Update on antibody biopolymer conjugates: optimizing immediacy and durability

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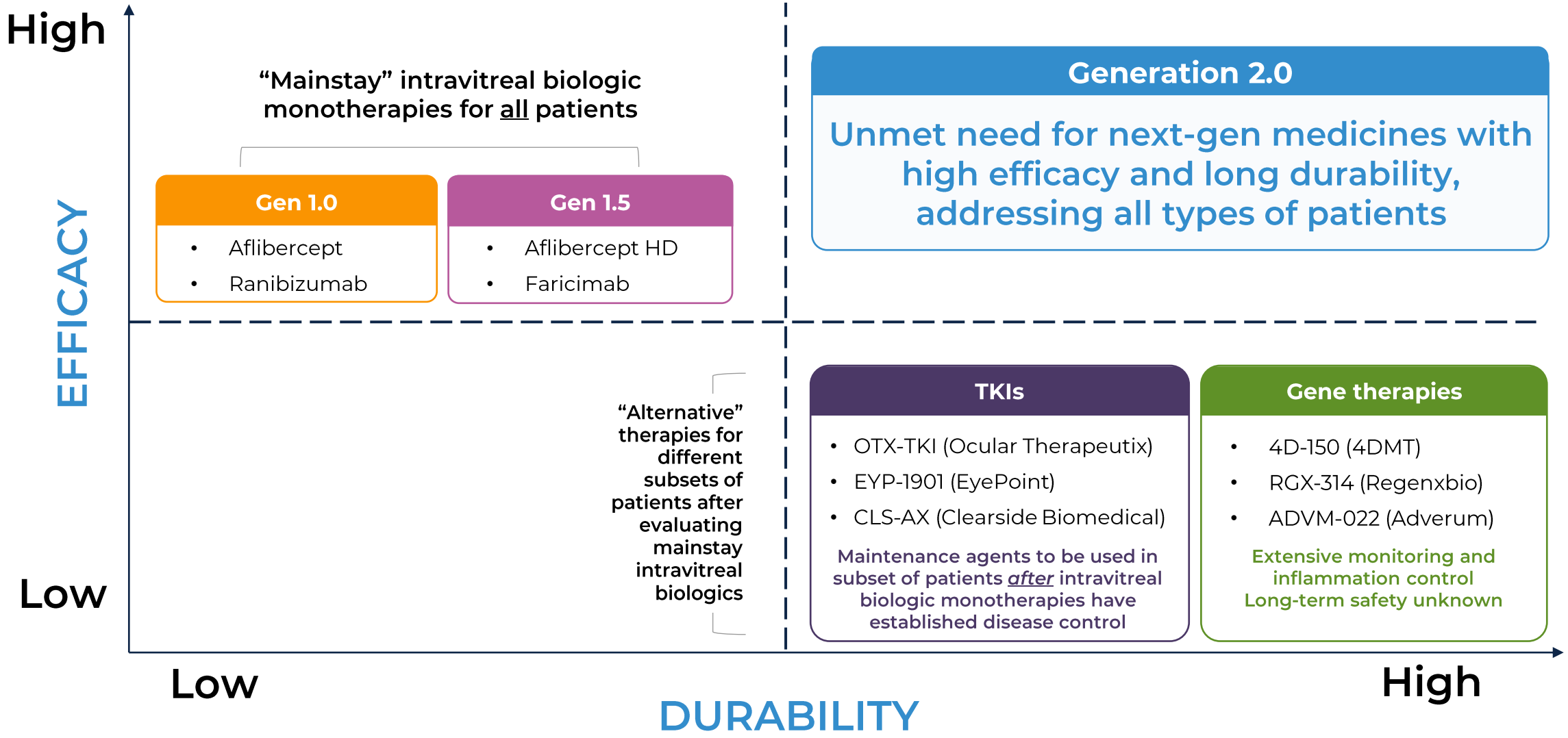
Disclosures

- Kodiak Sciences (C,R)
- The presentation will discuss IRB/IEC approved research of an investigational medicine

- AbbVie Inc[C]
- Adverum Biotech[CR]
- Alcon[BC]
- Alimera[C]
- Allegro[C]
- Allergan[C]
- AmerisourceBergen[C]
- Annexon Biosciences[CR]
- Apellis[BC]
- Arctic Vision[C]
- Astellas[BC]
- Bausch and Lomb[C]
- Biocryst[C]
- Biogen[C]
- Boehringer Ingelheim[C]
- CalciMedica[CR]
- Celltrion[C]
- Clearside Biomedical[CR]
- Coherus Biosciences[C]
- EyeBio[R]
- EyePoint Pharma[CR]
- Gemini Therapeutics[R]
- Genentech[BCR]
- Gyroscope Therapeutics[R]
- Harrow[C]
- Janssen[C]
- Kanghong/Vanotech[R]
- Kodiak Sciences[CR]
- Novartis[BCR]
- NeuBase[E]
- Neurotech[C]
- Ocular Therapeutix[CR]
- Oculis[CR]
- Opthea[CR]
- Outlook Therapeutics[C]
- Oxular[R]
- Oxurion[ER]
- Perfuse[R]
- Palatin Technologies[C]
- Regeneron[B]
- RegenxBio[CR]
- ReNeuron[R]
- RevOpsis Therapeutics[CE]
- Ribomic[R]
- Roche[C]
- Stealth Biotherapeutics[CR]
- Unity Biotechnology[R]

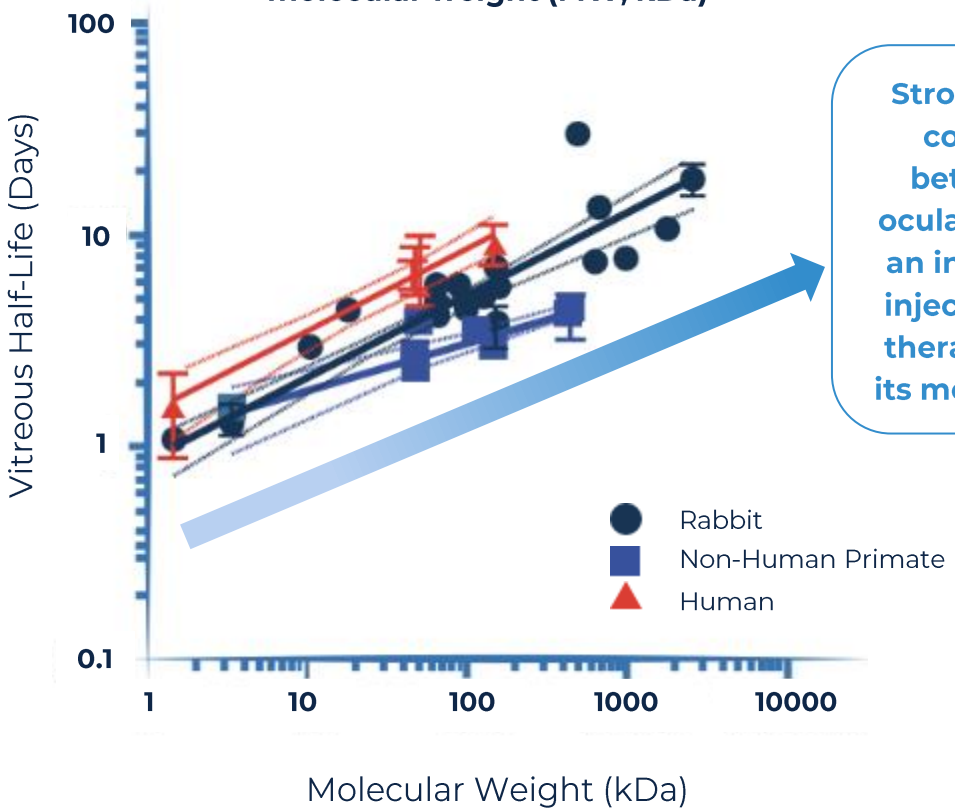
(B): Speakers' Bureau; (C): Consultant; (E): Equity; (R): Grants/Research Support

