu = \text{mean}$

$\sigma = \text{std. dev}$

# Is Twelve Weeks the New Norm?



For Average: YES- 12 weeks is the new norm!



For Lucky Slow Clearance Eyes: 14-16 weeks is the new norm

# Is Twelve Weeks the New Norm?



For Fast Clearance eyes- 5-6 weeks is the new norm  
But That's Better than Monthly!

# Currently Available Options



- Increase Dosing Frequency
- Block Additional Targets
- Increase Molar Blockade of Anti-VEGF
- **ABC Platform – increasing drug half-life**

Thank You!



# In the era of faricimab, are more durable intravitreal biologics still needed today for the treatment of retinal vascular diseases?

## Patients switching to faricimab achieve only a modest extension in dosing

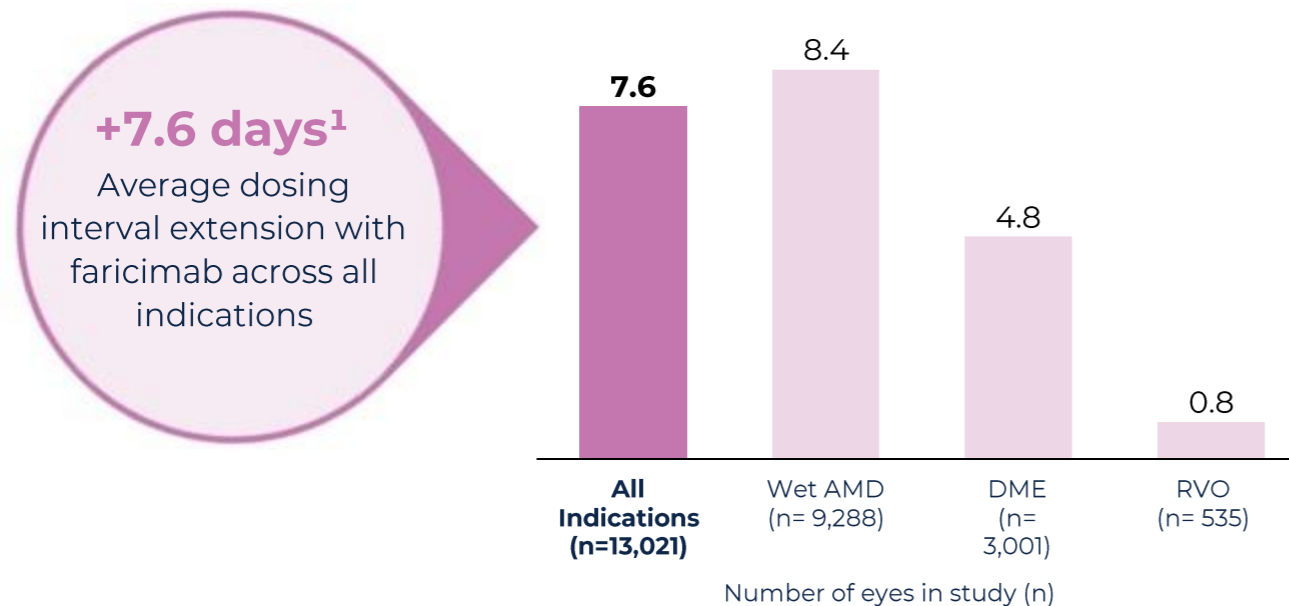
- In clinical trials, **less than half of faricimab patients achieved 4-month dosing** in Year 1
- Real-world evidence shows that switching anti-VEGF experienced patients to faricimab, however, achieves very modest extension in dosing intervals

## Retina specialists are still looking for more durable therapies

“With the second-generation anti-VEGFs, which we’ve started to incorporate quite a bit in practice, I have to say that by study design it exaggerates the durability of those drugs. You might see presentations that say some of these drugs, for example Eylea HD, can go 16 or 20 weeks in most patients. In practice that won’t happen. They are a little more durable but not to that degree.”

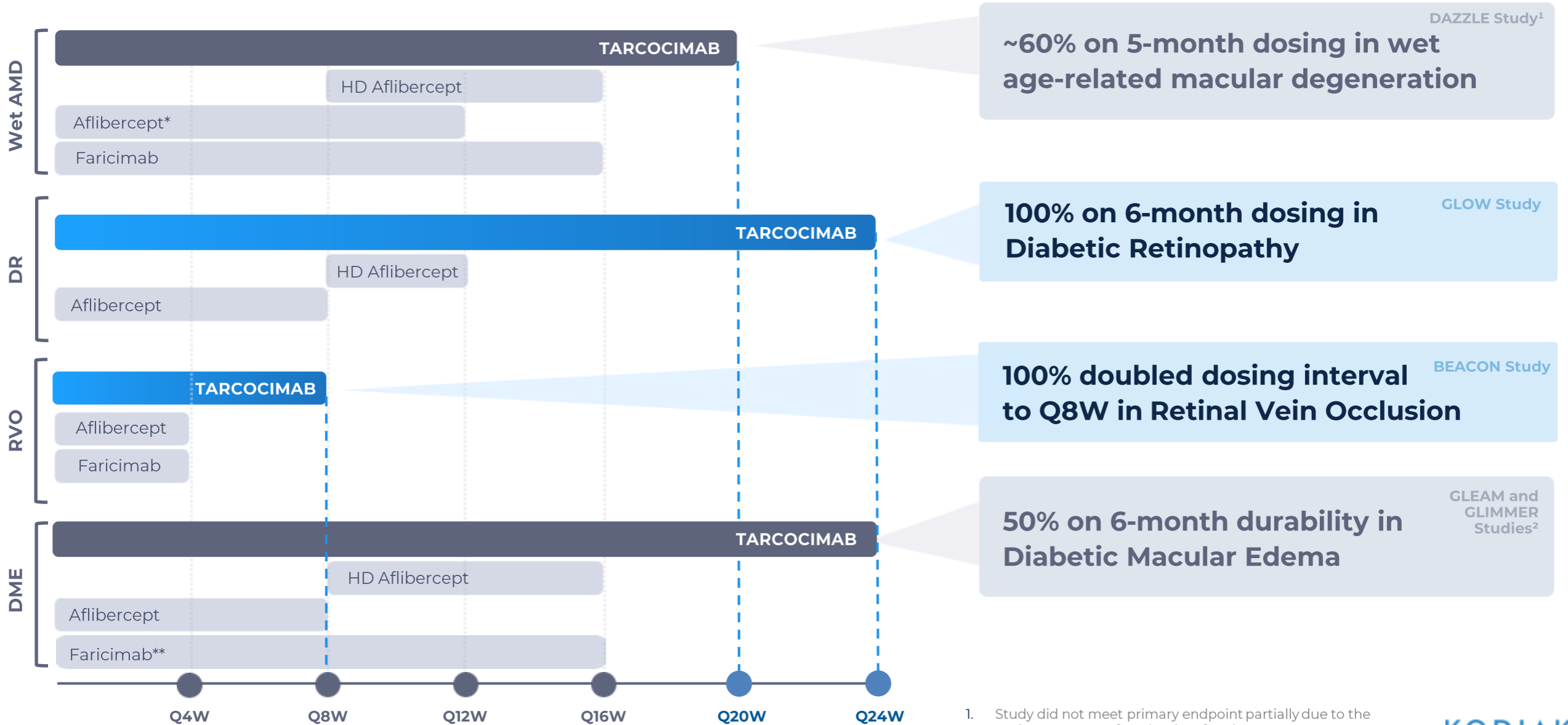
“I think a lot of clinical trial investigators are excited about a true durability agent. You look back at the PAT survey from the ASRS conference last year, I think retina specialists are at large still looking for more durable agents, and in particular agents that combine high efficacy with high durability.”

Mean extension in dosing interval by faricimab (days)





# Tarcocimab consistently demonstrated 5- to 6-month durability in multiple retinal vascular diseases across its pivotal studies



57 \*Q12W after 1 year of effective therapy.  
 \*\*Based on dosing interval at primary endpoint at year 1 in pivotal studies YOSEMITE and RHINE

1. Study did not meet primary endpoint partially due to the undertreatment of a minority of patients.  
 2. Studies did not meet primary endpoints due to an unforeseen increase in cataracts in tarcocimab-treated patients; Kodiak's enhanced formulation may mitigate this liability.

# Tarcocimab's extended durability stems directly from its underlying science of durability

Tarcocimab and the ABCD platform are supported by our **science of durability**

4 key elements support the science of durability



## CONJUGATE DESIGN

The ABCD Platform leverages a proprietary, high molecular weight, phosphorylcholine-based biopolymer that enables an extended ocular residence time

## POTENCY

Tarcocimab demonstrates strong potency in *in vitro* assays that is comparable to aflibercept

## ANIMAL OCULAR HALF-LIFE

Tarcocimab and other ABCD molecules demonstrate 3x longer ocular half-life in rabbit models compared to aflibercept or faricimab

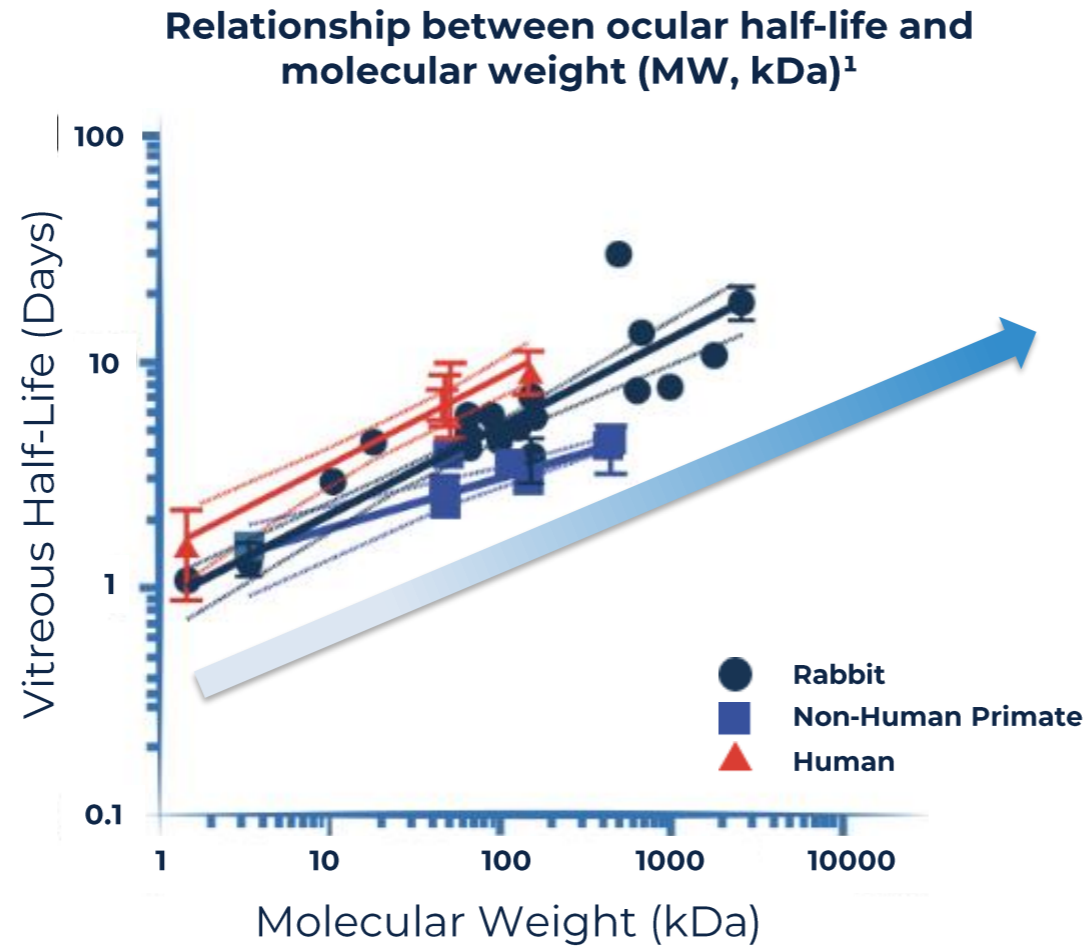
## HUMAN OCULAR HALF-LIFE

Tarcocimab demonstrates 3x longer human ocular half-life compared to aflibercept or faricimab



# CONJUGATE DESIGN

# Principal of Design: Ocular half-life increases proportionally with molecular size



**Strong positive correlation  
between the ocular half-life of  
an intravitreally injected  
protein therapeutic and its  
molecular size**

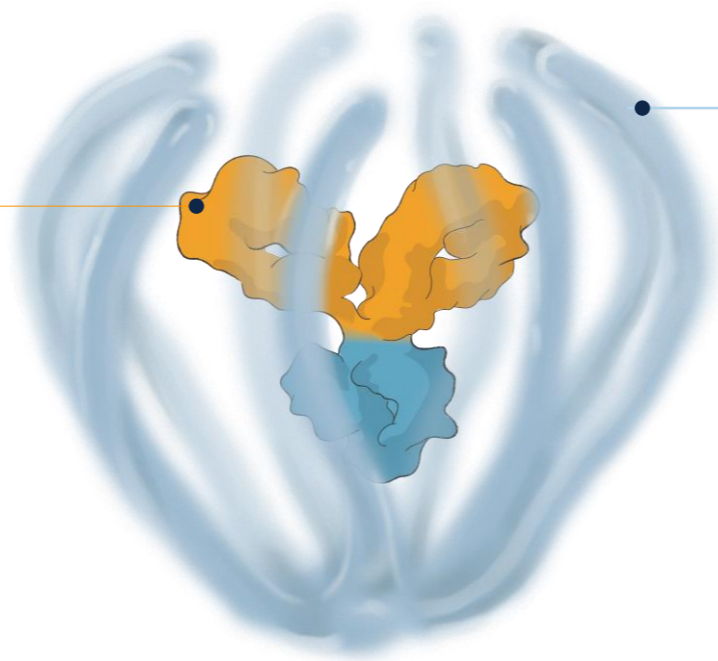
1. Adapted from Crowell SR, et al. Trans Vis Sci Tech. 2019;8(6):1.

# Kodiak's ABCD platform leverages a proprietary, high molecular weight, phosphorylcholine-based biopolymer to enable an extended ocular residence time

The Antibody Biopolymer Conjugate Drug ("ABCD") Platform is the foundation of tarcocimab tedromer and KSI-501

## Antibody or Other Biologic

Any biologic such as an antibody can be conjugated to the biopolymer via a stable, site-specific linkage



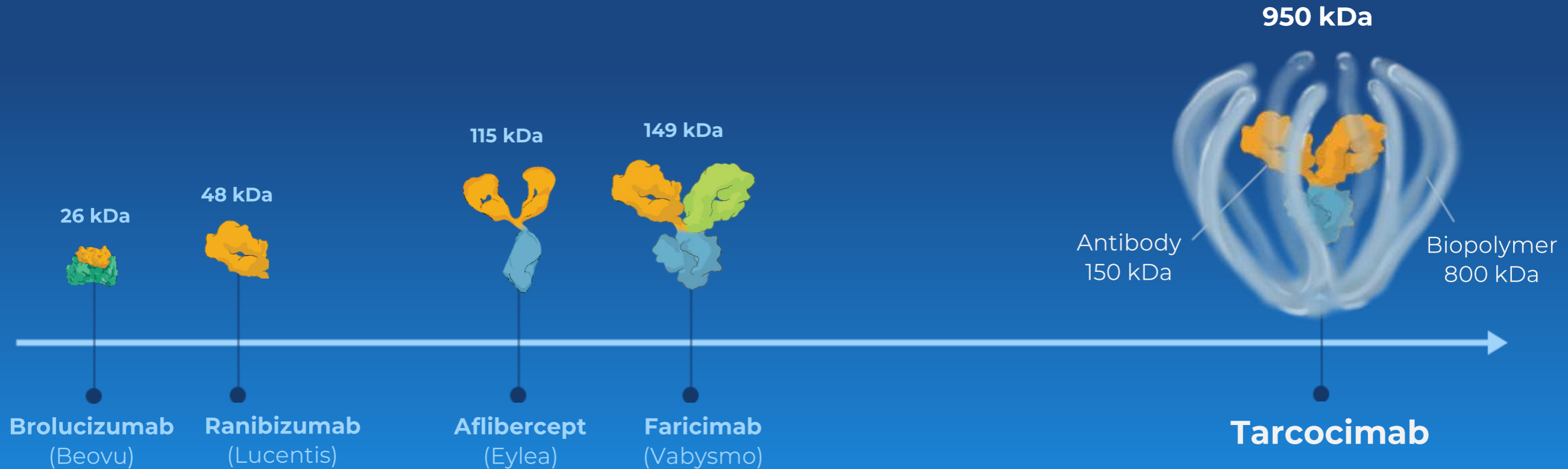
## High molecular weight Biopolymer

Engineered to make medicines last longer and extend their therapeutic benefit.






The biopolymer is optically clear and made of phosphorylcholine, the primary hydrophilic component of human cell membranes

Antibody Biopolymer Conjugate Drug ("ABCD")

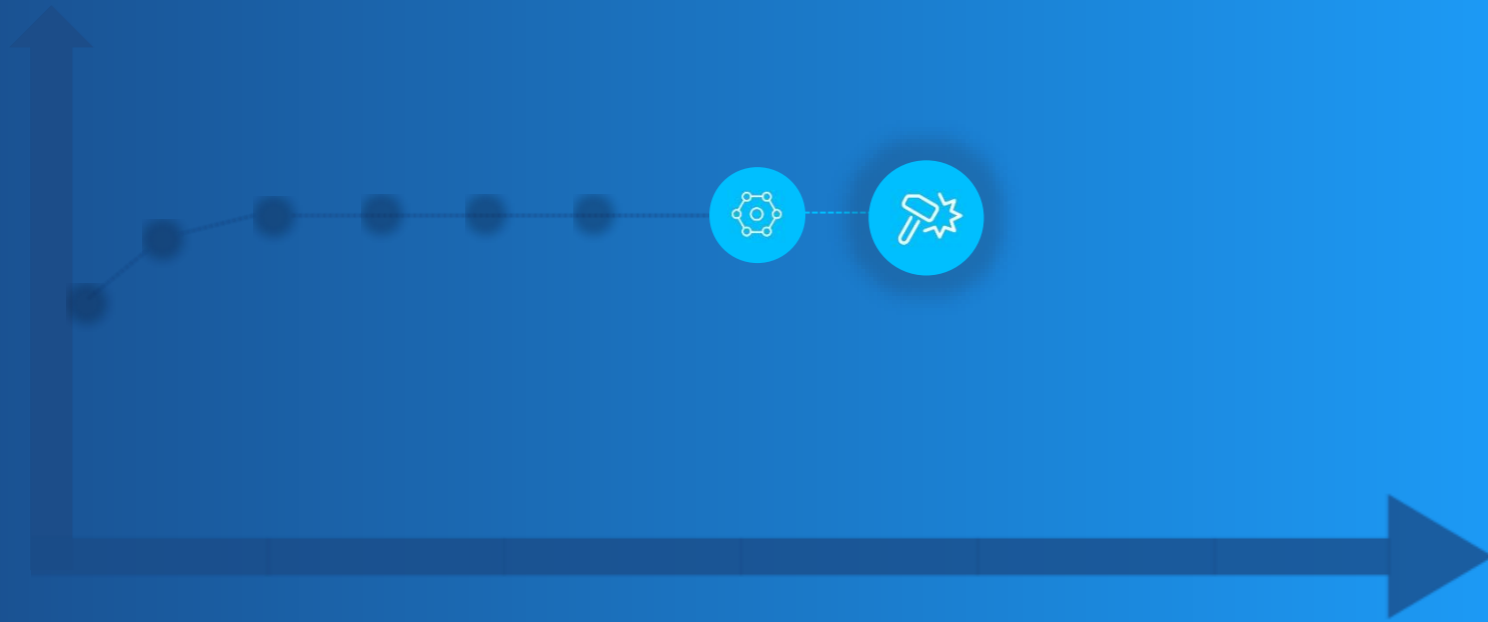
# Tarcocimab has a high molecular weight which increases its ocular half-life compared to today's anti-VEGFs



# Tarcocimab also has a high formulation strength to provide a meaningful dosing advantage

	<b>Brolucizumab</b>	<b>Ranibizumab</b>	<b>Aflibercept</b>	<b>Aflibercept HD</b>	<b>Faricimab</b>	<b>Tarcocimab Tedromer</b>
Molecule Type	Single-Chain Antibody Fragment	Antibody Fragment	Recombinant Fusion Protein		Antibody	<b>Antibody Biopolymer Conjugate Drug</b>
Molecular Structure						
Molecular Weight	26 kDa	48 kDa	115 kDa		149 kDa	<b>950 kDa</b>
Clinical Dose	6 mg	0.3-0.5 mg	2 mg	8 mg	6 mg	<b>5 mg</b> By weight of antibody
Equivalent Molar Dose	11	0.5	1	4	2	<b>3.5</b>

Equivalent values are shown as fold changes relative to aflibercept. kDa = kilodalton



POTENCY



# Tarcocimab unconjugated protein and conjugated protein both demonstrate high binding affinity and potency in pre-clinical assays

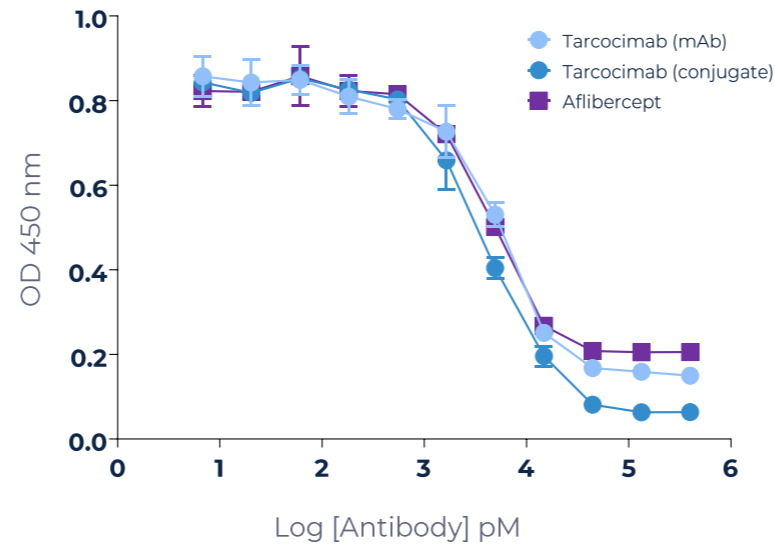
## High Binding Affinity for VEGF-A

Both the tarcocimab conjugate and the anti-VEGF antibody demonstrate similarly high binding affinity for VEGF-A.

	Binding Affinity to VEGF-A <sup>1</sup>
Tarcocimab (conjugate)	6.75 pM
Tarcocimab (mAb)	3.43 pM

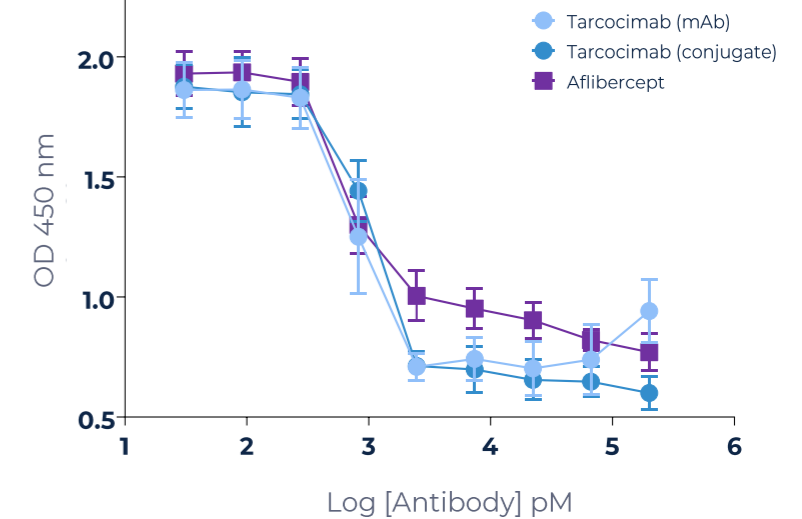
1. Tarcocimab unconjugated protein and conjugated protein have the same or similar binding affinity and potency as aflibercept.
2. The increased molecular size from conjugation to the biopolymer does not impact binding affinity or potency.

## High Potency in Inhibiting VEGF Binding to its Receptors

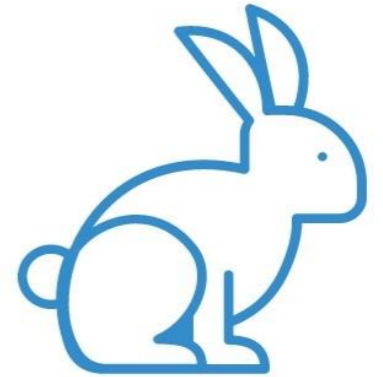


Inhibition of VEGF:VEGFR Binding	IC <sub>50</sub> (nM)	Maximal Inhibition (%)
Tarcocimab (conjugate)	3.72	94%
Tarcocimab (mAb)	3.97	84%
Aflibercept	4.50	75%

## High Potency in Inhibiting VEGF-mediated cell proliferation\*

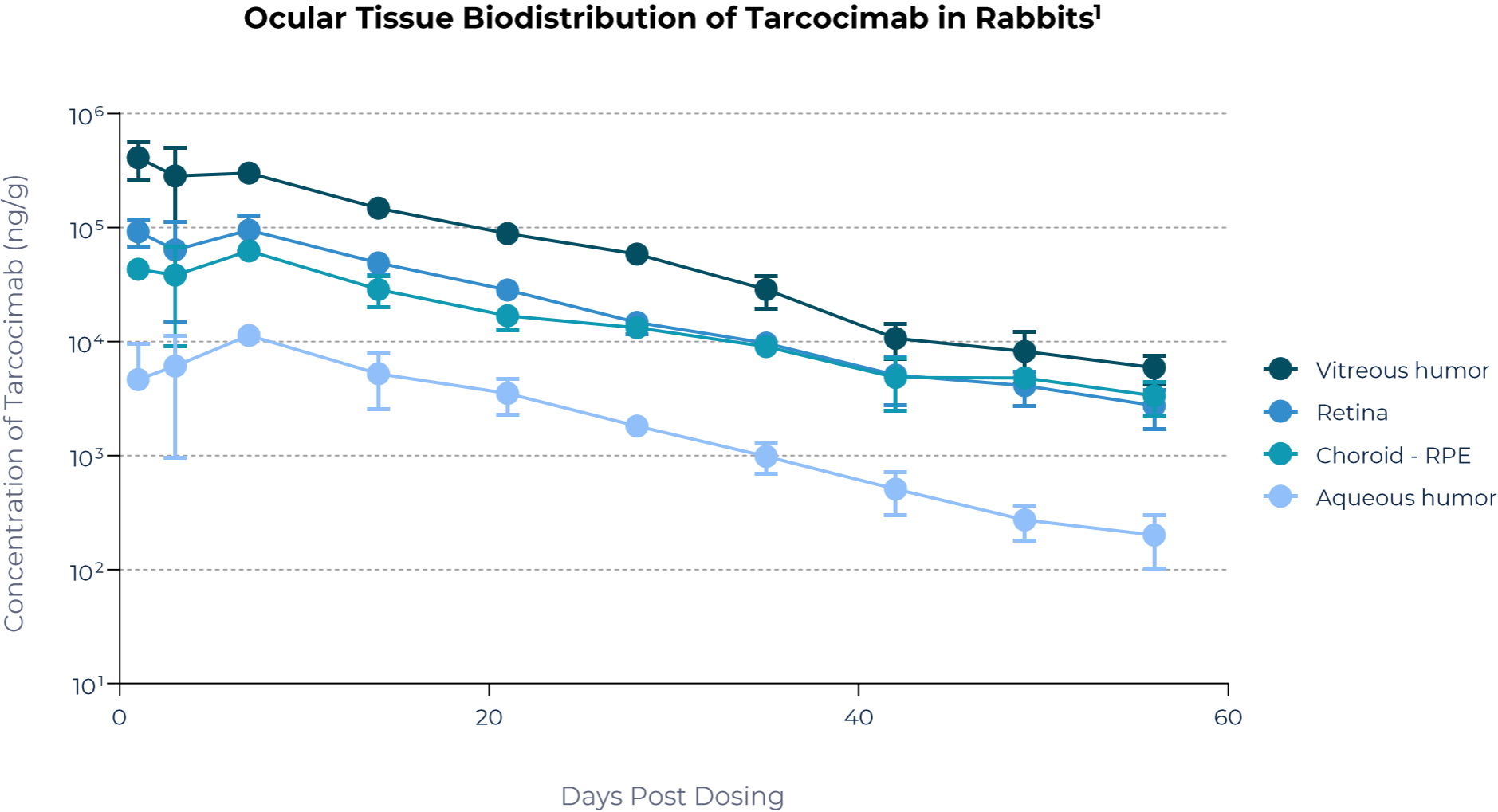


Inhibition of HRMVEC Proliferation	IC <sub>50</sub> (nM)	Maximal Inhibition (%)
Tarcocimab (conjugate)	0.96	65%
Tarcocimab (mAb)	0.85	59%
Aflibercept	0.74	54%



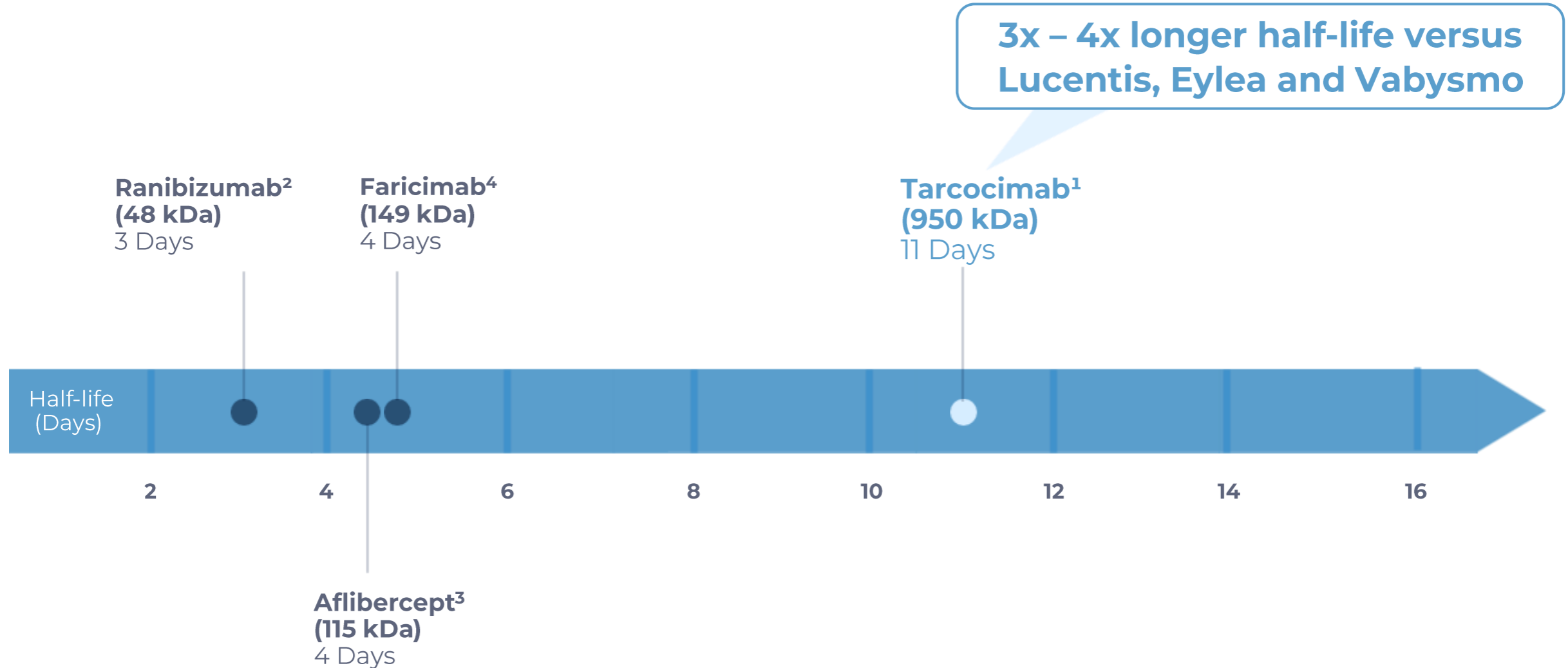
ANIMAL  
OCULAR  
HALF-LIFE

# Tarcocimab demonstrates excellent ocular tissue biodistribution in rabbits



RPE: retinal pigment epithelium  
1. Kodiak data on file. Ocular tissue bioavailability was determined from a single 50  $\mu$ L intravitreal injection of 0.725 mg of tarcocimab (conjugate) in rabbits.

# Tarcocimab's ocular half-life is significantly longer than approved intravitreal biologics in the rabbit model

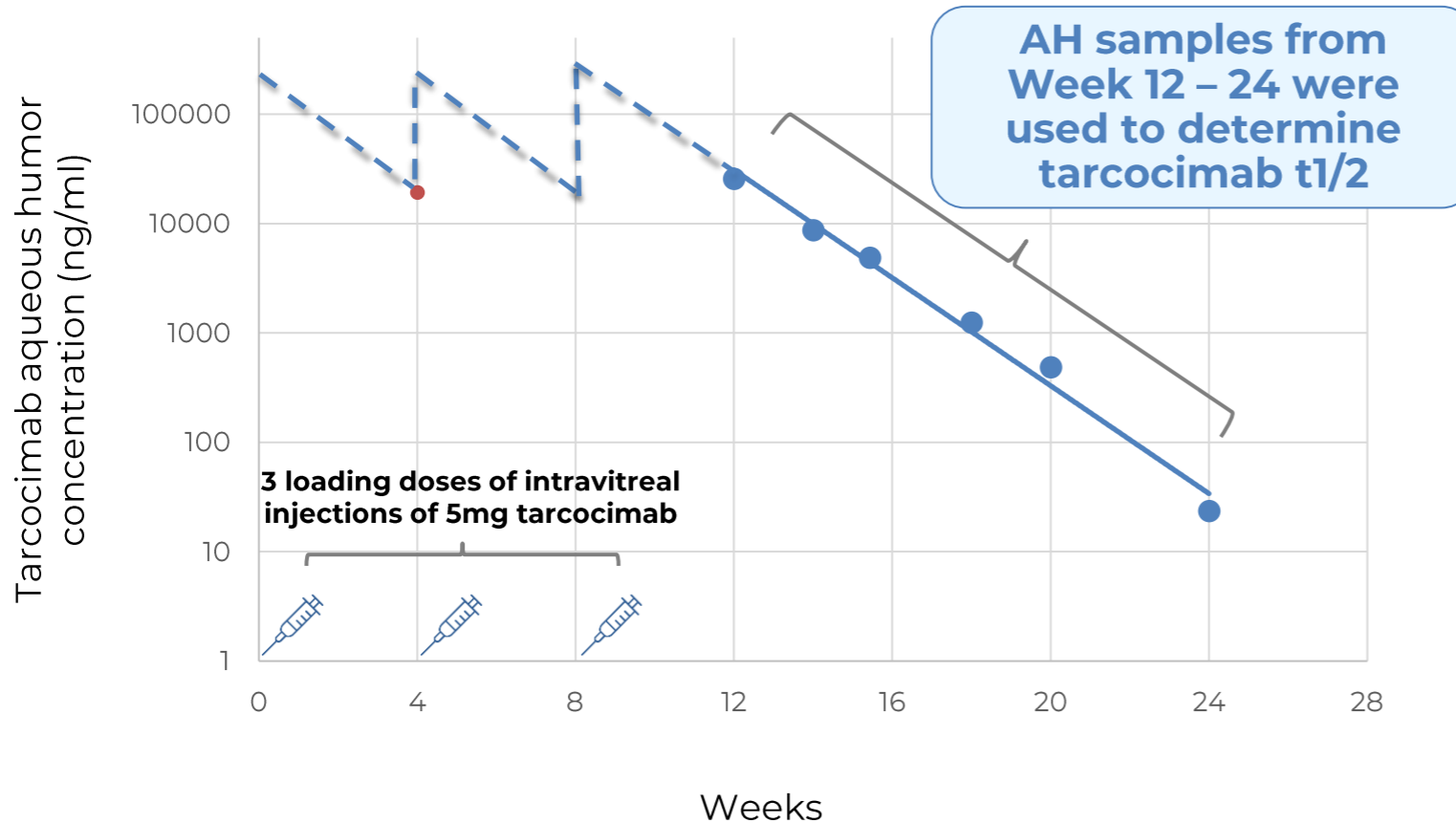




HUMAN  
OCULAR  
HALF-LIFE

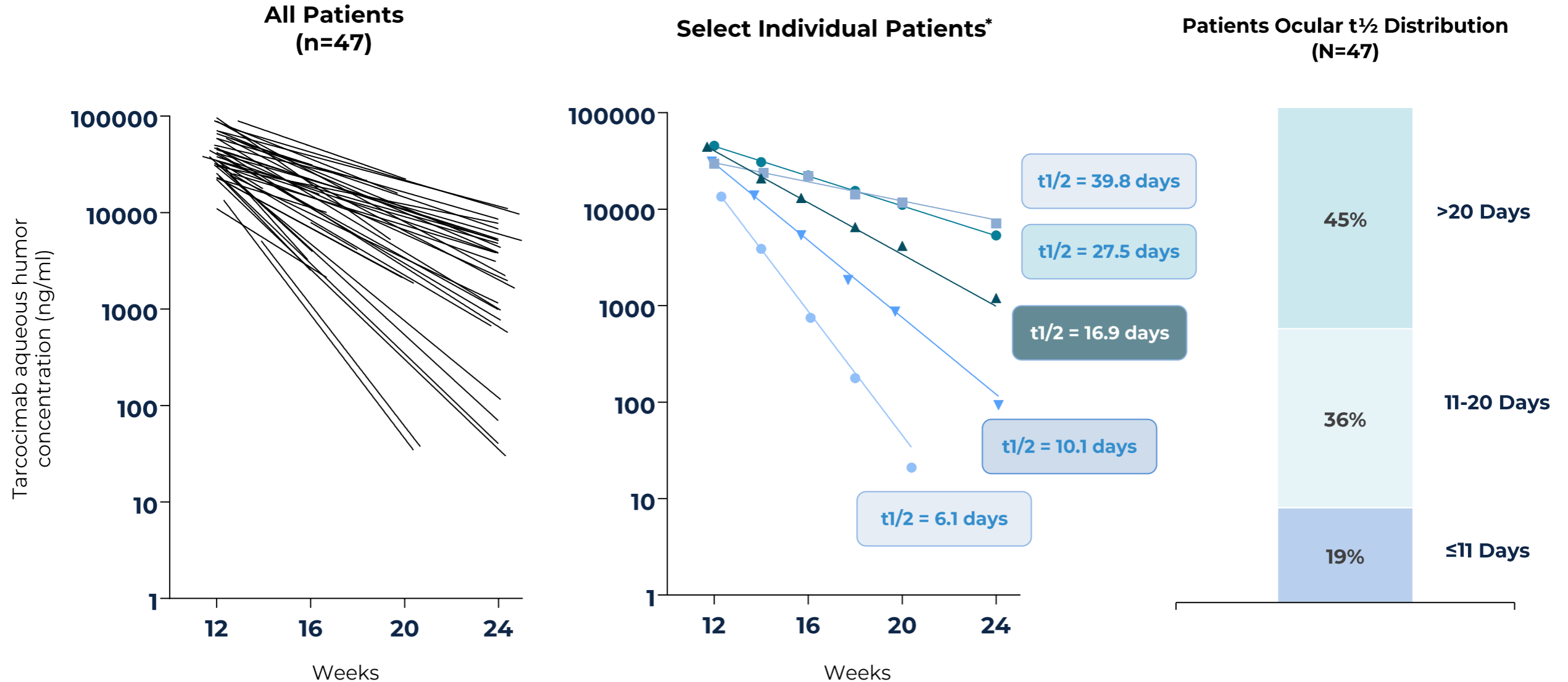
# Tarcocimab's ocular half-life in humans was calculated by measuring aqueous humor concentrations over time from patients in the Phase 1b Study

Using Aqueous Humor Concentration of Tarcocimab to Determine Ocular t<sub>1/2</sub> in human



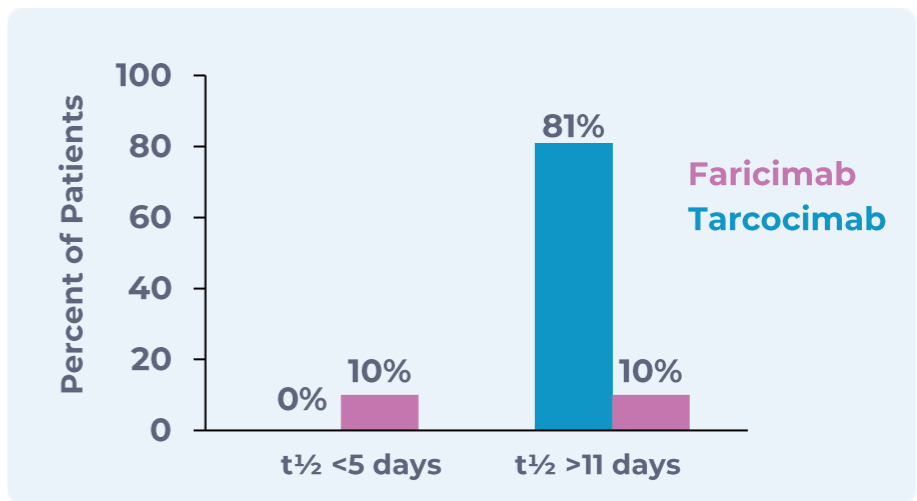
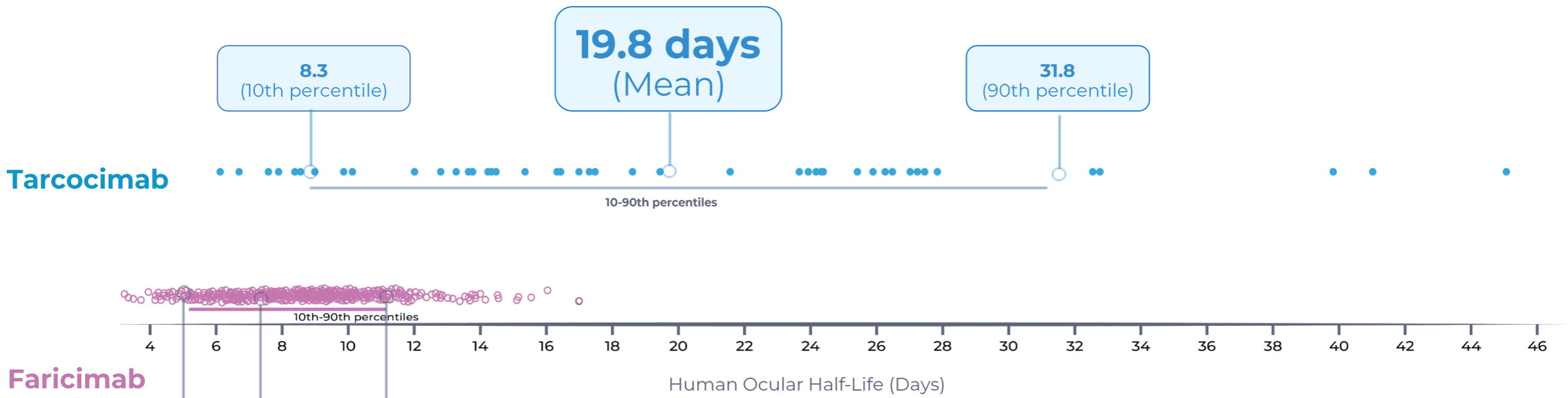
- Aqueous humor samples were collected from 47 subjects in the tarcocimab Phase 1b study in patients with wet AMD, DME and RVO and were used to evaluate tarcocimab ocular half life in patients
- Aqueous humor samples were collected at baseline and at Week 4, 12, 14, 16, 18, 20 and 24 and measured for tarcocimab concentrations
- Samples collected between the last loading dose and the next re-dose were used to determine ocular half-life of tarcocimab

