

**A Study to Evaluate the Efficacy and Safety of Tarcocimab Tedromer
and Tabirafusp Tedromer Compared to Aflibercept in Participants
with Wet Age-related Macular Degeneration**

**First-time One-year Primary Efficacy and Safety
Outcomes of the Phase 3 DAYBREAK Study**

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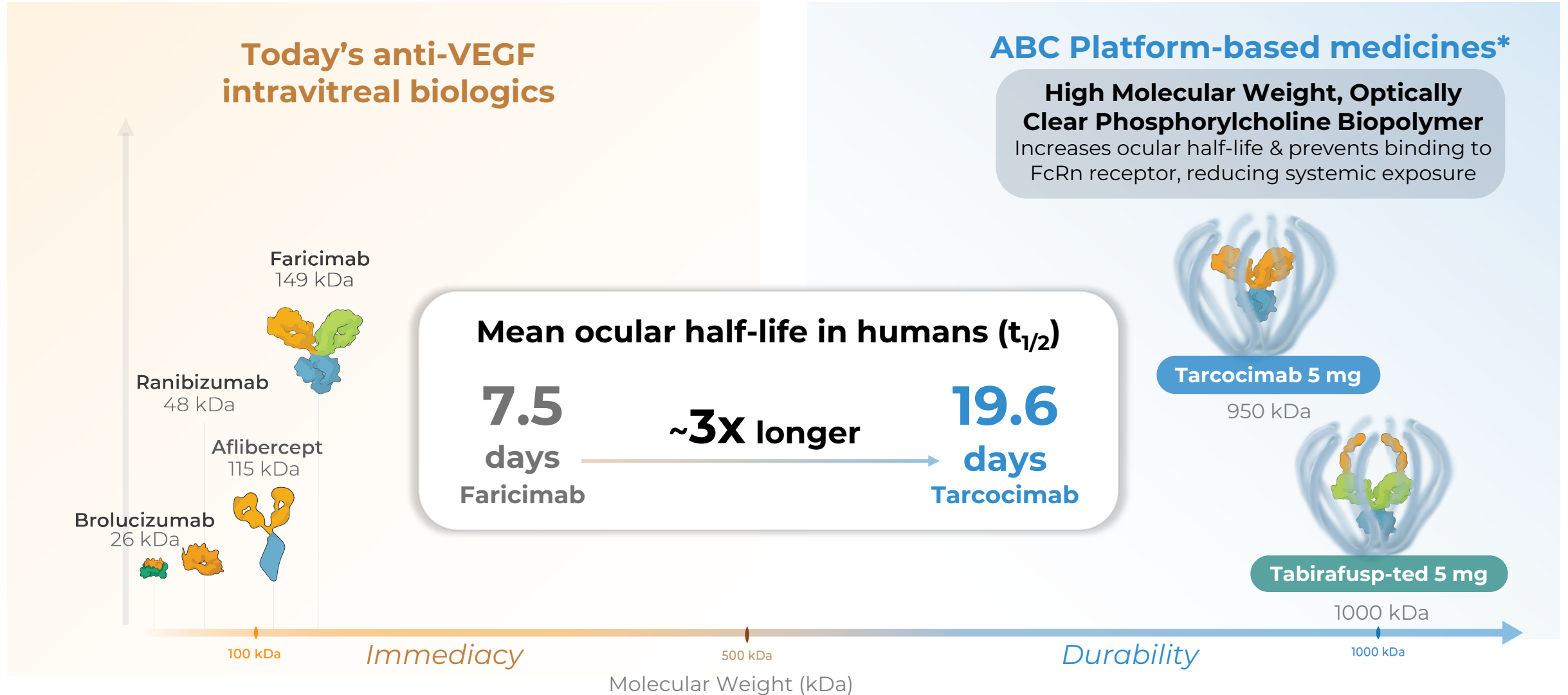
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Institute, Houston Methodist Hospital, Houston Texas**

on behalf of the DAYBREAK Study Group

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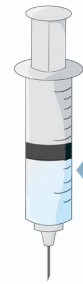
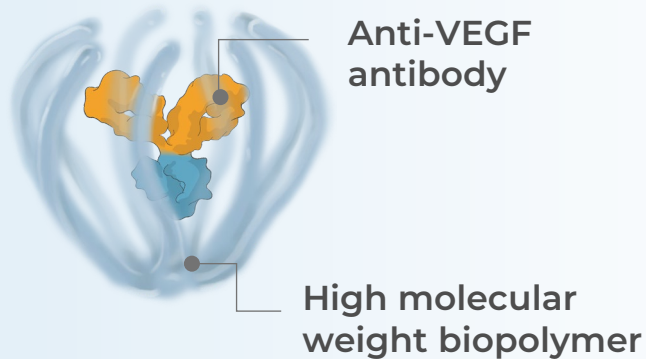
Antibody Biopolymer Conjugate (ABC) medicines leverage high molecular weight to deliver longer ocular durability



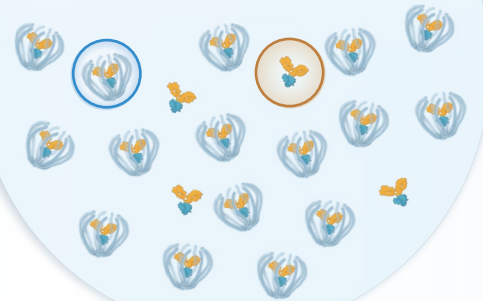
*Conjugated portion shown. ABC medicines tarcocimab and tabirafusp-ted combine conjugated and unconjugated protein in a single intravitreal injection.