While there are treatment options currently available to treat retinal vascular diseases, and a few more in development, there continues to be a clear unmet need



Increasing the molecular size has a direct correlation with extending the ocular half-life of intravitreal biologics. The ABCD platform leverages high molecular weight to deliver extended clinical durability

Relationship between ocular half-life and molecular weight (MW, kDa)[1]



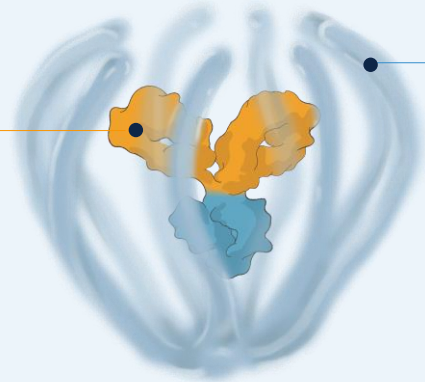
Strong positive correlation between the ocular half-life of an intravitreally injected protein therapeutic and its molecular size

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

The ABCD platform leverages a high molecular weight, phosphorylcholine-based biopolymer to enable an extended ocular residence time

Antibody or Other Biologic

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

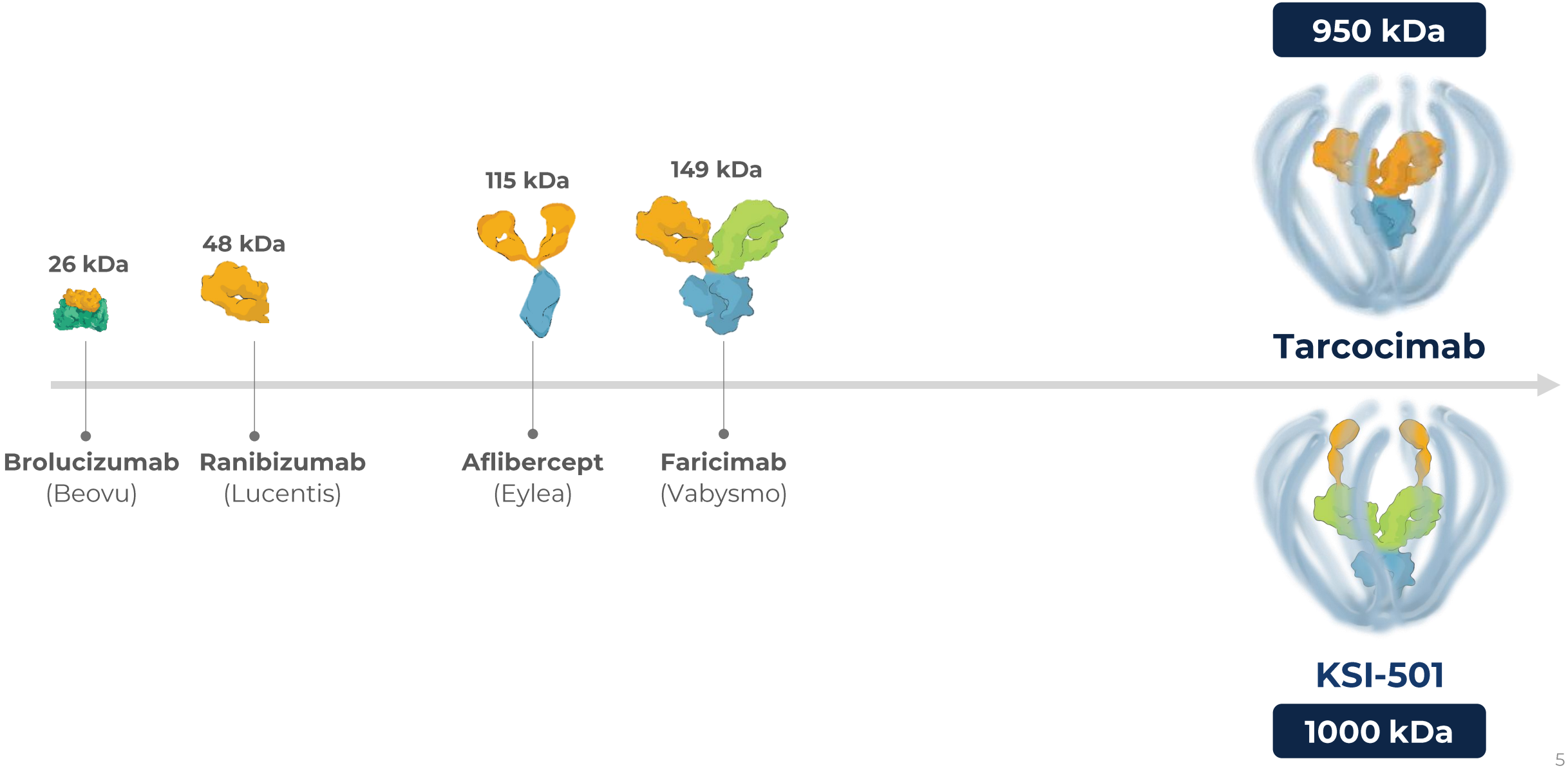


High molecular weight biopolymer

Engineered to make medicines last longer and extend their therapeutic benefit

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

Tarcocimab and KSI-501 have a high molecular weight which increases their ocular half-life and clinical durability compared to today's anti-VEGFs



From design to clinical data, tarcocimab translates extended ocular residence time into extended clinical durability

SCIENCE OF DURABILITY

Designed-in Extended Tissue Residence Time

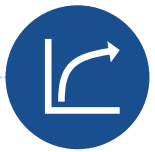
High molecular weight extends ocular half-life