# Tarcocimab achieved an extended ocular half-life of >20 days in 45% of sampled patients from the Phase 1b Study



71 Each line represents one individual patient from the Phase 1b study of tarcocimab in patients with wet AMD, DME and RVO. N= 47 patients, all received an intravitreal injection of 5mg tarcocimab clinical formulation on day 1. \*Mean and standard deviations are plotted, though SDs are not visible due to small magnitude

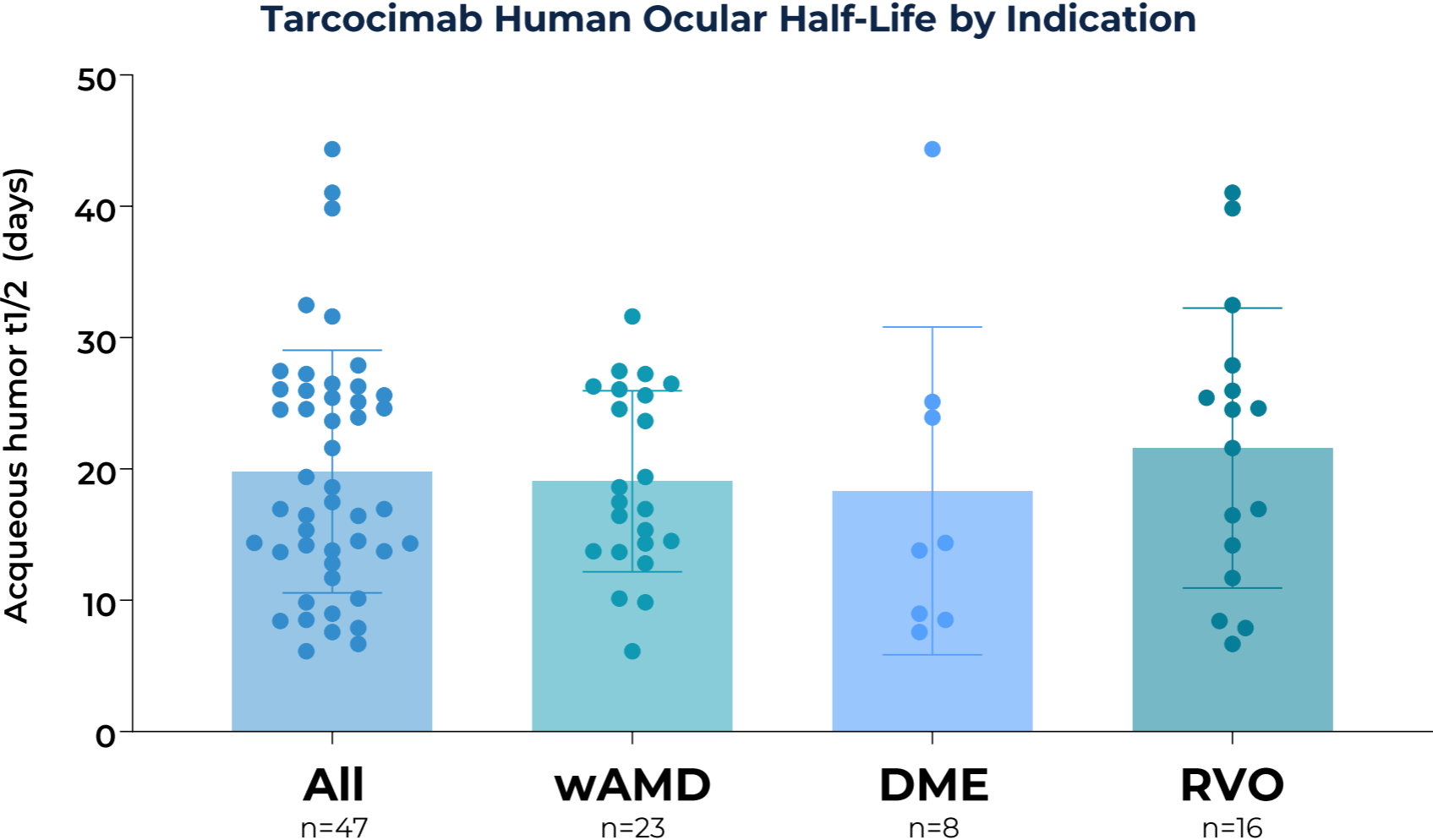
# Tarcocimab has a mean ocular half-life in humans of 20 days, which is 3x longer than faricimab



72 Each dot represents an individual patient. VABYSMO™ (faricimab solution for injection) Prescribing Information. South San Francisco, USA: Genentech, Inc. PK and ER of Faricimab, Report # 1105763

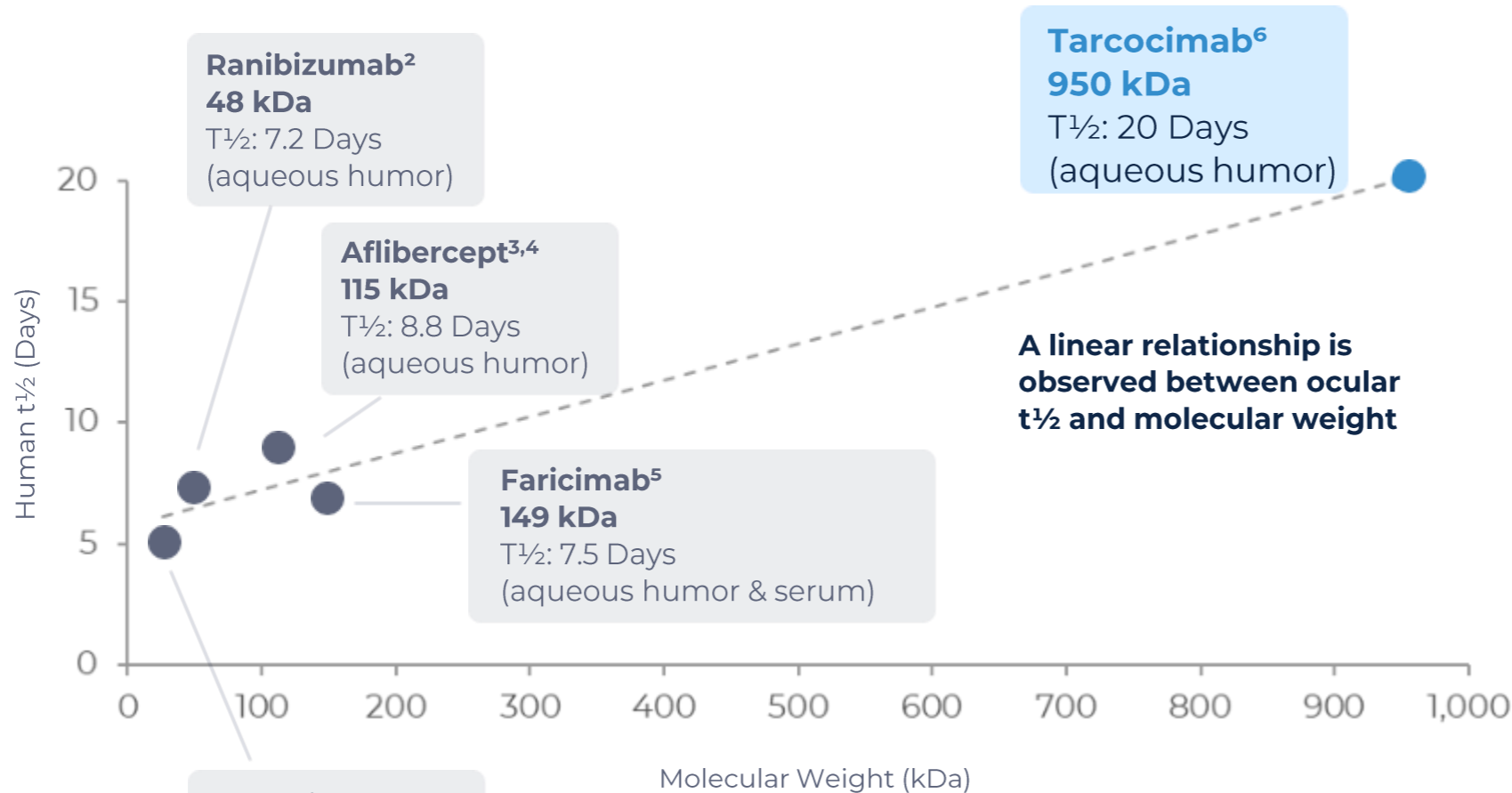


# Tarcocimab demonstrated consistent ocular half-life across wet AMD, DME and RVO Patients



# From Principal of Design to Human Durability (“A Science of Durability”): Tarcocimab's Ocular Half-Life in Human is Much Longer Than Approved Intravitreal Biologics

## Human Ocular Half-Life and Molecular Weight of Current Intravitreal Biologics<sup>1,2</sup>



**The design of tarcocimab translates in human into an extended ocular half-life of approximately 3X compared to marketed intravitreal biologics**

**A linear relationship is observed between ocular t<sub>1/2</sub> and molecular weight**

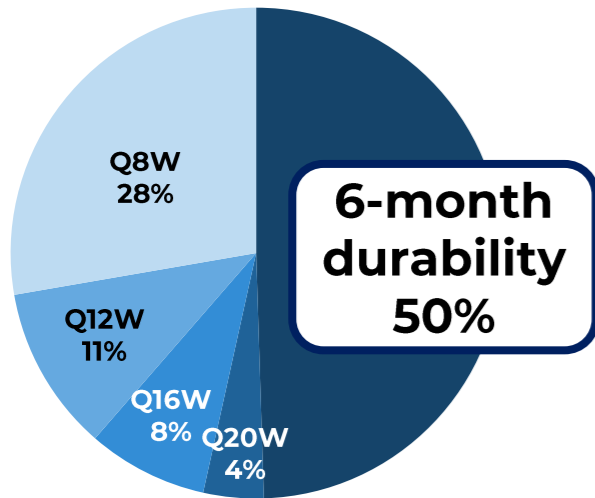
\*Half-life for brolucizumab is systemic half-life determined from serum pharmacokinetics  
1. Holz FG, et al. *Ophthalmology* 2016;123:1080-1089. 2. Krohne TU, et al. *Am J Ophthalmol* 2012;154:682-686.e2. 3. Do DV, et al. *Retina* 2020;40:643-647; 4. Caruso A, et al. *Retina*. 2020 Apr;40(4):e13. doi. 5. VABYSMOTM (faricimab solution for injection) Prescribing Information. South San Francisco, USA: Genentech, Inc. 6. Kodiak data on file.

**What is the evidence this longer ocular half-life  
in human translates into clinical durability?**

# Consistent with its science of extended ocular half life, tarcocimab has shown a differentiated clinical durability profile in all retinal vascular diseases tested

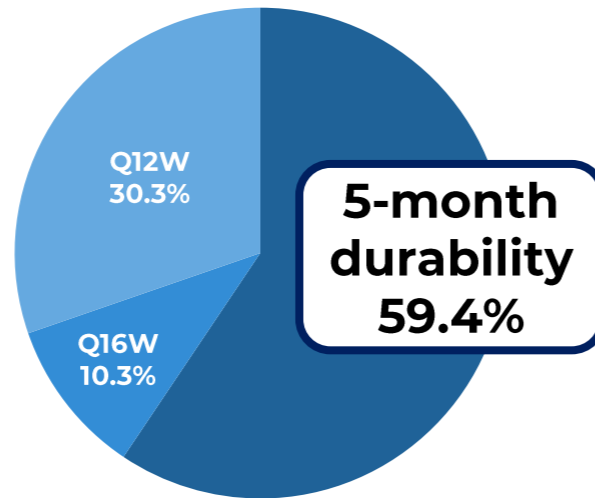
## Durability Interval at Year 1

## Number of doses in the second 6 months of Year 1



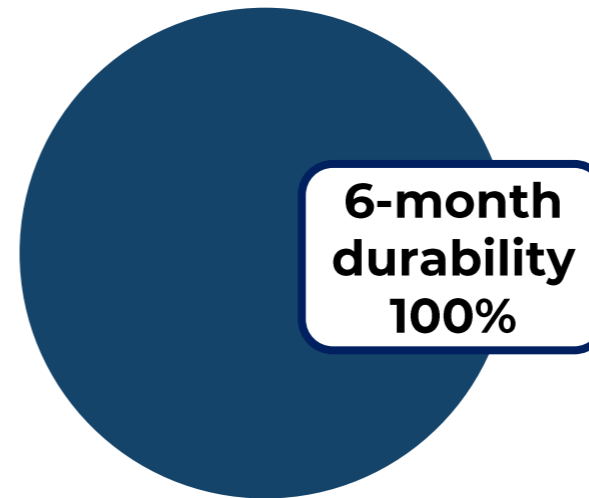
### DME

GLEAM and GLIMMER Studies<sup>1</sup>



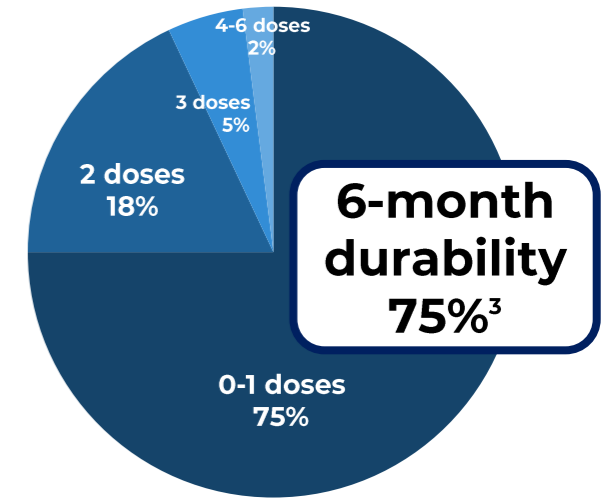
### WAMD

DAZZLE Study<sup>2</sup>



### DR

GLOW1 Study



### RVO

BEACON Study

DME: diabetic macular edema; DR: diabetic retinopathy; RVO: retinal vein occlusion; wAMD: wet age-related macular degeneration.

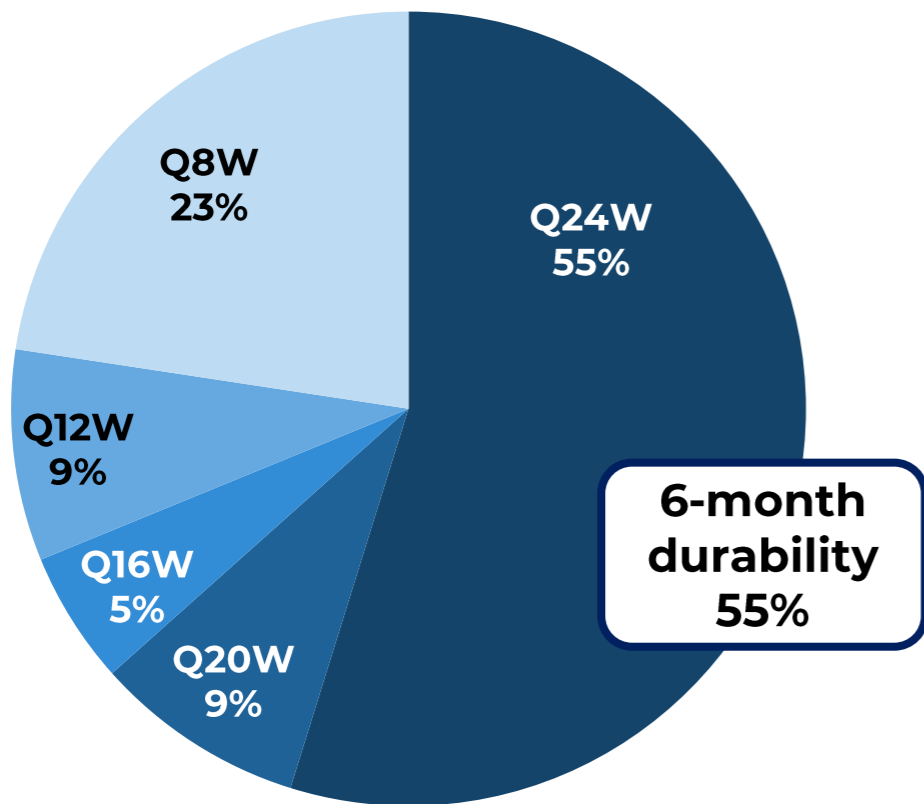
1. Pooled analyses. The studies did not meet the primary endpoint.

2. Treatment intervals were capped at 5 months (6-month dosing was not tested). The study did not meet the primary endpoint.

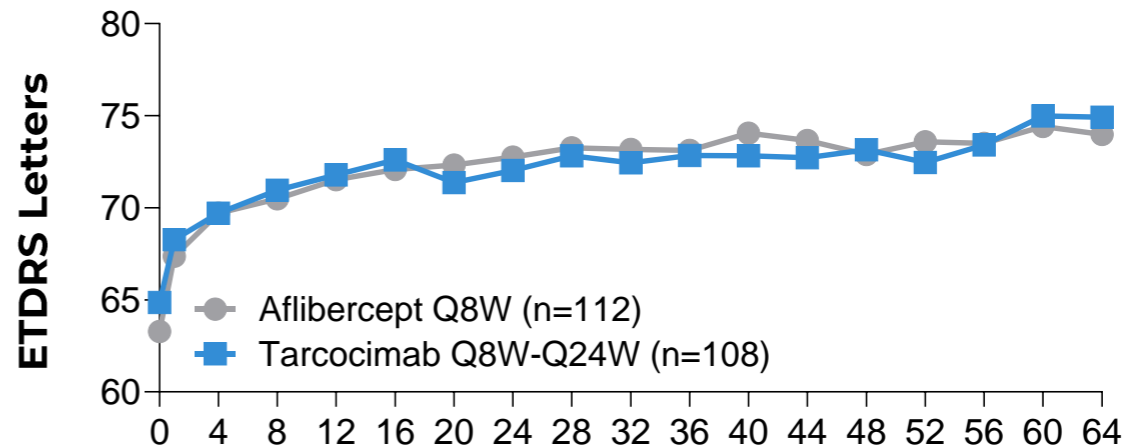
3. Estimated durability interval based on patients that received no injections (46%) or 1 injection (29%) over the second 6 months of Year 1.

Wait a minute. The DME studies did not meet their primary endpoint. How do we know the durability is real? Pseudophakic patients treated with tarcocimab achieved comparable improvements vs aflibercept patients, with significantly fewer doses (5 tarcocimab vs 10 aflibercept)

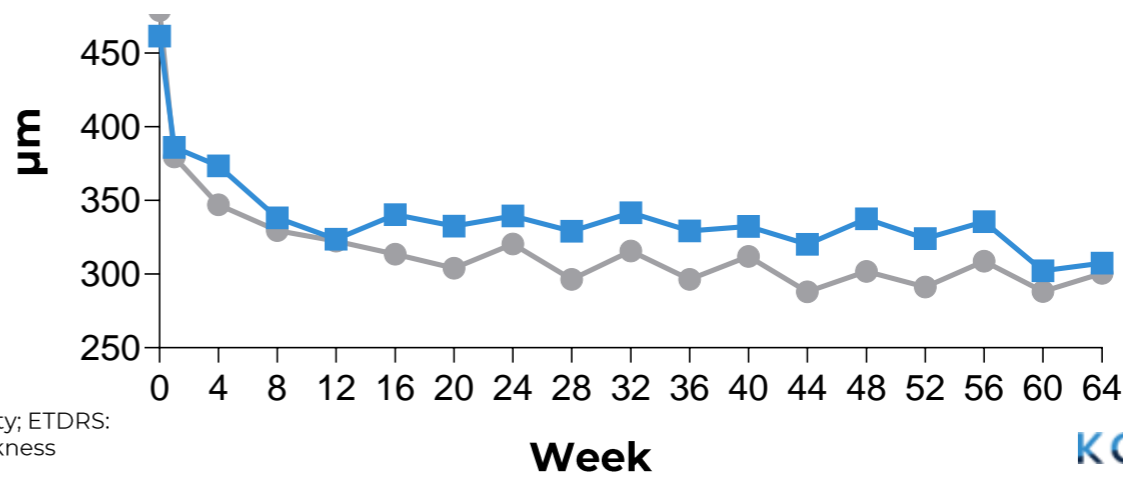
**Durability intervals for pseudophakic patients at Year 1 in the GLEAM & GLIMMER Studies<sup>1</sup>**



**GLEAM and GLIMMER Pooled Mean BCVA Over Time in Pseudophakic Patients**



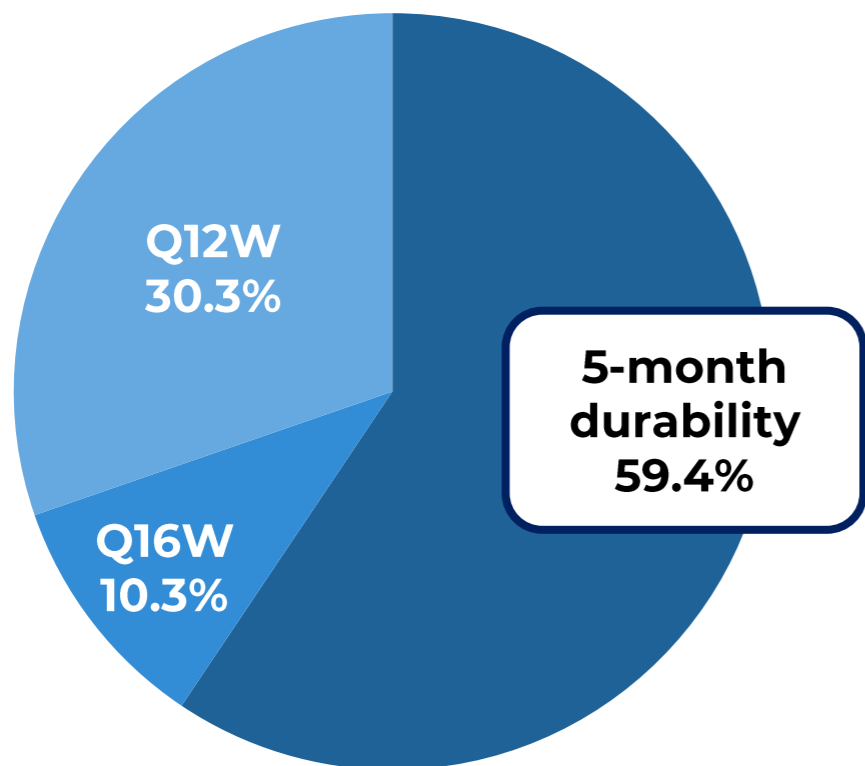
**Mean OCT CST Over Time in Pseudophakic Patients**



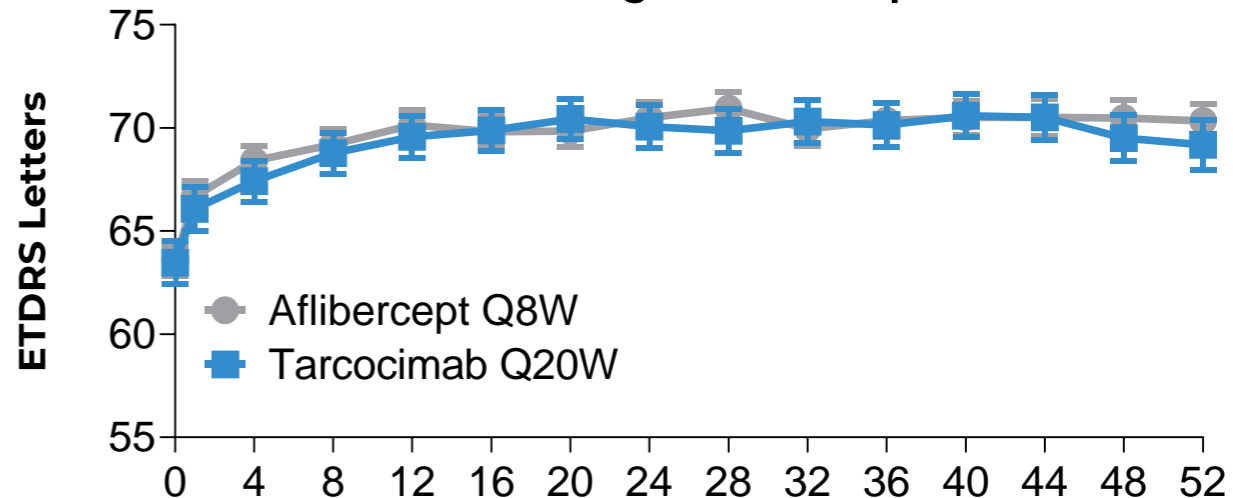
<sup>1</sup>. Data points may not add up to 100% due to rounding. Observed values. BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study. OCT: optical coherence tomography; CST: central subfield thickness

Wait a minute. The wAMD durability study did not meet its primary endpoint. What is the durability evidence here? In DAZZLE, ~2/3 of tarcocimab patients achieved 5-month durability with visual and anatomical improvements comparable to the overall aflibercept group

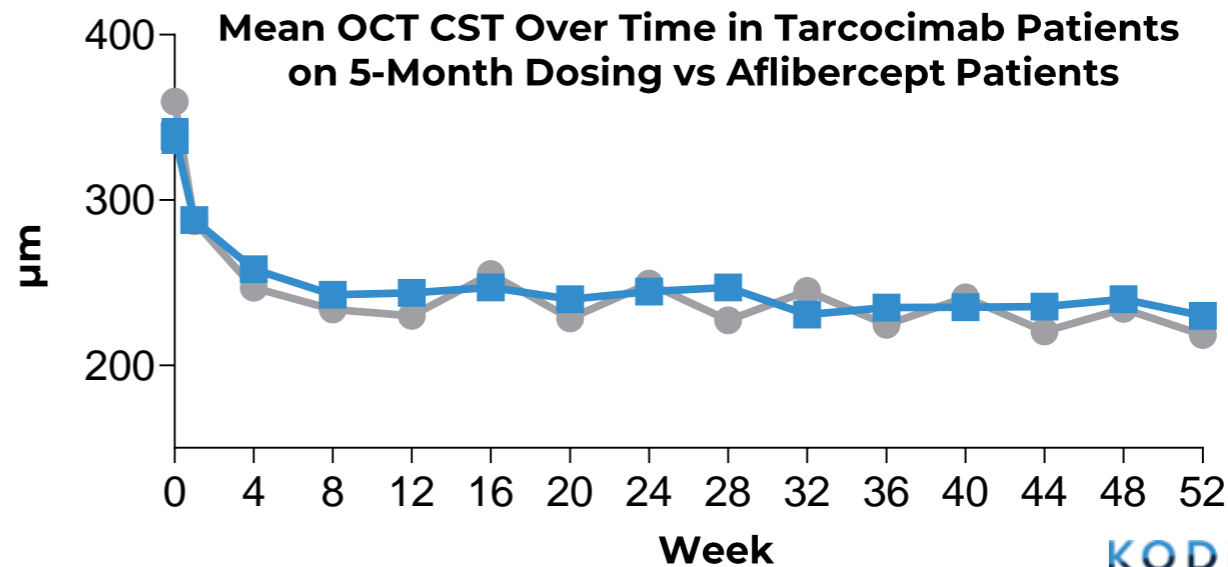
**Durability intervals at Year 1 in the DAZZLE Study**



**Mean BCVA Over Time in Tarcocimab Patients on 5-Month Dosing vs Aflibercept Patients**



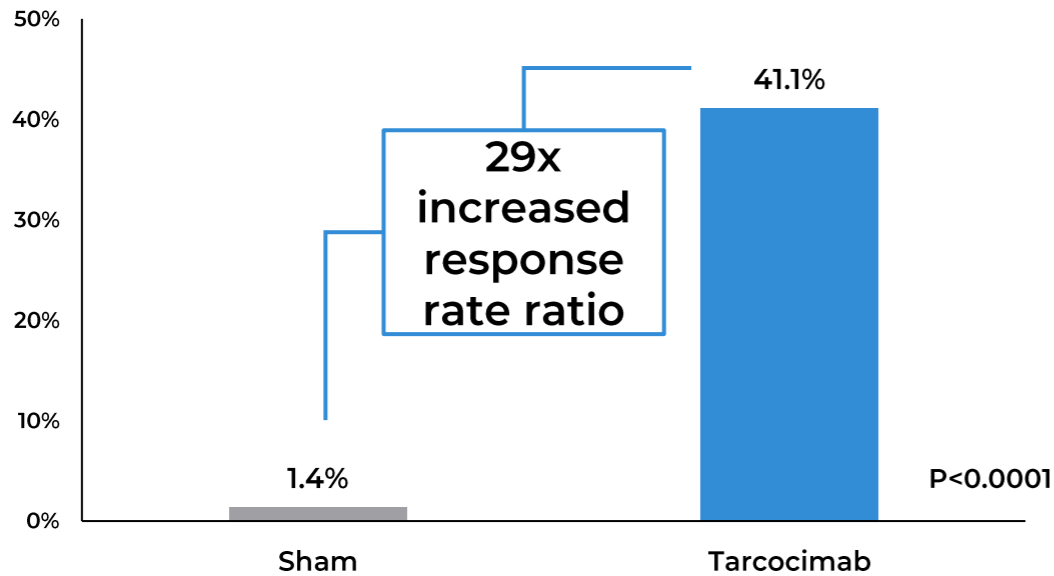
**Mean OCT CST Over Time in Tarcocimab Patients on 5-Month Dosing vs Aflibercept Patients**



# How relevant is 6-month durability in Diabetic Retinopathy? With only 4 doses in the first year (a 'gentle on-ramp') and 100% of tarcocimab patients on 6-month dosing, the drug *treats current retinopathy and prevents diabetic complications*

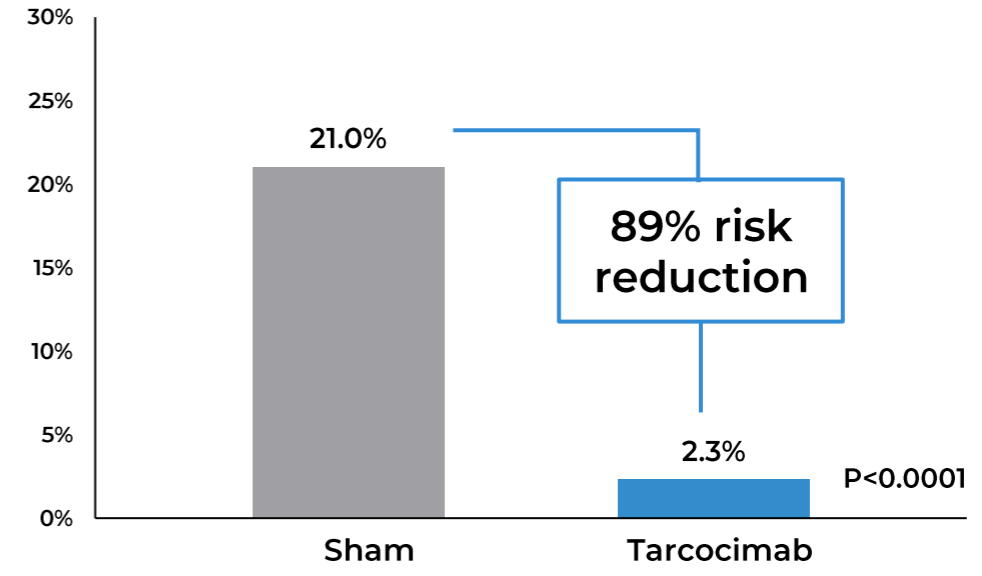
Primary endpoint met

Proportion of patients with  $\geq 2$ -Step improvement in DRSS from Baseline to Week 48



**Treatment of Retinopathy**

Proportion of patients developing any sight-threatening complication from Baseline to Week 48



**Prevention of Complications**

- All patients were randomized to receive either tarcocimab every six months after 3 initiating doses or to receive sham injections.

DRSS: diabetic retinopathy severity scale; DME; diabetic macular edema; PDR; proliferative diabetic retinopathy; ASNV: anterior segment neovascularization; CST; central subfield thickness; BCVA; best corrected visual acuity; NVD: neovascularization of the disc; NVE; neovascularization elsewhere; VH: vitreous hemorrhage; NVG; neovascular glaucoma.

Weighted percentages are based on weighted average of observed estimates across strata using CMH weights. p-values are based on the difference in response rates

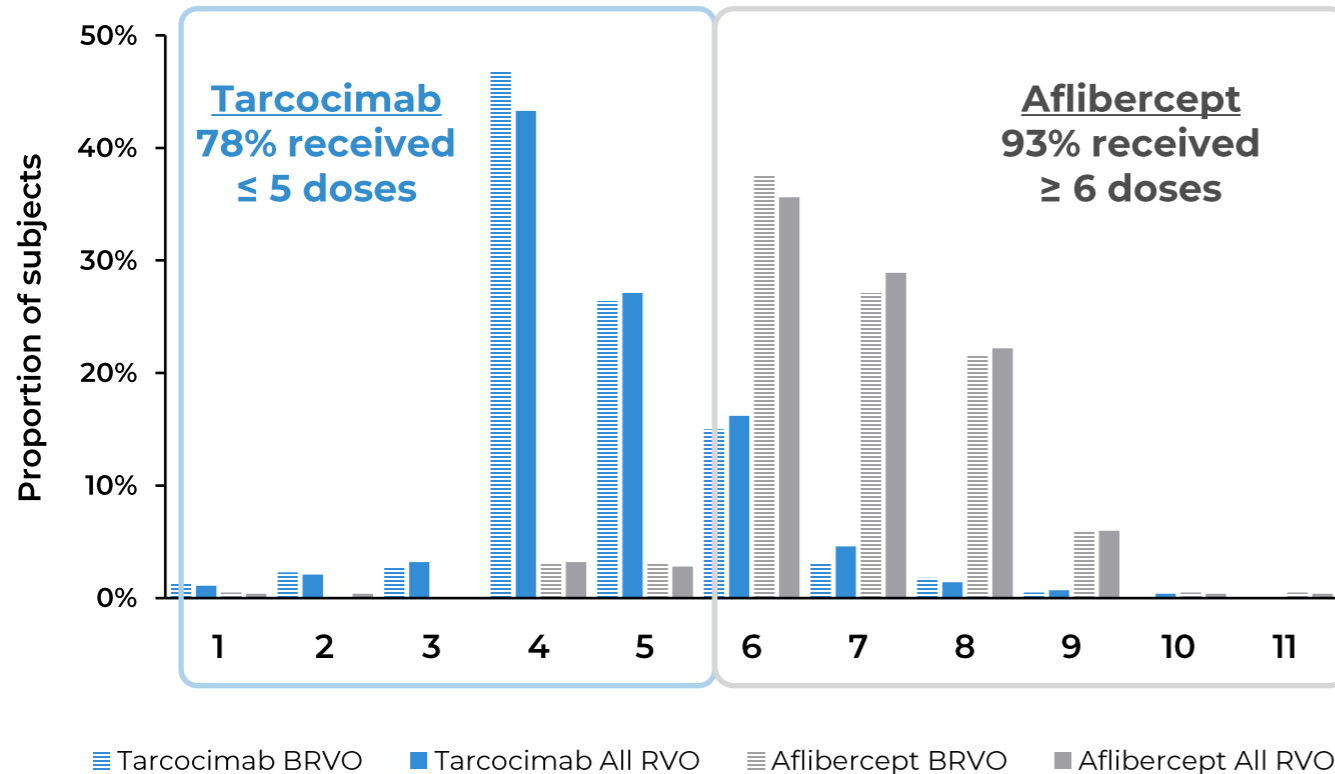
Any Sight-Threatening Complication

DME	CST of $\geq 320 \mu\text{m}$ and a 5-letter decrease in BCVA from Day 1; <u>or</u> CST of $\geq 350 \mu\text{m}$
PDR	NVD, NVE, or VH
ASNV	ASNV or NVG

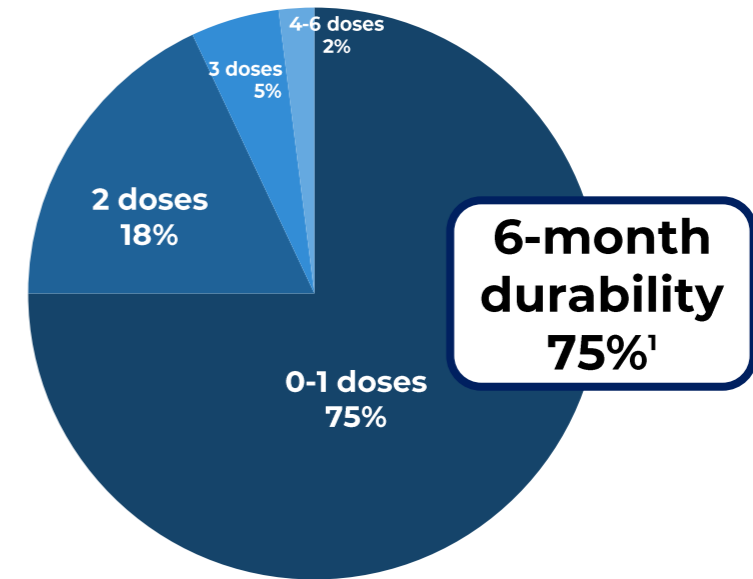
# Is there any durability benefit in RVO? Even after receiving 2 fewer initiating doses (4 vs 6, respectively), tarcocimab treated patients at one year had a ~30% higher chance of not requiring any additional doses versus aflibercept

Primary endpoint met

### Number of injections through Year 1



### Tarcocimab Number of doses in the second 6 months of Year 1





Tarcocimab and the ABC platform are supported by our

# SCIENCE OF DURABILITY



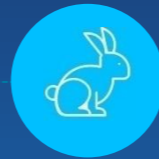
## Designed-in Extended Tissue Residence Time

A proprietary phosphorylcholine-based polymer is conjugated to an antibody to increase molecular size which extends ocular half-life



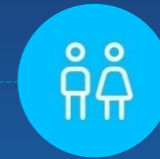
## High in-Vitro Potency

Both unconjugated protein and conjugated protein demonstrate high VEGF-A binding affinity and anti-VEGF potency *in vitro*, comparable to aflibercept



## Extended Ocular Half-Life in Animals

3x the ocular  $t_{1/2}$  of approved intravitreal biologics when measured in rabbits following an intravitreal injection



## Extended Ocular Half-Life in Humans

3x the ocular  $t_{1/2}$  of faricimab when measured from aqueous humor in patients following an intravitreal injection



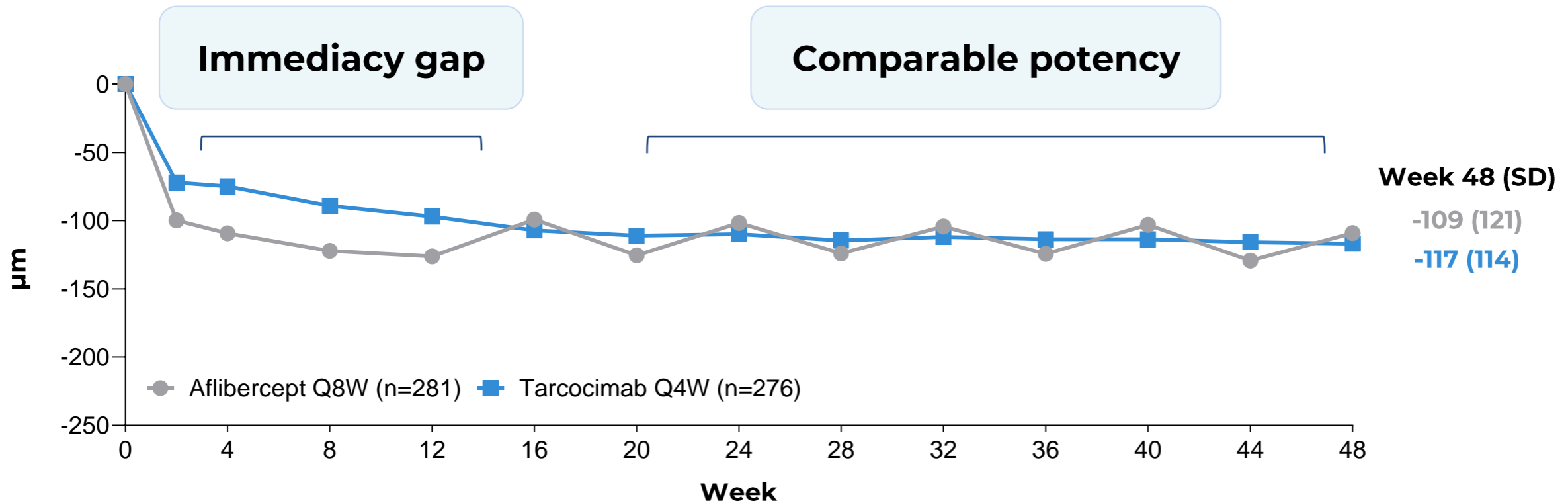
## Extended Clinical Durability

5 to 6-month predominant durability demonstrated in pivotal trials across all high-prevalence retinal vascular diseases

**Does this durability come at a cost?**

**Immediacy seems to be the cost.** A deficit is seen in the loading phase, in the “immediacy” of the effect. After the loading phase, the drying potential or “potency” is comparable to aflibercept

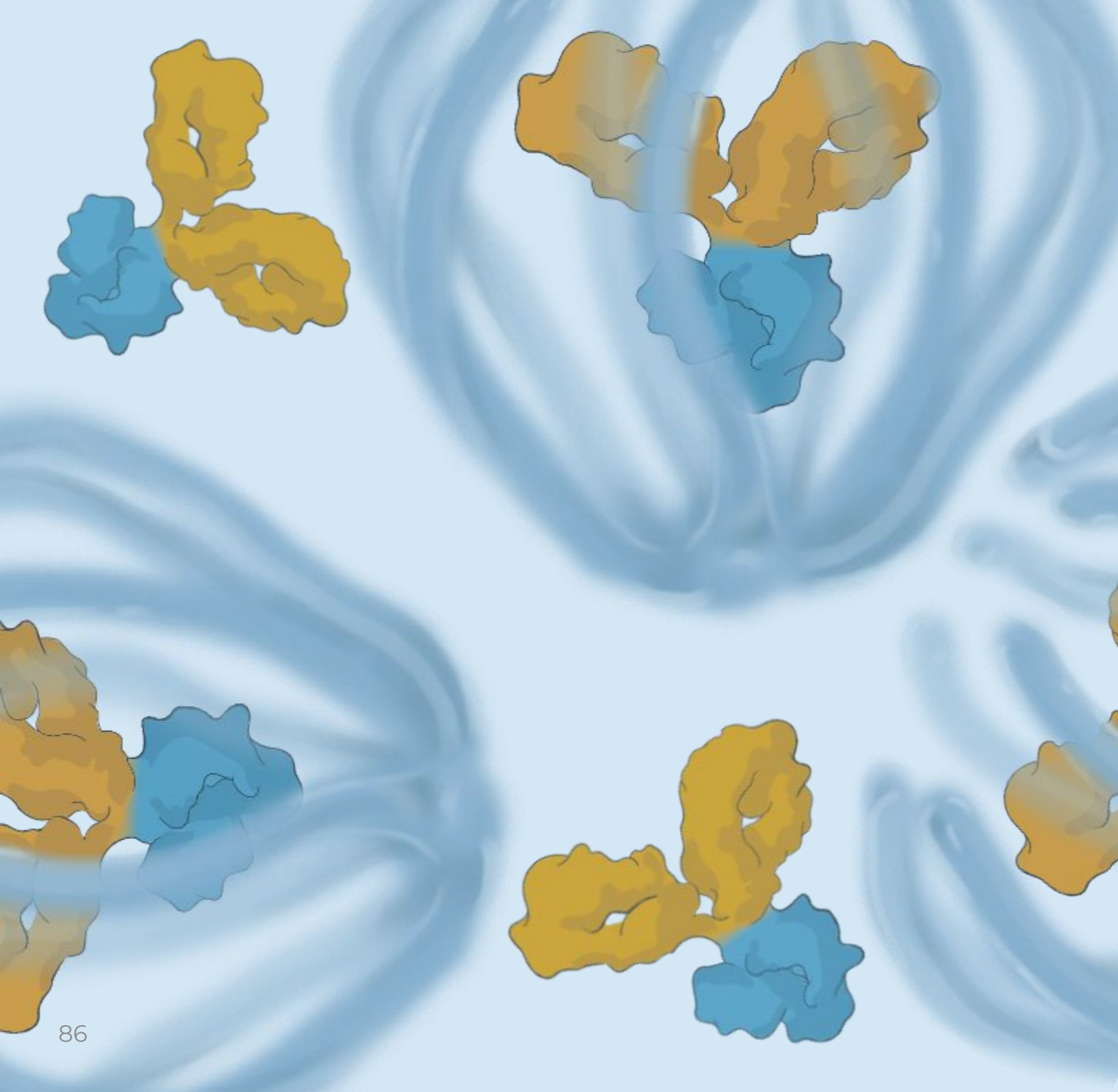
**Mean Change in OCT CST Over Time In the wet AMD DAYLIGHT Study**