Combining free and conjugated antibodies, ABC medicines are designed to optimize immediacy and durability in a single intravitreal injection

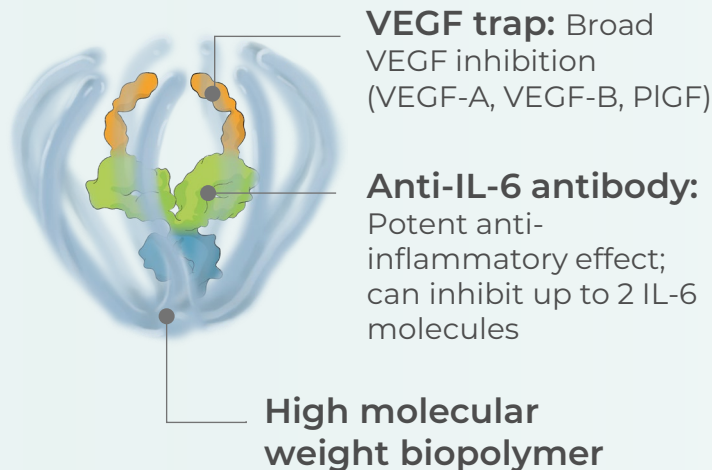
TARCOCIMAB 5 MG



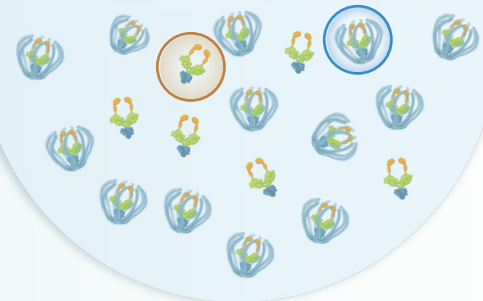
2-in-1 formulation
1 mg free protein +
4 mg ABC protein



TABIRAFUSP-TED 5 MG



2-in-1 formulation
1.5 mg free protein +
3.5 mg ABC protein



2-in-1 Formulation

Strong
Immediacy



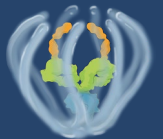
Strong Durability



Unconjugated
Protein



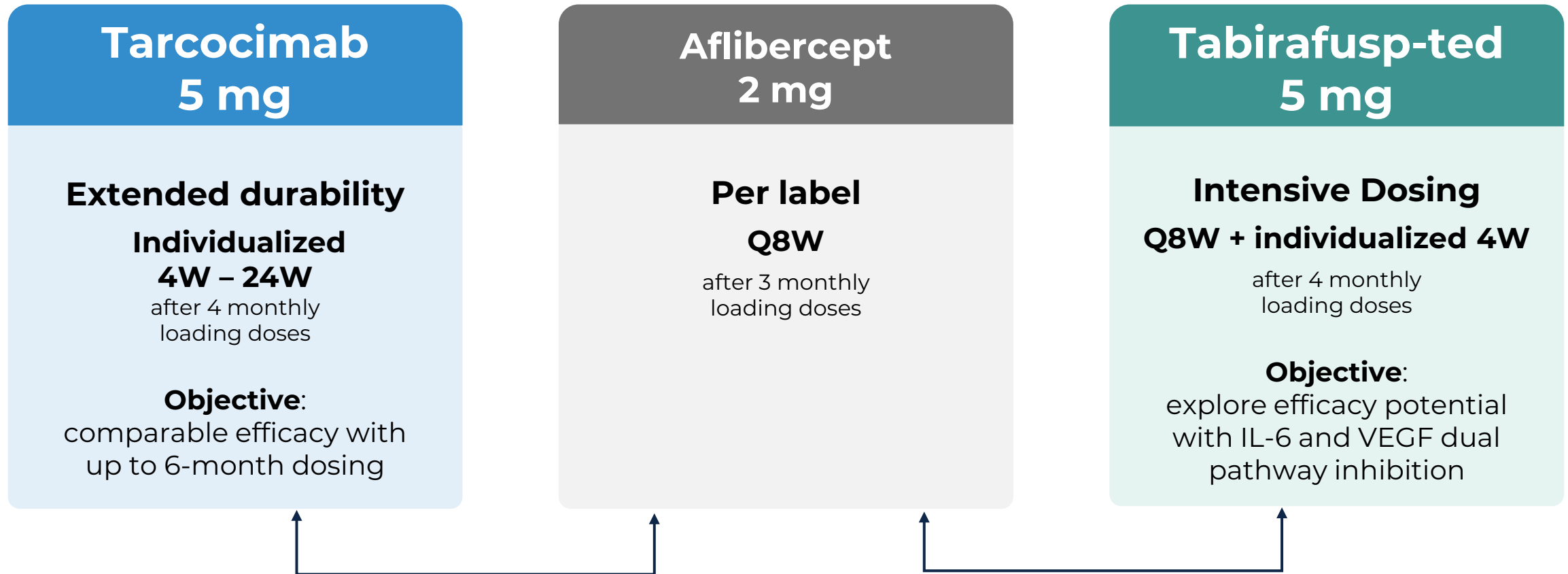
ABC (Conjugated)
Protein



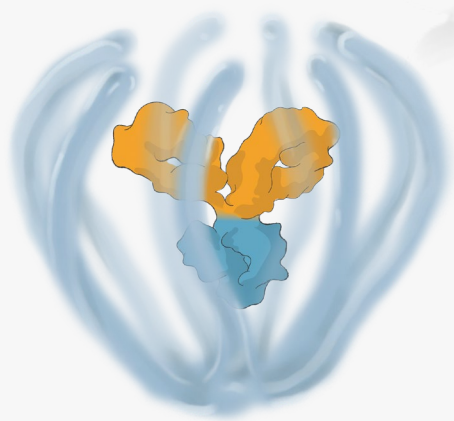
DAYBREAK: Phase 3, double-masked, randomized trial in treatment-naïve wet AMD (n=667)