Extended Ocular Half-Life in Animals

3x the ocular half-life of approved intravitreal biologics in rabbits

Extended Ocular Half-Life in Humans

3x the ocular half-life of faricimab in humans



Extended Clinical Durability

5 to 6-month predominant clinical durability

Designed-in Extended Tissue Residence Time

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

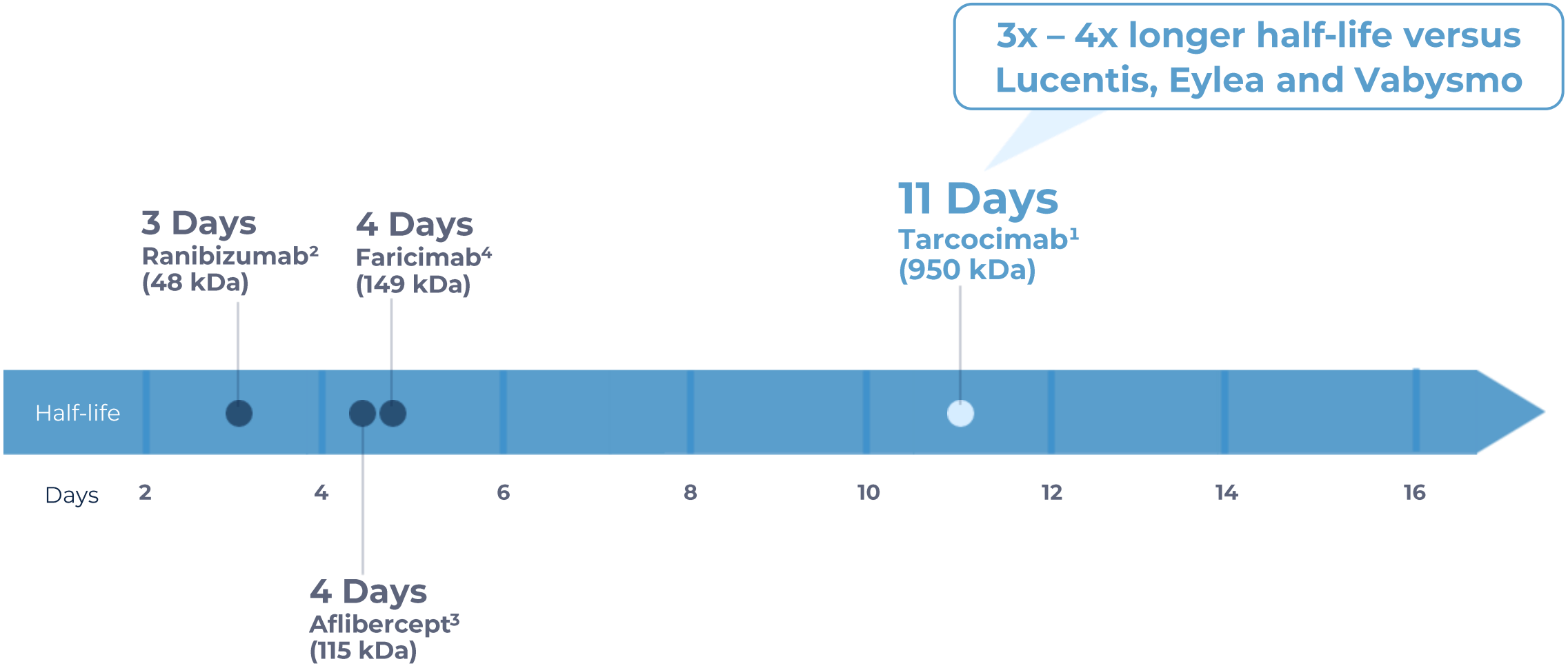
Tarcocimab is designed with a high molecular weight and a high formulation strength to provide extended ocular half life and a meaningful dosing advantage

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

Extended Ocular Half-Life in Animals

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

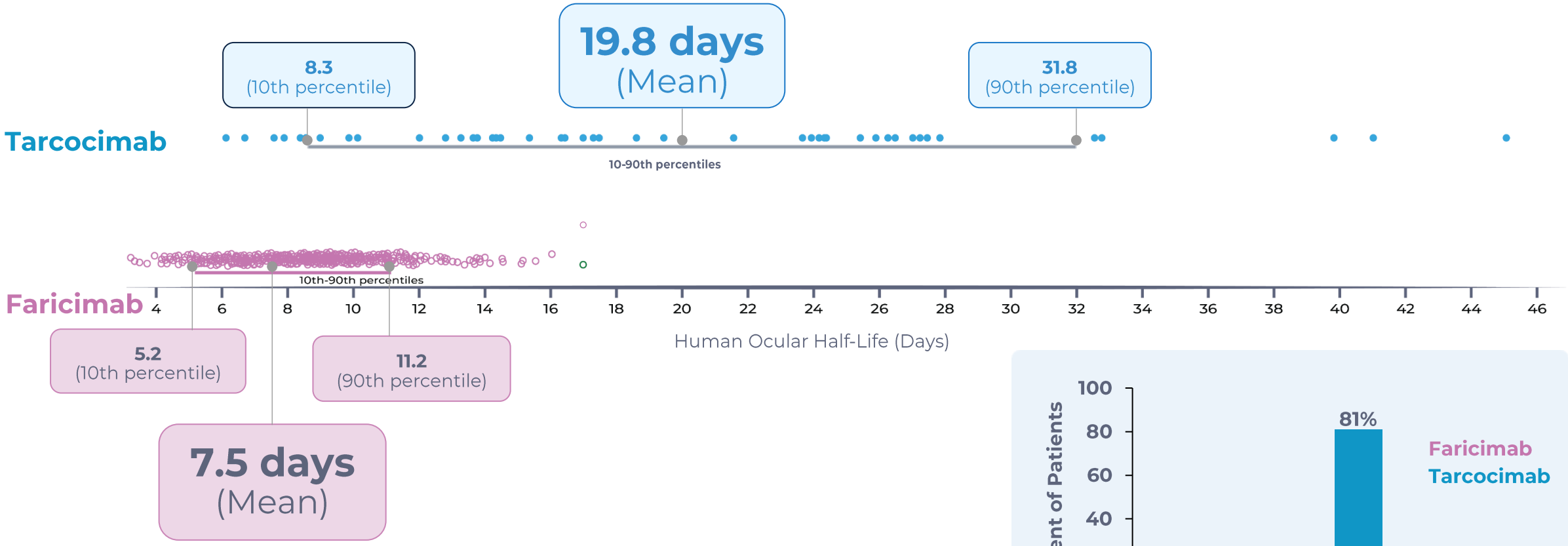
3x – 4x longer half-life versus Lucentis, Eylea and Vabysmo



1. Kodiak data on file. Ocular half life was determined from a single 50 µL intravitreal injection of 0.725 mg of tarcocimab (conjugate) in rabbits. 2. Gaudreault, et al. *Retina* 2007, 27: 1260-1266. 3. Park SJ, et al. *IOVS 2016, 57: 2612-2617*. 4. Pharmacology / Toxicology BLA Review and Evaluation

Extended Ocular Half-Life in Humans

Tarcocimab has 3x longer half life than faricimab

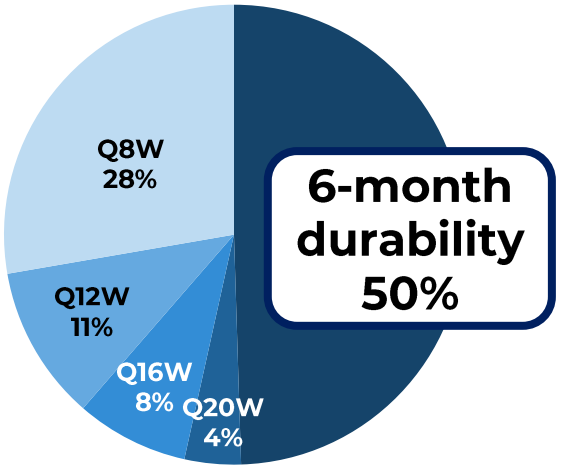


Each dot represents an individual patient. VABYSMO™ (faricimab solution for injection) Prescribing Information. South San Francisco, USA: Genentech, Inc.
PK and ER of faricimab, Report # 1105763