**We have applied course corrections to  
solve this challenge in immediacy**

# AGENDA

Why Kodiak?	Victor Perloth, MD Chairman and CEO
Science of Durability	David Brown, MD
<b>Science of the Enhanced Formulation</b>	<b>David Brown, MD</b>
Roundtable Discussion	Moderator: Victor Perloth, MD Chairman and CEO
Audience Q&A	All
Clinical Program Overview	Charles Wykoff, MD, PhD
The Kodiak Opportunity	Victor Perloth, MD Chairman and CEO
Roundtable Discussion	Moderator: Victor Perloth, MD Chairman and CEO
Audience Q&A	All
ABCD Platform Preview	Dolly Chang, MD, PhD Chief Scientific Officer
Summary and Takeaways	Victor Perloth, MD Chairman and CEO
Audience Q&A	All



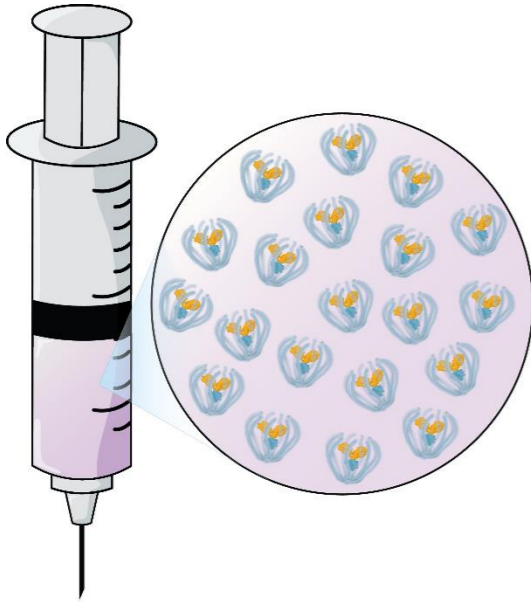
# ENHANCED FORMULATION



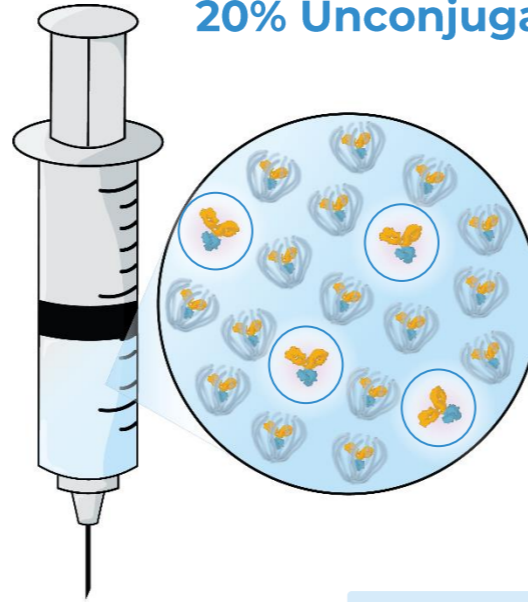
David Brown, MD

# How can the enhanced formulation solve the immediacy issue? By including free protein (unconjugated), the enhanced formulation is primed to solve the immediacy issue

## Tarcocimab Old Formulation 100% Conjugates



## Tarcocimab Enhanced Formulation 80% Conjugated 20% Unconjugated



5 mg	Strength (Total Anti-VEGF mAb)	5 mg
5 mg	Proportion of <b>Conjugates</b>	4 mg
n/a	Proportion of <b>Free Protein</b>	1 mg

Identical strength





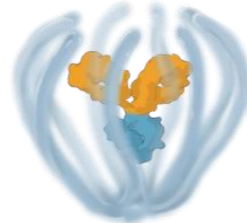
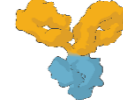
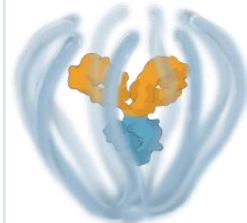
Reduced conjugates  
from 100% to 80%

Unconjugated protein  
at 20%

The enhanced formulation was designed to confer several key benefits:

- Improved **manufacturability**
  - Increased **ease of dosing** and **safety**
  - Maintenance of **dose** and **potency**
  - Maintenance of **signature durability**
- and**
- Improved **immediacy**

# The unconjugated portion of the enhanced formulation of tarcocimab contains A high molar equivalent to approved intravitreal biologics

	Brolucizumab	Ranibizumab	Aflibercept	Faricimab	Tarcocimab Old Formulation	Tarcocimab Enhanced Formulation	
Molecule Type	Single-Chain Antibody Fragment	Antibody Fragment	Fusion Protein	Antibody	Antibody Biopolymer Conjugate (ABC)	Unconjugated Antibody + ABC	
Molecular Structure							
Molecular Weight	26 kDa	48 kDa	115 kDa	149 kDa	950 kDa	150 kDa	950 kDa
Clinical Dose	6 mg	0.3-0.5 mg	2 mg	6 mg	5 mg By weight of antibody	5 mg <b>1 mg</b> <b>4 mg</b>	
Equivalent Molar Dose	11	0.5	<b>1.0</b>	2	3.5	<b>0.7</b>	<b>2.8</b>

Equivalent values are shown as fold changes relative to aflibercept. kDa = kilodalton

Equivalent to  
0.7 mg of  
ranibizumab

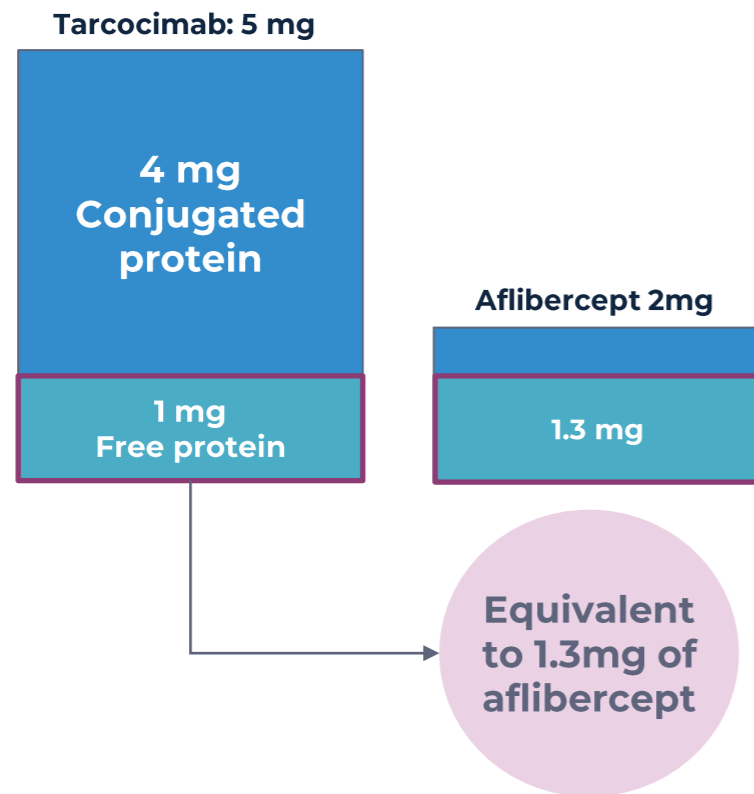
Equivalent to  
1.3 mg of  
aflibercept

Equivalent to  
2 mg of  
faricimab

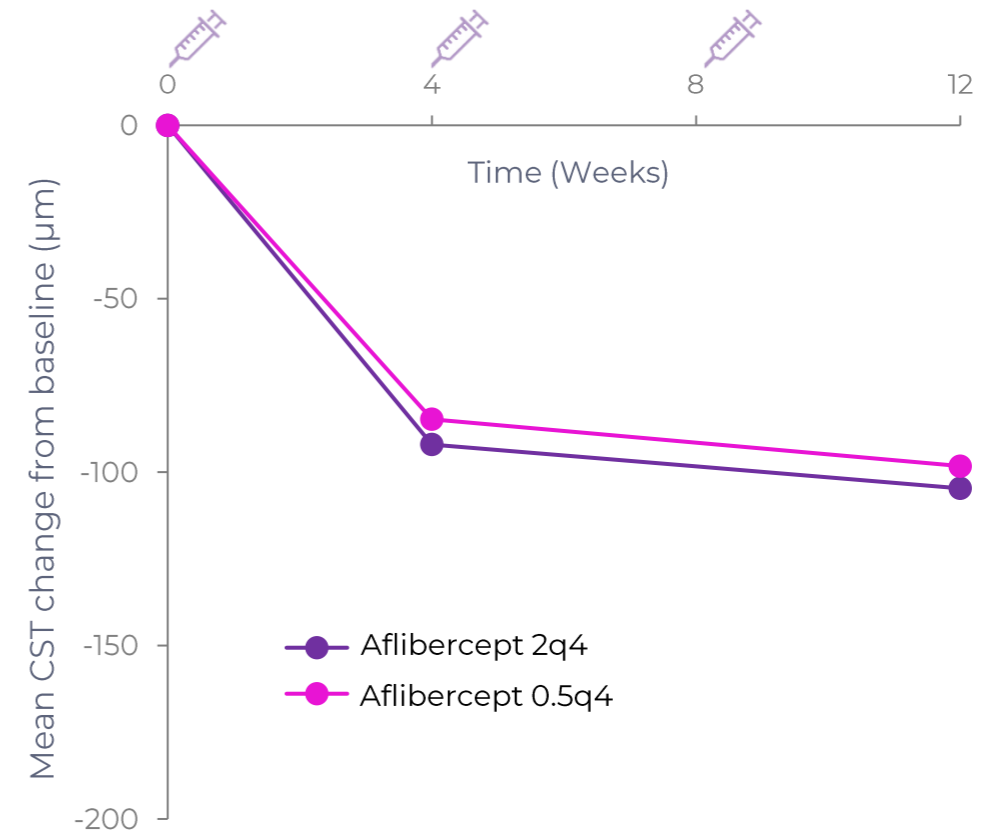


# How much unconjugated protein is there? Is it enough? The unconjugated portion is equivalent to 1.3 mg of aflibercept, sufficient to provide a strong immediacy after dosing

The 20% of free protein alone in the enhanced formulation is equivalent to 67% of the full clinical dose of aflibercept



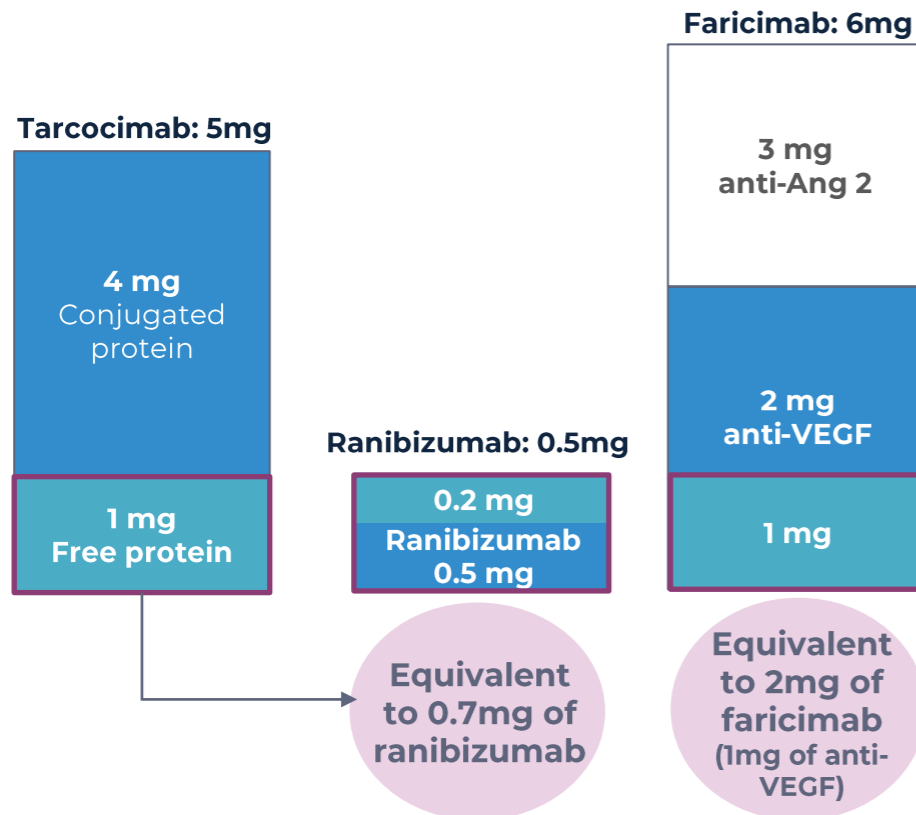
0.5 mg aflibercept achieved similar CST improvements as the full clinical dose of aflibercept (2 mg) in wAMD



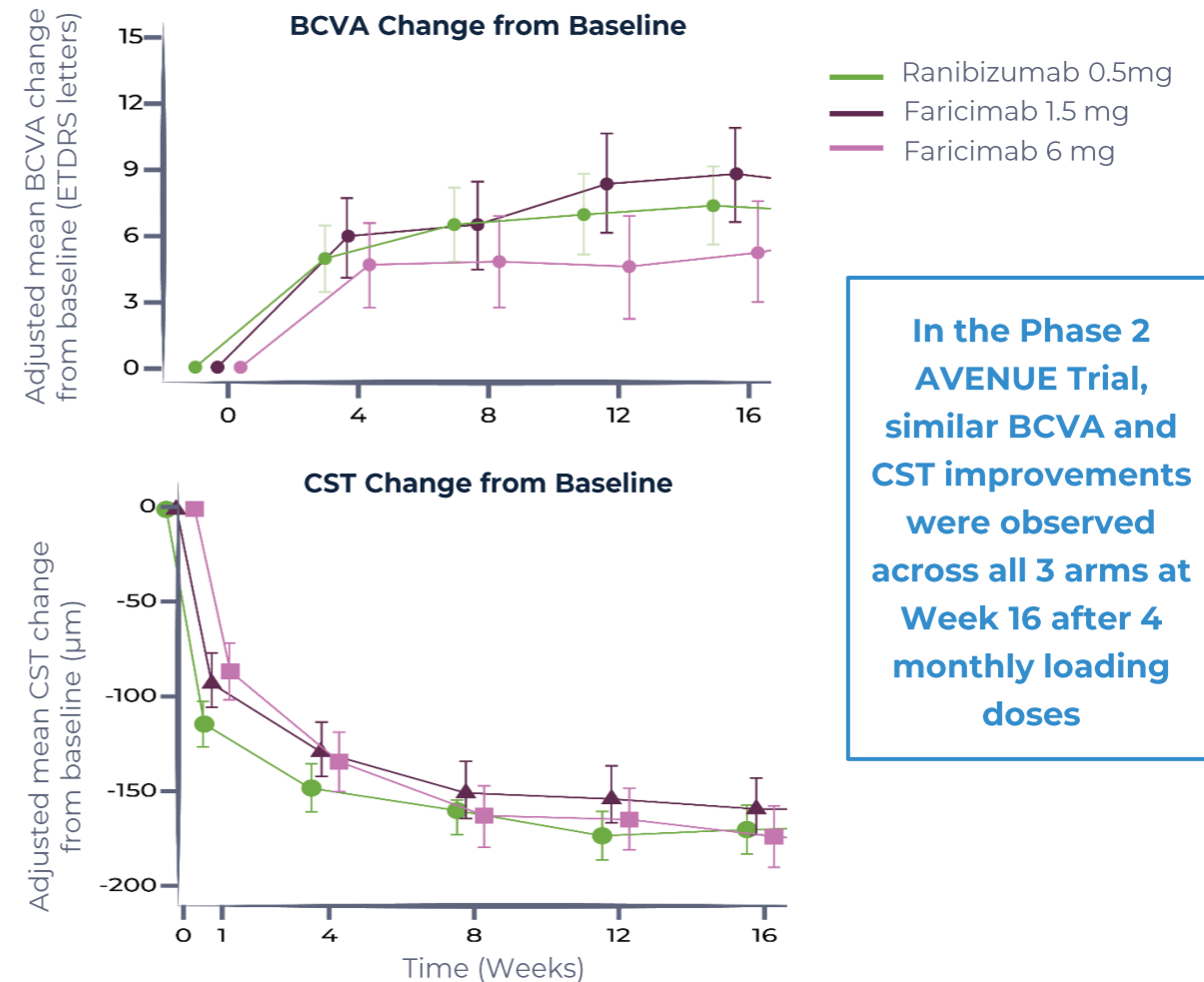
# What is the objective of each component? The unconjugated protein delivers a strong “pulse” of VEGF inhibition, meanwhile the conjugate continues to deliver sustained durability

The 1 mg of free protein in the enhanced formulation is expected to meaningfully improve immediacy

- The high molar equivalent of the 1 mg free protein suggests it should meaningfully improve immediacy to that similar or slightly superior to 1.5 mg faricimab or 0.5 mg ranibizumab



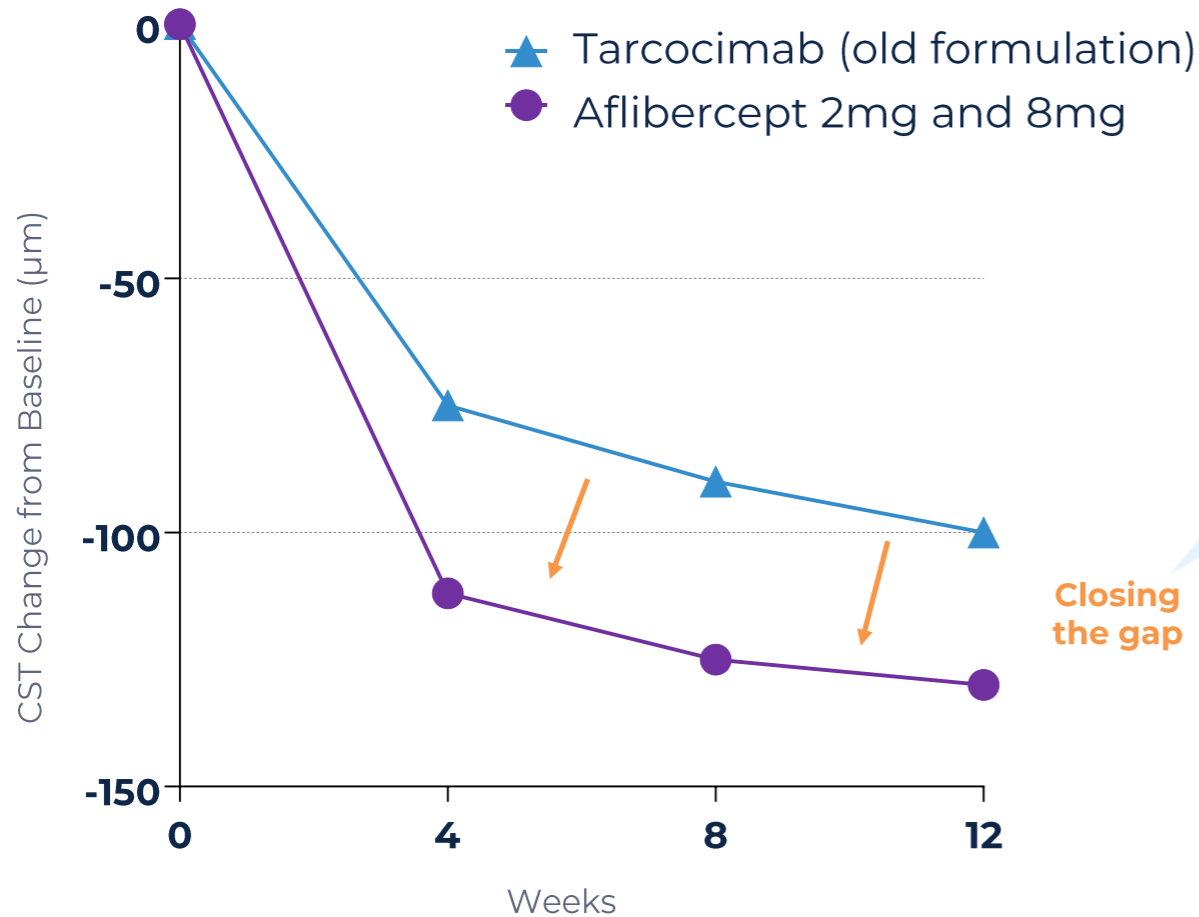
Similar efficacy benefits were observed among ranibizumab 0.5 mg, faricimab 1.5 mg and faricimab 6 mg



In the Phase 2 AVENUE Trial, similar BCVA and CST improvements were observed across all 3 arms at Week 16 after 4 monthly loading doses

# What is the objective? A key objective of the enhanced formulation was to close the immediacy gap, while improving manufacturability, dose administration and patient safety

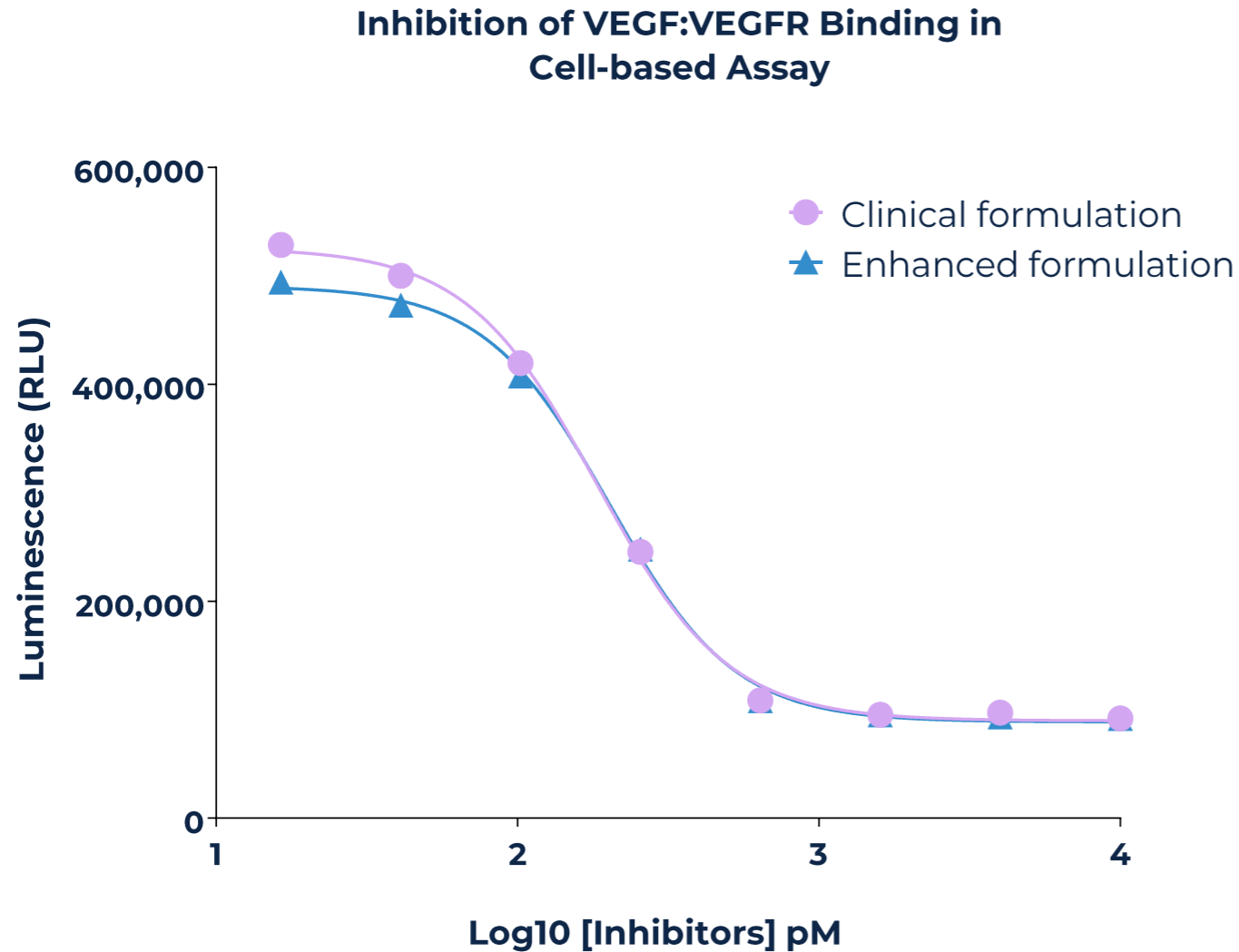
CST Reduction Through Loading Dose Phase in Wet AMD\*



The purpose of the 20% unconjugated protein (1 mg) is to improve the immediacy of the drying effect during the loading dose phase, "closing the gap"

The purpose of the 80% conjugated protein (4 mg) is to maintain the 6-month predominant durability as seen in tarcocimab pivotal studies to date

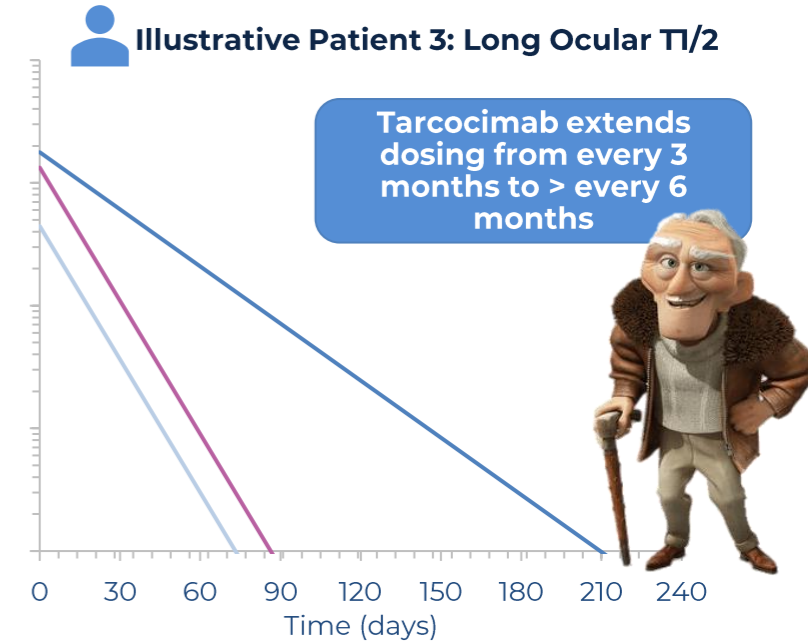
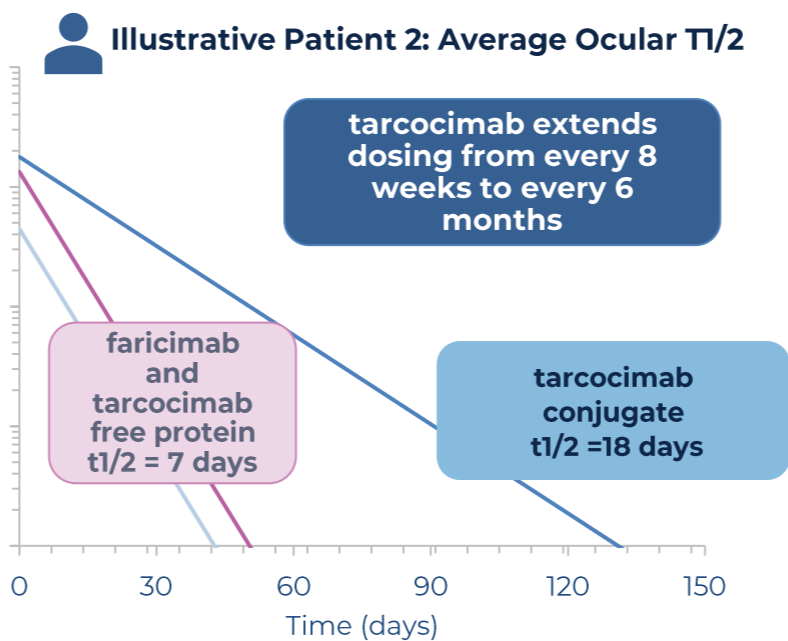
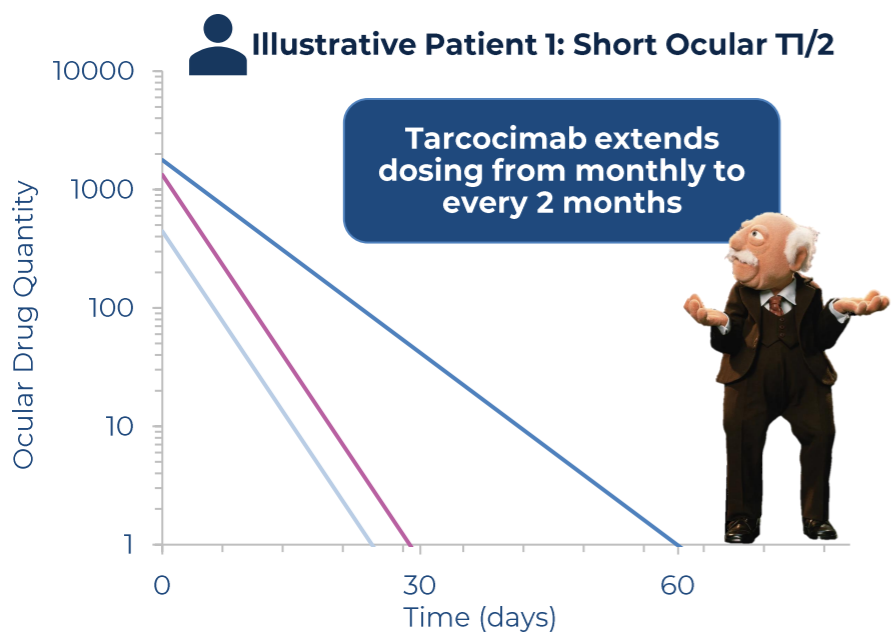
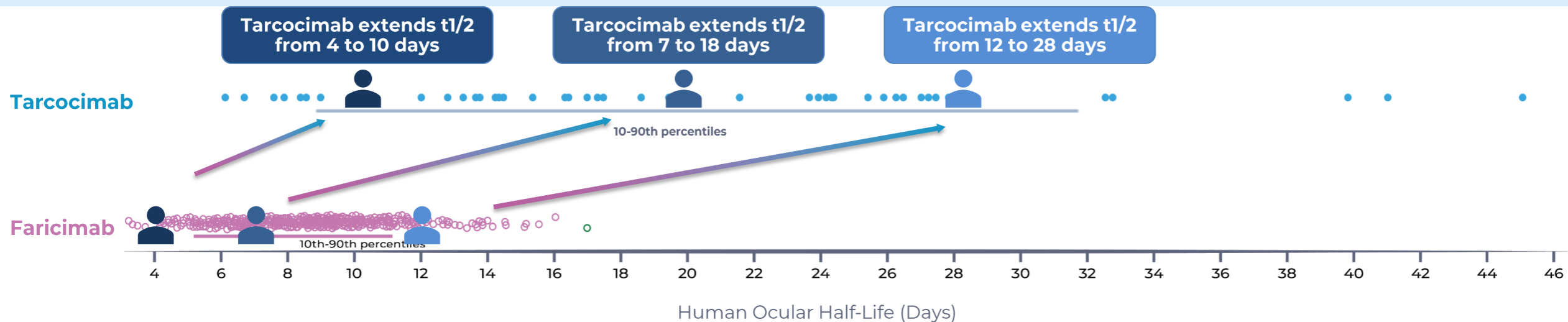
# Are you sacrificing potency? The enhanced formulation has nearly identical anti-VEGF potency as the old clinical formulation in preclinical assays



Inhibition of VEGF:VEGFR Binding	IC <sub>50</sub> (pM)
Clinical Formulation	184
Enhanced Formulation	202

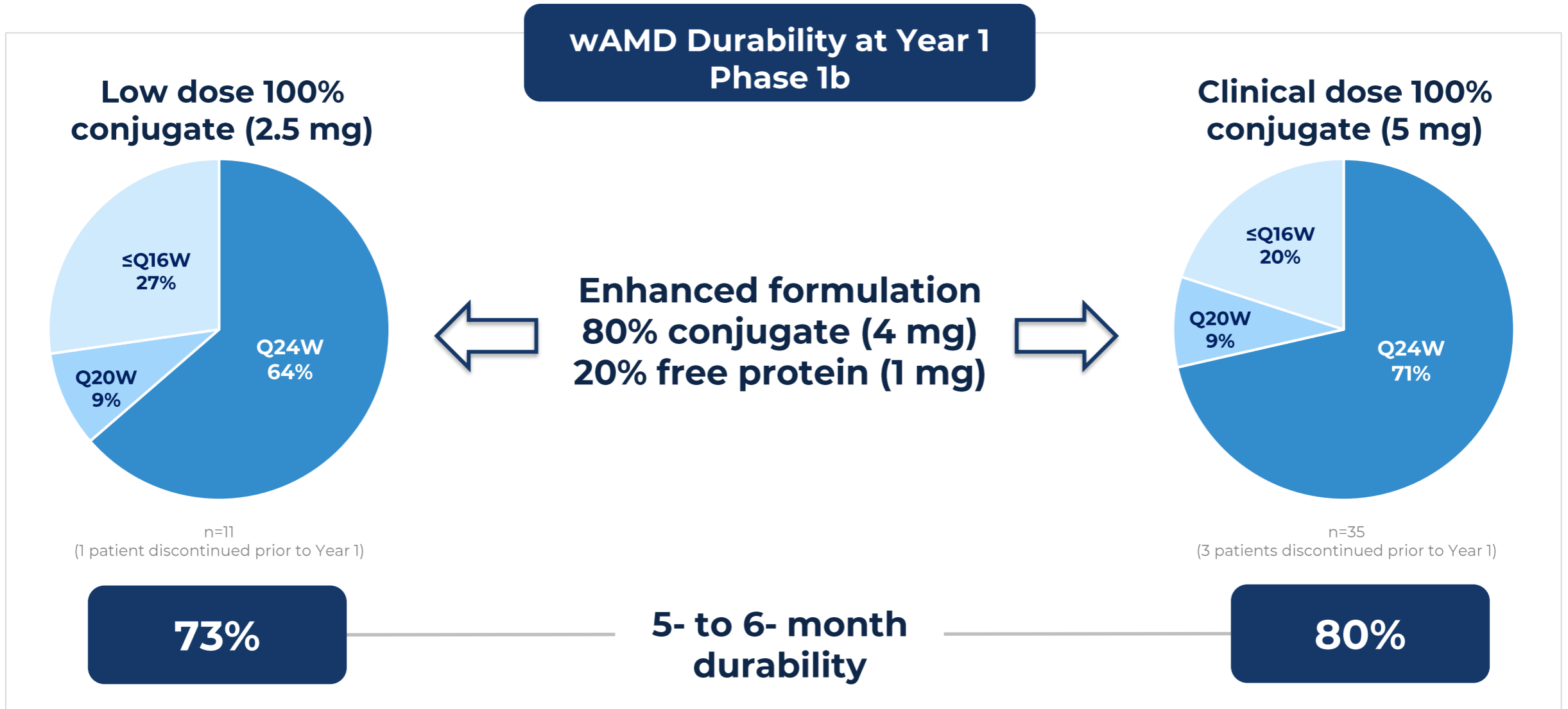
**Bringing it all together:  
modeling the expected pharmacology  
of tarcocimab in patients**

# Tarcocimab extends human ocular t1/2 by 3x vs faricimab; modeling suggests tarcocimab may meaningfully extend dosing intervals for patients while providing immediacy



— Faricimab — Tarcocimab Unconjugated Protein — Tarcocimab Conjugated Protein

# Are you sacrificing durability? The enhanced formulation is expected to have a similar durability profile as the 100% conjugated formulation



**Another benefit of the enhanced formulation is  
we believe it will solve the issue of increased  
cataracts in DME patients**



# The cataract imbalance in GLEAM and GLIMMER was not observed with monthly dosing in DAYLIGHT. Thus, exposure or accumulation was not the culprit

	GLEAM + GLIMMER (DME)		DAYLIGHT (wAMD)	
<b>Duration of Follow-Up</b>	<b>64 Weeks</b>		<b>48 Weeks</b>	
<b>Cataract in Study Eye up to Primary Endpoint</b>	<b>Tarcocimab Q8W-Q24W (n=458)</b>	<b>Aflibercept Q8W (n=459)</b>	<b>Tarcocimab Q4W (n=276)</b>	<b>Aflibercept Q8W (n=281)</b>
<b>Subjects with Cataract AEs in the Study Eye, n (%)</b>	89 (19.4%)*	40 (8.7%)	9 ( <b>3.3%</b> )	13 ( <b>4.6%</b> )
<b>Median number of doses</b>	5	10	<b>12</b>	<b>7</b>

In DAYLIGHT, the Phase 3 **monthly dosing** study in wAMD patients, an imbalance in cataracts is **not** seen, even though tarcocimab treated patients received:

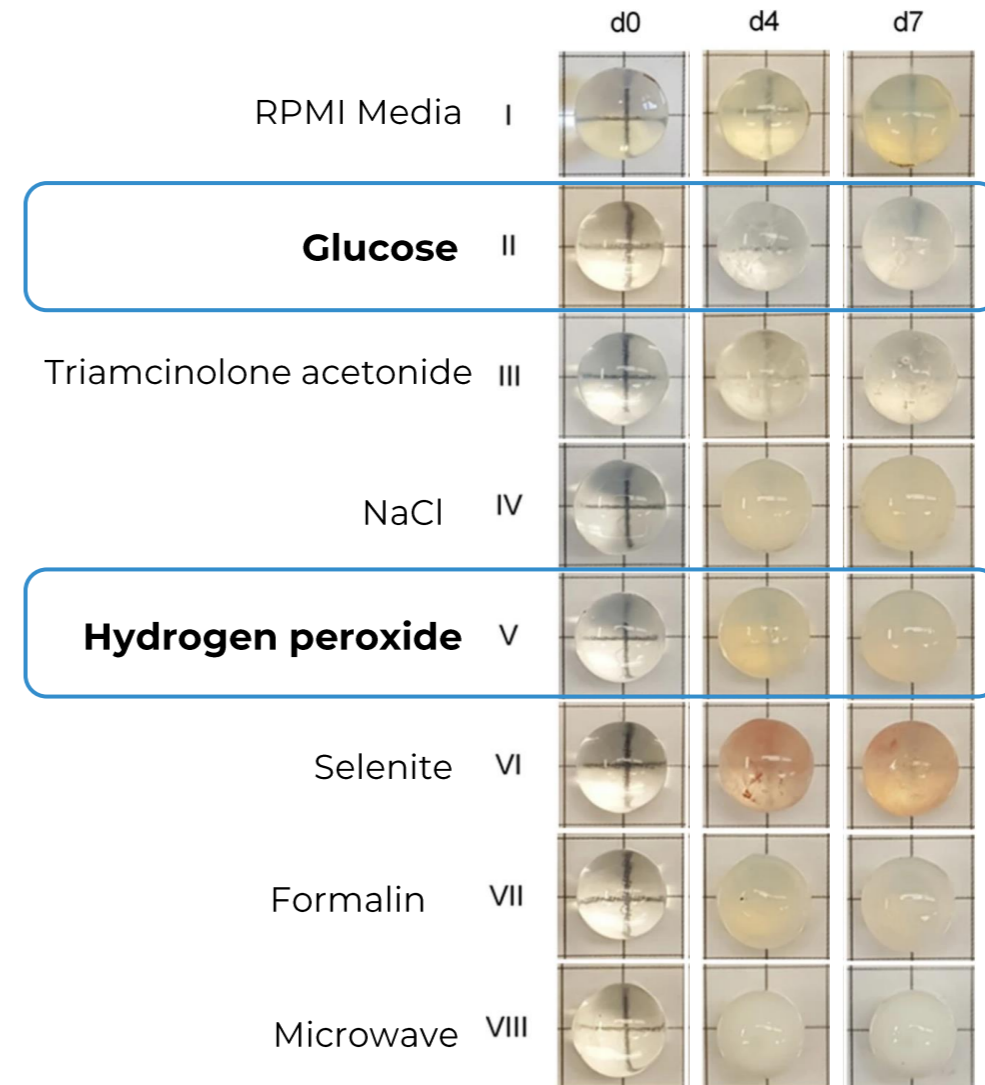
- (i) 5 more injections than aflibercept treated patients in DAYLIGHT, and
- (ii) 7 more injections than tarcocimab treated patients in GLEAM and GLIMMER

The lens is highly susceptible to stress, leading to cataract formation. Glucose is a known stress factor, as it is seen in diabetics.