2 molecules independently tested at full alpha vs a single comparator

Single Comparator



Separate pivotal analyses using independent SAPs

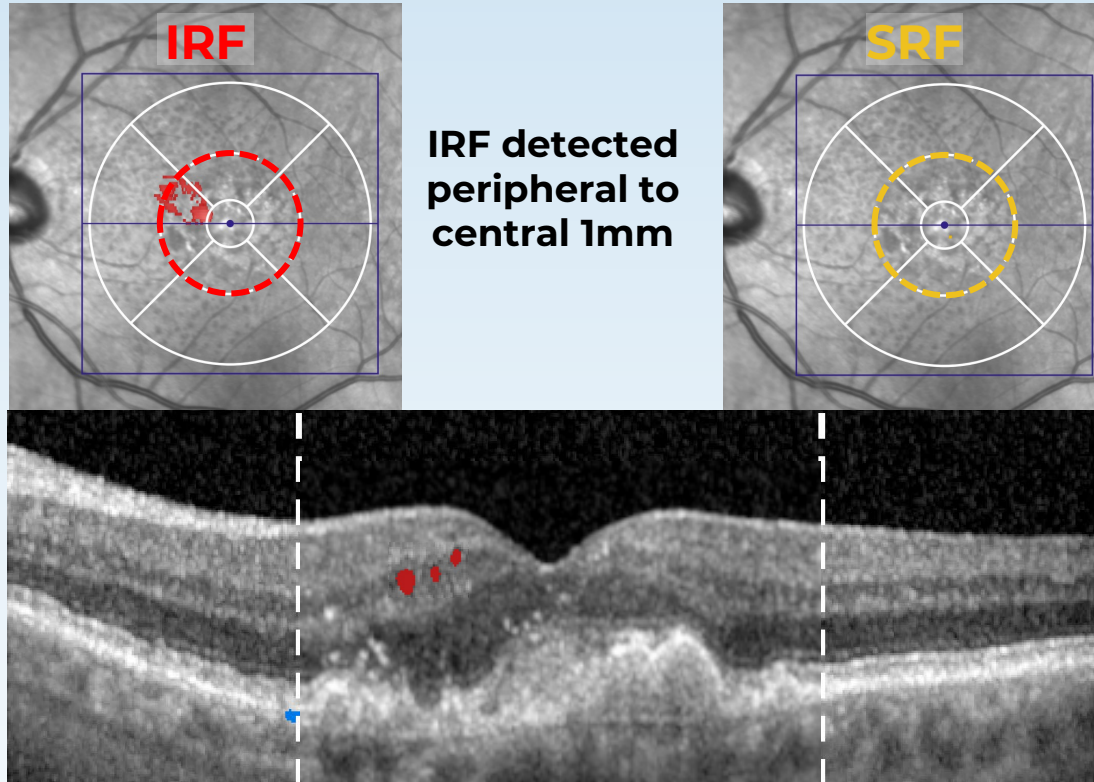


One-year primary efficacy and safety outcomes of the Phase 3 DAYBREAK Study in wet AMD

**Efficacy and safety of [tarcocimab tedromer](#)
compared to aflibercept**

An AI-algorithm assessed IRF and SRF presence in the central 3mm to determine retreatment. Real-world decision-making → *Fluid = Treatment*

Central 3 mm has 9-fold the evaluable area of CST (central 1mm)



DAYBREAK disease activity criteria (any of the following)

- Presence of intraretinal fluid (IRF) in central 3mm
- Presence of subretinal fluid (SRF) in central 3mm
- Presence of macular hemorrhage

Goal:

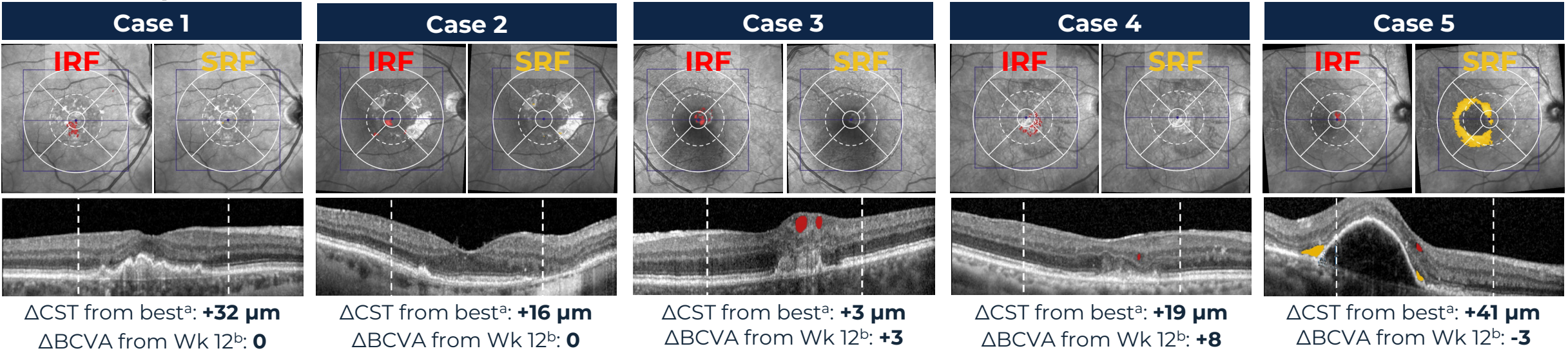
Operationalize how retina specialists determine exudative disease activity using a treat-to-dry approach

Intentionally NOT required:
Specific CST increase and/or visual acuity loss

DAYBREAK's retreatment criteria strict by design. No undertreatment allowed.

Would these meet disease-activity criteria in any other modern pivotal wAMD trial?