Extended Clinical Durability

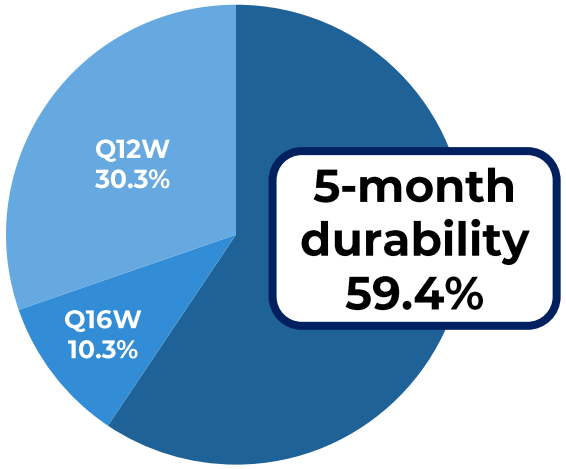
Durability Interval at Year 1

Number of doses in the second 6 months of Year 1



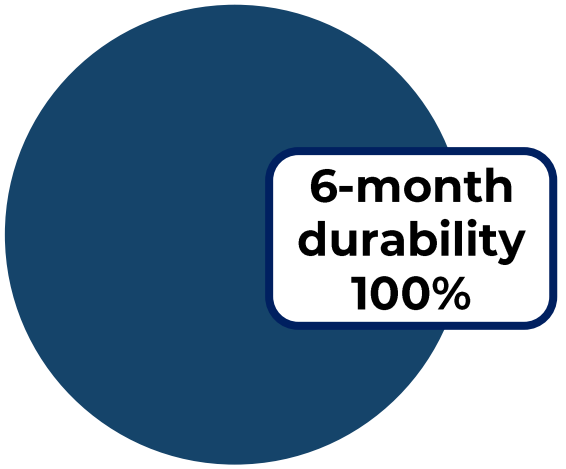
DME

GLEAM and GLIMMER Studies[1]



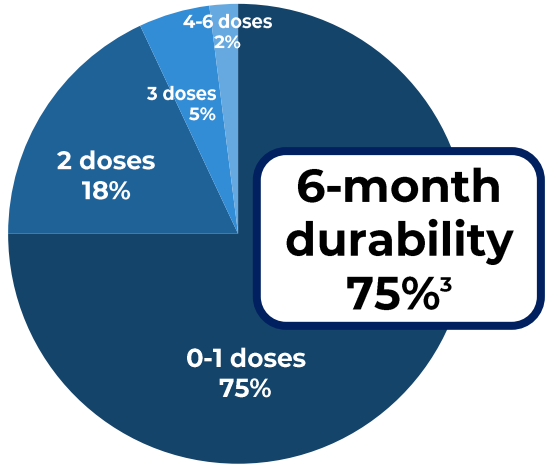
wAMD

DAZZLE Study[2]



DR

GLOW1 Study



RVO

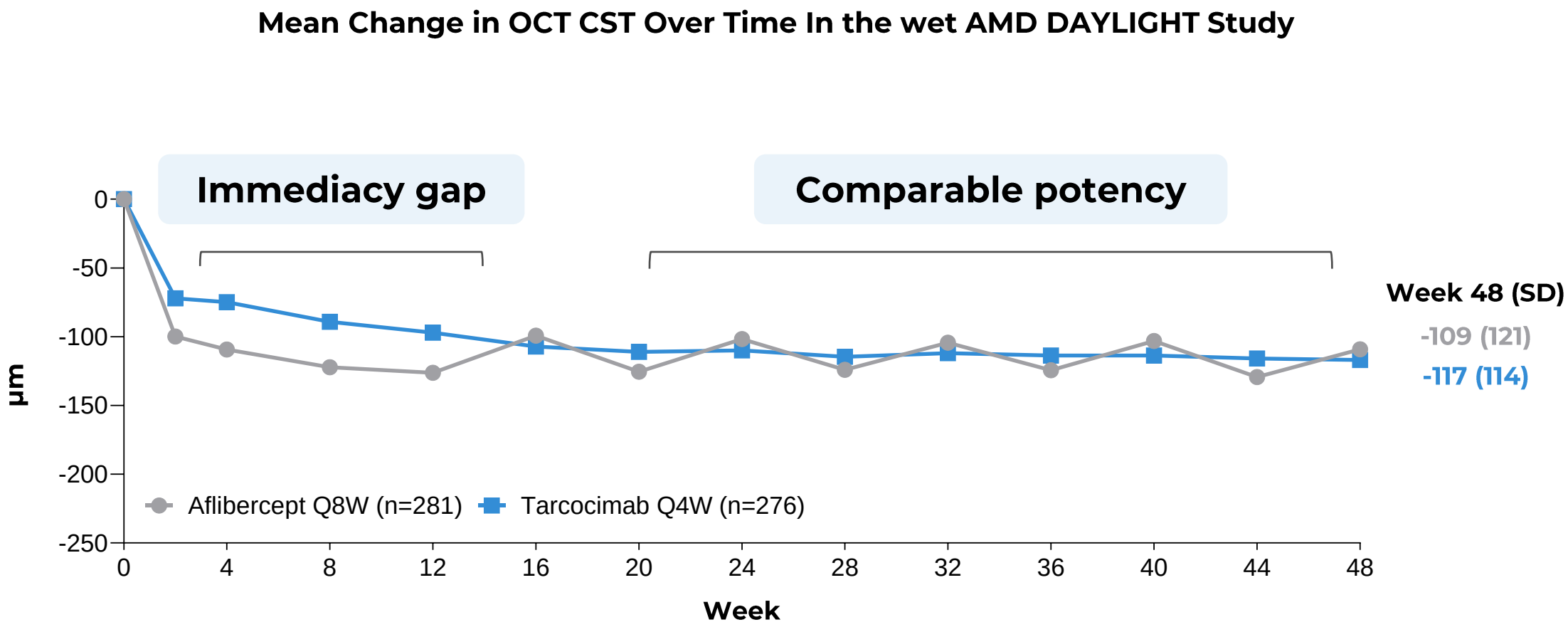
BEACON Study

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

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.