## Many cataract associated stresses induce *ex vivo* porcine lens opacification

### Key take-aways

- Lens gradually opacify by 7 days in regular media (RPMI)
- Positive controls: Strong insults increase opacification
  - 5% w/v NaCl
  - 10mM H<sub>2</sub>O<sub>2</sub>
  - 10% non-buffered Formalin
  - Microwave
- Difference in background color of images suggesting inconsistent illumination and image acquisition



# Experimentally, tarcocimab does not contribute to *ex vivo* lens opacification under multiple conditions

## Objective: Measuring the effect of tarcocimab on porcine lens opacification

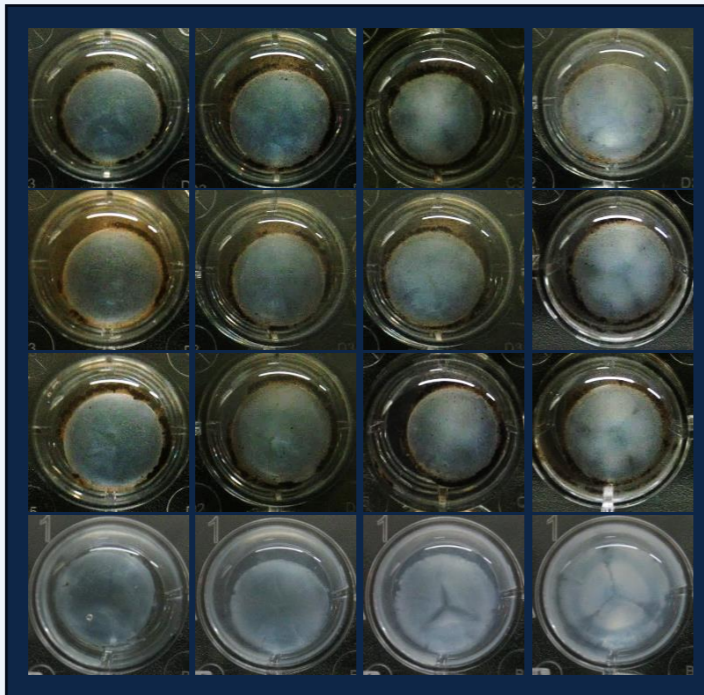
Day 0    Day 2    Day 4    Day 7

Untreated

Old Clinical formulation

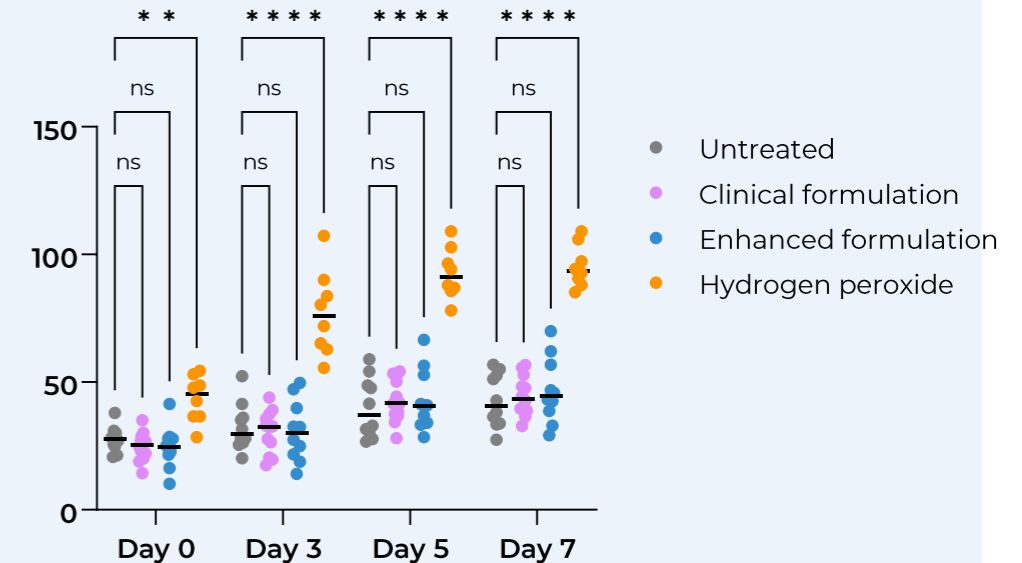
Enhanced formulation

Positive control  
Hydrogen Peroxide



Tarcocimab formulations at maximal clinical dose did not cause differences in lens opacification compared to untreated samples in both tissue culture media and artificial human vitreous

Quantification of Opacification (pixel intensity)

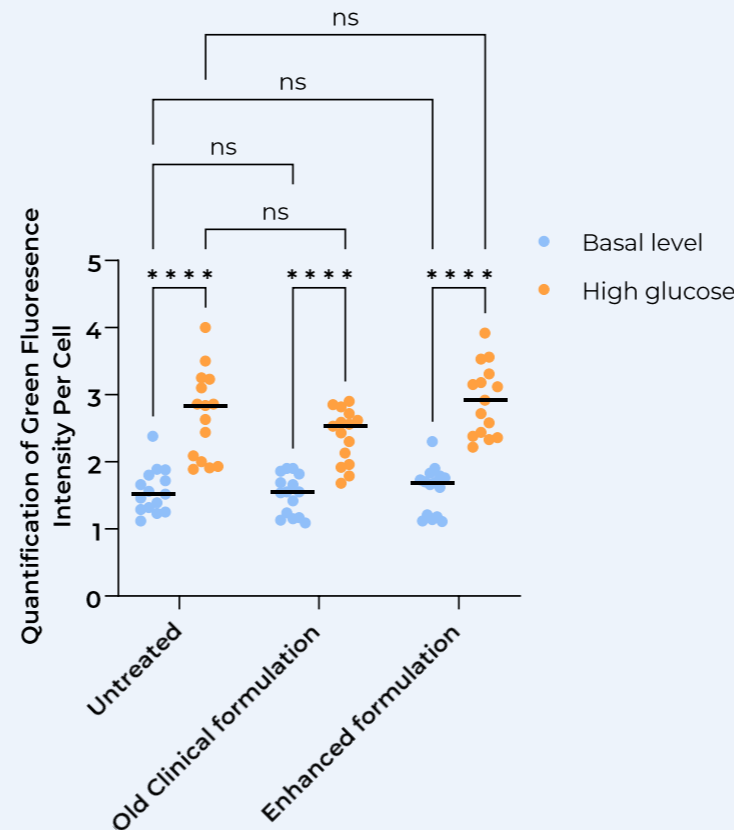
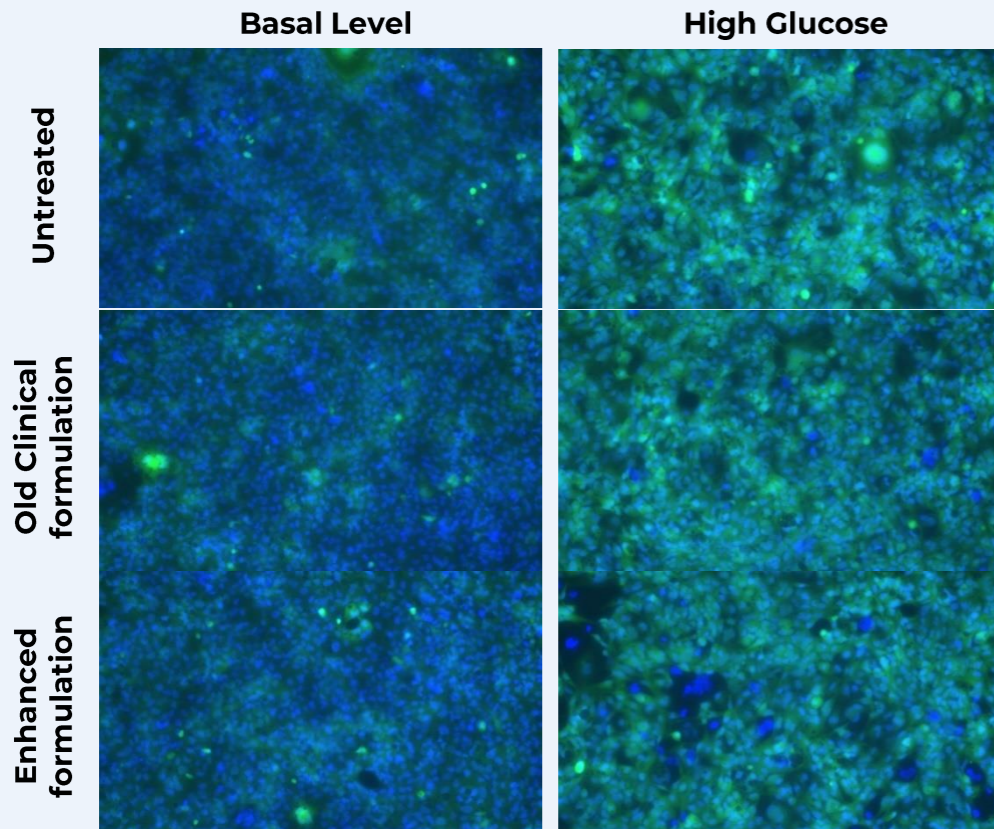


# Tarcocimab does not cause oxidative stress to human lens epithelial cells at basal or at high glucose concentration

## Experiment

- Human lens epithelial cells were treated with tarcocimab, with or without high level of glucose to simulate the physiological concentration in the eyes of a diabetic patient
- **The cells were stained with a dye responsive to oxidative stress (green) and nuclear stain (blue) to identify each cell**
- Oxidative stress dye signal was quantified and normalized per cell

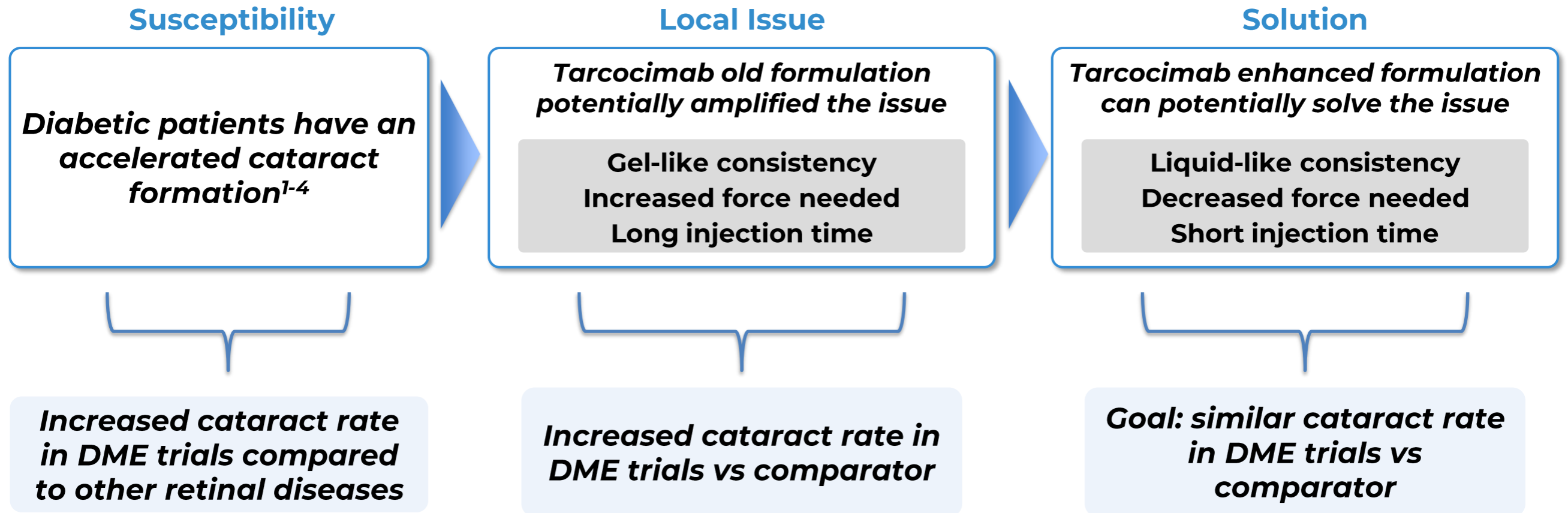
Objective: Measure if tarcocimab worsens the oxidative stress of glucose on lens epithelial cells



- High glucose increased oxidative stress as previously reported in the literature
- Tarcocimab formulations did not affect oxidative stress levels beyond the effect of high glucose alone

**The results show that tarcocimab does not compound the oxidative effect of glucose**

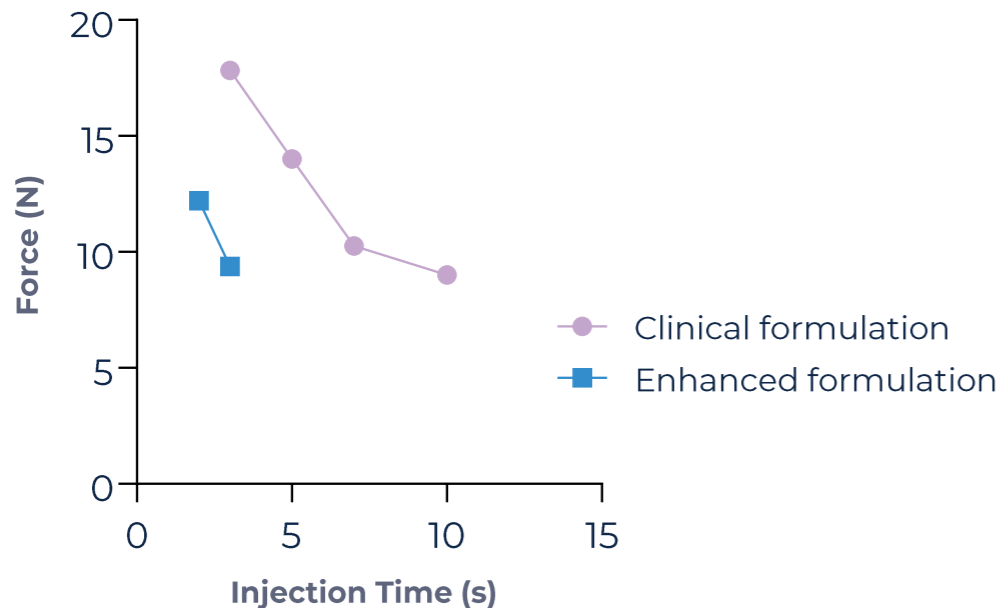
# Ease of dosing and patient safety. The enhanced formulation improves dispersion, with a liquid-like consistency, decreasing force and time needed



# Ease of dosing and patient safety

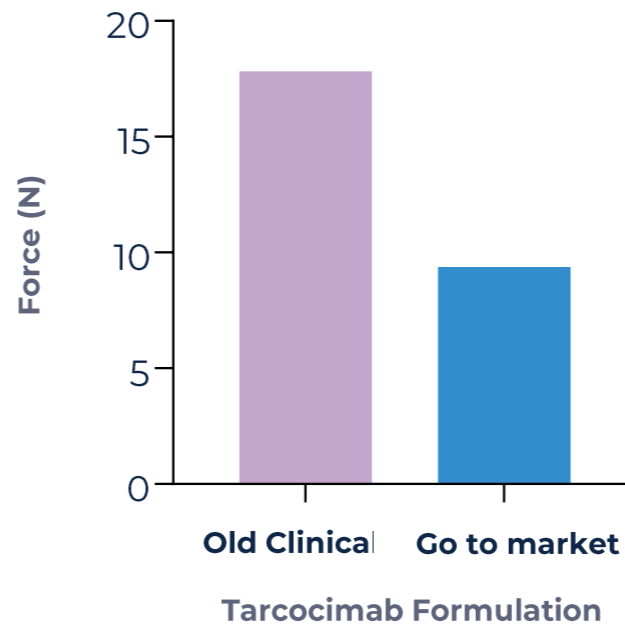
## The enhanced formulation requires less injection time and force

Injection Force Over Time



**Injection time reduced from 8 - 10 seconds to 2 - 3 seconds**

Matched Injection Time (3s)



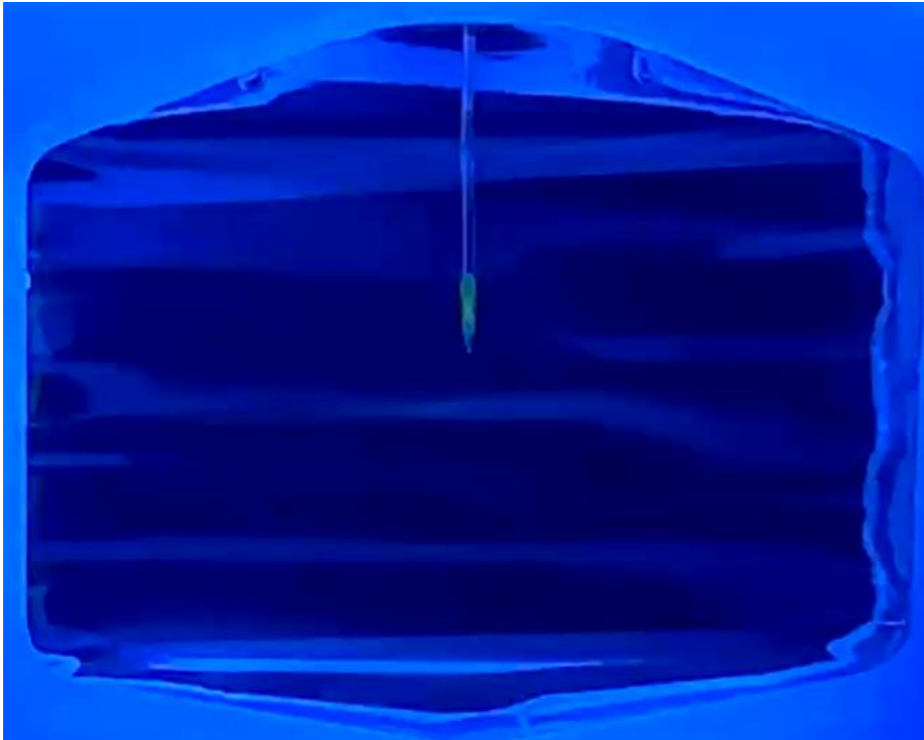
**The injection force is reduced by half**

**The enhanced formulation requires less injection time and force, which may lead to improved safety**

## Ease of dosing and patient safety. The enhanced formulation improves immediate dispersion, with a liquid-like consistency

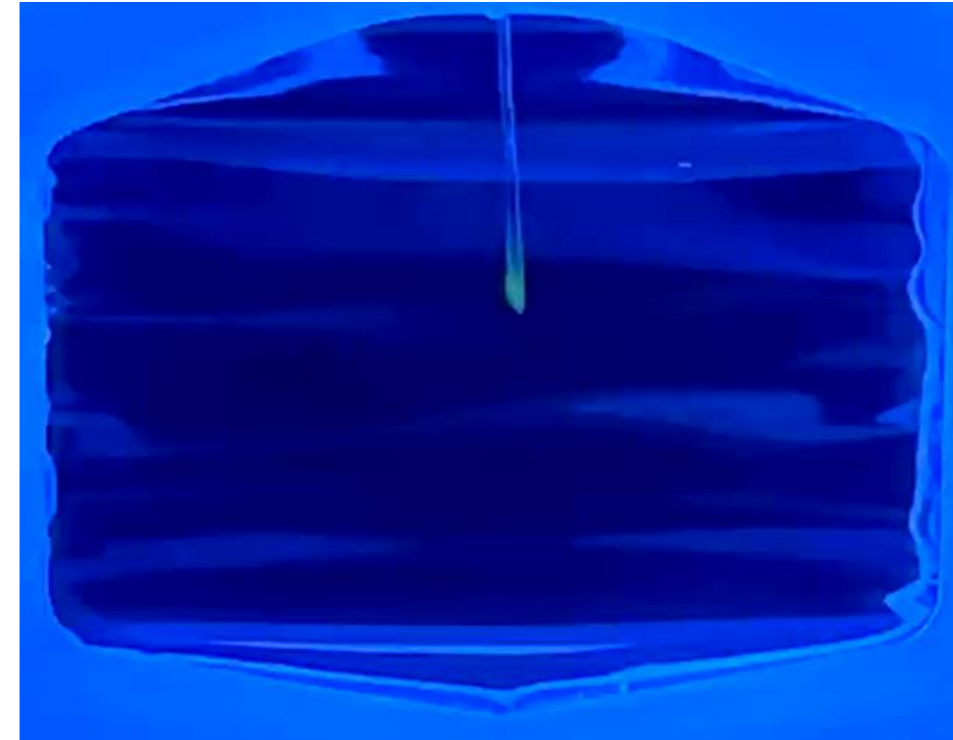
Tarcocimab clinical and enhanced formulations were labeled with green fluorescent dye and injected into artificial vitreous at the clinical ratios / volumes to compare dosing and administration of the two formulations

### Old Clinical formulation



**8 - 10 seconds to inject with high force and cohesiveness**

### Enhanced formulation



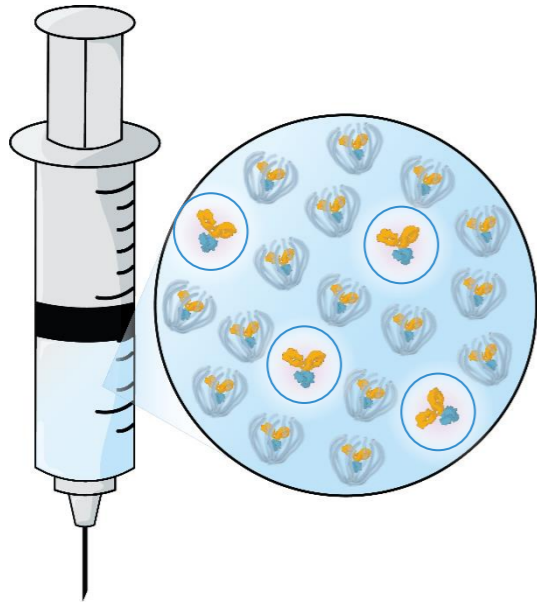
**2 - 3 seconds to inject with reduced force and improved dispersibility**

**We have extended these formulation  
improvements into all our ABCD medicines**

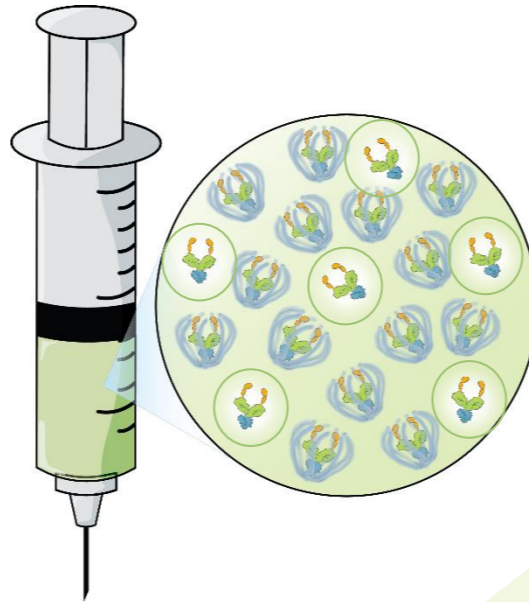


# We have incorporated the enhanced formulation into KSI-501

## Enhanced Formulation Tarcocimab



## Enhanced Formulation KSI-501



The enhanced formulation for KSI-501 also features an optimized combination of conjugated and unconjugated (free protein) forms

5.0 mg	Strength	<b>5.0 mg</b>
4.0 mg	Proportion of <b>Conjugates</b>	<b>3.5 mg</b>
1.0 mg	Proportion of <b>Free Protein</b>	<b>1.5 mg</b>

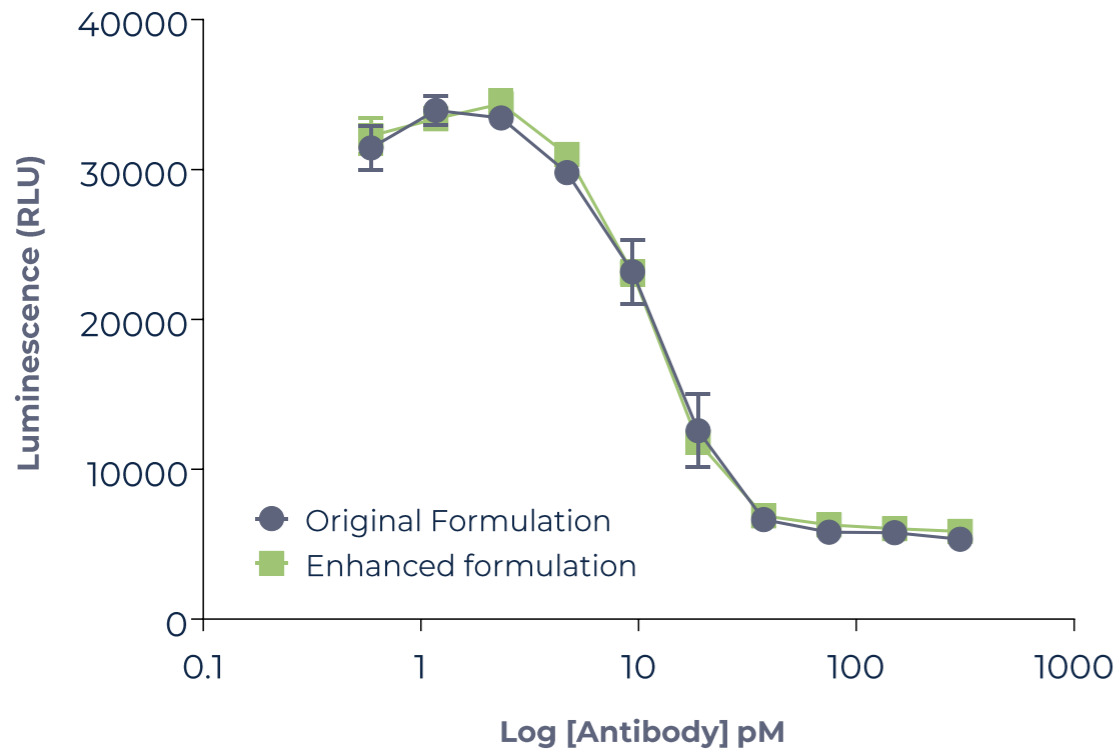
Based on antibody mass (injection volume of 100  $\mu$ L at 50 mg/mL)

Proportion of conjugates further reduced to 3.5 mg due to larger protein size

1.5 mg of unconjugated free protein

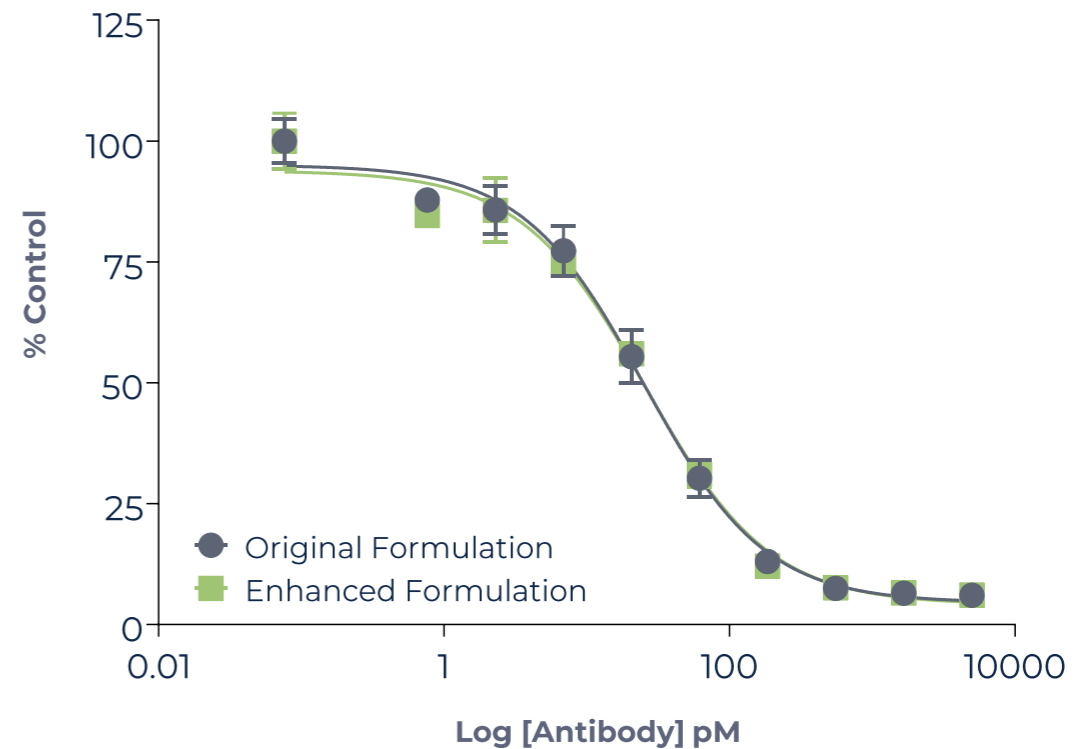
# The enhanced formulation demonstrates the same anti-VEGF and anti-IL-6 potency as the KSI-501 original formulation in preclinical assays

**Inhibition of VEGF:VEGFR Binding in a Cell-Based Assay**



Inhibition of VEGF:VEGFR Binding	IC <sub>50</sub> (pM)
KSI-501 Original Formulation	12.0
KSI-501 Enhanced Formulation	11.4

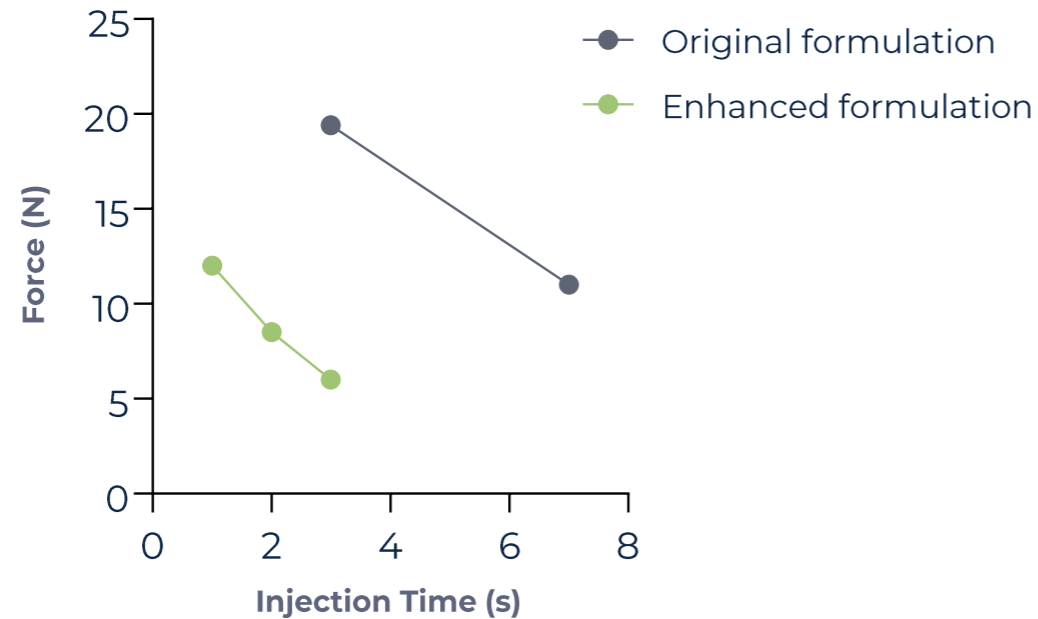
**Inhibition of IL-6 *cis* Signaling in a Cell-Based Assay**



Inhibition of IL-6 <i>cis</i> Signaling	IC <sub>50</sub> (pM)
KSI-501 Original Formulation	25.1
KSI-501 Enhanced Formulation	25.8

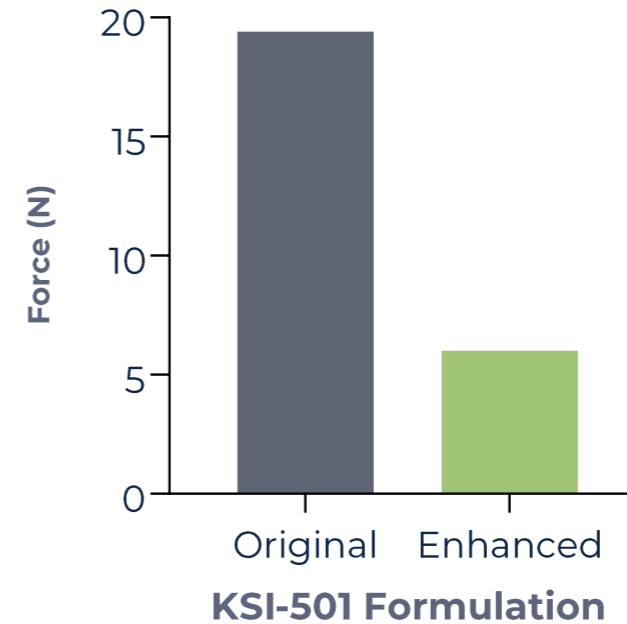
# Similar to tarcocimab, the enhanced formulation for KSI-501 requires less injection time and force

### Injection Force Over Time



**Injection time reduced from ~7 seconds to ~3 seconds**

### Matched Injection Time (3s)



**The injection force is reduced by >3x**

# AGENDA

Why Kodiak?	Victor Perloth, MD Chairman and CEO
Science of Durability	David Brown, MD
Science of the Enhanced Formulation	David Brown, MD
<b>Roundtable Discussion</b>	<b>Moderator: Victor Perloth, MD</b> Chairman and CEO
Audience Q&A	All
Clinical Program Overview	Charles Wykoff, MD, PhD
The Kodiak Opportunity	Victor Perloth, MD Chairman and CEO
Roundtable Discussion	Moderator: Victor Perloth, MD Chairman and CEO
Audience Q&A	All
ABCD Platform Preview	Dolly Chang, MD, PhD Chief Scientific Officer
Summary and Takeaways	Victor Perloth, MD Chairman and CEO
Audience Q&A	All

# ROUNDTABLE DISCUSSION

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## Moderator



**Victor Perloth, MD**  
Chairman and CEO

## KOL Participants



**David Brown, MD**



**Charles Wykoff, MD, PhD**

# AGENDA

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Q&A

# AGENDA

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# TARCOCIMAB TEDROMER

## CLINICAL PROGRAM OVERVIEW



Charles Wykoff, MD, PhD

KSI-501

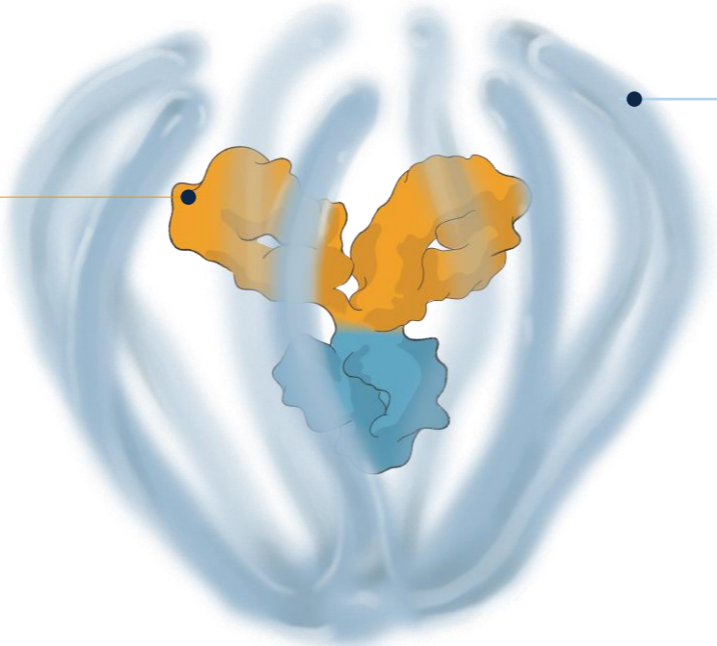
KSI-101

# Kodiak's ABCD Platform leverages a proprietary, high molecular weight, phosphorylcholine-based biopolymer to enable an extended ocular residence time

The Antibody Biopolymer Conjugate Drug ("ABCD") Platform is the foundation of tarcocimab tedromer and KSI-501

### Antibody or Other Biologic

Any biologic such as an antibody can be conjugated to the biopolymer via a stable, site-specific linkage



Antibody Biopolymer Conjugate Drug ("ABCD")

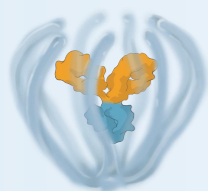
### High molecular weight Biopolymer

Engineered to make medicines last longer and extend their therapeutic benefit.

The biopolymer is optically clear and made of phosphorylcholine, the primary hydrophilic component of human cell membranes

# Kodiak has a portfolio of three differentiated clinical programs intended to address key limitations of today's therapies across a broad spectrum of retinal diseases

## ABCD Platform-derived biologics: Mainstay biologics for high-prevalence retinal vascular diseases



**Tarcocimab**  
Anti-VEGF ABCD

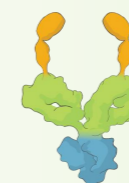
- **Objective:** to have a compelling first-line durability profile with uncompromising immediacy
- Longest-acting anti-VEGF biologic (6-month predominant) while preserving the flexibility to dose monthly
- An intravitreal biologic that can be used in any patient whether they be in the loading (immediacy) phase or in the maintenance (durability) phase
- **Enhanced 50 mg/mL formulation**



**KSI-501**  
Bispecific Anti-IL-6,  
VEGF Trap ABCD

- **Objective:** to address the opportunity for first-line efficacy with the best durability
- First-in-class bispecific “ABCD” designed to address retinal inflammation and vascular permeability simultaneously
- Reflects 10 years of learnings of the “ABCD” platform to maximize each patient’s efficacy and durability potential
- **Enhanced 50 mg/mL formulation**

## Unconjugated biologic: For inflammatory retinal diseases



**KSI-101**  
Bispecific Anti-IL-6,  
VEGF Trap Protein

- **Objective:** to address the underlying disease mechanisms of macular edema secondary to inflammation (“MESI”) for which no approved intravitreal biologic therapies exist today
- First-in-class bispecific protein designed to address retinal inflammation and vascular permeability simultaneously
- **100 mg/mL formulation provides high strength and potency**

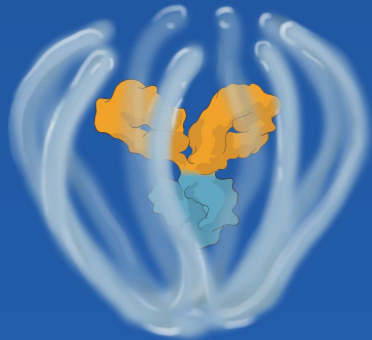
### Science Updates for our “ABCD” Investigational Medicines

1. Supported by our true science of durability
2. Enhanced formulation delivers immediacy and durability

VEGF: vascular endothelial growth factor; IL-6: interleukin 6; mAb: monoclonal antibody

# TARCOCIMAB TEDROMER

- Only intravitreal biologic that has demonstrated consistent 6-month predominant durability in high-prevalence retinal vascular diseases
- Intended to be a mainstay biologic that can be used in all patients
- Supported by a clinical science of immediacy and durability



## Design

- Anti-VEGF antibody biopolymer conjugate drug (“ABCD”)
- Only intravitreal biologic supported by the science of durability
- Enhanced formulation delivers “the pulse and the durability”

Uncompromising  
Immediacy with  
go to market  
formulation

## Differentiation

- High efficacy with high durability remains a key unmet need
- 6-month durability profile across retinal vascular diseases
- Developed for all retinal vascular disease patients
- Flexible dosing, from monthly to 6-month dosing

“Why wouldn’t I  
use it in all my  
patients after  
Avastin?”

## Development

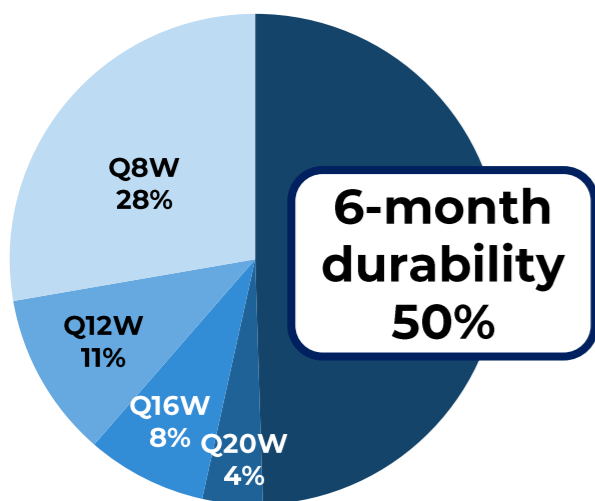
- 1 successful pivotal study away from BLA submission
- BLA package in 3 indications
- Anticipate high PTRS study outcomes
- ~90% of all investment needed completed

~90% of clinical &  
manufacturing  
activities already  
completed

# Tarcocimab tedromer and the ABCD platform have consistently shown a differentiated durability profile across all retinal vascular diseases

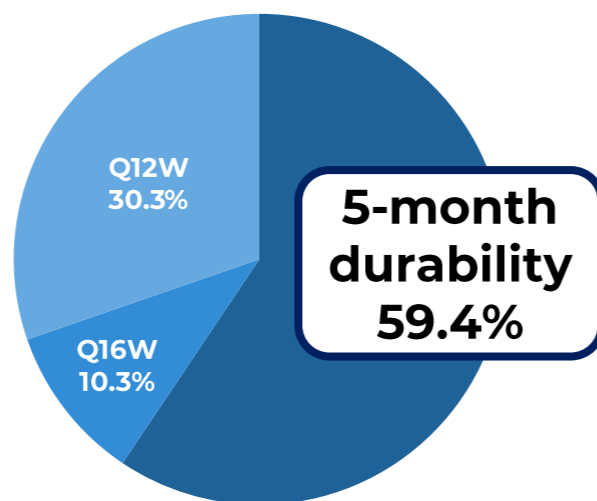
## Durability Interval at Year 1

## Number of doses in the second 6 months of Year 1



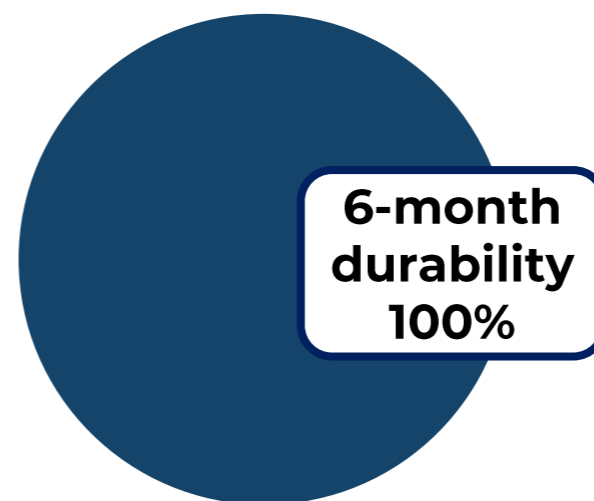
### DME

GLEAM and GLIMMER Studies<sup>1</sup>



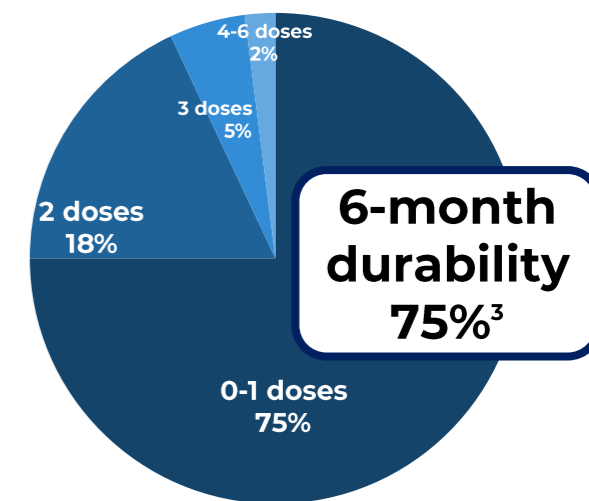
### wAMD

DAZZLE Study<sup>2</sup>



### DR

GLOW1 Study



### RVO

BEACON Study

DME: diabetic macular edema; DR: diabetic retinopathy; RVO: retinal vein occlusion; wAMD: wet age-related macular degeneration.

1. Pooled analyses. The studies did not meet the primary endpoint.

2. Treatment intervals were capped at 5 months (6-month dosing was not tested). The study did not meet the primary endpoint.

3. Estimated durability interval based on patients that received no injections (46%) or 1 injection (29%) over the second 6 months of Year 1.

# With three positive Phase 3 studies, tarcocimab is one positive study away from a multi-indication BLA submission package

## Completed Phase 3 studies:

Primary endpoint met and extended durability demonstrated using the original clinical formulation



DAYLIGHT Study

BEACON Study

GLOW1 Study

## Two Phase 3 studies actively enrolling:

using the go to market formulation of tarcocimab



GLOW2 Study

DAYBREAK Study



**Planned BLA package in 2026 for 3 disease indications supported by 5 pivotal studies in diabetic retinopathy, wet age-related macular degeneration & retinal vein occlusion**

# We had numerous positive and collaborative interactions with the FDA over the past 12 months

## GLOW2 in Diabetic Retinopathy

- FDA meetings and protocol reviews to discuss GLOW2 clinical trial
  1. Alignment on study design, population and primary endpoint (similar to GLOW1)

## DAYBREAK in wet AMD

- FDA meetings and protocol reviews to discuss DAYBREAK clinical trial
  1. Alignment on study design, population and primary endpoint
  2. FDA considered that the inclusion of both tarcocimab and KSI-501 is appropriate
  3. FDA considered that the proposed combination of active and comparator arms is appropriate.