5 different patients: all resulted in re-treatment in DAYBREAK



Would treatment be triggered in different Phase 3 studies?^c

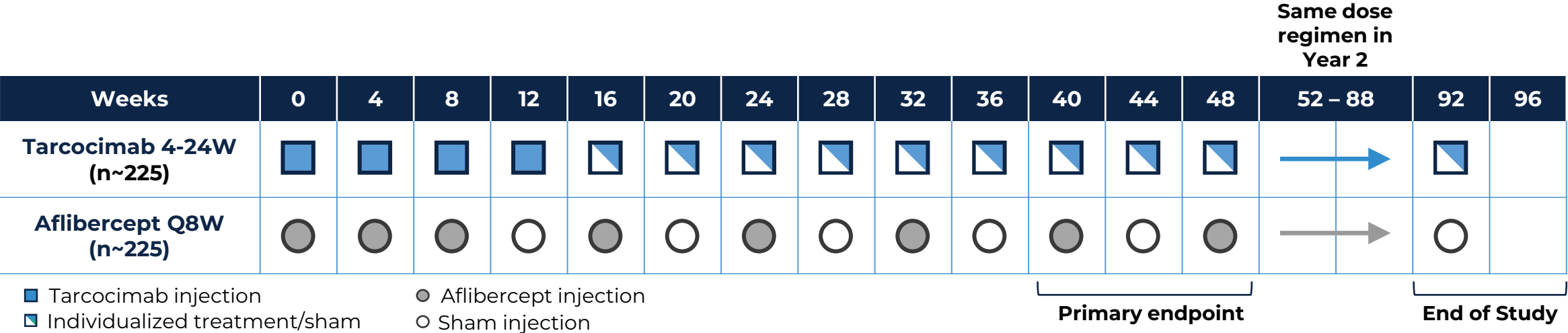
PULSAR ¹	No treatment	No treatment	No treatment	No treatment	No treatment
TENAYA & LUCERNE ²	No treatment	No treatment	No treatment	No treatment	No treatment
DAYBREAK					

DAYBREAK used strict fluid-based retreatment criteria. Treat-to-dry and maintain dry

a. CST increase measured from best previous CST measurement;
b. BCVA change measured compared to Week 12 value;
c. Refers to treatment decision visits. In TENAYA & LUCERNE, disease activity was assessed at Weeks 20 and 24 and patients were then assigned to fixed Q8W, Q12W, or Q16W dosing through Week 60.
1. Lanzetta, P. et al. *Lancet* (2024) doi:10.1016/S0140-6736(24)00063-1. 2. Khanani, A. M. et al. *Ophthalmol Sci* 1, (2021).

DAYBREAK – tarcocimab: evaluated the potential for dosing intervals of up to 6 months in wAMD





Treatment paradigm

Treat-to-dry with individualized 4W-24W (capped) dosing

Objective

Comparable efficacy with up to 6-month dosing

Primary endpoint

Mean change in BCVA from baseline (Day 1) to the average of Week 40, 44 and 48

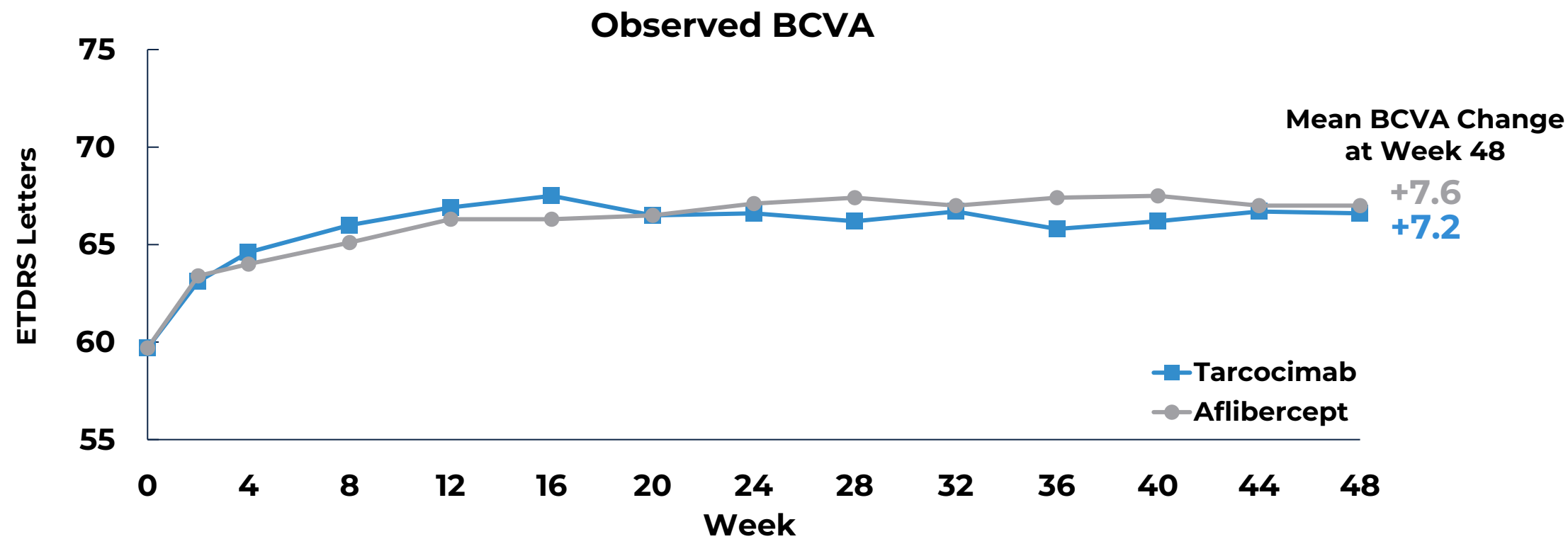
Baseline ocular characteristics were balanced and consistent with treatment-naïve wAMD patients