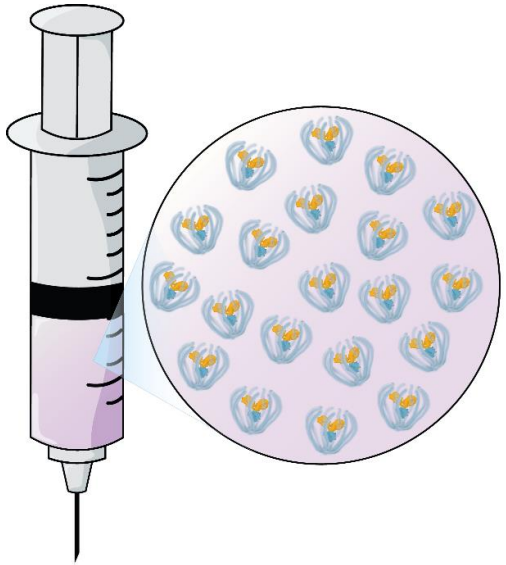
Does the durability come at a cost? Immediacy seems to be the cost. A deficit is seen in the loading phase, in the “immediacy” of the effect. After the loading phase, the drying potential or “potency” is comparable to aflibercept



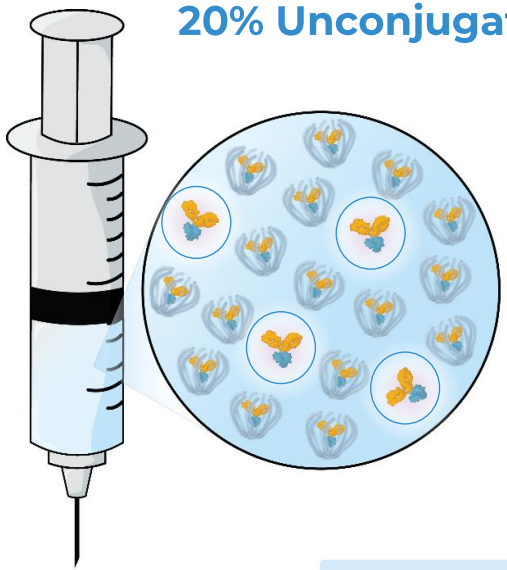
Observed values. OCT: optical coherence tomography; CST: central subfield thickness.

An enhanced formulation is primed to solve the immediacy deficit. By including 20% free protein (unconjugated), the enhanced formulation can deliver the immediacy of a traditional biologic

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 **Conjugates**	**4 mg**
n/a	Proportion of **Free Protein**	**1 mg**

Identical strength

Reduced conjugates from 100% to 80%

Unconjugated protein at 20%

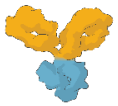
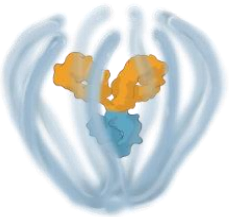
The enhanced formulation was designed to confer several key benefits:

- 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	
						1 mg	**4 mg**
Equivalent Molar Dose	11	0.5	**1.0**	2	3.5	**0.7**	**2.8**

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

Equivalent to 0.7 mg of ranibizumab

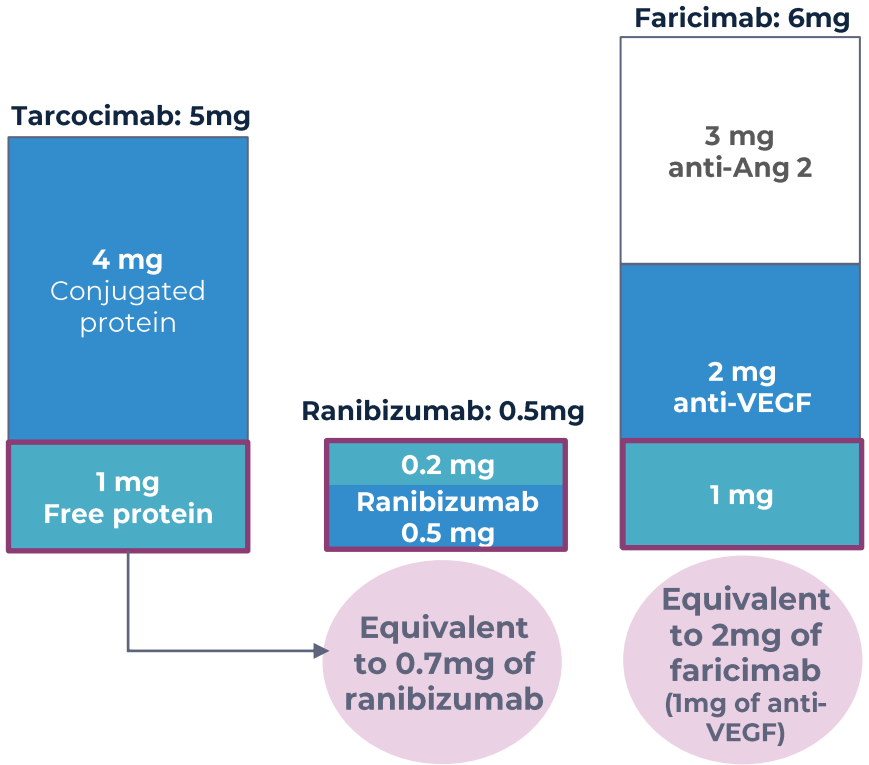
Equivalent to 1.3 mg of aflibercept

Equivalent to 2 mg of faricimab

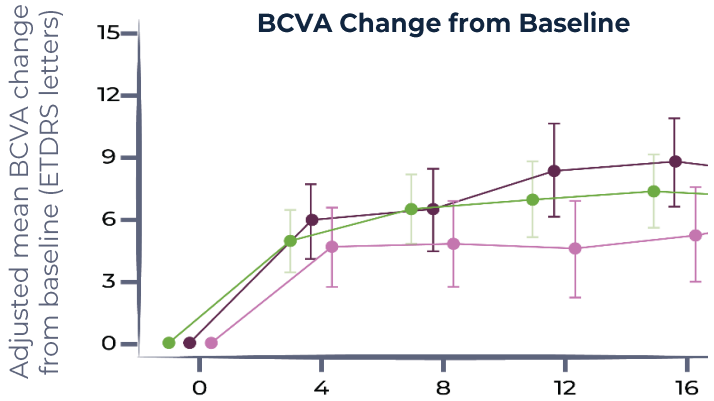
Is the unconjugated portion enough? The unconjugated protein should deliver a strong “pulse” of VEGF inhibition, with a clinically meaningful molar dose

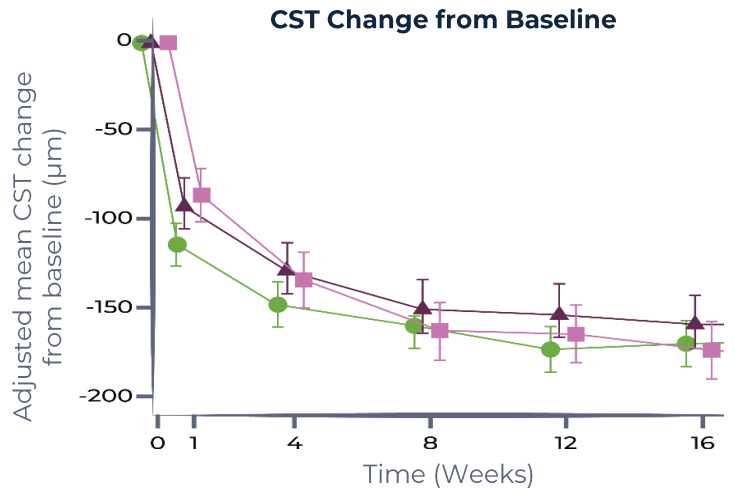
The 1 mg of free protein in the enhanced formulation is expected to meaningfully improve immediacy