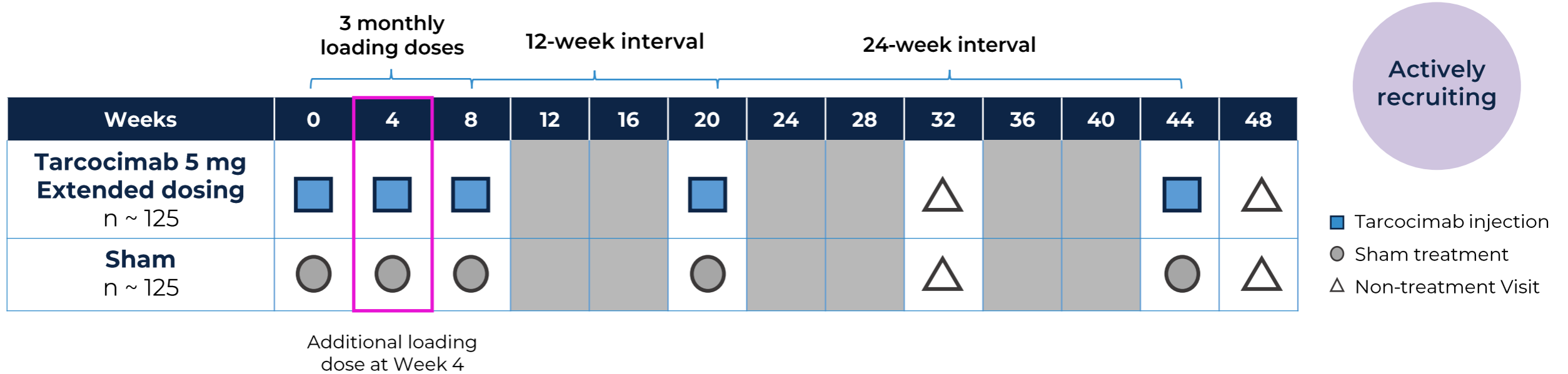
## Bridging of Go to Market Formulation

- FDA meetings to discuss go to market formulation
  1. FDA considered that a single additional Phase 3 study is sufficient to bridge the go-to-market formulation
  2. Kodiak is running two additional Phase 3 studies

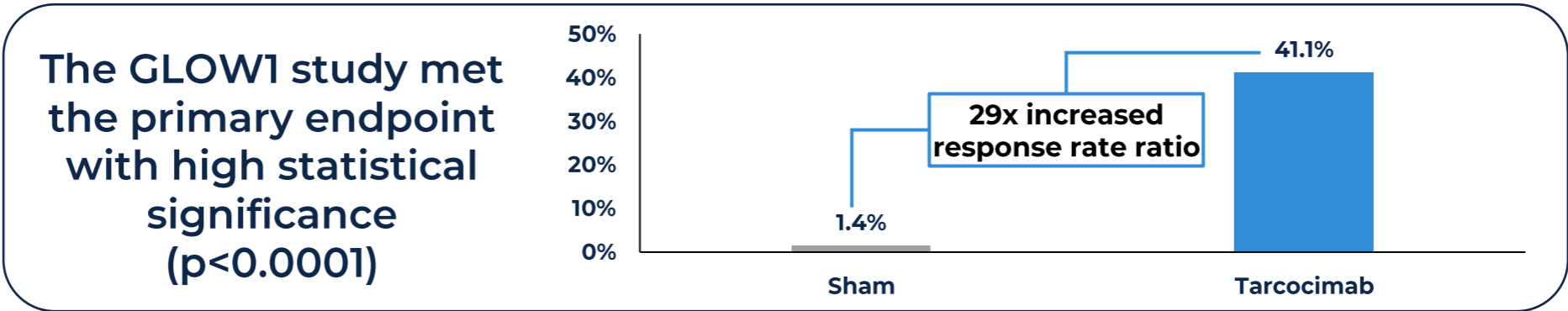
## **Biologics License Application:**

- FDA meetings to discuss tarcocimab and BLA filing
- FDA considered that the package of five Phase 3 studies (three Phase 3 studies of DAYLIGHT, BEACON, GLOW 1 run with the old clinical formulation; and two Phase 3 studies of GLOW 2, DAYBREAK run with the go to market formulation, if successful) is acceptable and sufficient to file a BLA for the 3 indications of DR, RVO and wAMD

# New DR Phase 3 study: GLOW2 features a similar study design as the successful GLOW1 study, with the benefit of an additional 3rd monthly loading dose



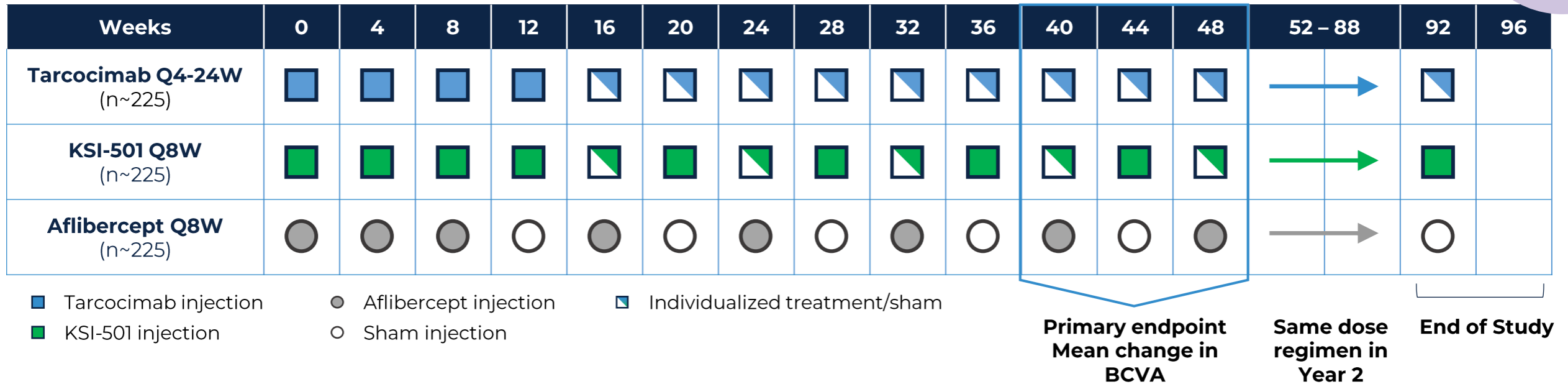
**Primary endpoint** • Proportion of eyes improving  $\geq 2$  steps on DRSS from baseline at Week 48





# New wAMD Phase 3 study: DAYBREAK is designed as a registrational study for both tarcocimab tedromer and KSI-501

Actively recruiting



The study optimizes treatment for each individual patient using objective disease activity criteria that are relevant to how physicians practice in their clinics

## Tarcocimab objective

Assess 6-month durability potential with individualized Q4W to Q24W dosing

## KSI-501 objective

Explore the efficacy potential of bispecific IL-6 and VEGF inhibition in fixed Q8W dosing with additional individualized monthly dosing

## Tarcocimab already failed in a wAMD durability study. What has changed? The DAYBREAK Study is designed to address each of the flaws of the DAZZLE Study

DAZZLE Study  
Allowed Intervals

Q12W Q16W Q20W

DAYBREAK Study  
Allowed Intervals

Q4W Q8W Q12W Q16W Q20W Q24W

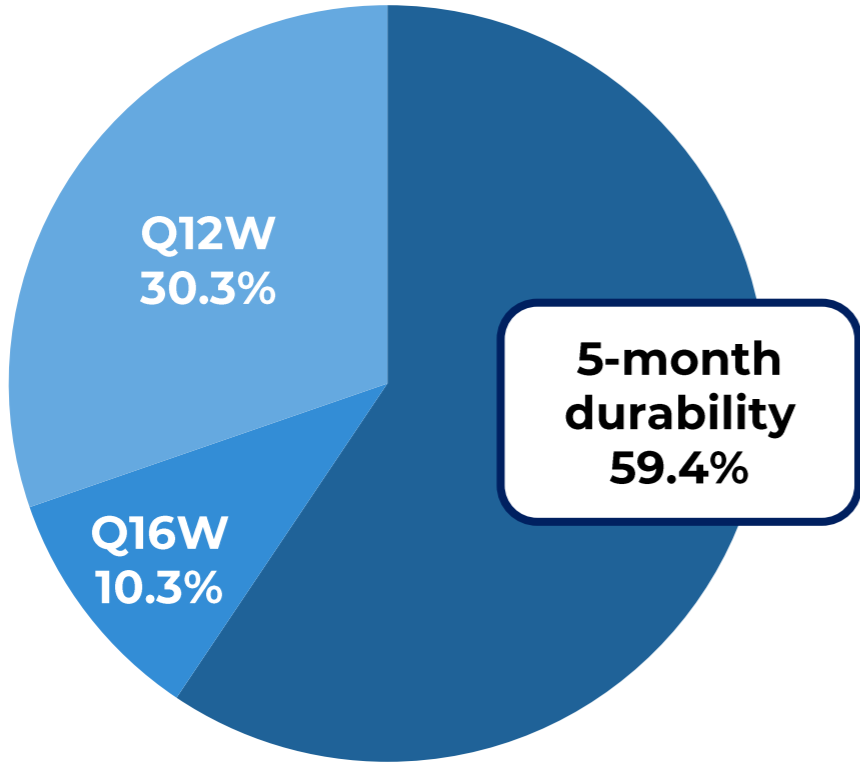
Shorter intervals  
prevent underdosing

Enables 6-month  
durability evaluation

DAZZLE Flaw	DAYBREAK Solution
<b>Underdosing</b>	<ul style="list-style-type: none"> <li>Adding a 4<sup>th</sup> loading dose</li> <li>Allowing shorter intervals, down to monthly dosing</li> <li>Having flexible intervals</li> </ul>
<b>Reactive dosing</b>	<ul style="list-style-type: none"> <li>A treat-to-dryness proactive dosing, enabled by using presence of fluid as a disease activity marker</li> </ul>
<b>Loose retreatment criteria</b>	<ul style="list-style-type: none"> <li>Using presence of fluid as a disease activity marker, instead of a combination of CST and vision loss, and expanding the evaluable area 9-fold (from 1mm<sup>2</sup> to 3mm<sup>2</sup>)</li> </ul>
<b>Lack of immediacy</b>	<ul style="list-style-type: none"> <li>Using the enhanced formulation of tarcocimab</li> </ul>

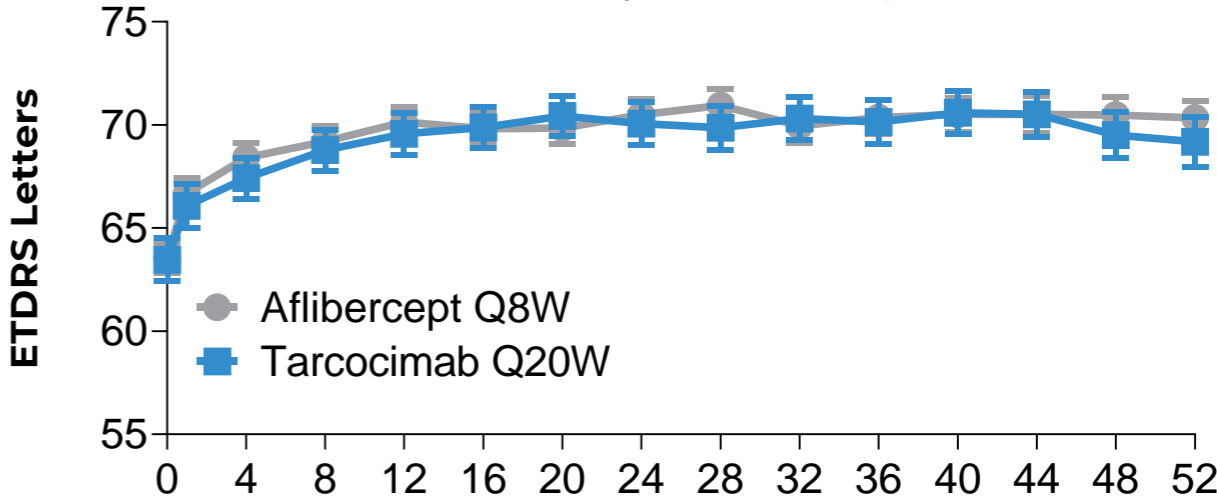
**Why go beyond 5 months?** In DAZZLE, ~60% of tarcocimab patients achieved 5-month durability with visual/anatomical improvements comparable to the overall aflibercept group

**Durability intervals at Year 1 in the DAZZLE Study**

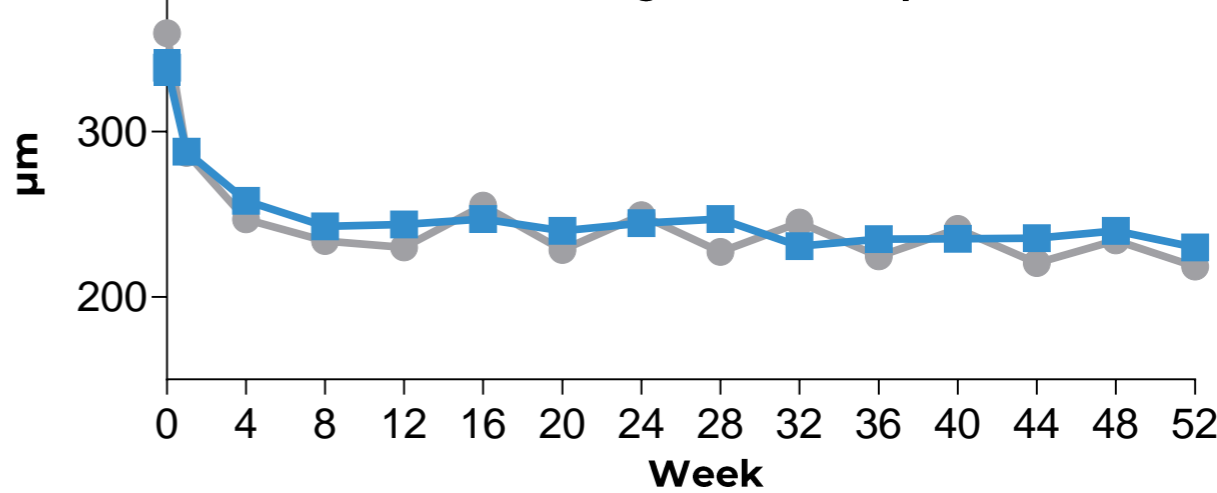


Q12W: every 12 weeks; Q16W: every 16 weeks; Q20W: every 20 weeks. BCVA: best corrected visual acuity; ETDRS: early treatment diabetic retinopathy study. CST: central subfield thickness

**Mean BCVA Over Time in Tarcocimab Patients on 5-Month Dosing vs Aflibercept Patients**



**Mean OCT CST Over Time in Tarcocimab Patients on 5-Month Dosing vs Aflibercept Patients**



**What is so special about DAYBREAK's disease activity criteria? Using fluid volumes instead of CST as a marker of disease activity resembles retina specialists' practice, optimizes each patient's treatment, and generates data on how the molecule will perform in the real world**

354 microns of OCT CST

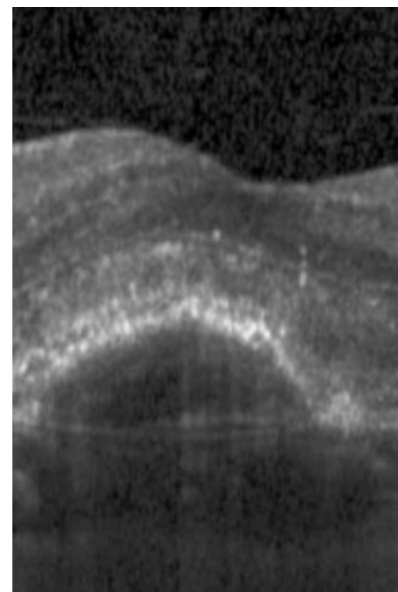
?

Loss of 5 letters

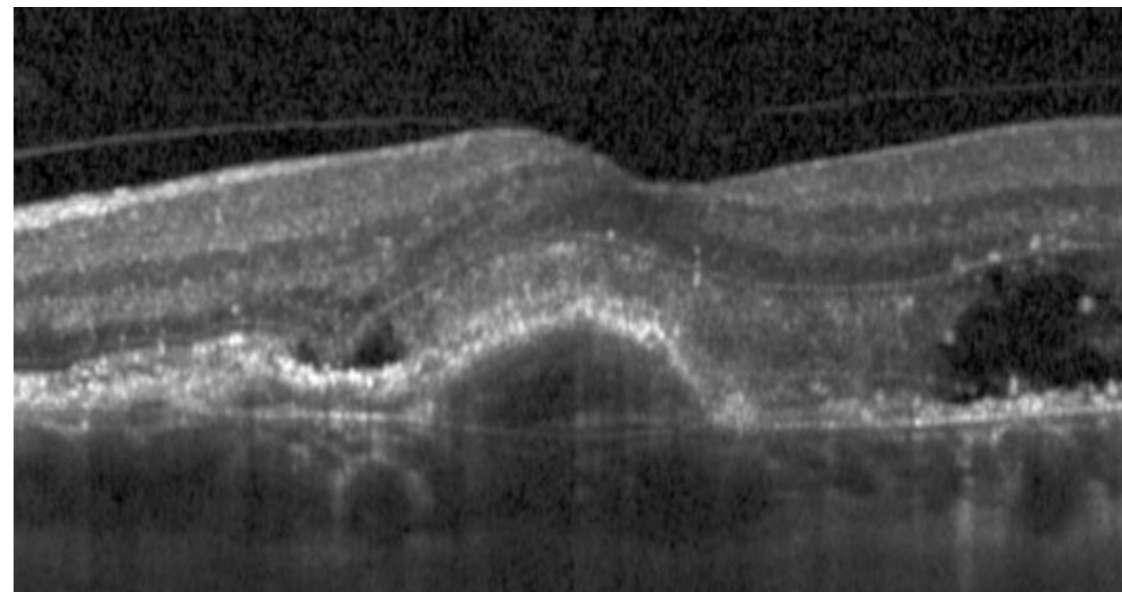
?

From best prior BCVA

?



1 mm<sup>2</sup>  
**Maybe?**



3 mm<sup>2</sup>  
**Definitely**

Would you treat?

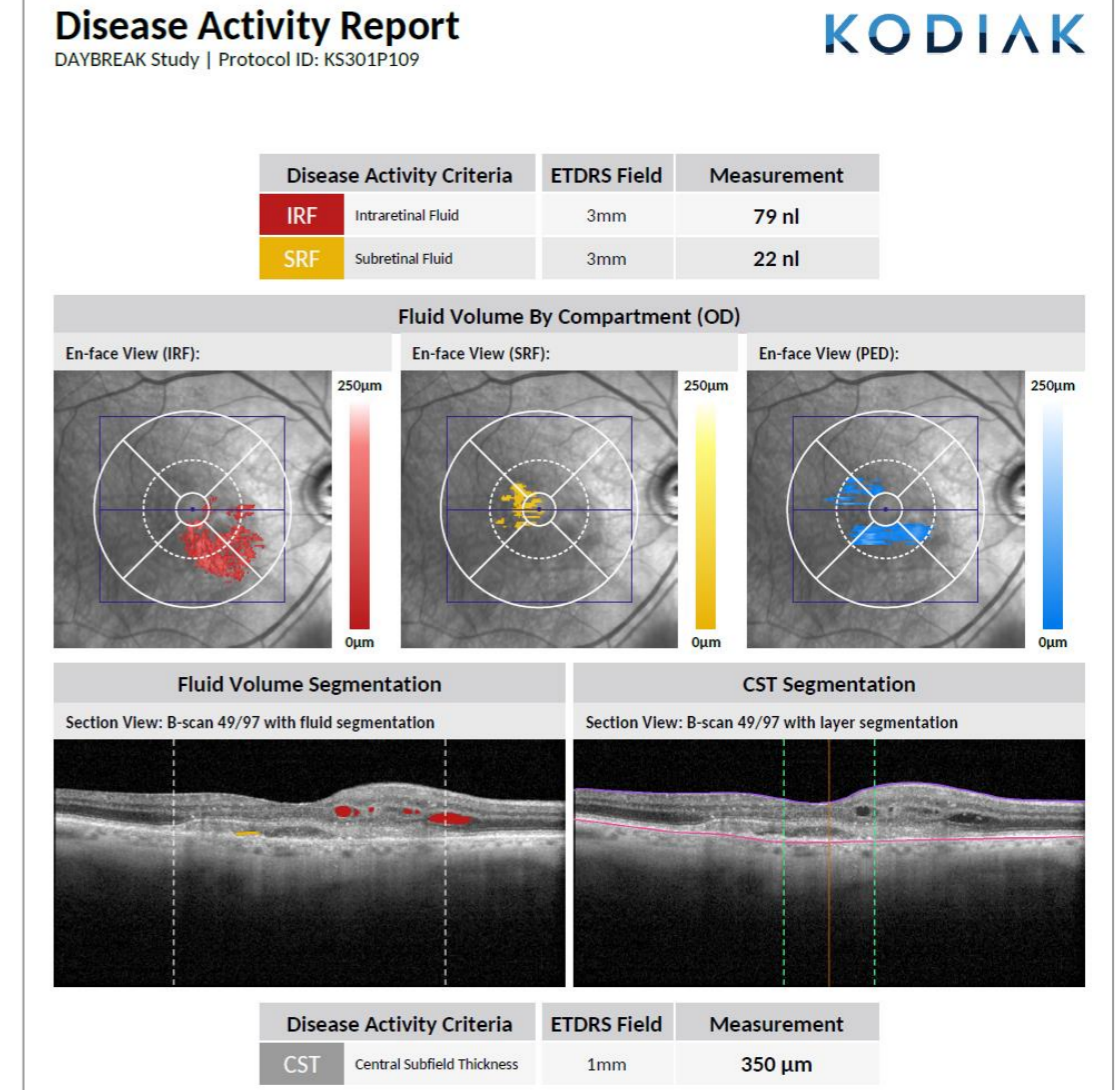
**So patients will be treated more. That means less durability, right? Not necessarily. It means that patients will receive treatment only when indeed needed. This is intended to maximize both the chance of meeting non-inferiority and having a strong and real durability profile**

### DAYBREAK disease activity criteria

- Presence of intraretinal fluid (IRF) in central 3mm<sup>2</sup>
- Presence of subretinal fluid (SRF) in central 3mm<sup>2</sup>
- Presence of macular hemorrhage

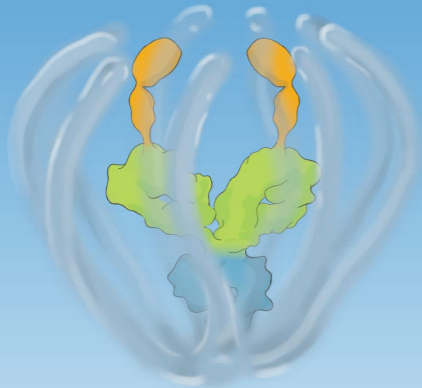
### Using a fluid tool provides meaningful advantages by treating patients only when they truly need it

- Optimizes treatment for *each* patient
  - **High need patients:** treats until dry, enables monthly dosing and detects disease reactivations earlier
  - **Long durability patients:** allows patients without active disease to *safely* go to 6-month dosing
- **Standardized, quantitative, objective evaluation:** a precision medicine tool for each patient



# KSI-501

First-in-class bispecific ABCD designed to address vascular permeability and retinal inflammation simultaneously with the potential for best efficacy and best durability in high prevalence retinal vascular diseases



## Design

- First-in-class dual inhibition: anti-IL-6 and VEGF Trap
- Supported by our science of durability of the “ABCD” platform
- Enhanced ABCD formulation

Enhanced formulation delivers both immediacy and durability

## Differentiation

- Designed to address two key unmet needs: higher efficacy and higher durability
- Bispecific mechanism demonstrates superior blood retinal barrier normalization effect vs monotherapies

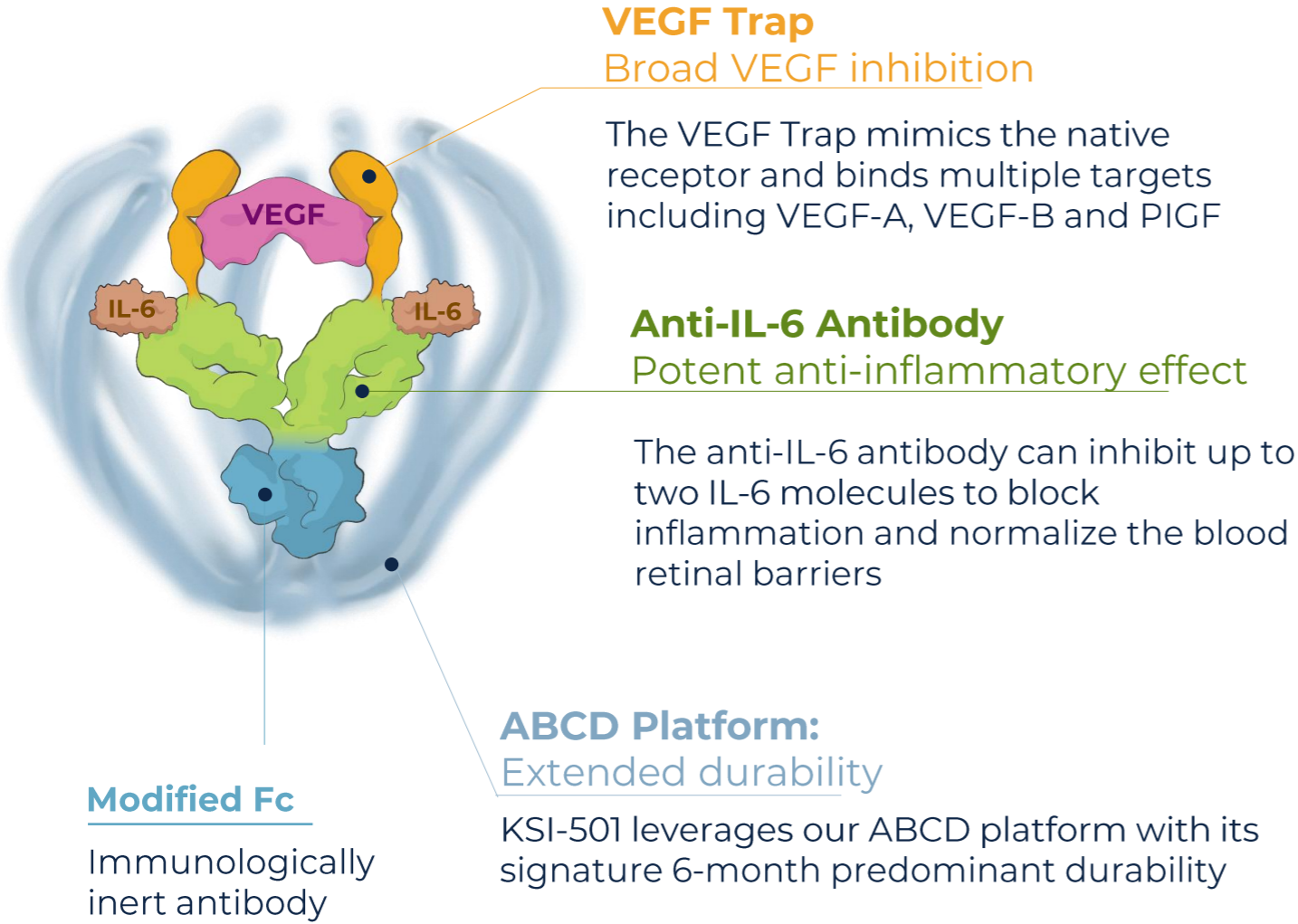
Potential for better efficacy and best durability

## Development

- Exploring potential for better efficacy with intensive dosing also optimizes for high PTRS
- After DAYBREAK, 1 study away from BLA package

After DAYBREAK, 1 study away from BLA submission

# Built on Kodiak's ABCD platform, KSI-501 is a first-in-class bispecific designed for highly efficient binding to both IL-6 and VEGF

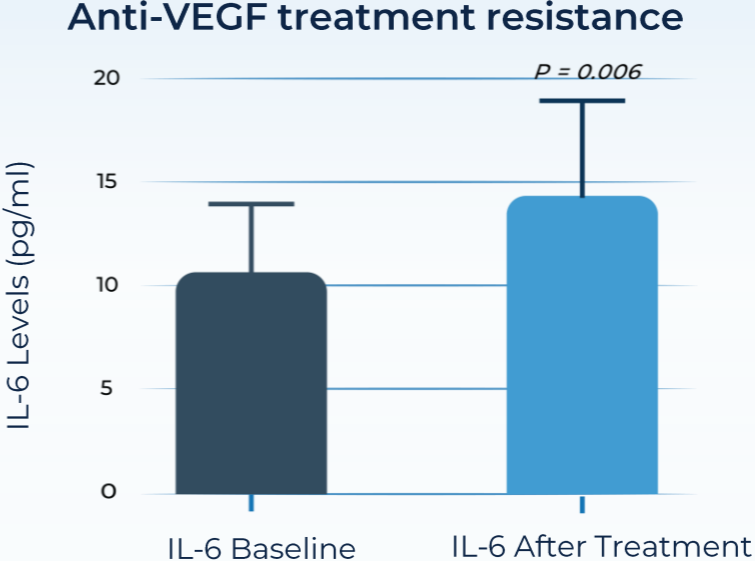
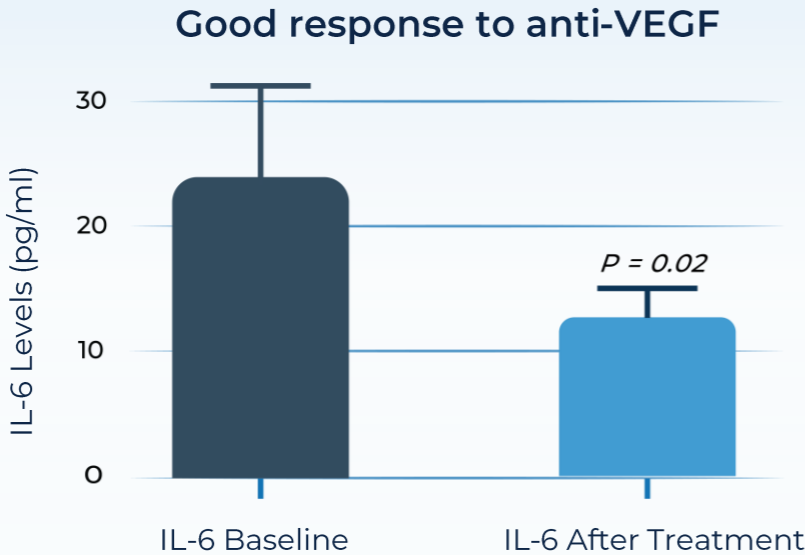


**VEGF inhibition is the primary effector**, with potential for additional clinical benefits based on the anti-permeability effect of the anti-inflammatory effect of IL-6 inhibition

**Enhanced ABCD formulation designed to maximize durability and efficacy**, with conjugated and unconjugated forms

# In addition to VEGF, IL-6 driven inflammation is implicated in retinal vascular disease

Aqueous humor IL-6 levels significantly correlate with anti-VEGF treatment response in wAMD<sup>1</sup>



**IL-6 is a pro-inflammatory cytokine and immune growth factor stimulates defective angiogenesis independent of VEGF and is implicated in anti-VEGF treatment resistance**

1. Adapted from Chalam et al. (2014). Journal of Ophthalmology, Article ID 502174. Mean with SEM plotted.



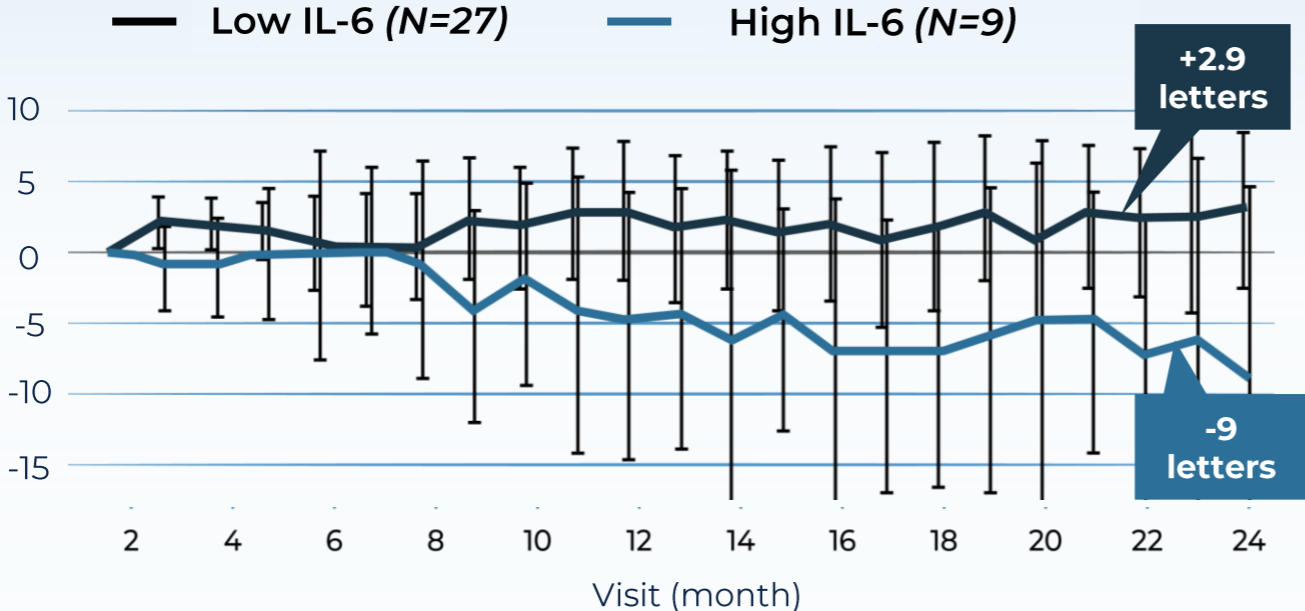
# Increased levels of IL-6 are associated with poor visual outcomes when patients are treated with anti-VEGF monotherapy

## Visual response by IL-6 baseline levels

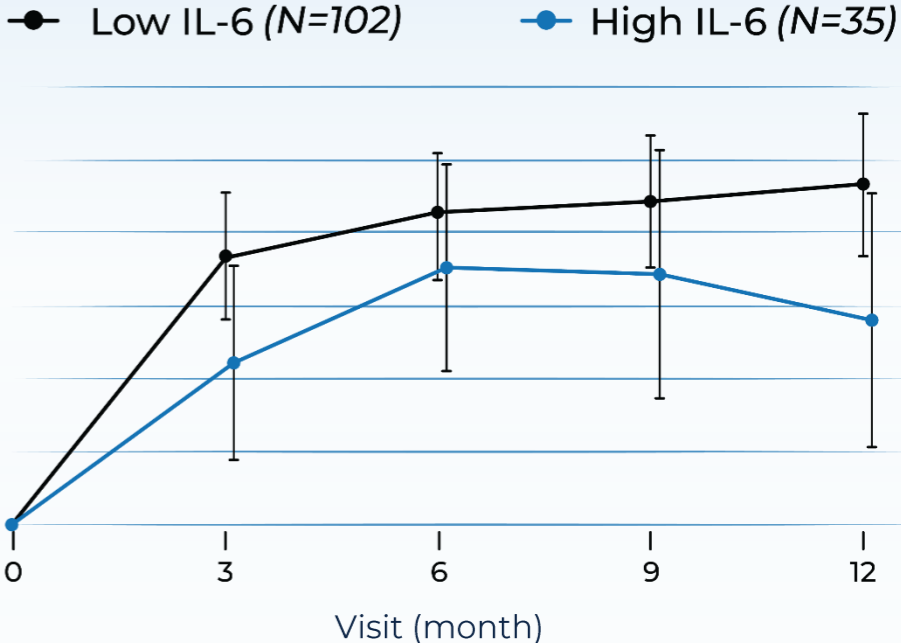
### wAMD

### DME

Mean change in BCVA (ETDRS letters) from month 2



Mean change in BCVA (ETDRS letters) from baseline



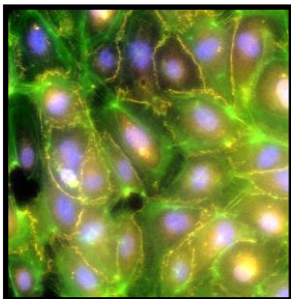
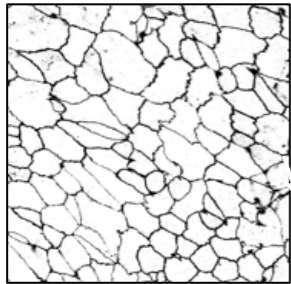
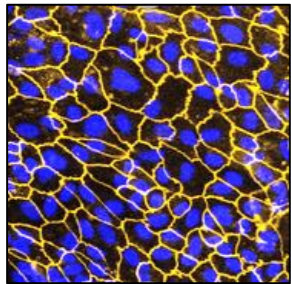
Higher levels of IL-6 in aqueous humor are correlated with poor BCVA outcomes over time in wet AMD and DME<sup>1</sup>

# Dual inhibition of VEGF and IL-6 by KSI-501 confers superior normalization of barrier biology vs anti-VEGF or anti-IL-6 monotherapy in preclinical studies

Normal

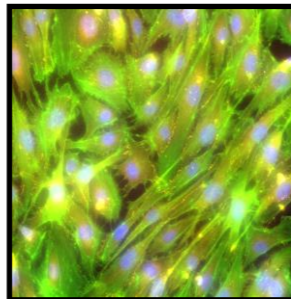
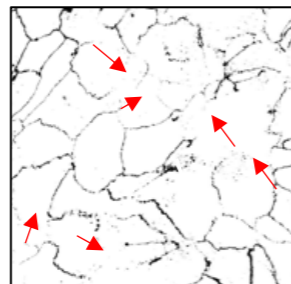
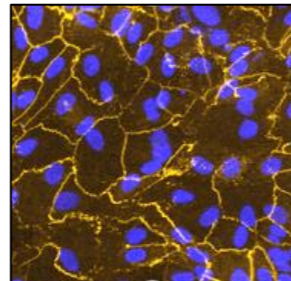
Exogenous VEGF and IL-6  
Tight junction disruption and changes in cell morphology

RPE Cells



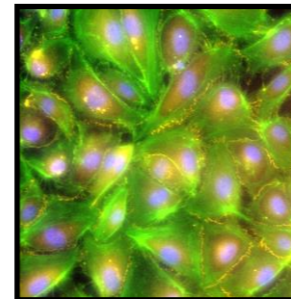
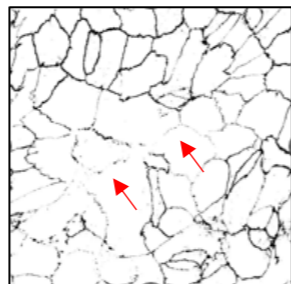
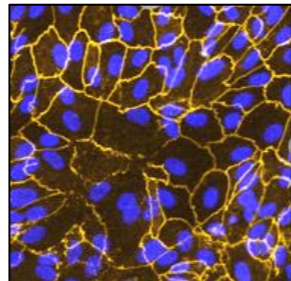
Vascular Cells

No Inhibitors

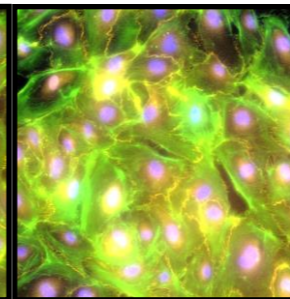
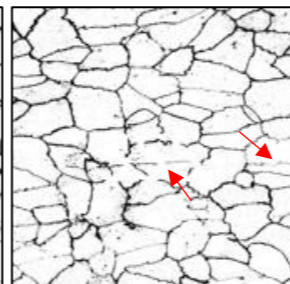
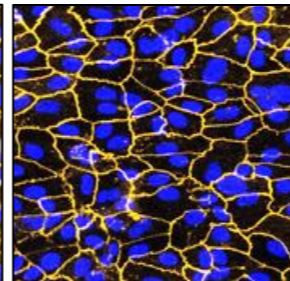


Monotherapy Inhibition

Aflibercept

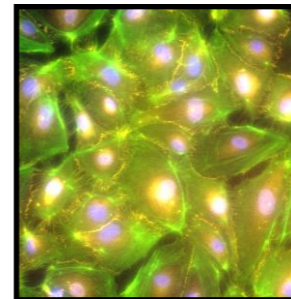
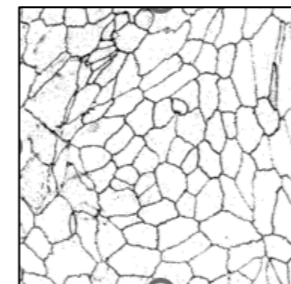
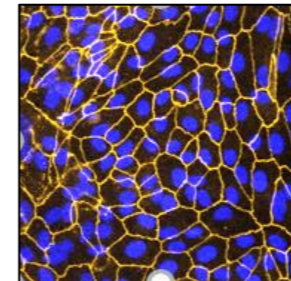


Anti-IL-6



Dual inhibition

KSI-501

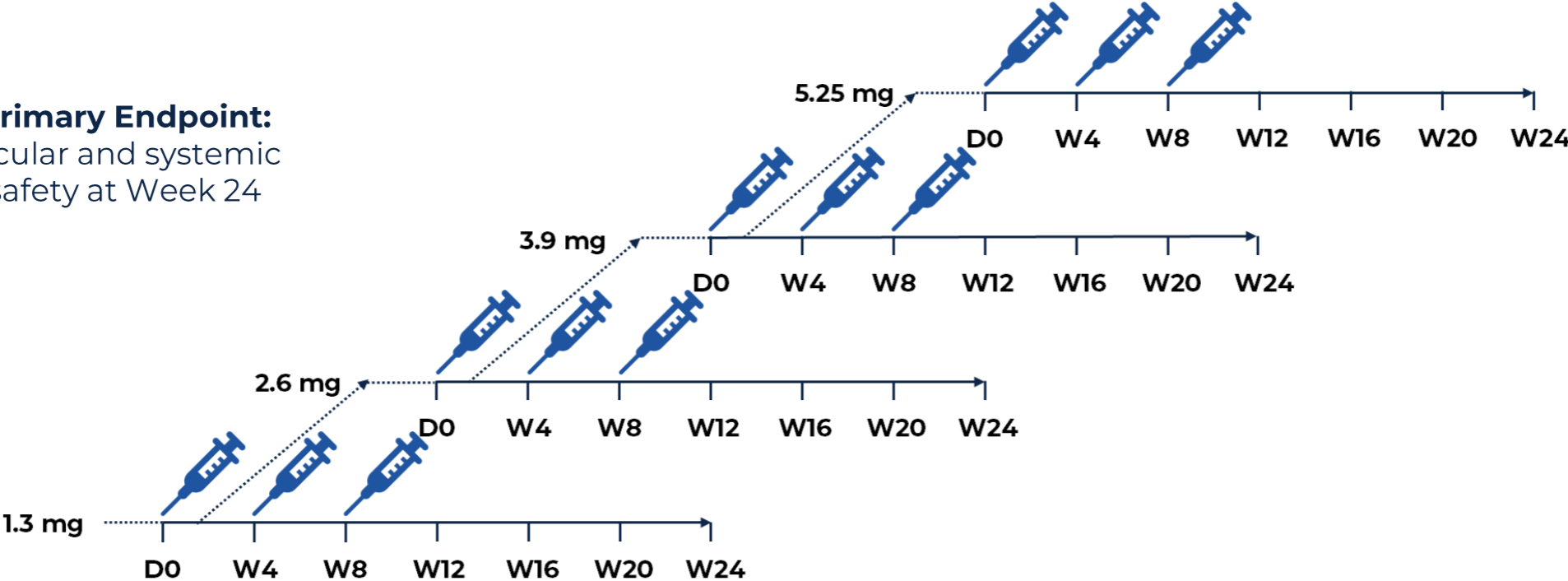


In additional preclinical studies, KSI-501 inhibits endothelial cell proliferation and tube formation to a greater extent than anti-VEGF or anti-IL-6 monotherapy

With synergistic effect on the blood retinal barrier, KSI-501 holds potential to be a new disease-modifying therapy