	Tarcocimab Q4-24W n= 220	Aflibercept Q8W n= 224
BCVA, ETDRS Letters , mean (SD) ≥20/40 Snellen equivalent, n (%) ≤20/200 Snellen equivalent, n (%)	59.7 (13.48) 72 (32.7%) 26 (11.8%)	59.7 (13.29) 72 (32.1%) 21 (9.4%)
BCVA Category ≤ 49 ETDRS Letters, n (%) 50 – 69 ETDRS Letters, n (%) 70 – 78 ETDRS Letters, n (%)	 44 (20.0%) 115 (52.3%) 61 (27.7%)	 43 (19.2%) 119 (53.1%) 62 (27.7%)
BCVA – Low Luminance VA Difference < 33, n (%) ≥ 33, n (%)	 160 (72.7%) 59 (26.8%)	 166 (74.1%) 58 (25.9%)
OCT Central Subfield Thickness (CST), μm , mean (SD)	345.8 (113.09)	354.9 (108.12)
Lens Status , n (%) Phakic Pseudophakic	 90 (40.9%) 130 (59.1%)	 88 (39.3%) 136 (60.7%)
Intraocular Pressure, mmHg , mean (SD)	14.5 (2.90)	14.7 (3.05)

n = Number of participants treated; The denominator for percentages is the number of participants treated within each treatment arm. Snellen equivalent of 20/40 is 69 ETDRS letters and of 20/200 is 38 ETDRS letters. wAMD: wet age-related macular degeneration; BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; VA: visual acuity; OCT: optical coherence tomography

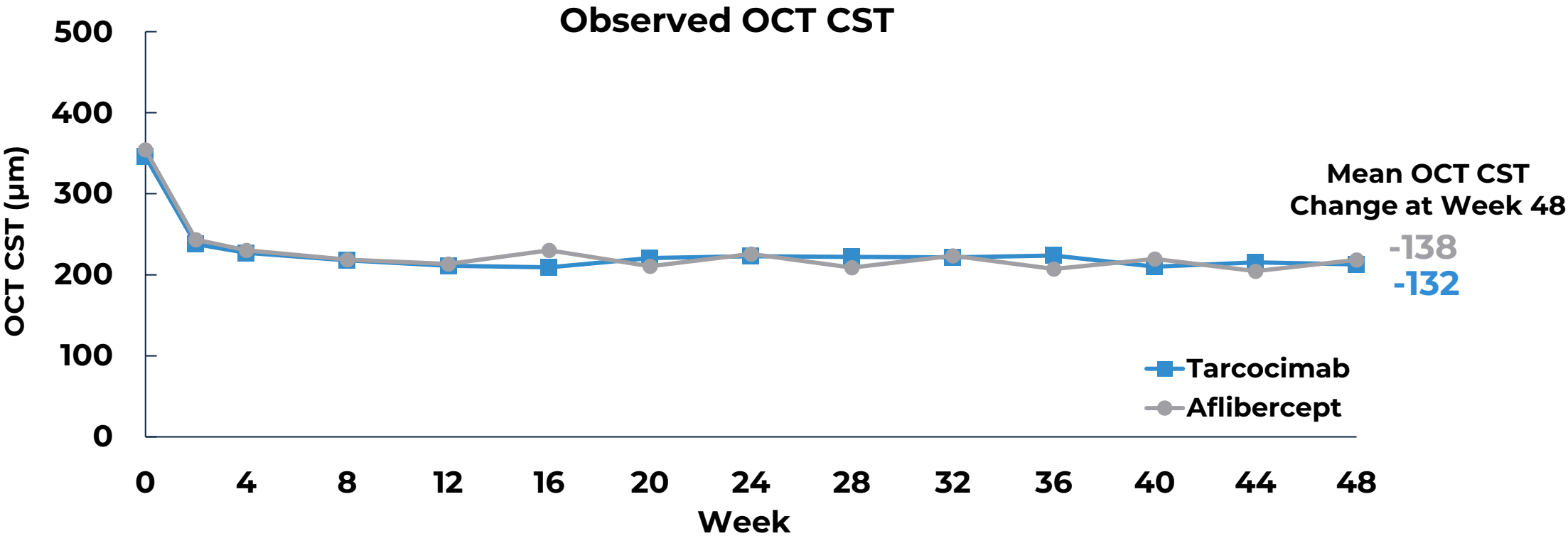
Primary endpoint met: tarcocimab demonstrated meaningful visual gains sustained with up to 6-month dosing



	LSM BCVA change Avg W40-48 (MMRM) ^a	LSM difference ^a (95.02% CI)	<i>p</i> -value ^a
Tarcocimab Q4-24W	6.1	-0.8 (-2.93, 1.32)	0.0007
Aflibercept Q8W	6.9		

LSM: least square mean; MMRM: mixed model for repeated measures. BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study.
^aResults for non-inferiority are based on a MMRM model including the change from baseline value as the dependent variable. Non-inferiority margin = 4.5 ETDRS letters.

Tarcocimab demonstrated rapid and sustained retinal drying in extended dosing with intervals up to 6-months



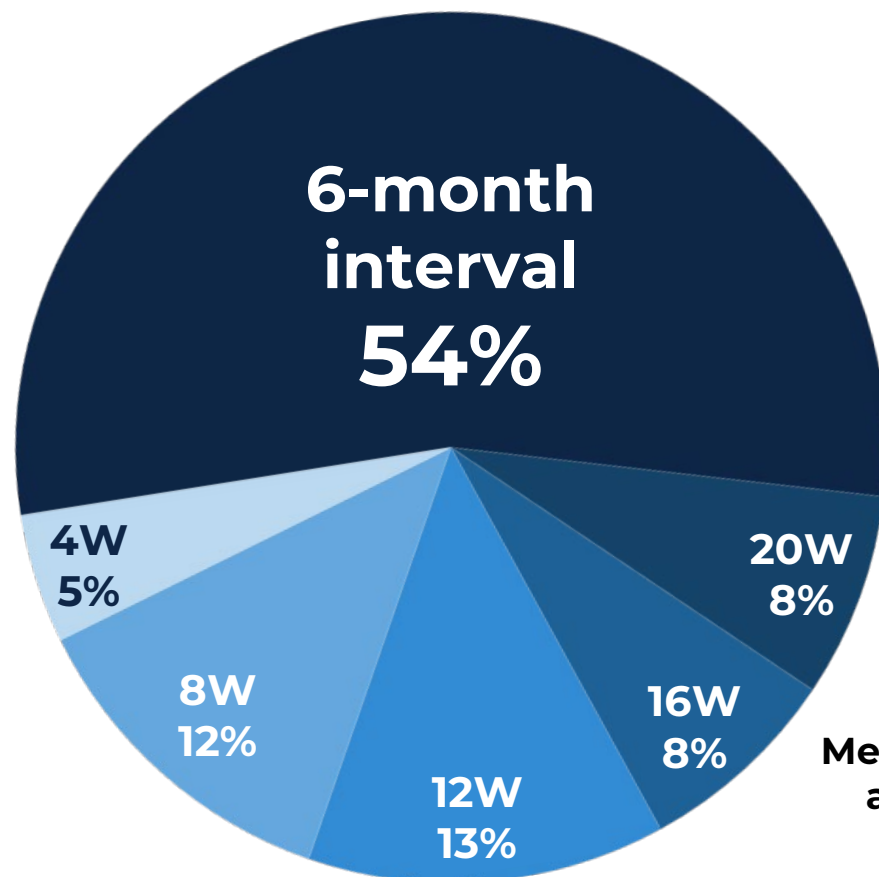
	LSM OCT CST change at W48 (MMRM) ^a	LSM difference ^a (95.02% CI)	Nominal <i>p</i> -value ^a
Tarcocimab Q4-24W	-139.3	-5.8 (-17.52, 5.90)	<0.0001
Aflibercept Q8W	-133.5		