- 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



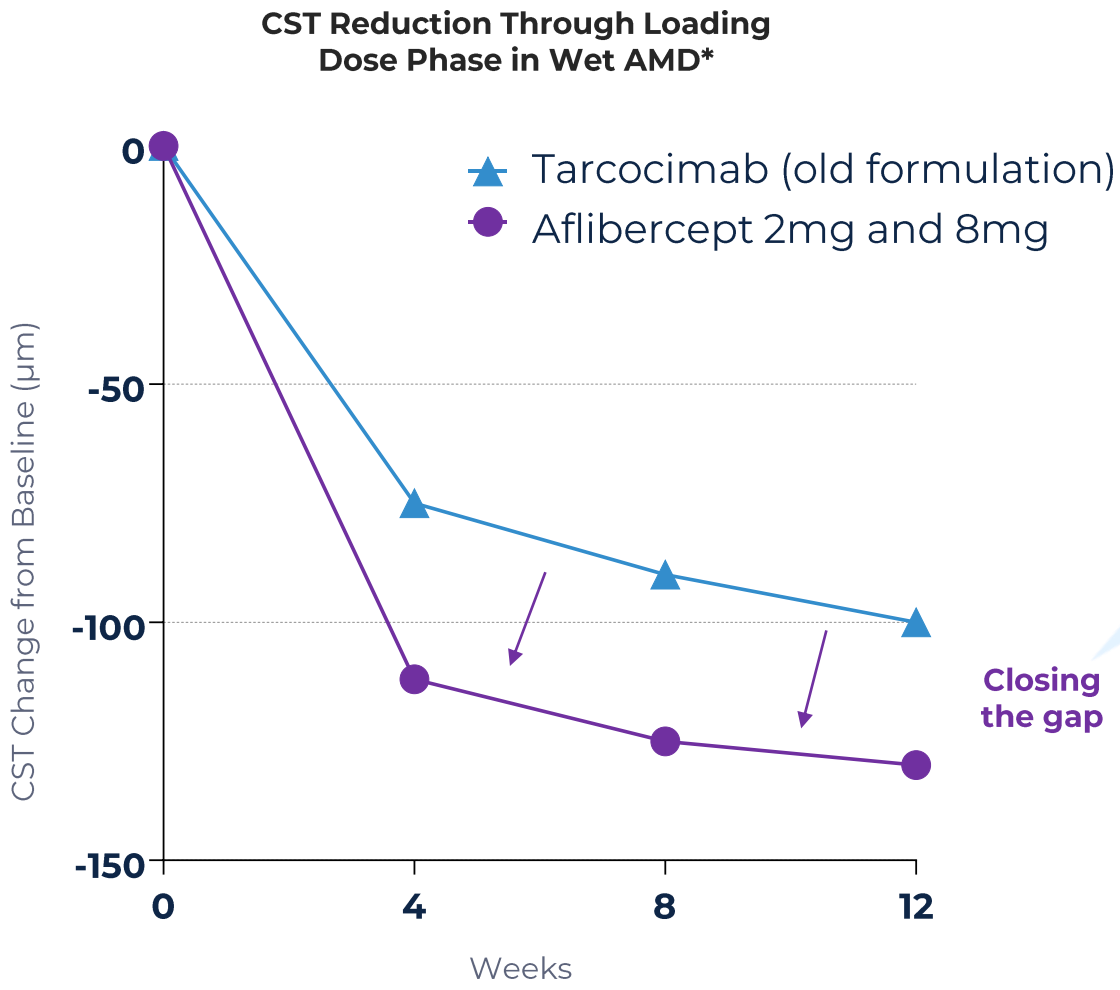
Similar efficacy benefits were observed among ranibizumab 0.5 mg, faricimab 1.5 mg and faricimab 6 mg





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

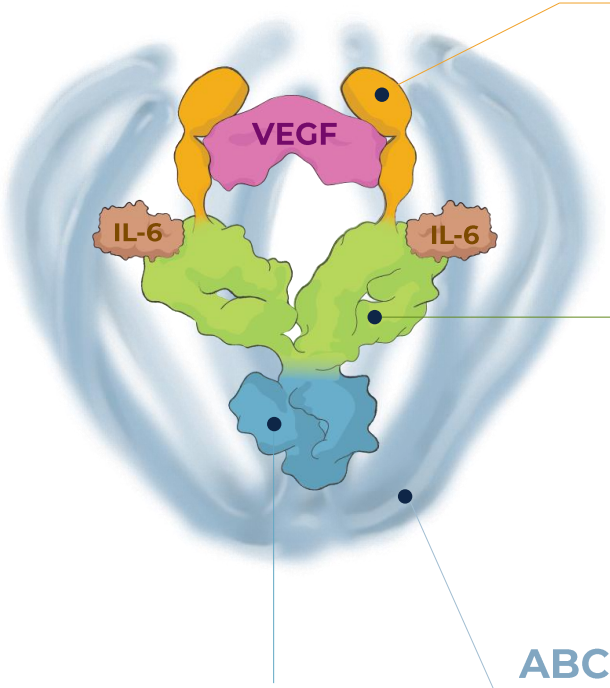


The purpose of the 20% unconjugated protein (1 mg) is to improve the immediacy of the drying effect during the loading dose phase, “closing the gap"

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

*Approximate CST changes are plotted based on pivotal clinical studies of approved intravitreal biologics. CST changes for tarcocimab enhanced formulation is a projection

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, leveraging the platform's durability profile



VEGF Trap
Broad VEGF inhibition

The VEGF Trap mimics the native receptor and binds multiple targets including VEGF-A, VEGF-B and PIGF

Anti-IL-6 Antibody
Potent anti-inflammatory effect

The anti-IL-6 antibody can inhibit up to two IL-6 molecules to block inflammation and normalize the blood retinal barriers

ABCD Platform:
Extended durability

KSI-501 leverages our ABCD platform with its signature 6-month predominant durability