# Phase 1 study of KSI-501 was a multiple ascending dose study in patients with diabetic macular edema

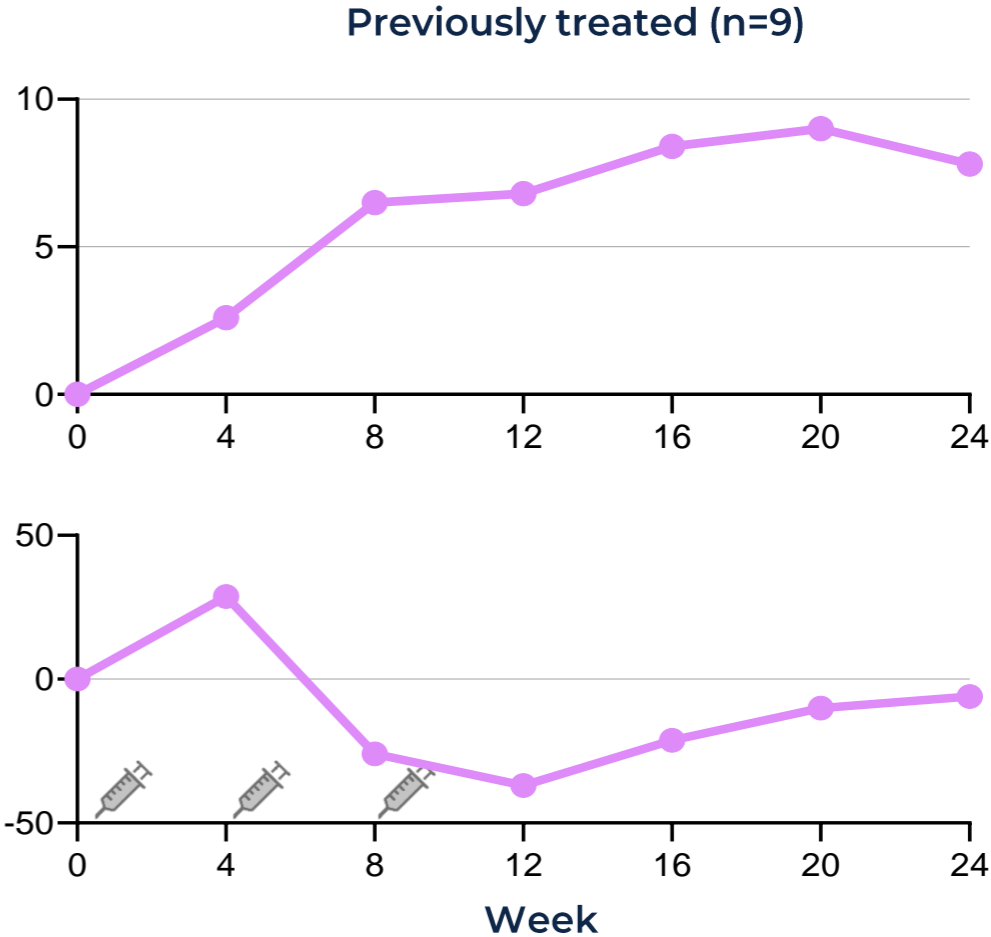
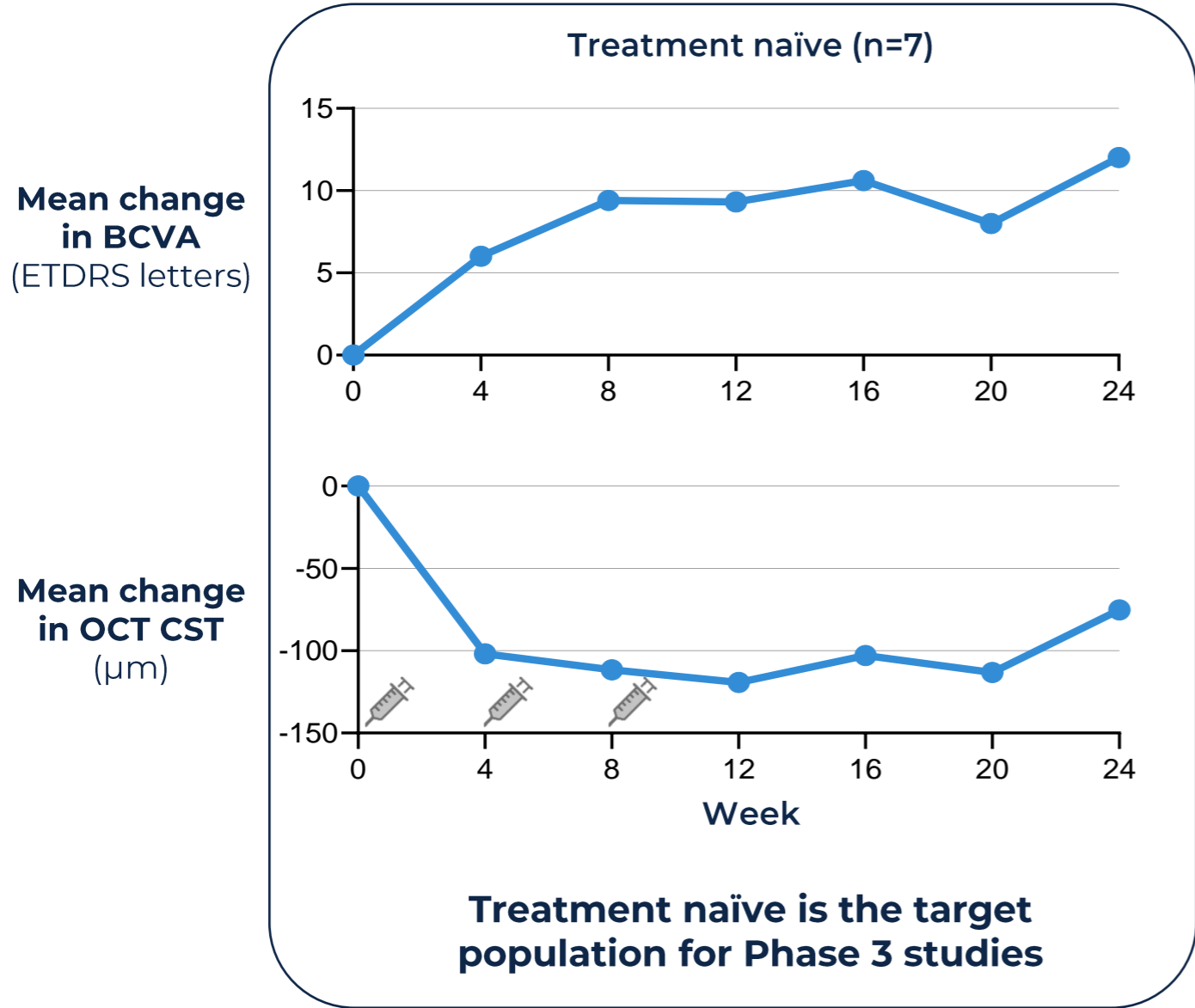
**Primary Endpoint:**  
Ocular and systemic safety at Week 24



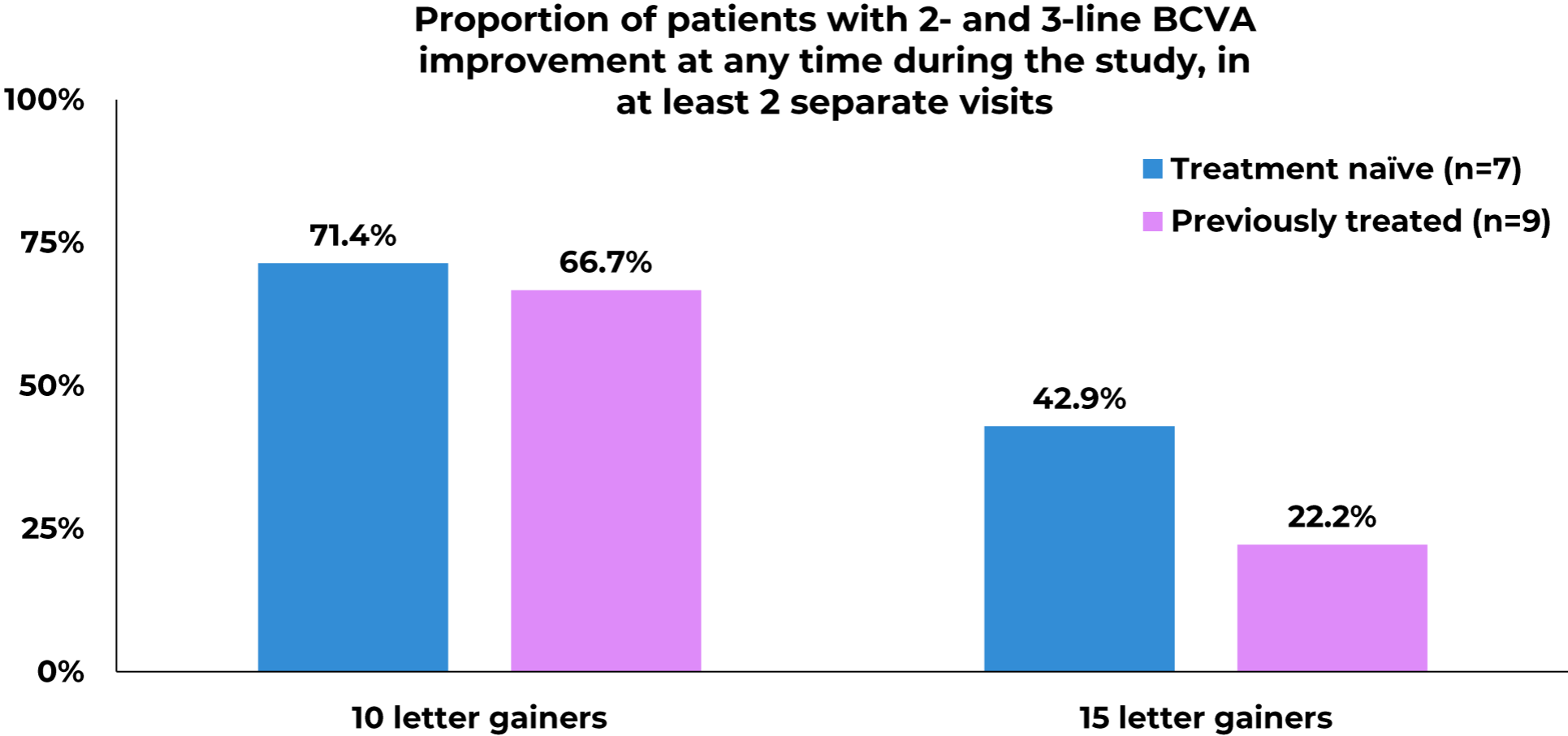
### Study Design

- Multiple ascending dose design
- Conducted at 5 sites in the US
- Each subject received 3 monthly doses and was followed for 24 weeks total

# KSI-501 demonstrated robust and meaningful visual acuity gains that were sustained over 16 weeks in both treatment naïve and pre-treated patients

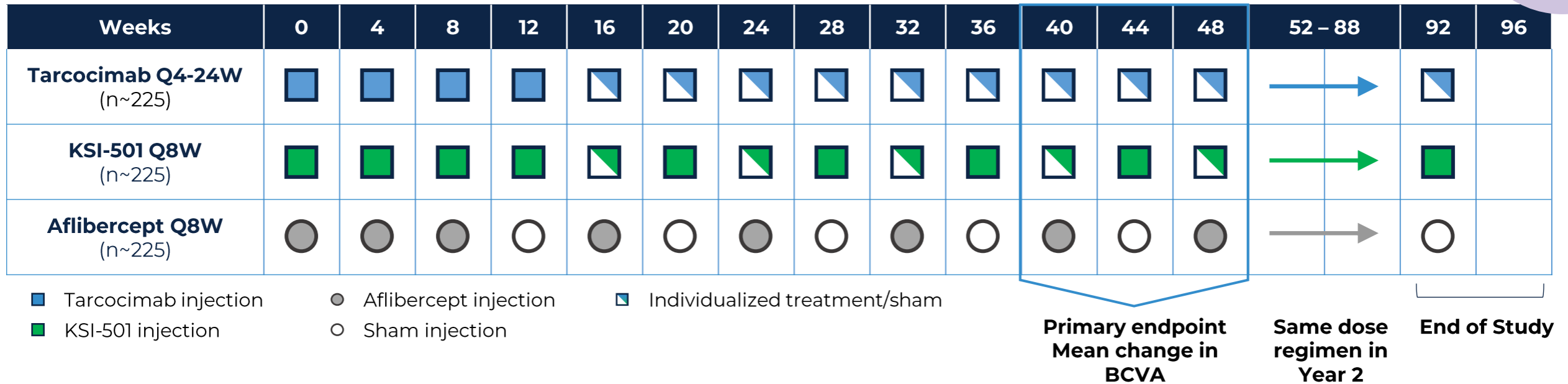


# Treatment with KSI-501 resulted in a meaningful increase of BCVA for the majority of patients during the study



# New wAMD Phase 3 study: DAYBREAK is designed as a registrational study for both tarcocimab tedromer and KSI-501

Actively recruiting



The study optimizes treatment for each individual patient using objective disease activity criteria that are relevant to how physicians practice in their clinics

## Tarcocimab objective

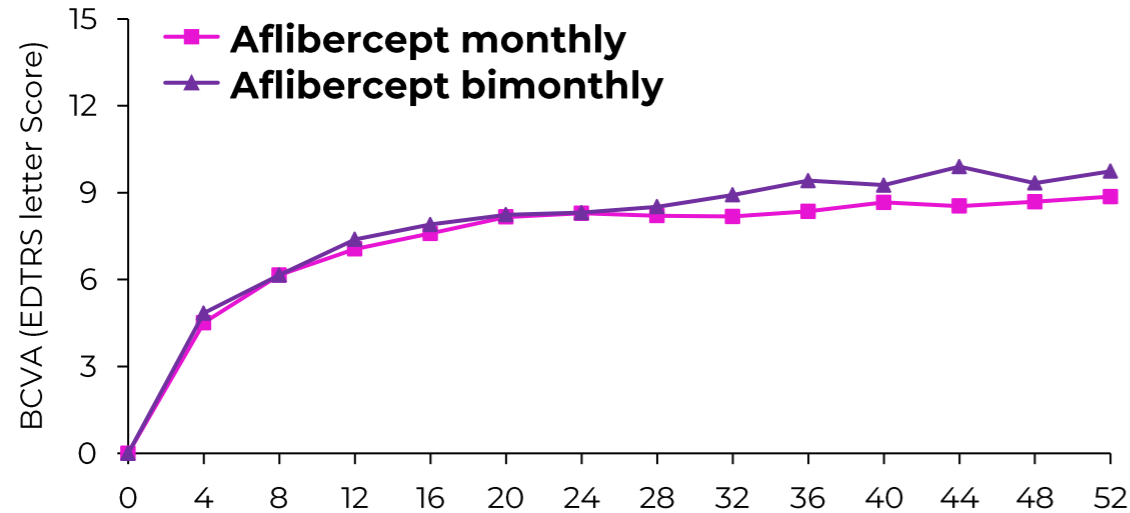
Assess 6-month durability potential with individualized Q4W to Q24W dosing

## KSI-501 objective

Explore the efficacy potential of bispecific IL-6 and VEGF inhibition in fixed Q8W dosing with additional individualized monthly dosing

# Why allow monthly dosing? Meaningfully better visual outcomes have been observed with monthly dosing in patients with persistent fluid

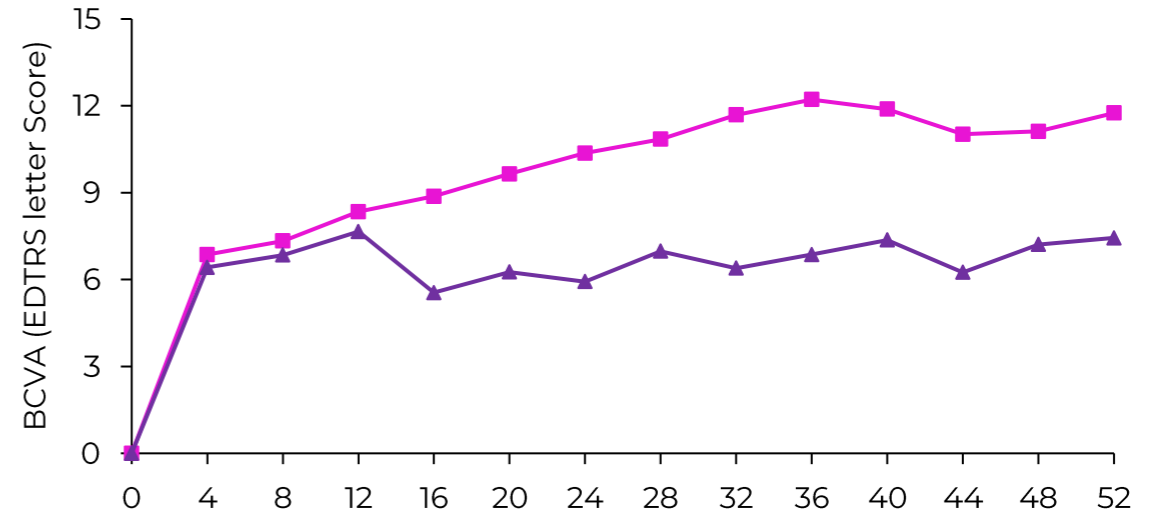
## BCVA in aflibercept's registrational VIEW studies in wAMD



### Patients *without* persistent fluid

(~80% of the population)

No differences in BCVA gains between monthly and every-other-month dosing with aflibercept



### Patients *with* persistent fluid

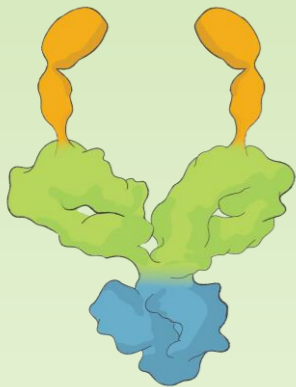
(~20% of the population)

**Significantly better BCVA gains are achieved** with monthly dosing (~4.2 letters)

**Allowing monthly dosing for KSI-501 enhances the possibility to observe better efficacy outcomes and assess the full potential of the bispecific IL-6 VEGF MoA**

# KSI-101

A potent, high-strength bispecific protein designed to address macular edema secondary to inflammation (“MESI”) for which no approved intravitreal biologic therapies exist today



## Design

- First-in-class dual inhibition: anti-IL-6 and VEGF Trap
- Uncorrelated from the ABCD Platform
- 100 mg/mL formulation provides high-strength and potency

High-strength formulation can provide disease control

## Differentiation

- Greenfield market segment
- Unmet need with no approved biologic
- Accelerated readout of pivotal data

Potential to be valuable in its own right

## Development

- Direct to Phase 3 approach
- Sham as comparator
- Exploring accelerated development options: Rare Pediatric Disease Designation, Orphan Disease Designation & Fast Track Designation

Phase 1b underway and exploring accelerated development paths

As an unconjugated protein, KSI-101 is a traditional intravitreal biologic with a profile uncorrelated to the ABCD Platform

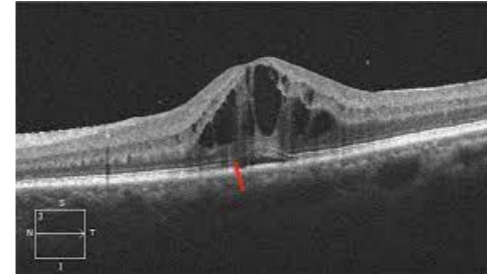


# Macular edema is the leading cause of vision loss among patients with intraocular inflammation



Intraocular inflammation is the 4th leading cause of vision loss in the developed world

- Up to 50% of patients experience reduced vision
- 10-15% of patients become blind



Macular edema is the leading cause of vision loss among patients with intraocular inflammation

- 1/3 of patients with intraocular inflammation develop macular edema (~110,000 patients in the U.S.)

**Studies show that inflammation and vascular permeability have a synergistic effect on driving disease progression and vision loss due to macular edema, but there are no approved therapies that target both drivers of disease**

# Current treatment algorithm for macular edema secondary to inflammation: unmet need for safer therapies that target the underlying mechanisms of disease

## First line: Mainstay of treatment

### Local or systemic corticosteroids

- Associated with **elevated intraocular pressure/glaucoma** that often require therapy and even surgery as well as cataract progression
- **30–40% of patients do not respond**

## Second line

### Immunomodulators

- Off-label use
- Used as steroid-sparing agents
- Up to 50% of patients do not have macular edema resolved
- ~35% of patients do not experience improvement in macular edema

## Second or third line

### Biologic

- Adalimumab (anti-TNF $\alpha$ ) is the only FDA-approved non-steroid therapy for NIU
- Used as a steroid-sparing therapy
- **~55% of patients experienced treatment failure** over 85 weeks
- Associated with **serious side effects** (e.g., infections, malignancies)

## Third or fourth line or adjunct

### Anti-VEGF agents

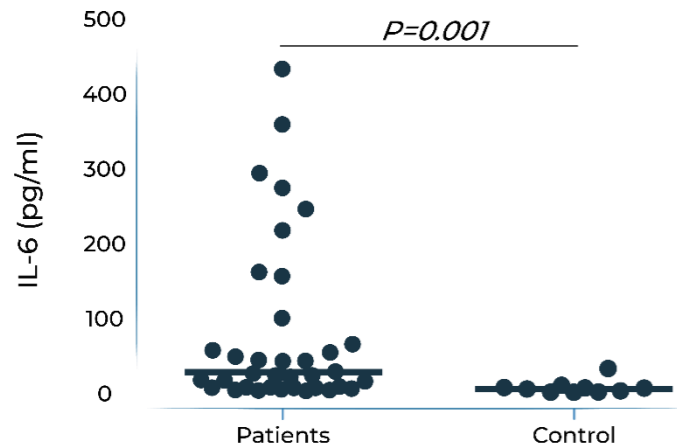
- Used for patients with persistent macular edema associated with inflammation that fail conventional therapies
- **However, the underlying inflammatory component of the pathophysiological process is not addressed by inhibiting VEGF alone**

**There is an unmet need for minimally invasive potent therapies with a better safety profile**

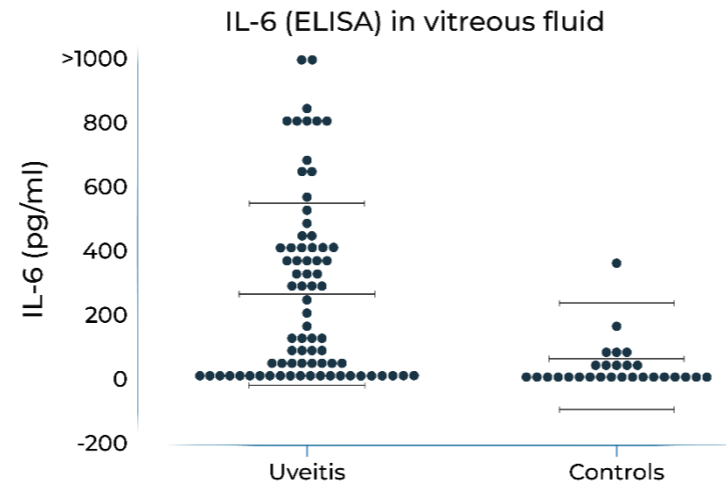
# Both IL-6 and VEGF play a key role in retinal inflammatory disease with IL-6 mediated pro-inflammatory signaling being a key disease driver

## IL-6 levels and role

Aqueous Humor IL-6 levels are elevated in patients with intermediate uveitis<sup>1</sup>

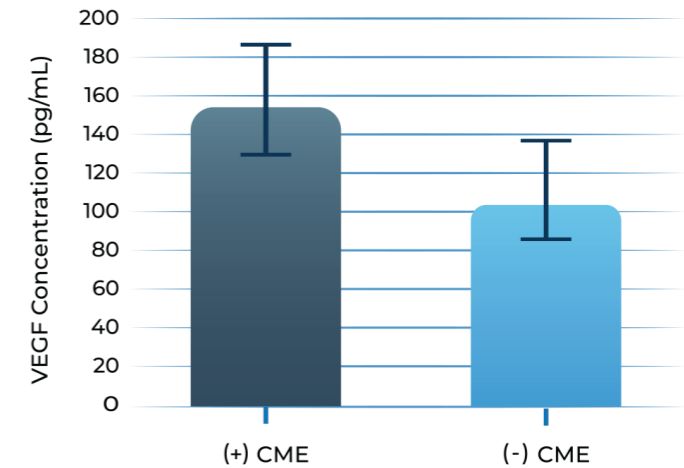


IL-6 levels are elevated in vitreous fluid of patients with active uveitis<sup>2</sup>



## VEGF levels and role

VEGF levels are elevated in aqueous humor of uveitis patients with macular edema vs without macular edema<sup>3</sup>



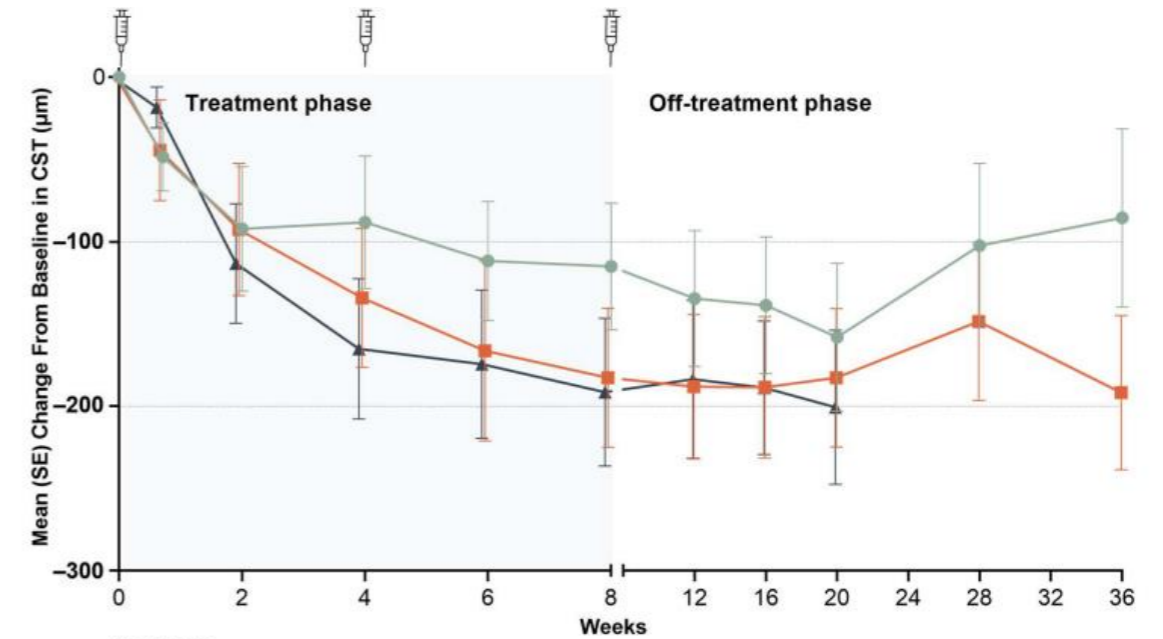
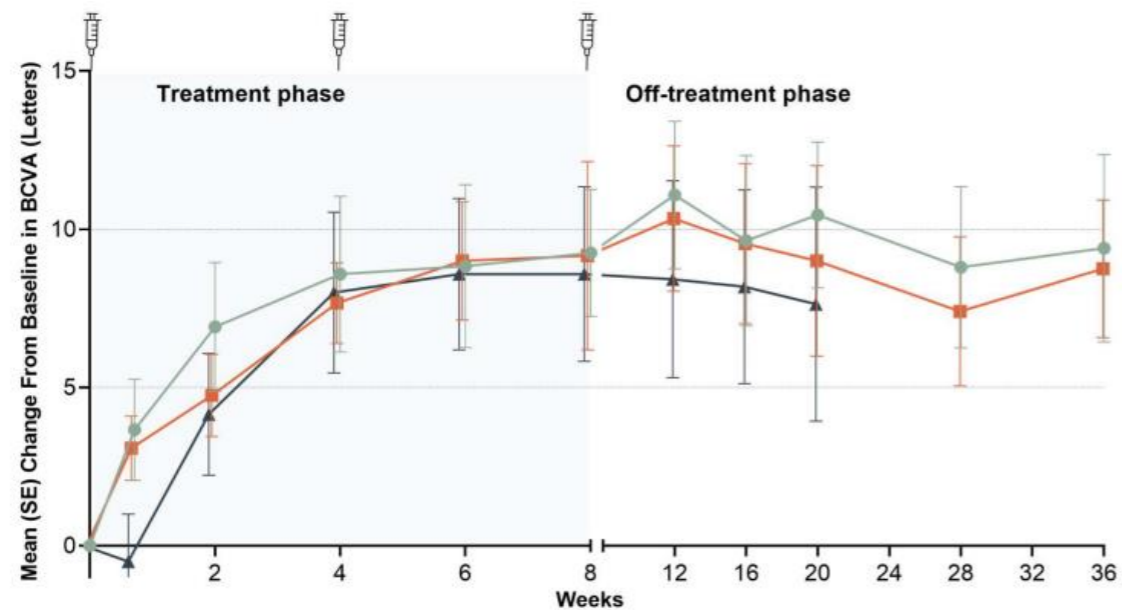
- IL-6 levels are elevated in ocular compartments and in serum in patients with non-infectious uveitis, and further elevated in uveitis patients with macular edema
- Signaling mediated by pro-inflammatory cytokines including IL-6 is a key disease driver of MESI because it leads to the disruption of the inner and outer blood-retina barrier and accumulation of fluid

- Persistent inflammation also triggers VEGF upregulation. VEGF levels are found to be elevated in aqueous humor of eyes with uveitis and uveitic macular edema, which can lead to angiogenesis, vascular leakage and blood-retinal barrier dysfunction

# Vamikibart (Roche, anti-IL-6) has shown that anti-IL-6 monotherapy can provide visual and anatomical improvement in patients with inflammatory macular edema

Change from Baseline in BCVA

Change from Baseline in CST

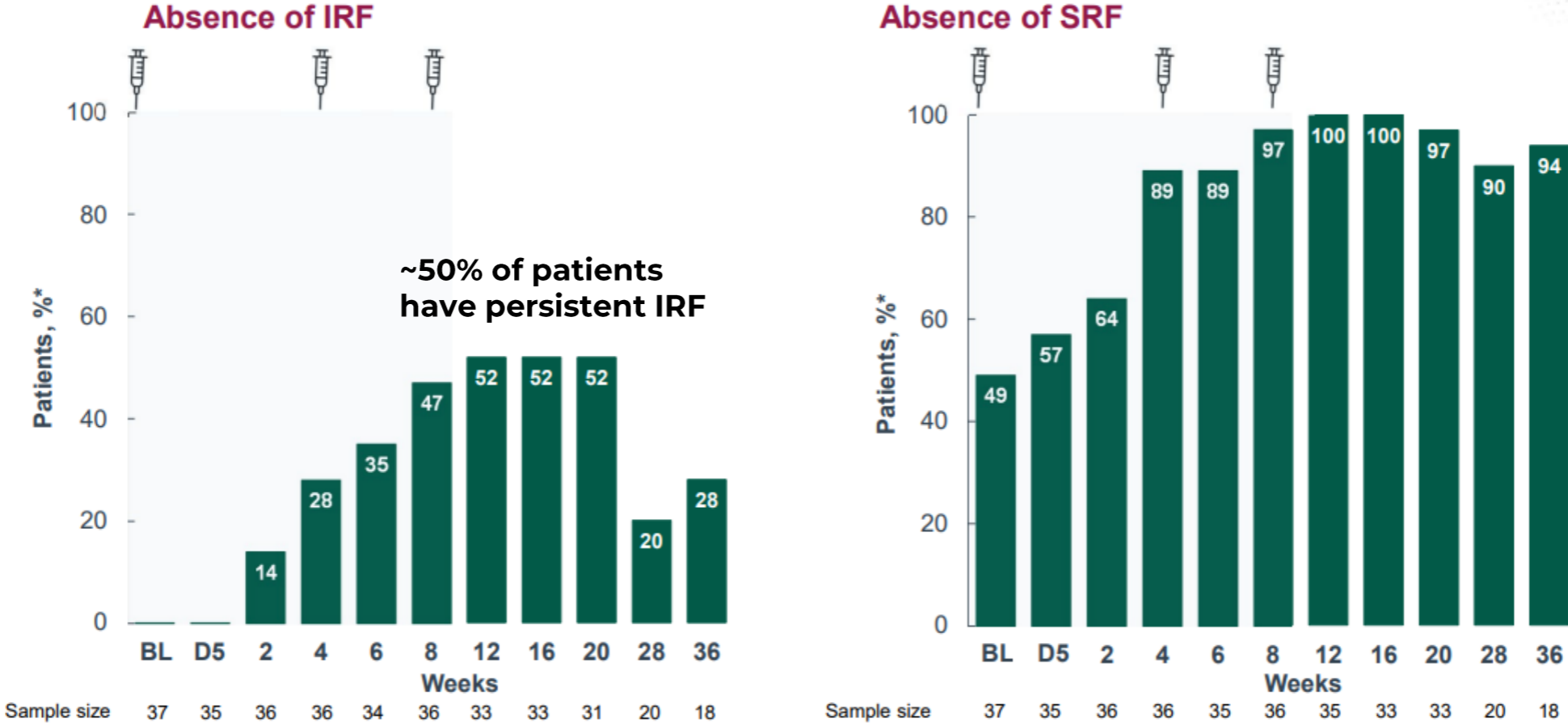


Sample size	0	2	4	6	8	12	16	20	28	36
0.25 mg (n)	12	12	12	12	12	12	11	11	10	10
1 mg (n)	12	12	12	12	11	12	11	11	10	8
2.5 mg (n)	13	12	13	12	12	12	11	11	2.5 mg cohort last F-up is W20	

Sample size	0	2	4	6	8	12	16	20	28	36
0.25 mg (n)	12	12	12	11	12	12	11	11	10	10
1 mg (n)	12	12	12	12	11	12	12	11	11	10
2.5 mg (n)	13	11	12	12	12	12	11	11	2.5 mg cohort last F-up is W20	

**A clear dose response is seen with IL-6 monotherapy in patient with inflammatory macular edema**

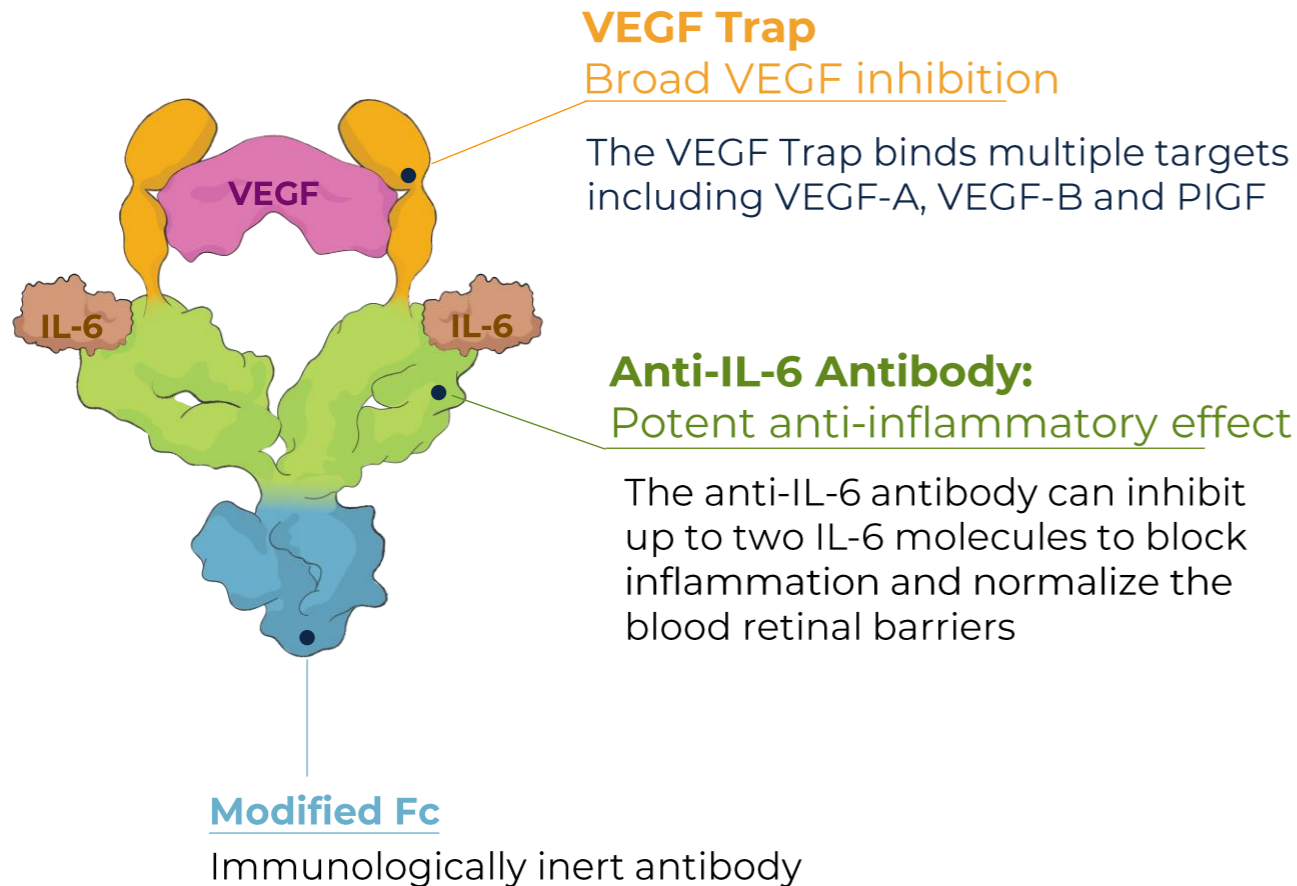
# While intravitreal IL-6 monotherapy is useful, ~50% of patients have persistent IRF, which is similar to the overall failure rate of systemic adalimumab<sup>1</sup>, leaving significant room for improvement



**Persistent intraretinal fluid (IRF) is known to cause deleterious and permanent effects in visual function**

# KSI-101 is a first-in-class bispecific protein for the powerful treatment of macular edema secondary to inflammation (“MESI”)

- KSI-101 is a bispecific protein designed to directly target both IL-6 mediated inflammation and edema, and VEGF-mediated vascular permeability



**The anti-inflammatory effect of IL-6 inhibition is the primary effector**, with the anti-permeability effect of VEGF inhibition having an additive and synergistic effect

With bispecific IL-6 and VEGF inhibition which confer a **synergistic anti-inflammatory and anti-permeability effect**, along with the proven safety profile of an intravitreal biologic, KSI-101 can become a first line therapy for all retinal diseases with an inflammatory component

# Phase 1b APEX study: multiple dose study of KSI-101 in patients with DME (Cohort 1) and macular edema secondary to inflammation (Cohort 2)

Actively recruiting

**Cohort 1: Subjects with treatment-naïve DME (n ~ 12)**

Weeks	0	4	8	12	16	20	24
2.5 mg	■	■	■	■	■		
5 mg	■	■	■	■	■		
10 mg	■	■	■	■	■		

**Cohort 2: Subjects with macular edema secondary to inflammation (MESI) (n ~ 36)**

Weeks	0	4	8	12	16	20	24
2.5 mg	■	■	■	■			
5 mg	■	■	■	■			
10 mg	■	■	■	■			

■ KSI-101 injection

End of Study

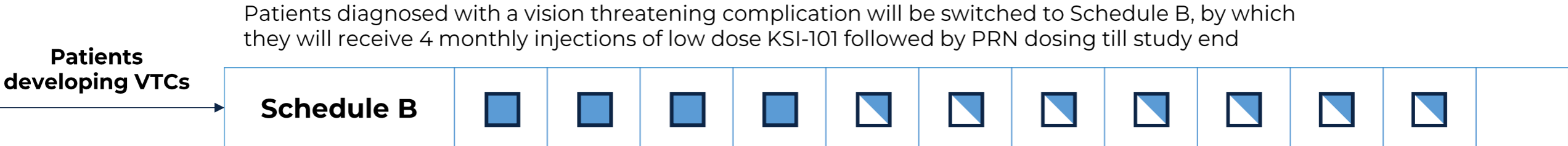
A low and high dose of KSI-101 will be selected to progress into dual Phase 2b/3 pivotal studies (PEAK and PINNACLE) in MESI

# Phase 2b/3 Studies PEAK and PINNACLE planned based on regulatory input: identically designed studies with primary endpoint at Week 16 and safety to Week 48

Weeks	0	4	8	12	16	20	24	28	32	36	40	44	48
<b>KSI-101 low dose (n ~ 75)</b>	■	■	■	■	◐	◐	◐	◐	◐	◐	◐	◐	
<b>KSI-101 high dose (n ~ 75)</b>	■	■	■	■	◐	◐	◐	◐	◐	◐	◐	◐	
<b>Sham (n ~ 75)</b>	○	○	○	○	○	○	○	○	○	○	○	○	

Primary endpoint

Last dosing visit Secondary endpoint



- KSI-101 low dose injection
- KSI-101 high dose injection
- Sham injection
- ◐ Individualized injection / sham

**Primary endpoint:** Proportion of eyes improving  $\geq 15$  ETDRS letters at **Week 16**



# KSI-101 has the potential to become an important medicine in treating pediatric patients with intraocular inflammation and macular edema

- Up to 15% of patients referred to tertiary uveitis clinics are pediatric patients
- Like adults, macular edema is a major vision-threatening complication in children with uveitis
- Following early indication of safety in APEX, a third pivotal cohort could be run in the pediatric setting towards an accelerated approval

## Management of pediatric patients presents unique challenges today



- **Diagnosis often delayed** with complications such as macular edema already present



- Systemic and local corticosteroids, immunosuppressants and biologics are often needed to treat macular edema—can take **>2 years to resolve**



- **Inflammation more likely to be recurrent or chronic** and can persist into adulthood

- **Macular edema can be refractory** to existing therapies



- **Risk of macular edema may increase over time** with persistent disease in some patients



- Systemic use of steroids or immunosuppressive agents have limited utility because they **have adverse effects on growth, nutrition, infectious diseases and fertility**

**There is a significant unmet need for effective and safe therapies that target underlying disease mechanisms in this patient population**

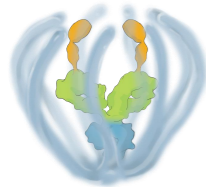
## Tarcocimab tedromer



### *Intended to be a mainstay intravitreal biologic monotherapy providing high efficacy and high durability and for use in all patients*

- Supported by our science of durability
- Enhanced formulation delivers “the pulse and the durability” while improving dose preparation, dose administration and safety
- 1 successful pivotal study away from BLA submission
- Phase 3 GLOW2 study in DR and Phase 3 DAYBREAK study in wet AMD are enrolling

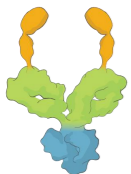
## KSI-501



### Designed to address the opportunity for improved efficacy with extended durability in high-prevalence retinal vascular diseases by targeting retinal inflammation and vascular permeability

- Supported by our science of durability
- Benefits from the science of immediacy and durability of the ABCD platform
- Phase 3 DAYBREAK study in wet AMD is actively enrolling, designed to explore the power of the dual MoA to deliver improved efficacy

## KSI-101



### A potent 100 mg/mL high strength bispecific protein being developed for the treatment of macular edema secondary to inflammation (MESI) for which no approved intravitreal biologic therapies exist today

- Uncorrelated from the ABCD platform
- In a greenfield market segment separate from the anti-VEGF market
- Potential to be a fast follower to Roche’s vamikibart (anti-IL-6) with differentiation of having dual inhibition MoA and a high strength 100mg/mL formulation
- Anticipated to be a low-risk asset with optionality
- Phase 1b APEX study is enrolling with objective to initiate twin pivotal studies in 1H2026