LSM: least square mean; OCT: optical coherence tomography; CST: central subfield thickness.
^a Nominal p-value as not prespecified for hypothesis testing. Results for non-inferiority are based on a MMRM model including the change from baseline value as the dependent variable. Non-inferiority margin = 75 microns.

Durability: using real-world retreatment criteria, more than half of tarcocimab patients achieved 6-month dosing

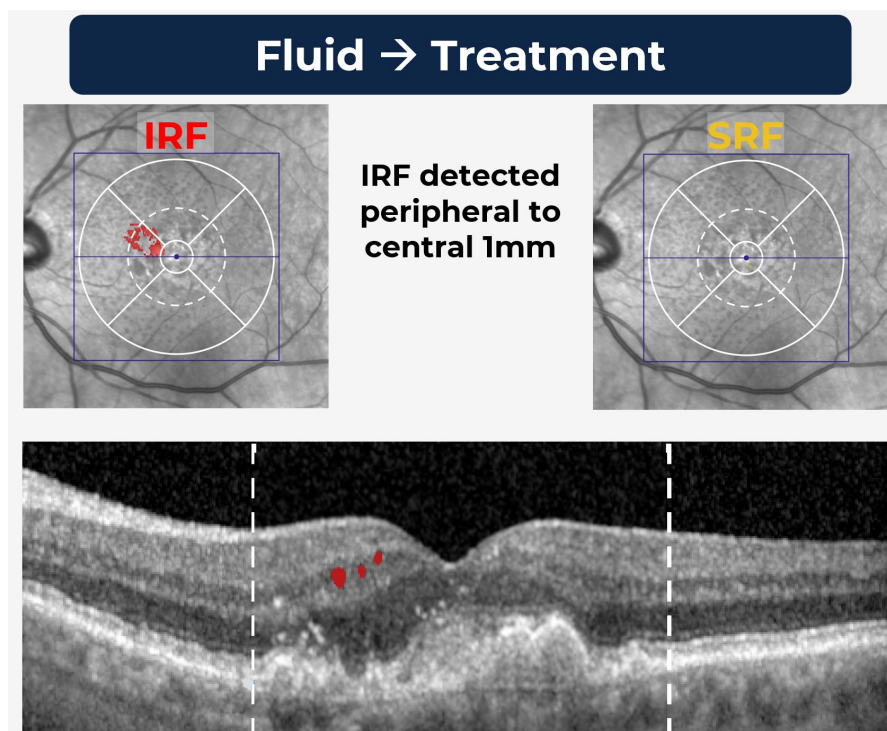


Interval at the Primary Endpoint^a



YEAR 1
Median number of injections
after the loading phase^b

Tarcocimab – 1
Aflibercept – 5



48% of patients achieved a 6-month interval immediately after the loading phase

Strict Treat-to-Dry & Maintain Dry Real-world Durability

a. Prespecified durability analysis includes tarcocimab patients with any completed visit on or after Week 36 (n=210).

b. Number of injections from Week 16 through Week 48 (tarcocimab n=220; aflibercept n=224)

IRF: Intraretinal fluid; SRF: Subretinal fluid; 4W, 4-week interval; 8W, 8-week interval; 12W, 12-week interval; 16W, 16-week interval; 20W, 20-week interval

Tarcocimab was well-tolerated

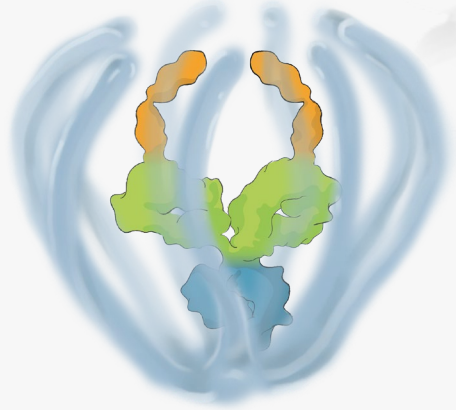
Ocular Adverse Events (AEs) up to Week 48	Tarcocimab n = 220	Aflibercept n = 224
Subjects with any AE in the Study Eye, n (%)^a		
Subjects with ≥1 AEs	89 (40.5%)	79 (35.3%)
Serious AEs	2 (0.9%)	1 (0.4%)
AEs leading to treatment discontinuation	1 (0.5%)	3 (1.3%)
Selected AEs in the Study Eye, n (%)^b		
Retinal hemorrhage	9 (4.1%)	12 (5.4%)
Eye Pain	8 (3.6%)	5 (2.2%)
Elevated IOP	2 (0.9%)	2 (0.9%)
Retinal pigment epithelial tear	2 (0.9%)	2 (0.9%)
Cataract ^c	1 (0.5%)	2 (0.9%)
Intraocular inflammation	0	0
Occlusive retinal vasculitis	0	0
Endophthalmitis	0	0

Results presented for the Safety Population. Events are investigator reported. Adverse events are events with start date ≥first study drug date and ≤last study drug date + 28 days.

a. Includes all adverse events (AE) reported. A single patient can have multiple events of the same AE term reported and can be counted in different AE terms.

b. Total number of patients with one or more adverse event. A patient with multiple events of the same AE term reported are only counted once.