Modified Fc

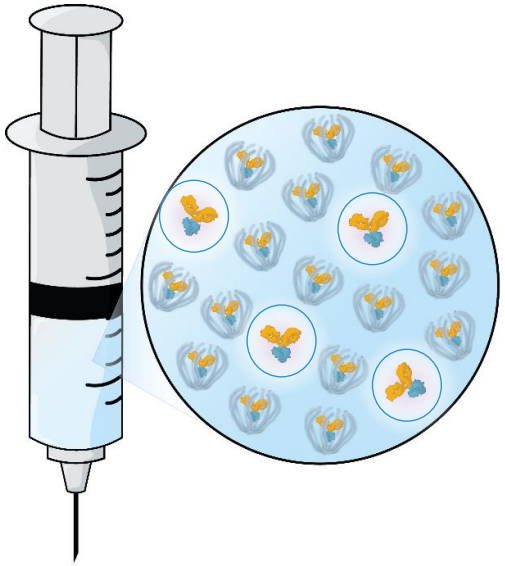
Immunologically inert antibody

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

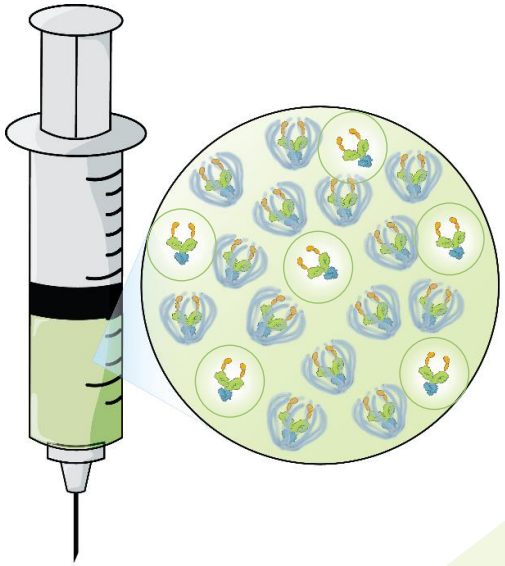
Enhanced ABCD formulation designed to maximize durability and efficacy, with conjugated and unconjugated forms

The enhanced formulation is implemented in all ABCD platform to solve the immediacy deficit, including 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	**5.0 mg**
4.0 mg	Proportion of **Conjugates**	**3.5 mg**
1.0 mg	Proportion of **Free Protein**	**1.5 mg**

Based on antibody mass (injection volume of 100 µL 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

Tarcocimab: planned BLA package in 2026 for 3 disease indications supported by 5 pivotal studies in diabetic retinopathy, wet AMD & retinal vein occlusion

Completed Phase 3 studies:

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

Wet AMD	Retinal vein occlusion	Diabetic retinopathy
DAYLIGHT Study	BEACON Study	GLOW1 Study

Two Phase 3 studies actively enrolling:

using the go to market formulation of tarcocimab

Diabetic retinopathy	Wet AMD
GLOW2 Study	DAYBREAK Study

AMD: age-related macular degeneration; BEACON: NCT04592419; GLOW1: NCT05066230; DAYLIGHT: NCT04964089; GLOW2: NCT06270836; DAYBREAK: NCT06556368

New wAMD Phase 3 study – DAYBREAK: Beyond the enhanced formulation, a variety of learnings have been applied in DAYBREAK, which incorporates both tarcocimab and KSI-501

Actively recruiting

	4 loading doses for tarcocimab and KSI-501										Primary endpoint Mean change in BCVA			Same dose regimen in Year 2	End of Study		
Weeks	**0**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44**	**48**	**52 – 88**	**92**	**96**	**Objective**
Tarcocimab Q4-24W (n~225)	■	■	■	■	◪	◪	◪	◪	◪	◪	◪	◪	◪	→	◪		**Assess 6-month durability potential** with individualized Q4W – Q24W dosing
KSI-501 Q8W (n~225)	■	■	■	■	◪	■	◪	■	◪	■	◪	■	◪	→	■		**Explore efficacy potential of bispecific IL-6 and VEGF inhibition** in fixed Q8W + individualized monthly dosing optionality
Aflibercept Q8W (n~225)	●	●	●	○	●	○	●	○	●	○	●	○	●	→	○		

■ Tarcocimab injection ■ KSI-501 injection ● Aflibercept injection ○ Sham injection ◪ Individualized treatment/sham

For tarcocimab: DAYBREAK corrects the flaws in DAZZLE and maximizes the probability of meeting non-inferiority

DAZZLE Flaw	DAYBREAK Solution
Underdosing	• Adding a 4th loading dose • Allowing shorter intervals, down to monthly dosing
Reactive dosing	• A treat-to-dryness proactive dosing, enabled by **using presence of fluid** as a disease activity marker
Loose retreatment criteria	• Using presence of fluid as a disease activity marker, instead of a combination of CST and vision loss, which **resembles retina specialists' practice and optimizes each patient's treatment**
	• Expanding the evaluable area 9-fold (from 1mm² to 3mm²)
Weak immediacy	• Using the enhanced formulation of tarcocimab

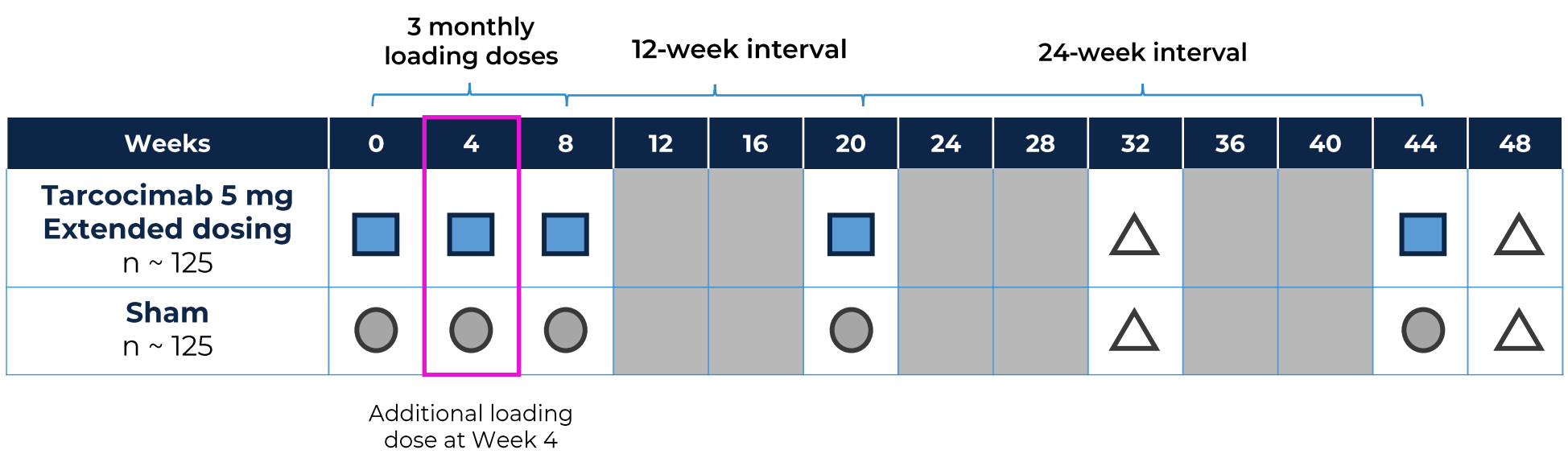
For KSI-501: dosing regimen designed to assess potential for better efficacy

Why allow monthly dosing?