# AGENDA

Why Kodiak?	Victor Perloth, MD Chairman and CEO
Science of Durability	David Brown, MD
Science of the Enhanced Formulation	David Brown, MD
Roundtable Discussion	Moderator: Victor Perloth, MD Chairman and CEO
Audience Q&A	All
Clinical Program Overview	Charles Wykoff, MD, PhD
<b>The Kodiak Opportunity</b>	<b>Victor Perloth, MD</b> Chairman and CEO
Roundtable Discussion	Moderator: Victor Perloth, MD Chairman and CEO
Audience Q&A	All
ABCD Platform Preview	Dolly Chang, MD, PhD Chief Scientific Officer
Summary and Takeaways	Victor Perloth, MD Chairman and CEO
Audience Q&A	All

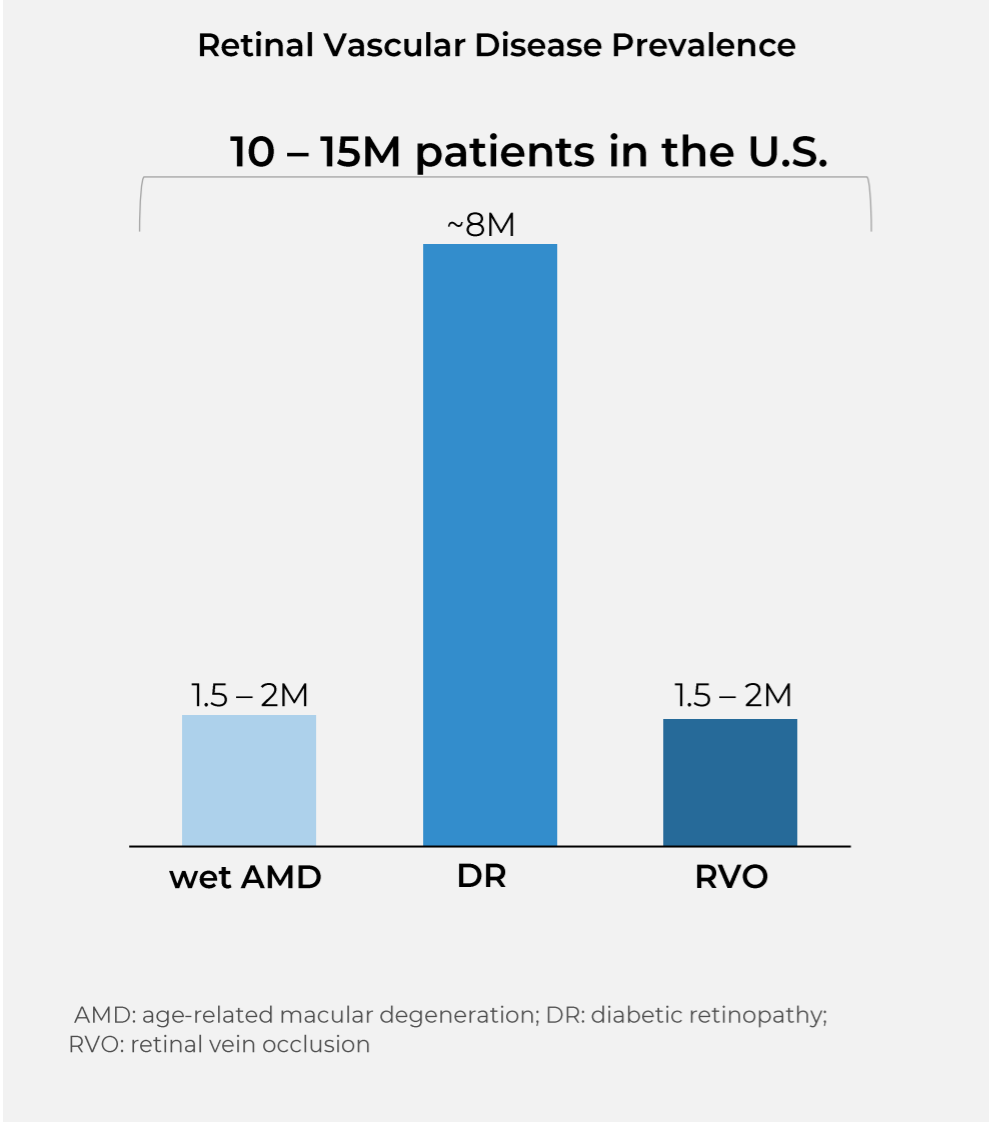
# THE KODIAK OPPORTUNITY



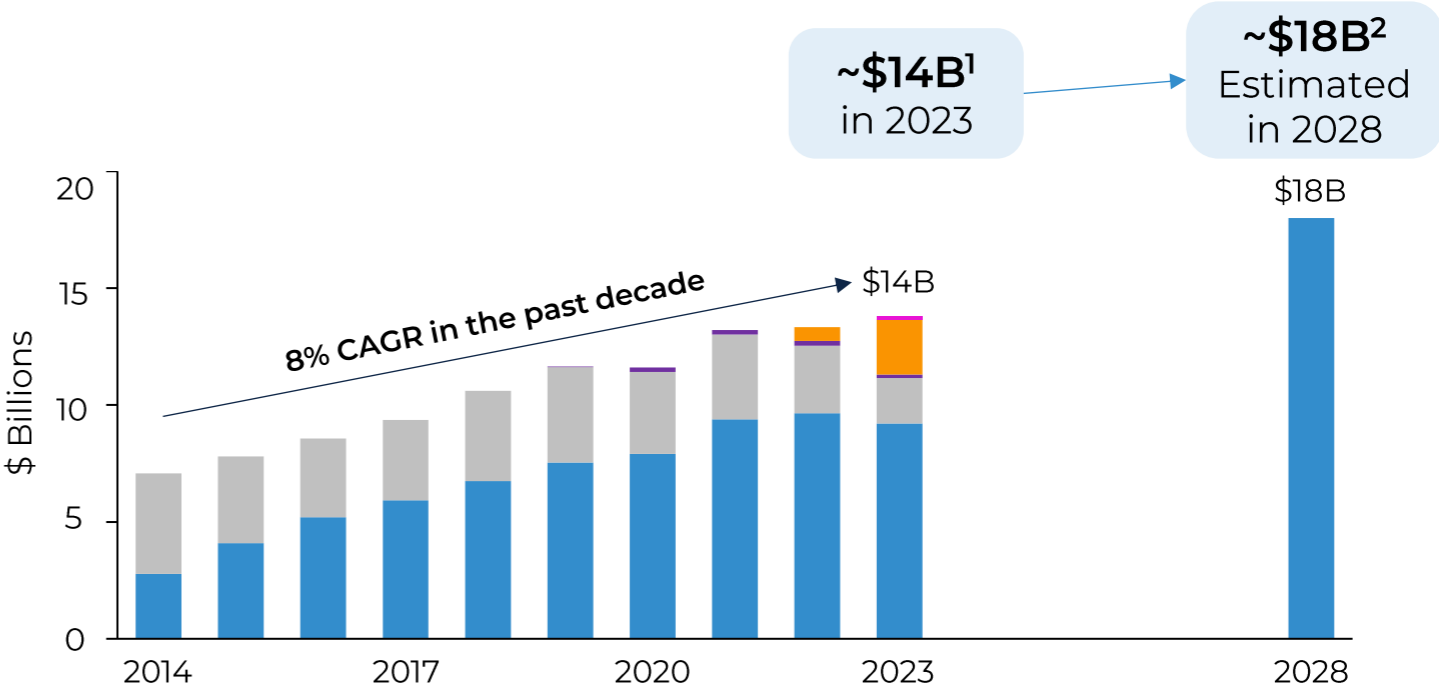
Victor Perloth, MD



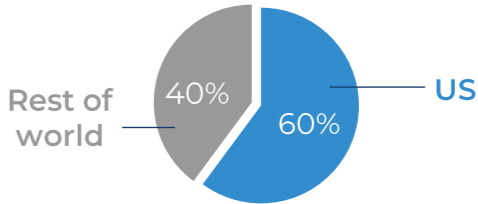
# Retinal vascular diseases remain a large and growing market driven by aging populations and increased prevalence of diabetes



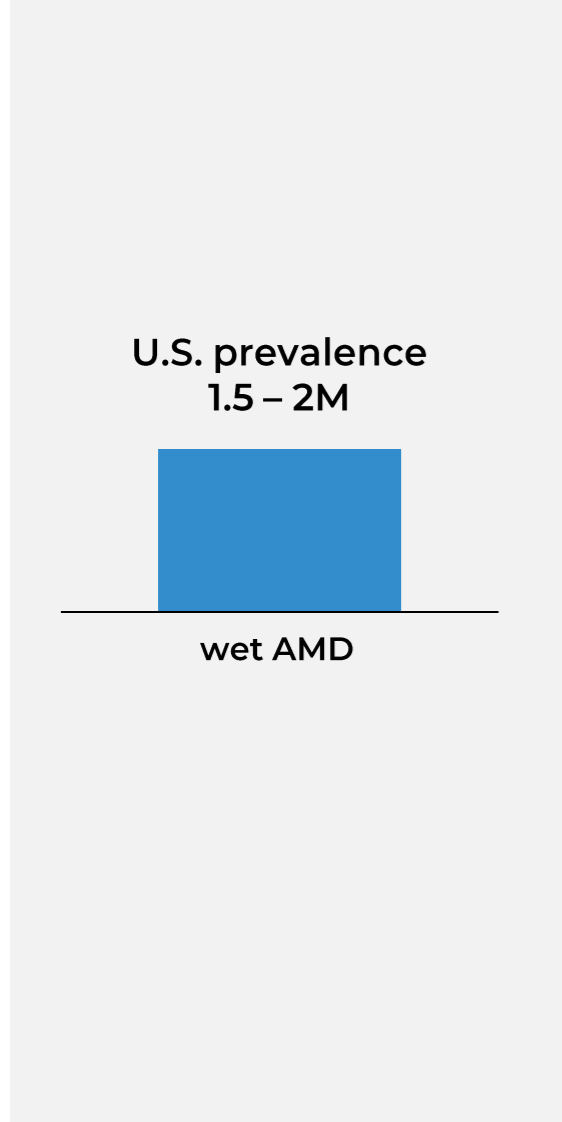
### Global Net Sales of Branded Intravitreal Biologics for Retinal Vascular Diseases



- U.S. remains the growth driver by geography
- 10% (US) vs 5% (rest of world) CAGR in the past decade



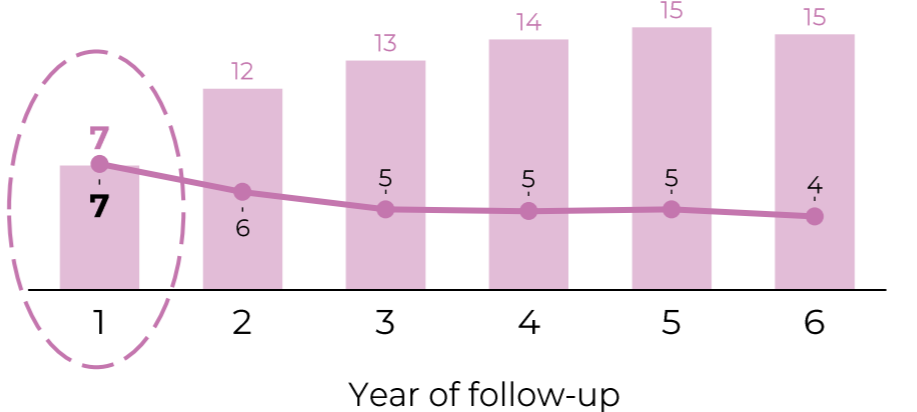
# In wet AMD, established Gen 1.0 anti-VEGF agents achieve modest vision gains in the real world and require frequent injections to maintain vision



- Gen 1.0 anti-VEGF agents achieve only modest vision gains in Year 1 despite frequent injections (7 injections with a mean interval of 7 weeks in between)

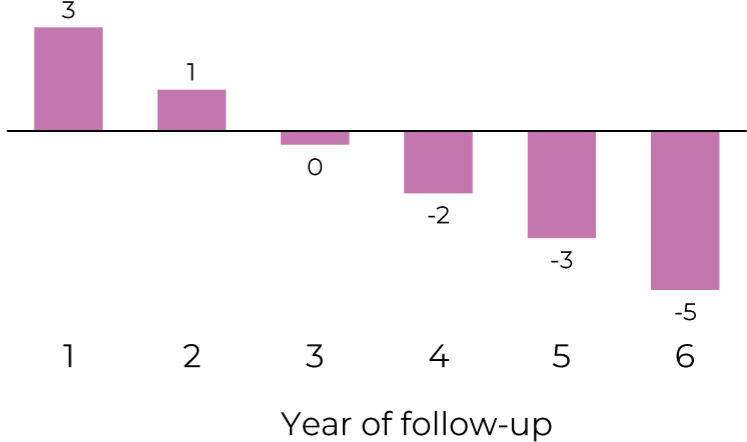
- Frequent injections are not sustained over the long term, which leads to vision loss over time

Real world treatment pattern of wet AMD patients<sup>1</sup>



● Mean no. of anti-VEGF injections per year      ■ Mean anti-VEGF injection interval (weeks)

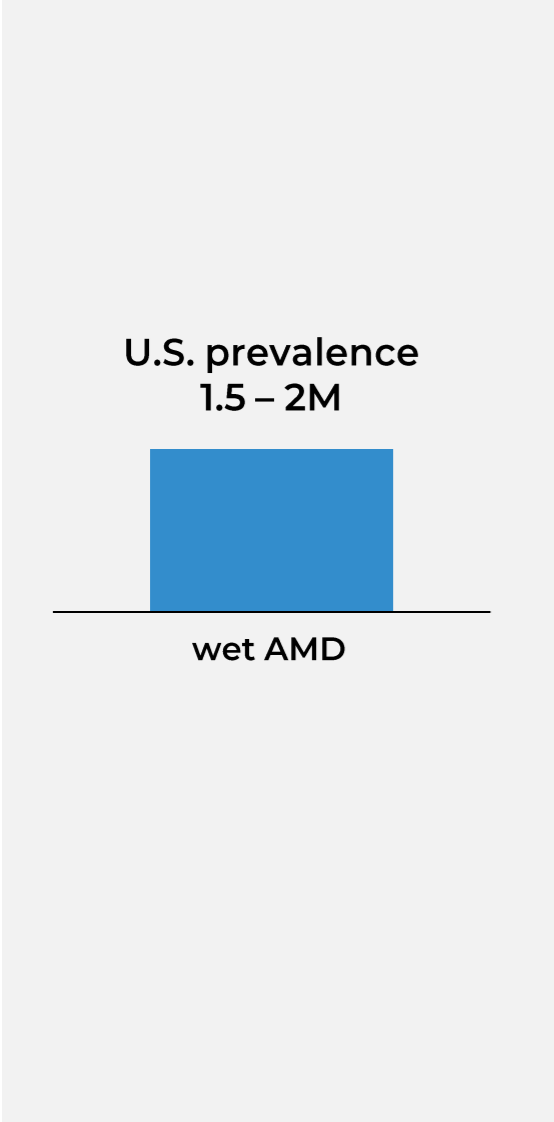
Real world visual outcomes of wet AMD patients<sup>1</sup>



■ Change in visual acuity from baseline (ETDRS letters)

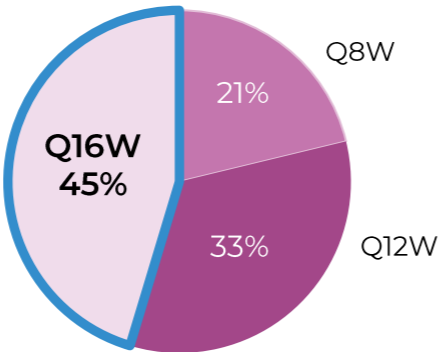
1. Adapted from Wykoff et al. Ophthalmology Science 2024; 4: 100421

# “Gen 1.5” anti-VEGFs provide modest dosing interval extension in the real world



- Accumulating evidence suggests newer anti-VEGF agents such as faricimab only achieves modest dosing intervals extension in real-world data
- **Real-world durability of faricimab does not match that demonstrated in Phase 3 studies<sup>1</sup>**

Phase 3 TENAYA / LUCERNE  
Year 1 treatment interval  
(Pooled analysis)

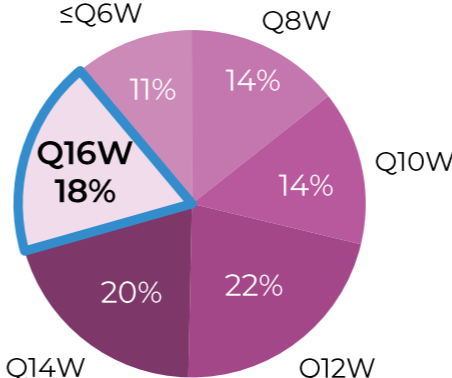


Q16W: 45%

Faricimab in wAMD  
Clinical Trials

Independent UK real-world data

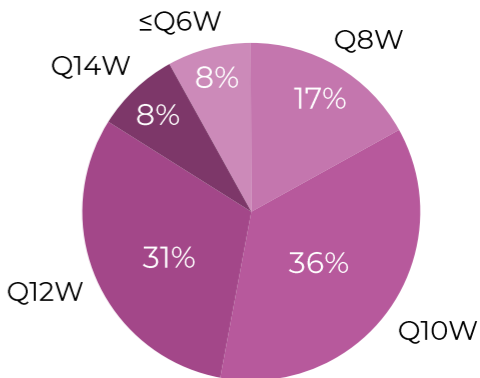
Year 1 Moorfields (n=172)



Q16W: 18%

Faricimab in wAMD  
Real World

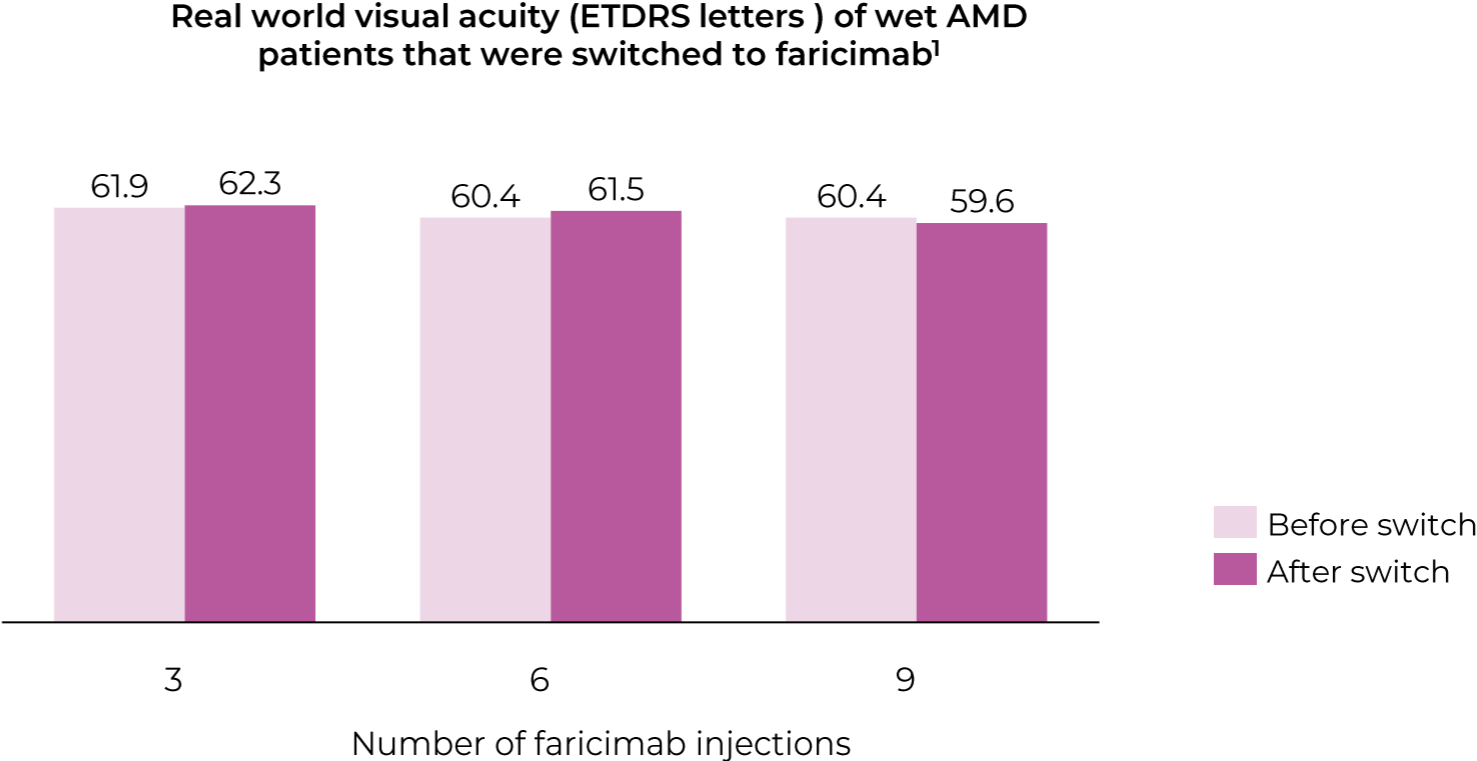
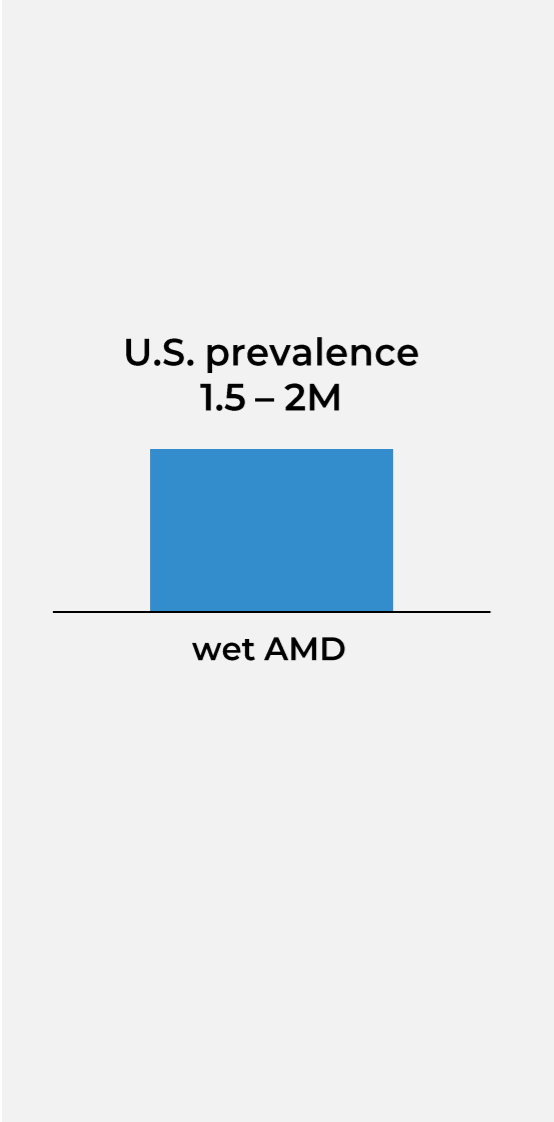
Year 1 Liverpool (n=101)



Q16W: 0%

# “Gen 1.5” anti-VEGFs also do not provide additional vision benefits in the real world over Gen 1.0 agents

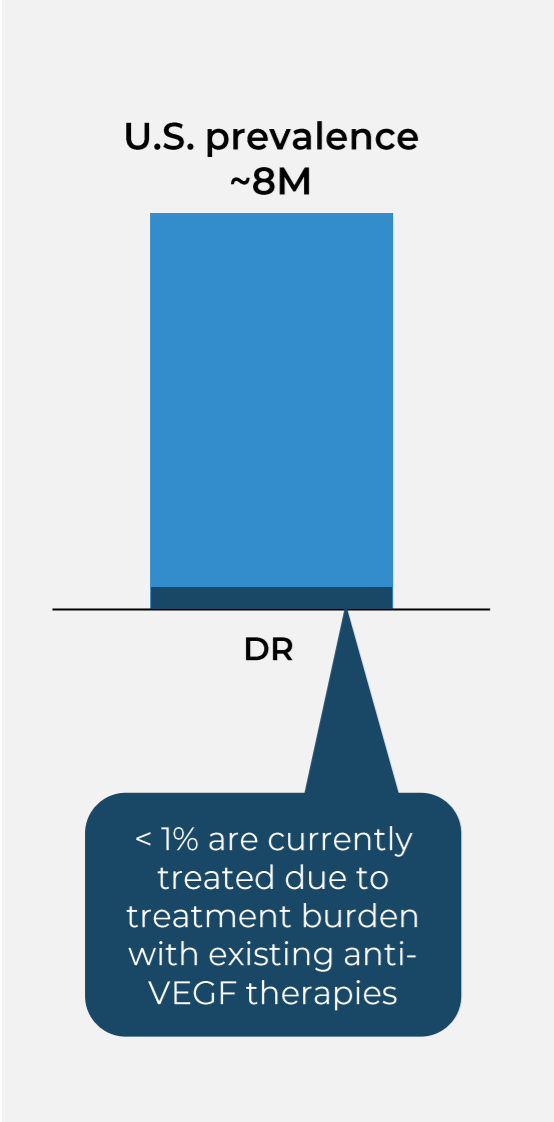
- Newer anti-VEGF agents such as **faricimab does not provide additional vision benefits in real-world data** compared to previously approved anti-VEGF agents



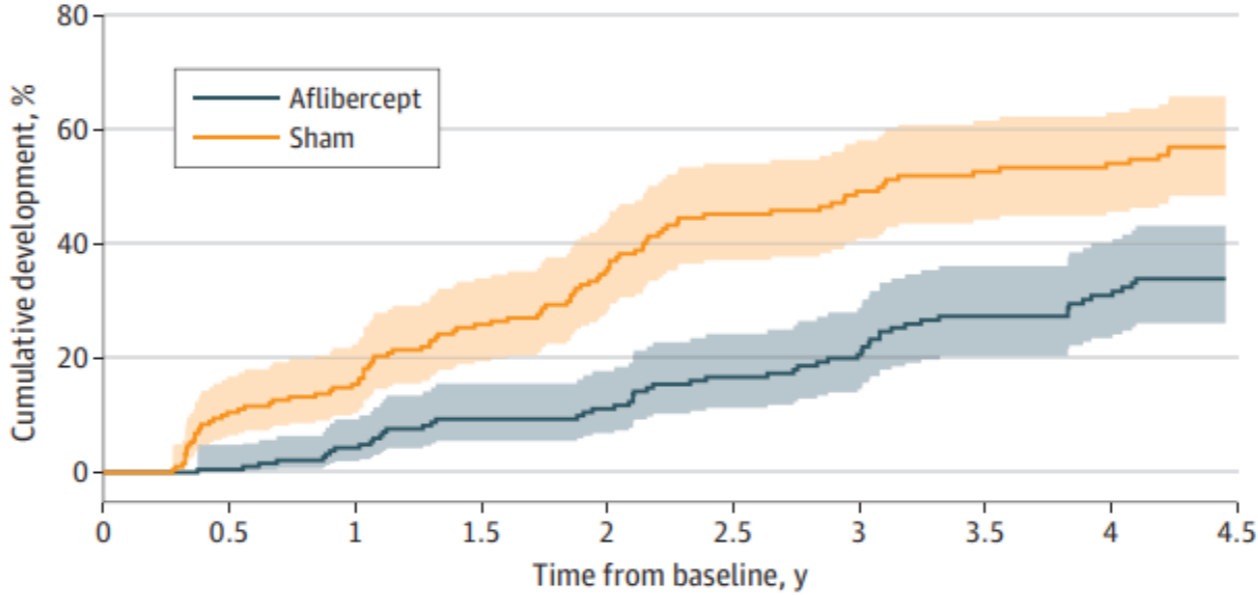
1. Adapted from Khanani presentation “The Real-World Efficacy and Safety of Faricimab in Neovascular Age-Related Macular Degeneration: The TRUCKEE Study – 2 years results” at Roche 2024 ASRS IR event



# In diabetic retinopathy, current “wait and watch” approach does not treat retinopathy or prevent progression to vision threatening complications

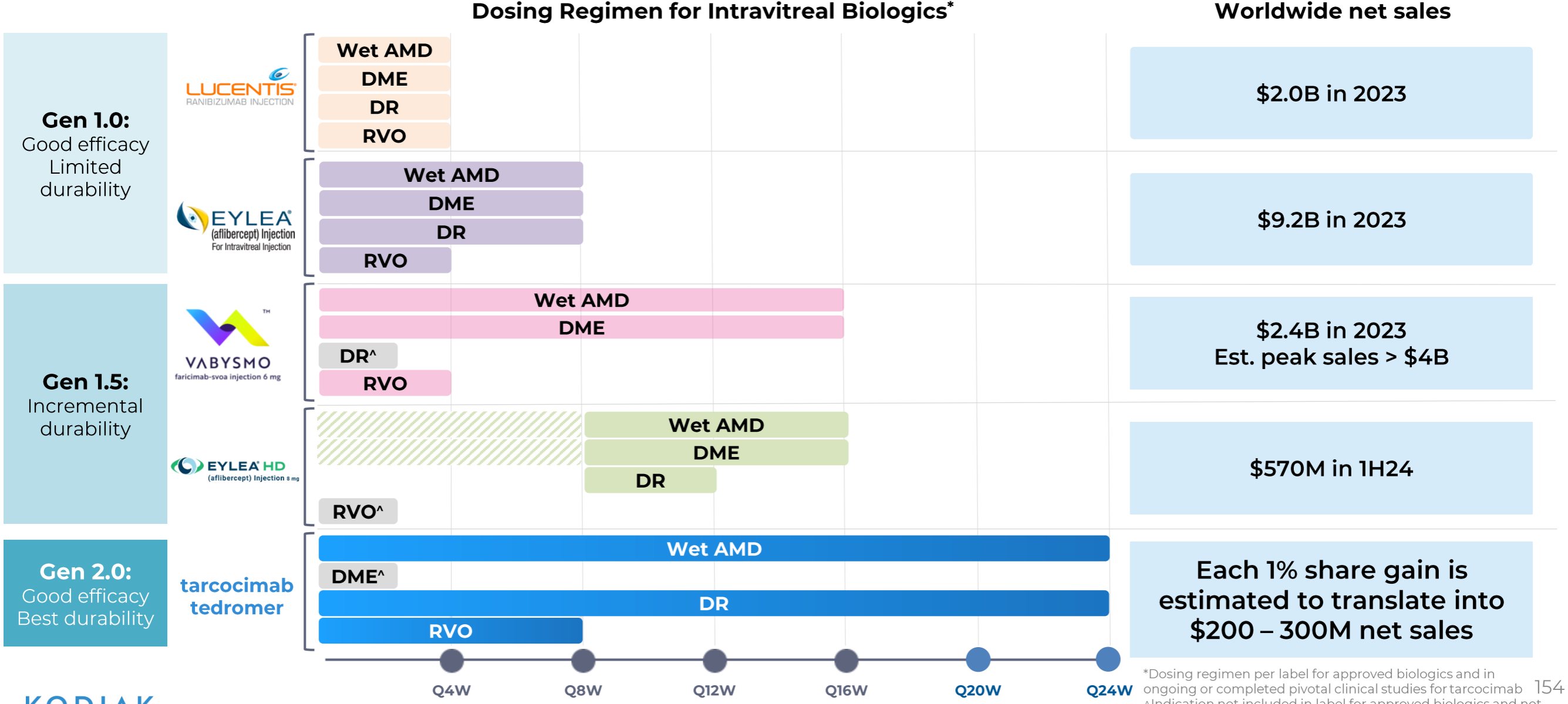


- Currently, patients with diabetic retinopathy are generally not treated given high treatment burden associated with frequent injections of approved therapies
- The “watch and wait” approach is known to result in progression of retinopathy and development of vision threatening complications



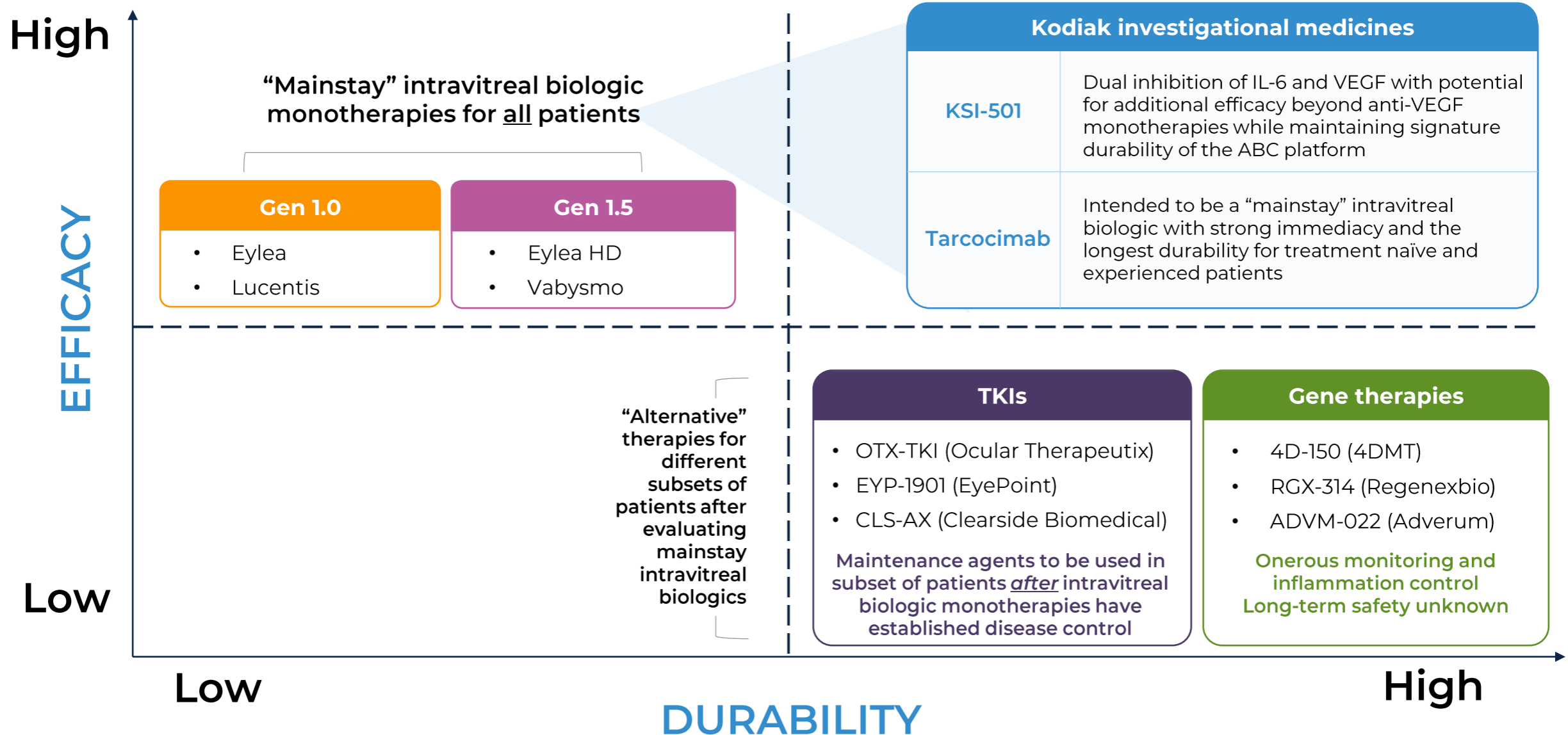
Left untreated, 57% of patients with NPDR progressed to PDR or developed CI-DME over 4 years<sup>1</sup>

# Despite limited differentiation and label limitations, each incremental improvement has resulted in blockbuster commercial opportunities for the mainstay biologics



\*Dosing regimen per label for approved biologics and in ongoing or completed pivotal clinical studies for tarcocimab  
 ^Indication not included in label for approved biologics and not expected to be in initial BLA for tarcocimab

Tarcocimab and KSI-501 are being developed as “mainstay” intravitreal biologic monotherapies that provide *high efficacy and high durability and a flexible 1-month through 6-month label*

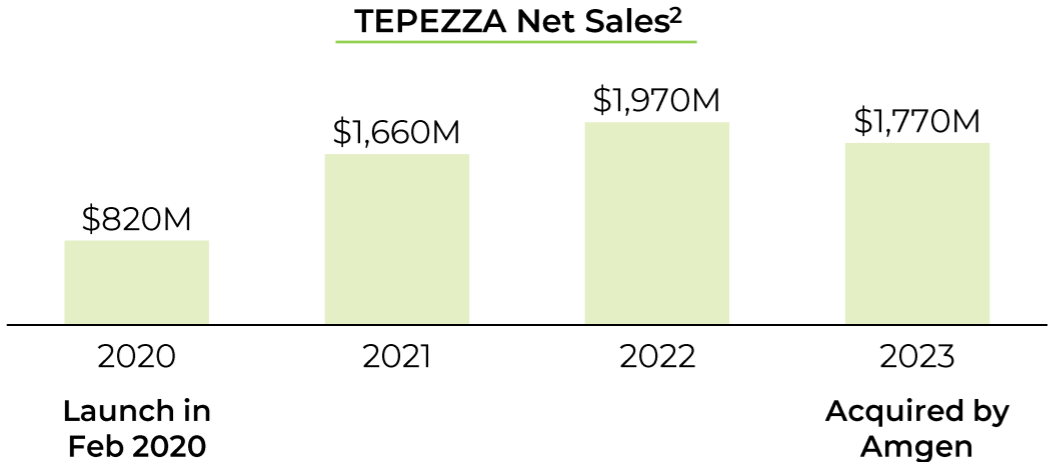


# In addition, KSI-101 has the potential to be an important and differentiated medicine in retinal inflammatory conditions, a greenfield market segment

## A relevant case study TEPEZZA in thyroid eye disease

**A Greenfield Market**

- Launched into a nonexistent market: high unmet need with no approved therapy
- Sales approached blockbuster status in 1<sup>st</sup> year of launch, substantially outperforming management expectation of “\$30 – 40 million”<sup>1</sup>



## The KSI-101 Opportunity

**Market opportunity**

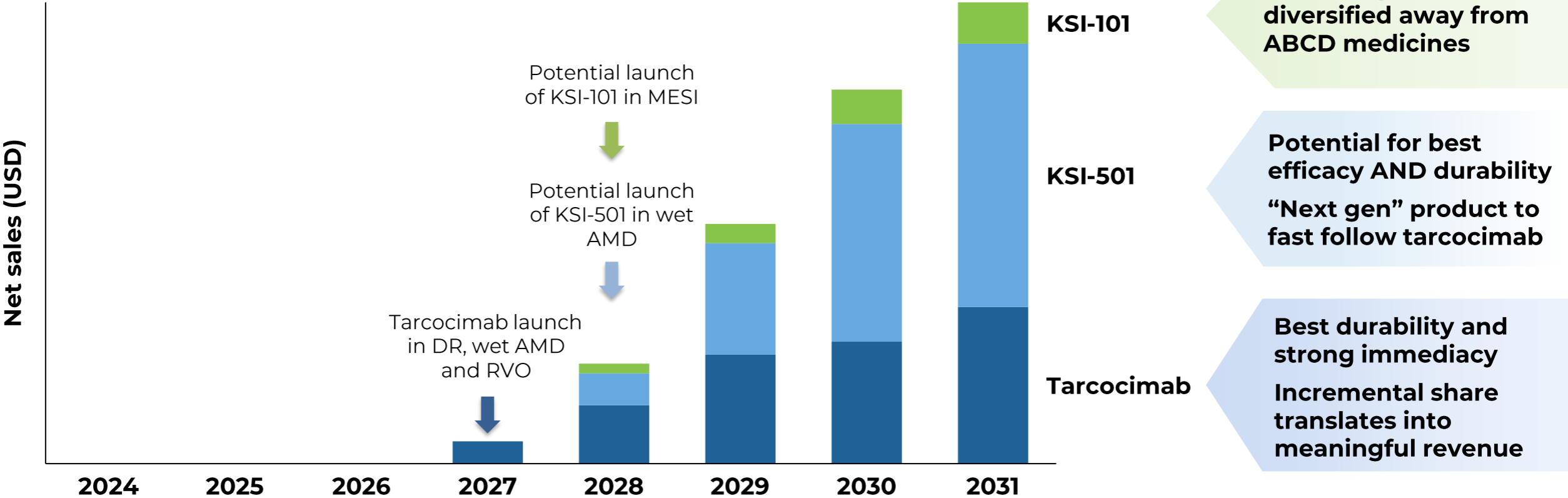
- **A similar greenfield market opportunity**
- Broad patient population
- High unmet need with no approved intravitreal biologics
- **Gateway indication** to a broad set of diseases; could include all retinal diseases that have inflammation and macular edema

**The KSI-101 Difference**

- **Dual inhibition** (anti-IL-6 and VEGF trap) with a **synergistic effect** on normalizing blood retinal barrier function vs. anti-IL-6 monotherapy
- **High strength formulation** (100 mg/mL) and **high potency** provide the fire power needed to treat “angry” inflammation and macular edema
- **Exploring accelerated development** options including pediatric population

# Kodiak's clinical portfolio has the potential to provide continued revenue stream starting from 2027, with built-in life cycle management and risk diversification

Net sales Potential of Kodiak Clinical Portfolio (Illustrative)



**Kodiak owns full commercial rights to our portfolio, which allows us the flexibility in our commercialization decisions to support adoption of our products**

# Longstanding and significant investment in commercial manufacturing has positioned Kodiak well to launch multiple ABCD products into large and growing markets

News Release

**Lonza**  
**KODIAK**

## Grand Opening of Kodiak Sciences' Purpose-Built Bioconjugation Facility to Support Potential Commercial Manufacture of KSI-301, an Antibody Biopolymer Conjugate for Retinal Diseases

- Purpose-built bioconjugation facility in Lonza's Ibex® Dedicate Biopark in Visp, Switzerland to support the potential commercial launch of Kodiak's lead product candidate KSI-301 for high-prevalence retinal diseases
- The opening ceremony took place on May 17, 2022 following mechanical completion of the facility in March 2022

**Basel, Switzerland and Palo Alto (CA), USA, 18 May 2022** – Kodiak Sciences Inc. (Nasdaq: KOD), a biopharmaceutical company committed to researching, developing and commercializing transformative therapeutics to treat high prevalence retinal diseases, and Lonza announced today the opening of a new, custom-built, bioconjugation facility within Lonza's Ibex® Dedicate manufacturing complex in Visp (CH).