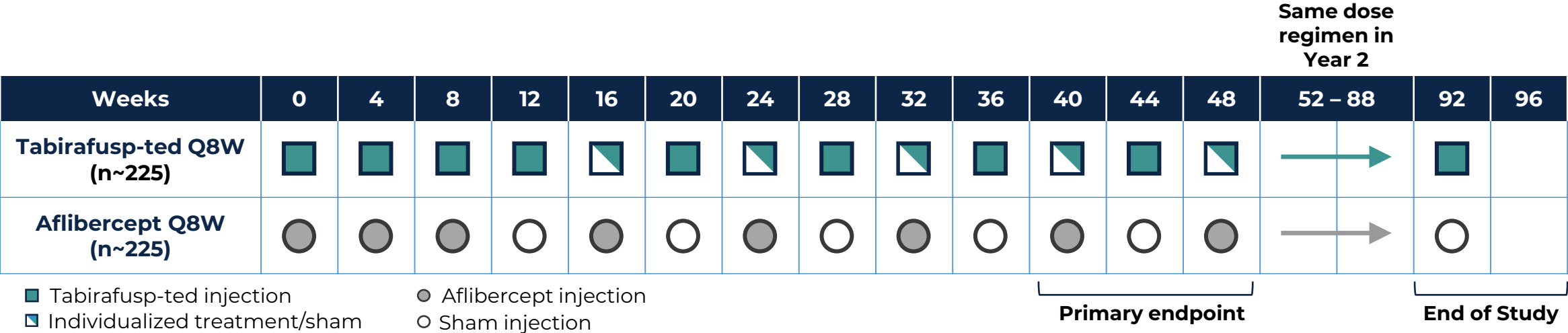
c. Includes the following cataract AE terms: cataract, cataract cortical, cataract nuclear, posterior subcapsular cataract and lenticular opacities.



One-year primary efficacy and safety outcomes of the Phase 3 DAYBREAK Study in Wet AMD

Efficacy and safety of **tabirafusp alfa tedromer
compared to aflibercept**

DAYBREAK – tabirafusp-ted: explored if dual VEGF and IL-6 inhibition can improve outcomes in treatment-naïve wAMD



Treatment paradigm

Proactive bi-monthly dosing, with individualized monthly doses

Objective

Explore efficacy potential with dual VEGF and IL-6 inhibition in treatment-naïve wAMD

Primary endpoint

Mean change in BCVA from baseline (Day 1) to the average of Week 40, 44 and 48

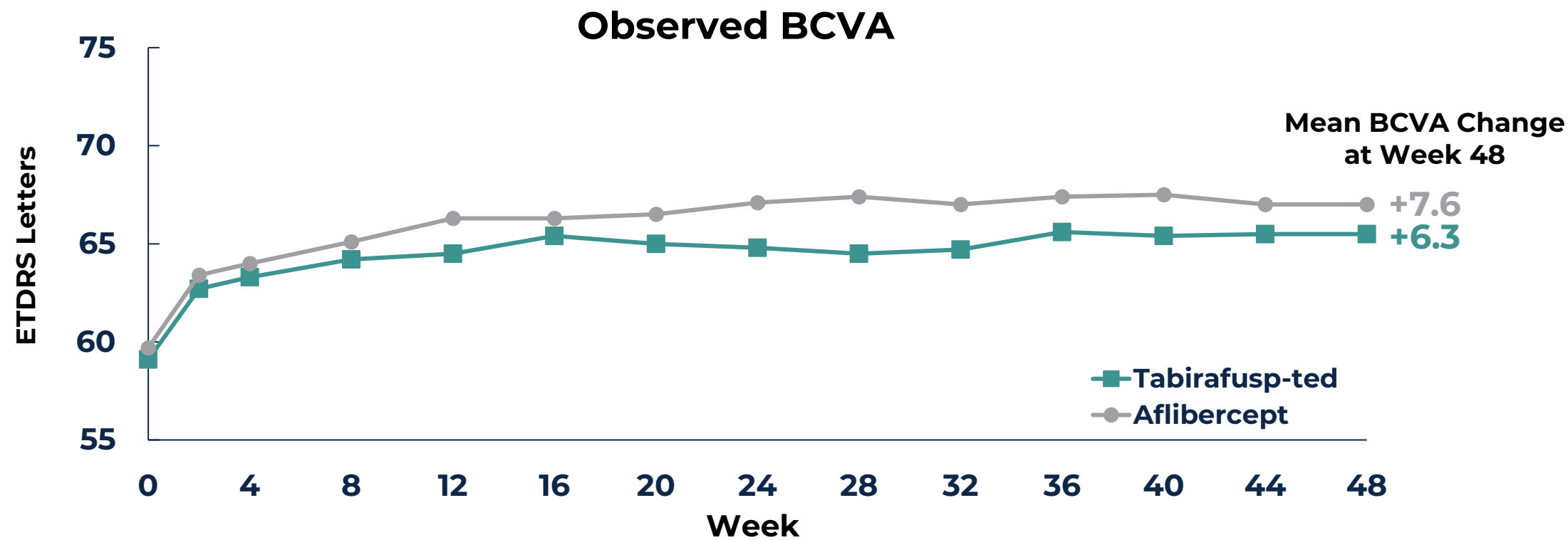
Baseline ocular characteristics were balanced and consistent with treatment-naïve wAMD patients