- Better vision outcomes are observed with monthly dosing vs Q8W dosing in wet AMD patients with persistent fluid[1]
- **Enhances the possibility to observe better efficacy outcomes** and assess the full potential of the bispecific anti-IL-6 VEGF trap mechanism of action

Q4W: every 4-week dosing; Q24W: every 24-week dosing; 1. Jaffe et al. Ophthalmology 2016;123:1856-1864

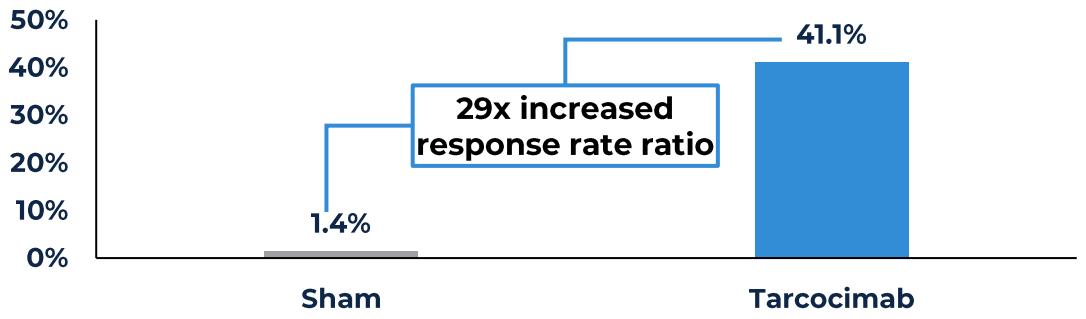
New DR Phase 3 study – GLOW2: features a similar study design as the successful GLOW1 study, with the benefit of an additional 3rd monthly loading dose



Primary endpoint

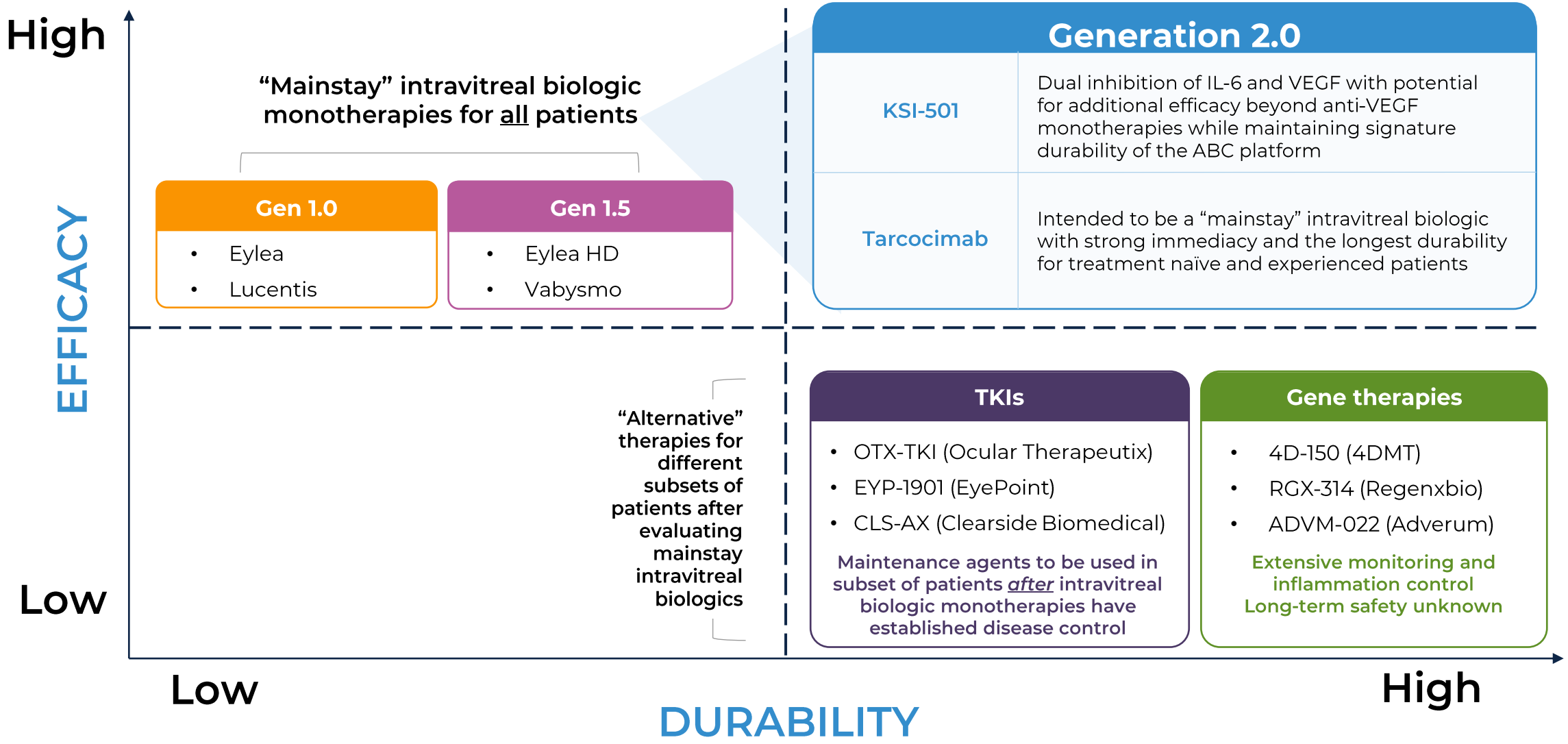
- Proportion of eyes improving ≥2 steps on DRSS from baseline at Week 48

The GLOW1 study met the primary endpoint with high statistical significance (p<0.0001)



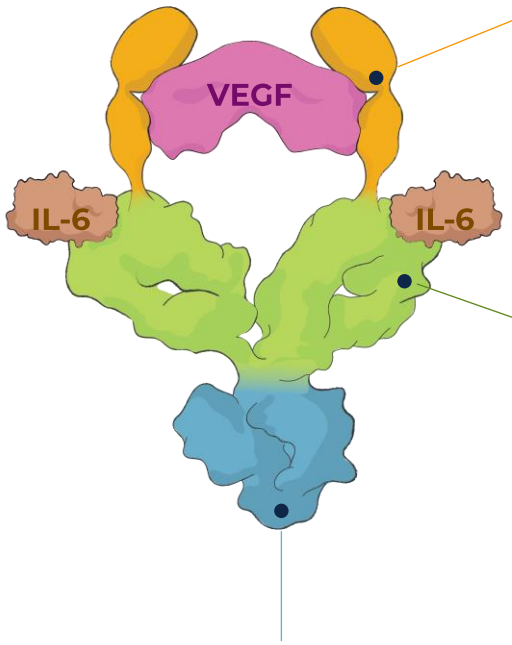
DRSS: diabetic retinopathy severity score; GLOW 1 study NCT05066230; GLOW2 study NCT06270836

Tarcocimab and KSI-501 have the fundamentals to become Generation 2.0 intravitreal biologics, addressing all patient types, providing high efficacy and extended durability



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



VEGF Trap
Broad VEGF inhibition

The VEGF Trap binds multiple targets including VEGF-A, VEGF-B and PIGF

Anti-IL-6 Antibody:
Potent anti-inflammatory effect

The anti-IL-6 antibody can inhibit up to two IL-6 molecules to block inflammation and normalize the blood retinal barriers

Modified Fc
Immunologically inert antibody

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

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 intended to deliver high efficacy and high durability for 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
- Differentiation of having dual inhibition mechanism and high strength 100 mg/mL formulation

Target indication: macular edema secondary to inflammation

Phase 1

Summary of clinical programs and timeline of anticipated milestones