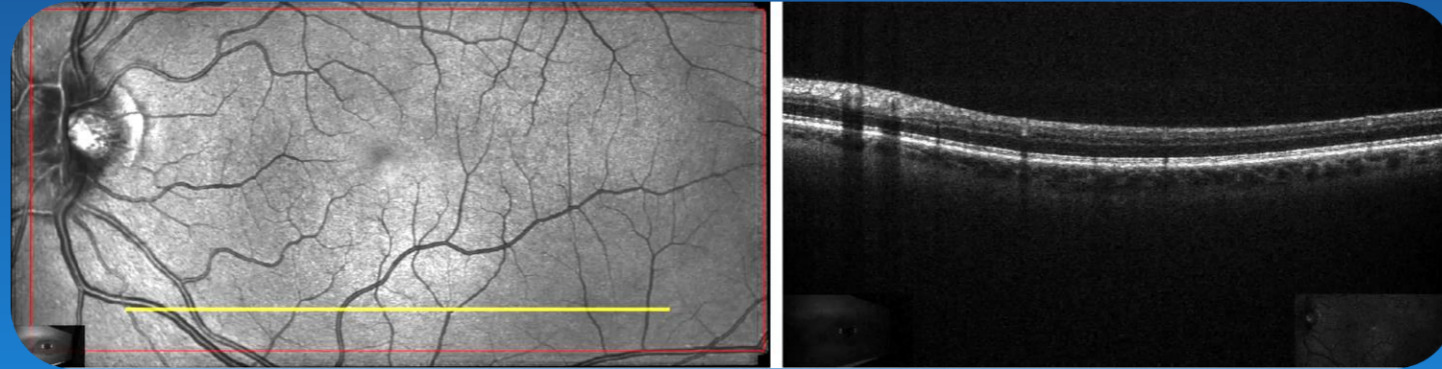
### *Ursus, a premium commercial manufacturing facility*

- A commercial scale facility dedicated to the manufacture of Kodiak's ABC medicines
- Custom designed for large scale **premium manufacturing of complex antibody conjugate biotherapies**
- Mechanical completion in 1H2022; commissioned as a cGMP facility in Jan 2023
- Successfully manufactured and released commercial scale cGMP of tarcocimab tedromer enhanced formulation in Nov 2023

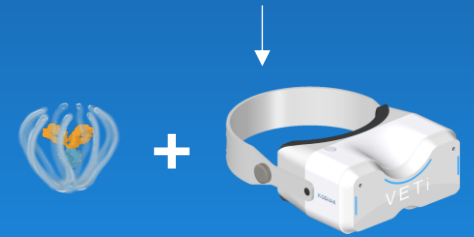


# VETi as Part of Kodiak's Commercial Franchise

Retinal images  
by VETi



VETi + tarcocimab  
for home monitoring



VETi + AI  
Many applications

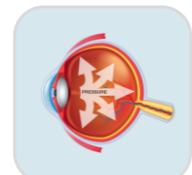
## Ophthalmology



Fluid Analysis



DRSS Scoring



Glaucoma  
Analysis



Pupillometry

## Neuro/Cardio



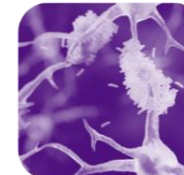
Metabolic  
Analysis



Blood Oxygen



Parkinson's  
Analysis



Alzheimer's  
Analysis

## Consumer



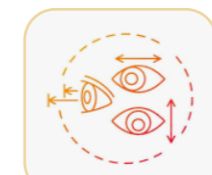
Train Your  
Brain



Visual Acuity



Biological  
Age



Train Your  
Vision

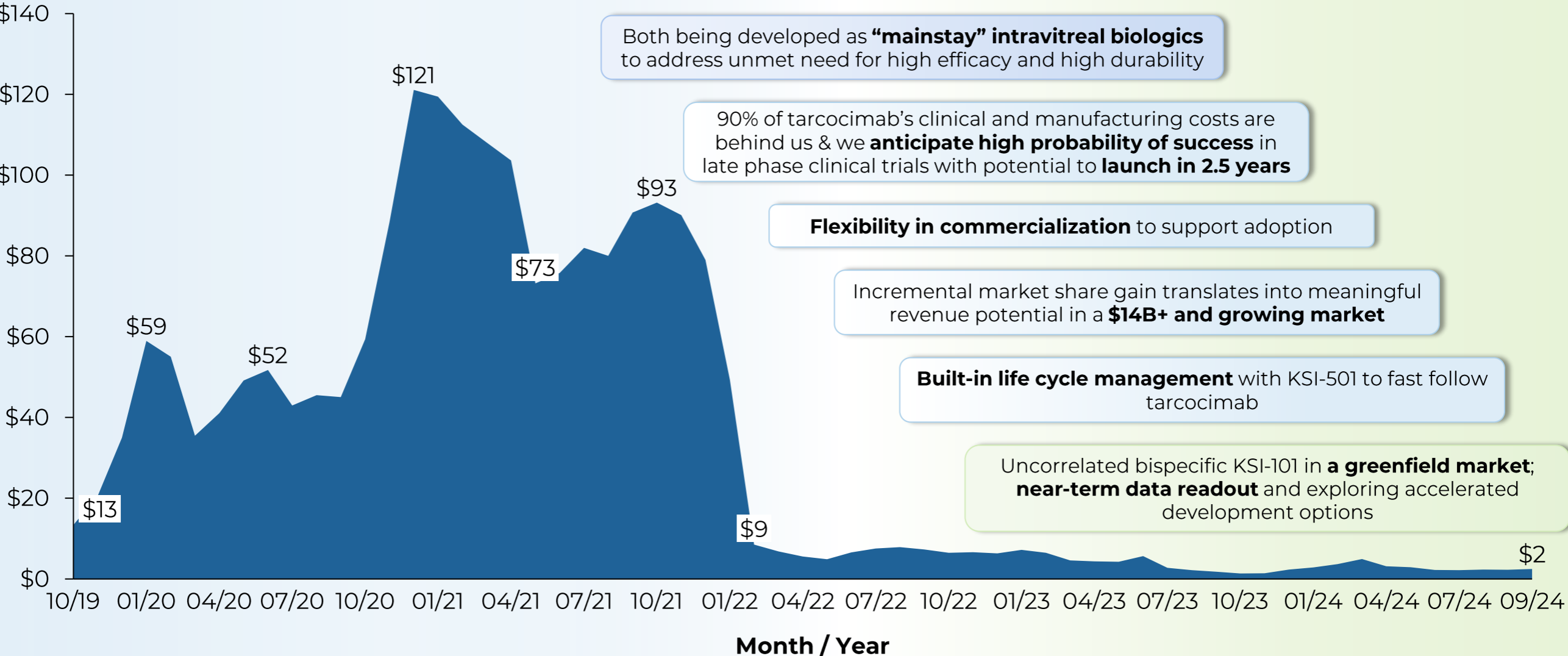
## Government



Population  
Health

**The Kodiak Opportunity: In our 15-year history we have made mistakes. The 3 clinical programs in our pipeline utilize the learnings from these mistakes to increase the probability of rebuilding significant value over the next several years.**

**Historical Stock Price of KOD (USD)**



Two ABCD investigational medicines built with **proprietary science of durability** and **enhanced formulation**

Both being developed as **“mainstay” intravitreal biologics** to address unmet need for high efficacy and high durability

90% of tarcocimab’s clinical and manufacturing costs are behind us & we **anticipate high probability of success** in late phase clinical trials with potential to **launch in 2.5 years**

**Flexibility in commercialization** to support adoption

Incremental market share gain translates into meaningful revenue potential in a **\$14B+ and growing market**

**Built-in life cycle management** with KSI-501 to fast follow tarcocimab

Uncorrelated bispecific KSI-101 in a **greenfield market**; **near-term data readout** and exploring accelerated development options



# AGENDA

Why Kodiak?	Victor Perloth, MD Chairman and CEO
Science of Durability	David Brown, MD
Science of the Enhanced Formulation	David Brown, MD
Roundtable Discussion	Moderator: Victor Perloth, MD Chairman and CEO
Audience Q&A	All
Clinical Program Overview	Charles Wykoff, MD, PhD
The Kodiak Opportunity	Victor Perloth, MD Chairman and CEO
<b>Roundtable Discussion</b>	<b>Moderator: Victor Perloth, MD</b> Chairman and CEO
Audience Q&A	All
ABCD Platform Preview	Dolly Chang, MD, PhD Chief Scientific Officer
Summary and Takeaways	Victor Perloth, MD Chairman and CEO
Audience Q&A	All

# ROUNDTABLE DISCUSSION

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## Moderator



**Victor Perloth, MD**  
Chairman and CEO

## KOL Participants



**David Brown, MD**



**Charles Wykoff, MD, PhD**

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Q&A

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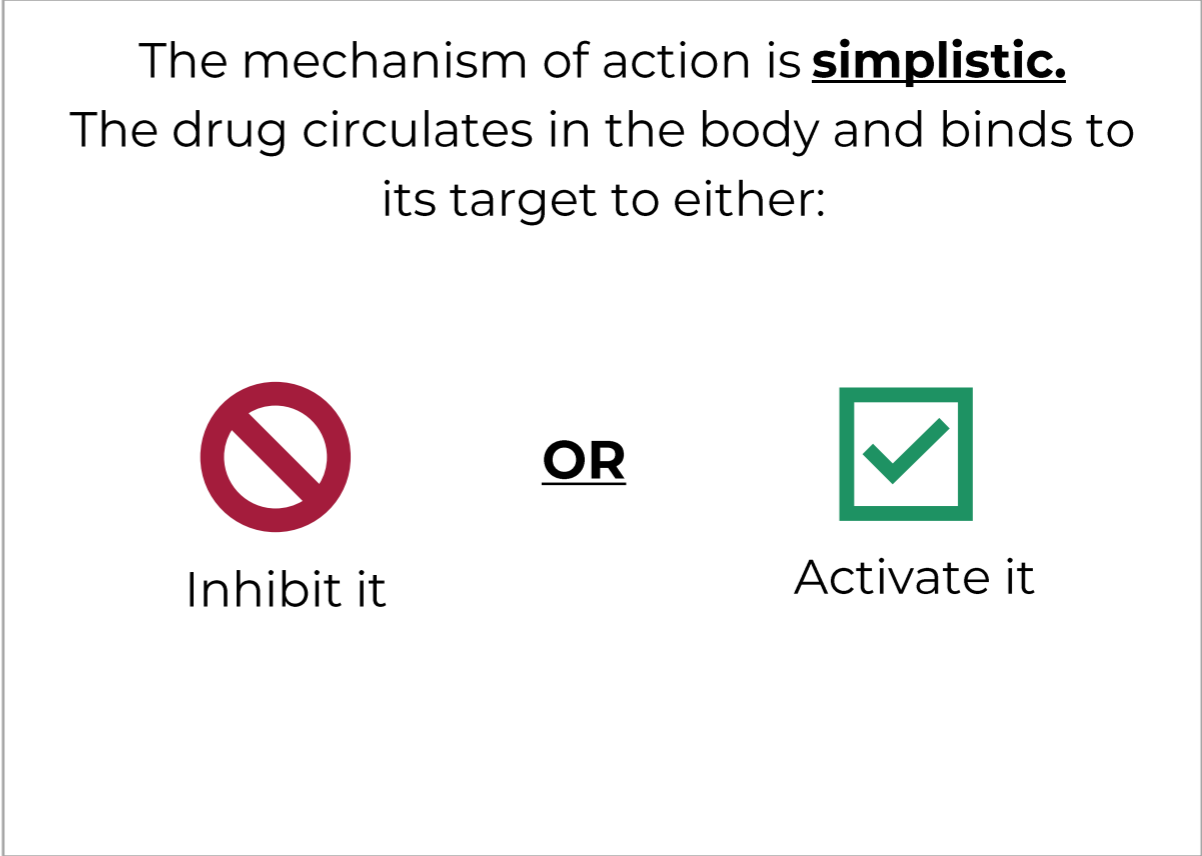
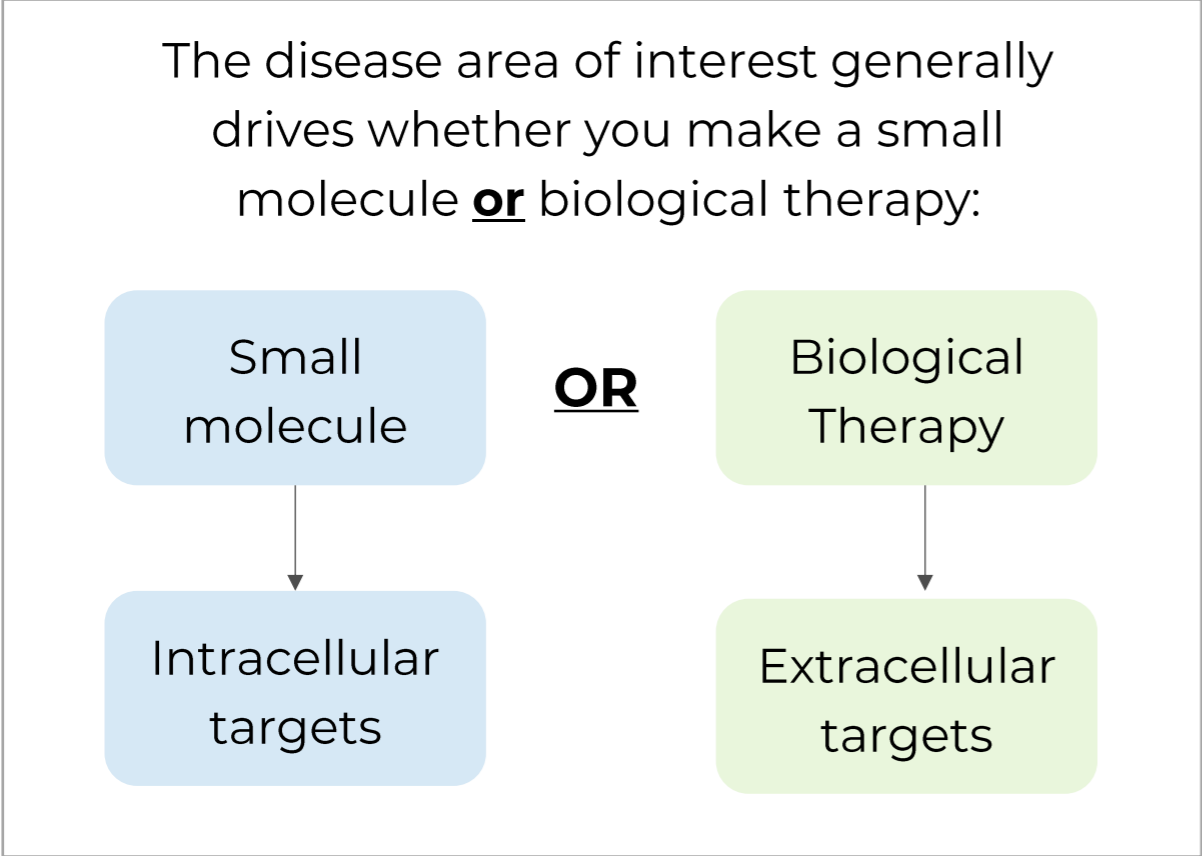
**Dolly Chang, MD, MPH, PhD**  
Chief Scientific Officer

ANTIBODY BIOPOLYMER CONJUGATE DRUG

A B C D

PLATFORM

# Today's medicines are designed based on the traditional “one drug-one target” approach



**This approach, while effective in many cases, may oversimplify complex biological systems and miss potential synergistic effects**

# Recent advancements in drug development are promising but have limitations

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RNAi Therapeutics

**Limited to liver and muscle.** Challenges with bioavailability, tissue specificity, limited cellular uptake

Bispecific and Trispecific Antibodies

**Limited to extracellular targets** and may have limited tissue penetration

Peptides and Small Protein Scaffolds

**Short residence time** and requires frequent redosing; patients may suffer from tolerability issues due to high Cmax

Antibody Drug Conjugates

**Limited DAR of 1-8** restricts use of drugs to cytotoxins or radioligands, which often have tolerability issues

Gene and Cell Therapies

**Significant challenges with immunogenicity,** tolerability and the ability to re-dose



# What if you could take a disease and impact it from many perspectives all at once?

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The medicine can be targeted **to a tissue of your choice**

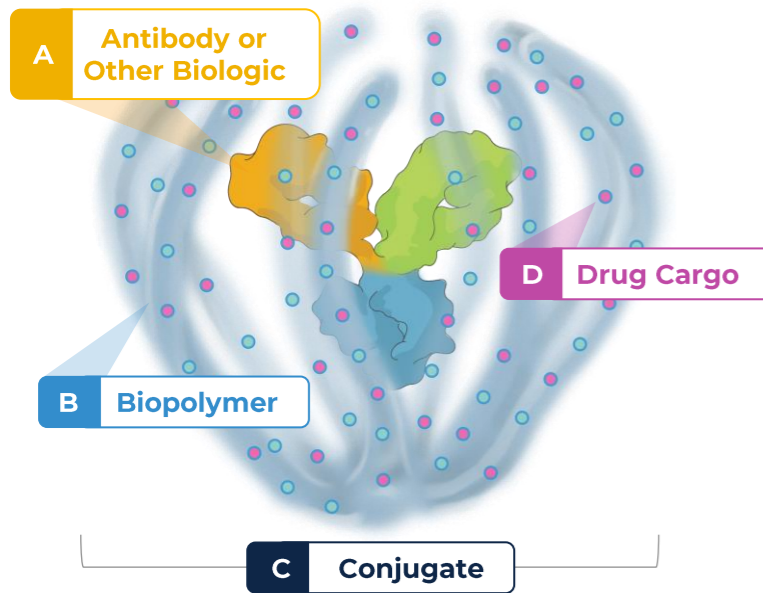
You can include **both intracellular and extracellular** mechanism of actions

You have the **flexibility on the number of different APIs** (2,3,4,5) and on the **number of each** (10s or 100s per API)

You can **tailor the pharmacokinetic profile per API**, such as fast or slow onset, fast or slow clearance, high or low cMax

This new drug concept is **designable, manufacturable and intended to be safe**

# Antibody Biopolymer Conjugate Drug (“ABCD”)



For targeted, high drug loading, multi-specific and tailored modulation of biological pathways

## Conjugates of diverse APIs

- Proteins, peptides, macrocycles, oligonucleotides, small molecules, antibodies can be embedded in the biopolymer

## High drug-antibody-ratio (DAR)

- Antibody targeted
- Targeting moiety can be expanded to protein, peptides or macrocycles
- APIs with DAR of 15 up to >250

## Tailored Release of APIs

- Release of payloads with tunable release rates enabled by pH modulation and/or enzymatic cleavage of linkers

## Embedded in phosphorylcholine biopolymers

- APIs of differing biophysics (size, solubility, charge) are embedded in a high biocompatibility phosphorylcholine biopolymer backbone

# The ABCD Platform is modular and each component (ABCD) can be custom designed and developed

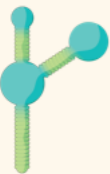
## Antibody or Other Biologic



**Antibody**  
(including monospecific, bispecific, and trispecific)



**Fusion Protein**



**Aptamer**

## Biopolymer

(Copolymer is customizable to match therapeutic need)



### 9-arm

- 10% drug loading
- 500 or 750kD
- DAR of 166 or 250



### 3-arm

- 3% or 10% drug loading
- 150 or 250kD
- DAR of 15 to 83



### Copolymers of variable sizes and percent loading

- Copolymer arm length and percent loading are both customizable

## Drug Cargo

(Diverse payloads with varying biophysical properties)



**Small molecules**



**Macrocycles**



**Peptides**

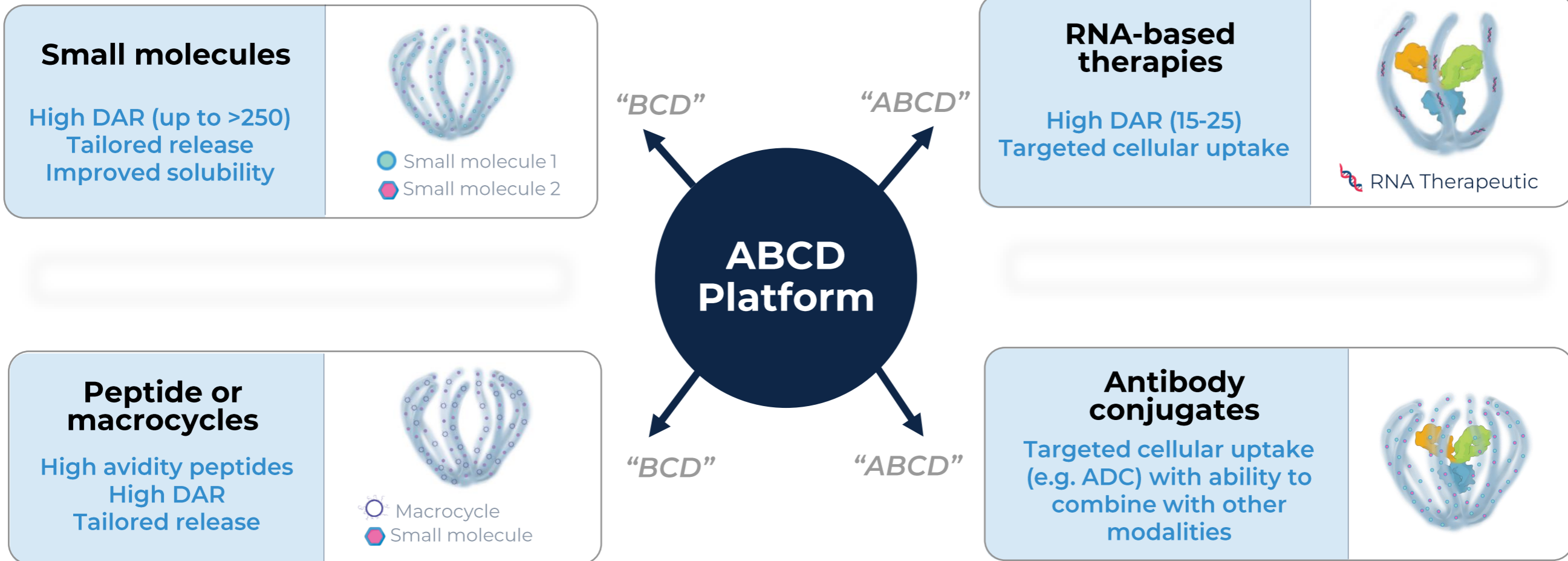


**Oligonucleotides**

Each drug cargo has a customizable release rate ( $t_{1/2}$ ) of 5 days, 10 days, 20 days or 30 days

Imagine the many possibilities where Kodiak can design a customized ABCD for your disease area of expertise?

# Tailoring the ABCD Platform: customized solutions for diverse therapeutic modalities



# GLAUCOMA

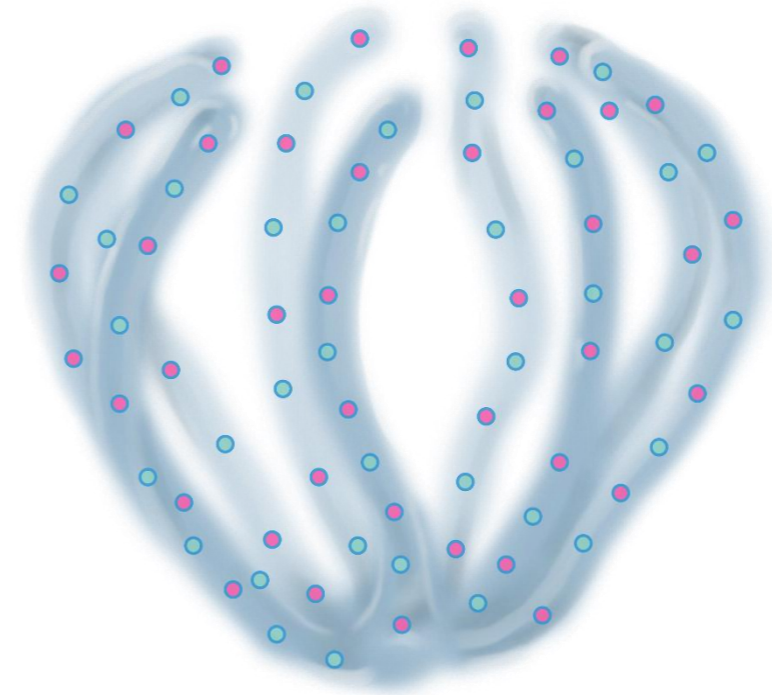
## Unmet need:

Current therapies focus on lowering intraocular pressure ("IOP") only, but many patients continue to experience disease progression and retinal damage

## ABCD Platform opportunity:

- NLRP3 inhibitors provide retinal neuroprotection
- Sustained release of an IOP lowering agent could replace or augment topical application

## Biopolymer with Small Molecules



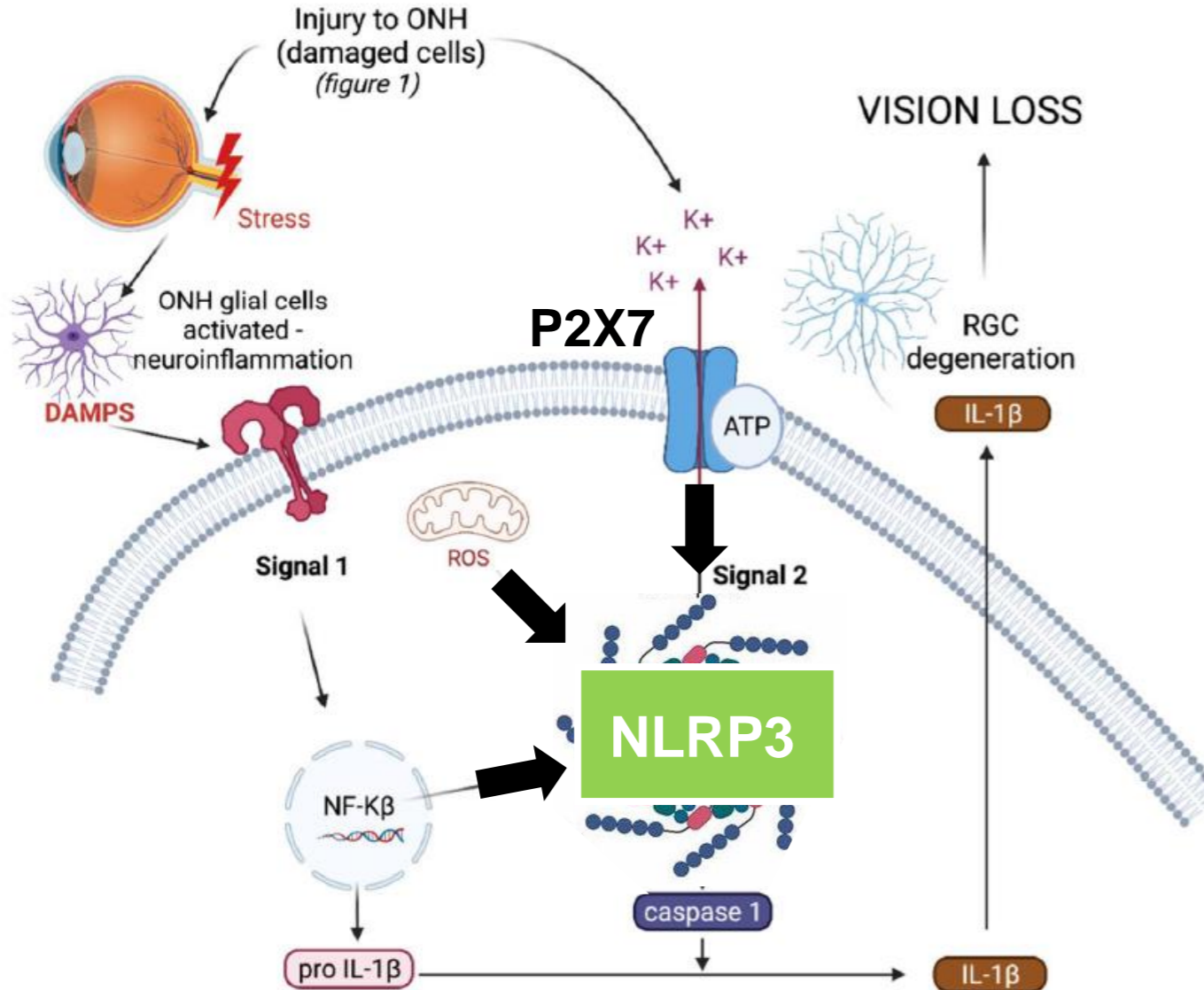
NLRP3i  
(neuroprotection)



IOP lowering agent

Administered via intravitreal injection

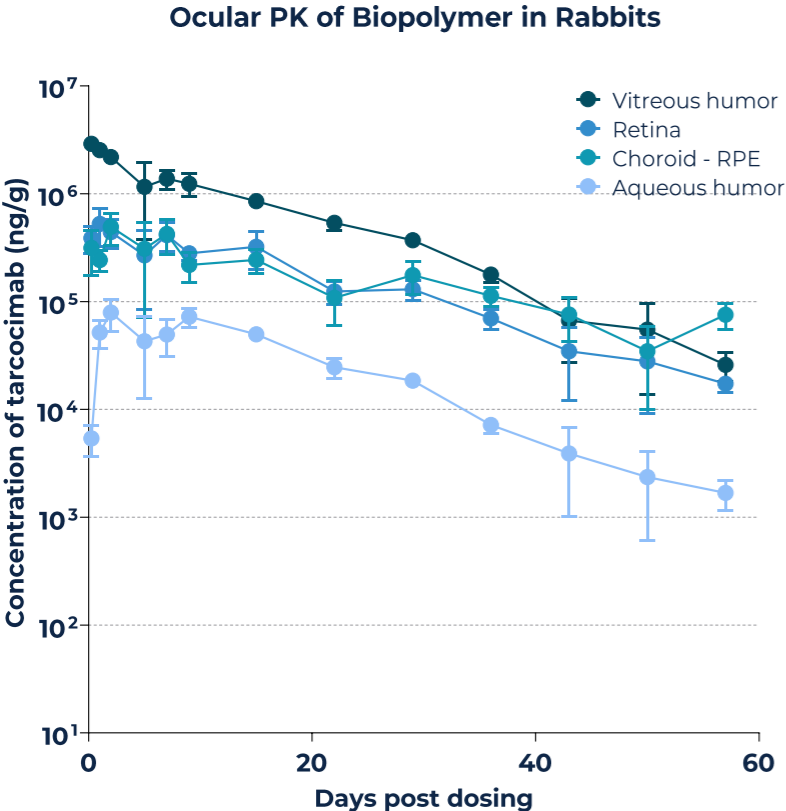
# NLRP3 a novel intracellular target for glaucoma neuroprotection



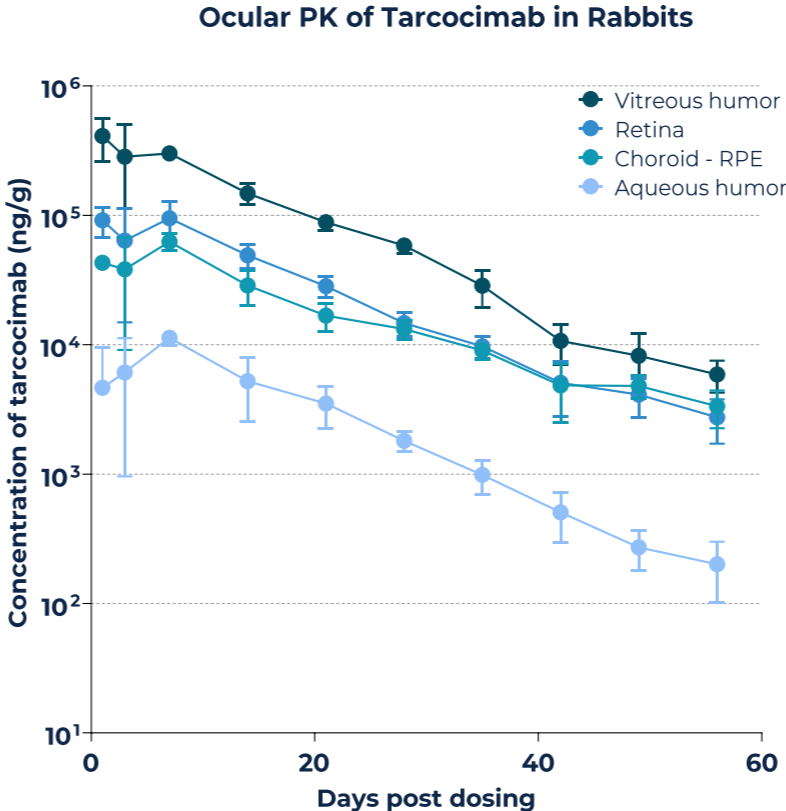
- **NLRP3 inflammasome contributes to optic nerve damage and retinal ganglion cell death**
  - NLRP3 inflammasome is activated in glaucoma<sup>1,2</sup>
  - Genetic and inhibitor data suggests a role for NLRP3 in preclinical models<sup>1, 3, 4</sup>
  - NLRP3 pathway perturbations show preclinical efficacy<sup>5</sup>
- **Intracellular NLRP3 inhibition is challenging**
  - Limitations of traditional small molecule approach
  - Overcoming ocular clearance limitations with the ABCD platform

Kodiak's proprietary biopolymer technology provides the backbone and the durability – the biopolymer alone demonstrates similar ocular tissue biodistribution and pharmacokinetics as tarcocimab and Kodiak's ABCD medicines

Biopolymer alone



Biopolymer + Antibody



Ocular half-life

Biopolymer	Tarcocimab
11.6	11.1

(Days)

# Tailored drug design: harnessing the ABCD platform for the glaucoma “duet”

## KEY INSIGHTS

### Extended Ocular Half-Life

- The biopolymer alone has a similar ocular half-life to Antibody Biopolymer Conjugates (“ABC”)

### Sequential Conjugation & Payload Release

- Multiple distinct drug linkers “clickable” onto a single copolymer
- Simultaneous release of different payloads (D)
- Compatible with varied chemical structures of payloads/linkers

### Consistent Linker Performance

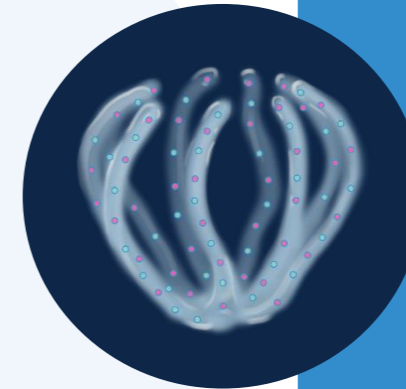
- Linkers show consistent half-lives
- Unaffected by single or multiple drug linker conjugations

## APPLICATION

### Glaucoma Duet Design

NLRP3 inhibitor +  
IOP-lowering  
small molecule

*Achieving  
targeted drug  
release in the eye*





# DRY AMD

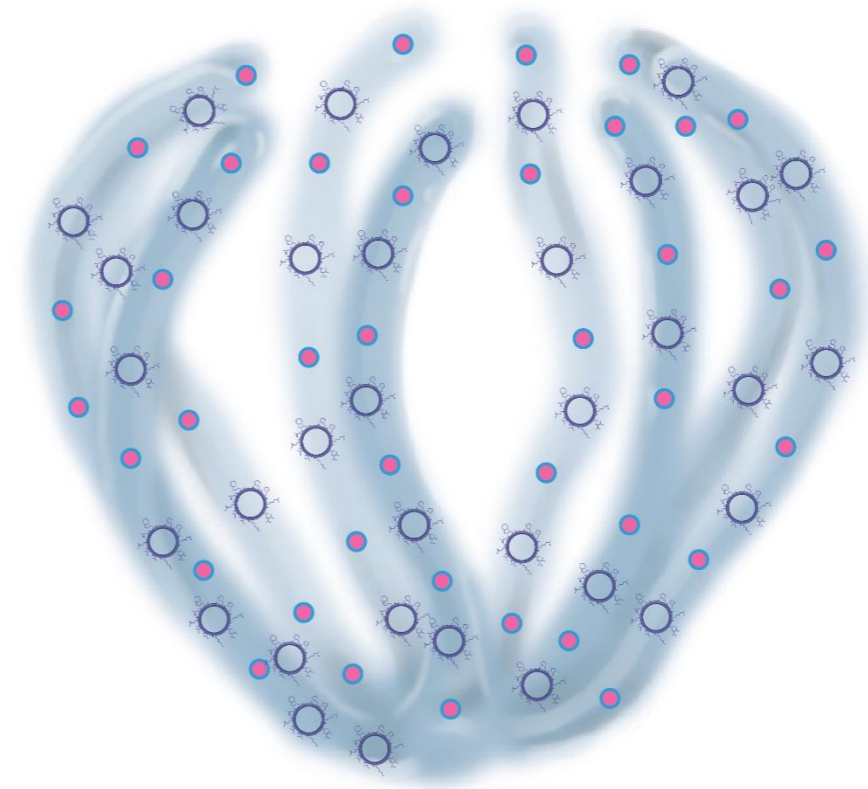
## Unmet need:

No approved treatments exist for early-stage dry AMD; current two complement therapies for late-stage disease require frequent injections, and neither of which sufficiently halts disease progression

## ABCD platform opportunity:

- **Macrocyclic peptides** are emerging as a new modality with several key advantages over small molecules and proteins
- **NLRP3 inhibitor** prevents inflammasome activation, which contribute to AMD pathology through the release of proinflammatory cytokines

## Macrocycle(s) Biopolymer Conjugates



Macrocycle  
complement  
inhibition



NLRP3 small molecule

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# SUMMARY & **TAKEAWAYS**



Victor Perloth, MD

# 3 clinical programs advancing in parallel, collectively addressing limitations of today's therapies across a broad spectrum of retinal diseases

## Retinal Vascular Diseases



### TARCOCIMAB TEDROMER

- Anti-VEGF “ABCD”
- Three Phase 3 studies complete
- Consistent 6-month predominant durability
- Two new Phase 3 studies actively enrolling
- Enhanced formulation designed to deliver “the pulse and the durability” while improving dose preparation, dose administration and safety
- A “mainstay” intravitreal biologic that delivers high efficacy and high durability for the \$14B market of retinal vascular diseases

**Target indications at launch:**  
wet AMD, DR and RVO

Phase 3



### KSI-501

- First-in-Class, bispecific anti-IL-6 , VEGF trap “ABCD”
- Designed to address vascular permeability and retinal inflammation simultaneously
- Benefits from the clinical science of immediacy and durability of the ABCD platform
- Phase 3 DAYBREAK study actively enrolling, designed to explore the power of the dual MoA to deliver improved efficacy

**Indications of interest:**  
wet AMD, DME, RVO and DR

Phase 3

## Inflammatory Retinal Diseases



### KSI-101

- First-in-Class, bispecific anti-IL-6 , VEGF trap protein
- Designed to address the underlying disease mechanisms of macular edema secondary to inflammation (“MESI”) for which no approved intravitreal biologic therapies exist today
- Uncorrelated from the ABCD Platform in a greenfield market
- Can be a fast follower to Roche’s vamiKIBART (anti-IL-6), with differentiation of having dual inhibition mechanism and high strength 100 mg/mL formulation

**Target indication:** macular edema secondary to inflammation

Phase 1

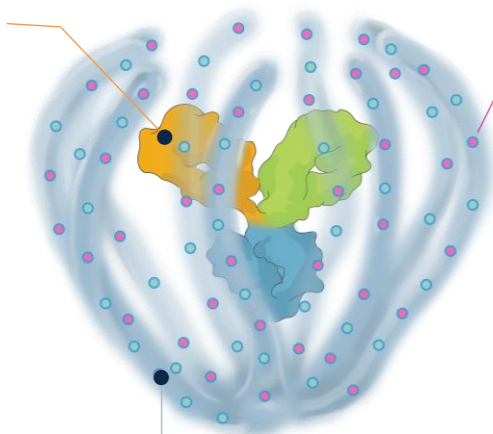
# Our ABCD Platform builds in modular fashion from our ABC Platform development and is maturing rapidly

## Antibody Biopolymer Conjugate Drug (“ABCD”):

Designed to embed small molecules and other **Active Pharmaceutical Ingredients (“API”)** such as oligonucleotides and peptides into the biopolymer backbone for release over a designed-in time period

### Antibody or other Biologic

Engineered to exhibit high binding affinity and specificity. Any biologic can be conjugated to the biopolymer



### Drug Cargo

Diverse APIs of varying biophysical properties including small molecules, macrocycles, peptides and oligonucleotides are embedded in the biopolymer and released over a designed-in time

### Biopolymer

Combines multiple APIs and can be tailored to meet a specific therapeutic goal. It is optically clear and made of phosphorylcholine, the primary hydrophilic component of human cell membranes

**Conjugates of diverse APIs +/- a biologic**  
Target both intracellular and extracellular pathways

**High Drug Antibody Ratio (“DAR”) medicines**  
Can include APIs with DAR of 10 up to >250

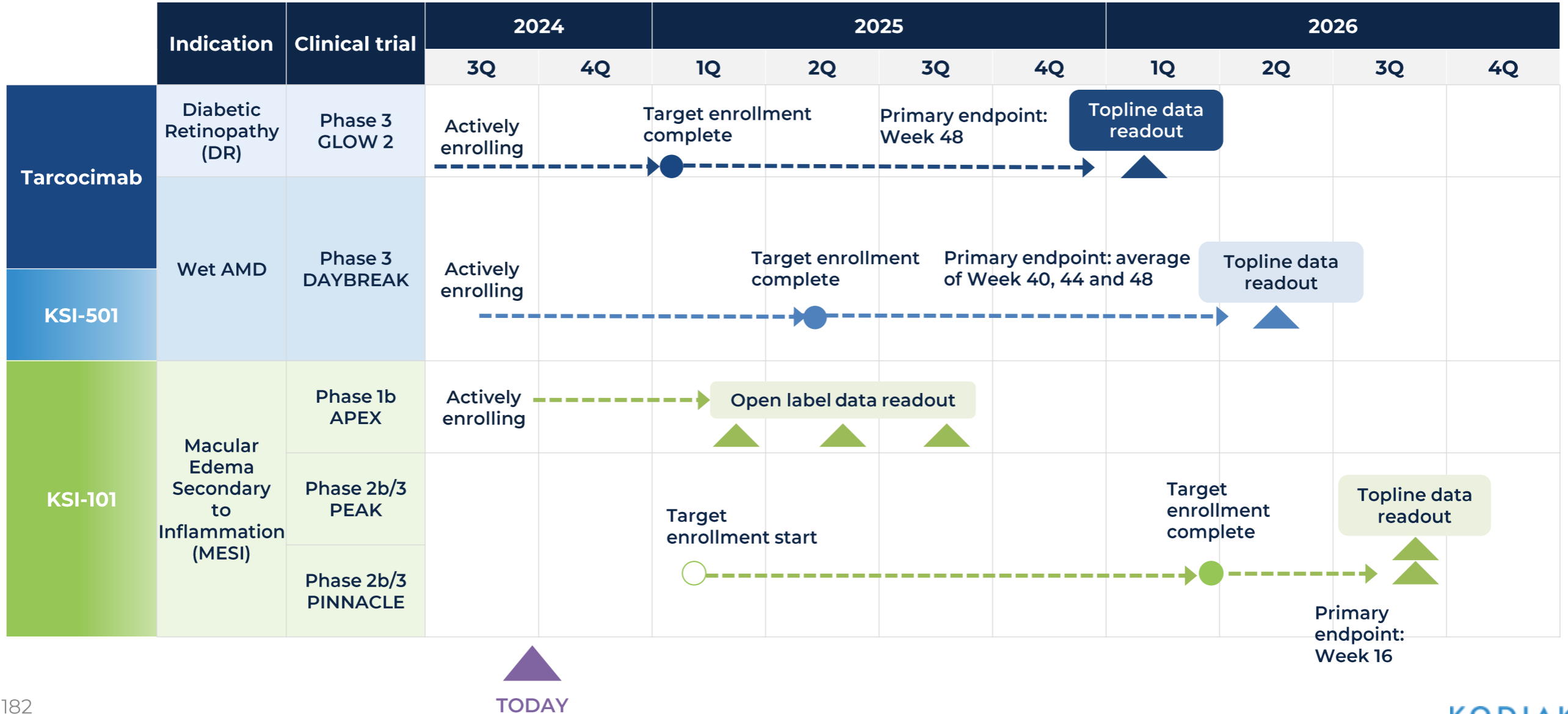
**Tailored release of APIs**  
Release of API payloads enabled by pH modulation or enzymatic cleavage of linkers

**Proven tolerability of the ABC Platform**  
>2,500 patient years of experience in patients

**A new combination of targeting, high drug loading, mixed API formats and tailored drug release – with applications in ophthalmic and systemic diseases**

Targeting one IND per year starting in 2025

# Summary of clinical programs and timeline of anticipated milestones



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Q&A



# We Are Here To Answer Your Questions



**Victor Perloth, MD**  
Chairman and CEO



**John Borgeson**  
CFO



**David Brown, MD**  
Key Opinion Leader



**Dolly Chang MD, MPH, PhD**  
Chief Scientific Officer



**Pablo Velazquez-Martin MD**  
Chief Medical Officer



**Almas Qudrat, M.Sc**  
Chief Quality Officer



**Charles Wykoff, MD, PhD**  
Key Opinion Leader



**THANK YOU**