	Tabirafusp-ted Q8W n=223	Aflibercept Q8W n= 224
BCVA, ETDRS Letters , mean (SD)	59.1 (13.54)	59.7 (13.29)
≥20/40 Snellen equivalent, n (%)	73 (32.7%)	72 (32.1%)
≤20/200 Snellen equivalent, n (%)	25 (11.2%)	21 (9.4%)
BCVA Category		
≤ 49 ETDRS Letters	45 (20.2%)	43 (19.2%)
50 – 69 ETDRS Letters	114 (51.1%)	119 (53.1%)
70 – 78 ETDRS Letters	64 (28.7%)	62 (27.7%)
BCVA – Low Luminance VA Difference		
< 33, n (%)	164 (73.5%)	166 (74.1%)
≥ 33, n (%)	59 (26.5%)	58 (25.9%)
OCT Central Subfield Thickness (CST), μm , mean (SD)	357.0 (114.22)	354.9 (108.12)
Lens Status , n (%)		
Phakic	90 (40.4%)	88 (39.3%)
Pseudophakic	133 (59.6%)	136 (60.7%)
Intraocular Pressure, mmHg , mean (SD)	14.9 (3.30)	14.7 (3.05)

n = Number of participants treated; The denominator for percentages is the number of participants treated within each treatment arm. Snellen equivalent of 20/40 is 69 ETDRS letters and of 20/200 is 38 ETDRS letters. wAMD: wet age-related macular degeneration; BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; VA: visual acuity; OCT: optical coherence tomography

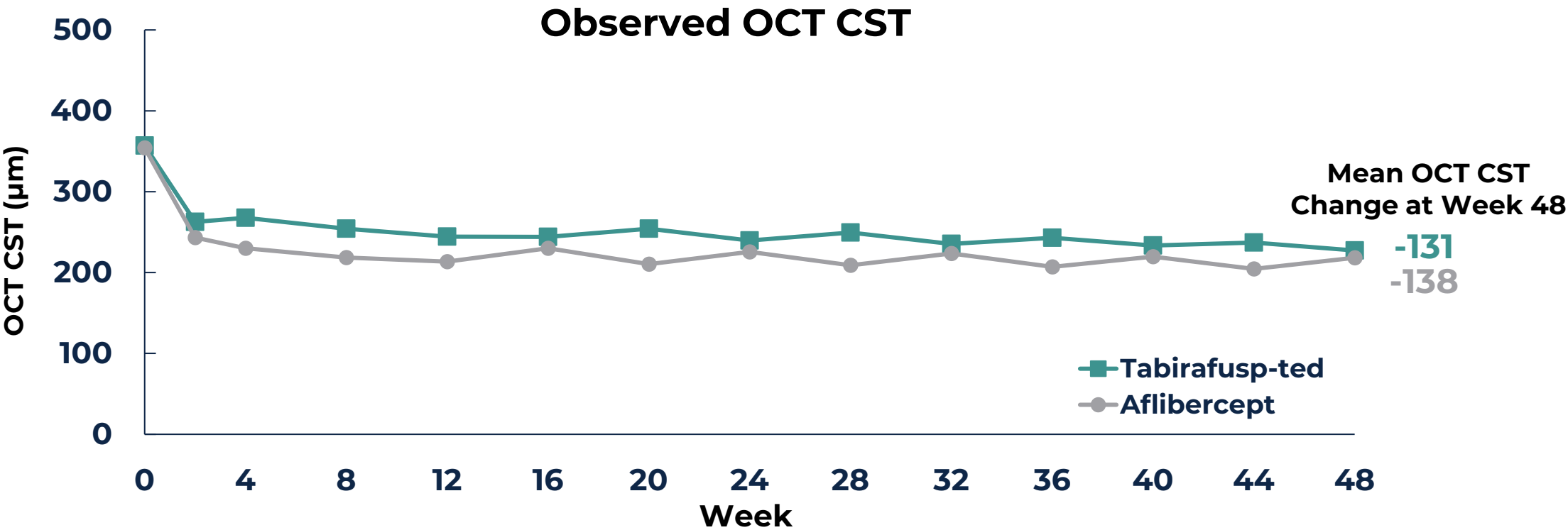
Primary endpoint met: tabirafusp-ted demonstrated meaningful visual gains



	LSM BCVA change Avg W40-48 (MMRM) ^a	LSM difference ^a (95.02% CI)	p-value ^a
Tabirafusp-ted Q8W	5.3	-1.3 (-3.45, 0.87)	0.0036
Aflibercept Q8W	6.6		

LSM: least square mean; MMRM: mixed model for repeated measures. BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; Q8W: every 8 weeks.
^a Results for non-inferiority are based on a MMRM model including the change from baseline value as the dependent variable. Non-inferiority margin = 4.5 ETDRS letters.

Tabirafusp-ted achieved non-inferior retinal drying compared to aflibercept



	LSM OCT CST change at W48 (MMRM) ^a	LSM difference ^a (95.02% CI)	<i>p</i> -value ^a
Tabirafusp-ted Q8W	-132.3	6.6 (-6.22 , 19.35)	<0.0001
Aflibercept Q8W	-138.8		

OCT: optical coherence tomography; CST: central subfield thickness; Q8W: every 8 weeks.
^aResults are based on a MMRM model including the change from baseline value as the dependent variable. Non-inferiority margin = 75 microns.

Tabirafusp-ted was well-tolerated

Ocular Adverse Events (AEs) up to Week 48	Tabirafusp-ted n = 223	Aflibercept n = 224
Subjects with any AE in the Study Eye, n (%)^a		
Subjects with ≥1 AEs	85 (38.1%)	79 (35.3%)
Serious AEs	0	1 (0.4%)
AEs leading to treatment discontinuation	1 (0.4%)	3 (1.3%)
Selected AEs in the Study Eye, n (%)^b		
Retinal hemorrhage	15 (6.7%)	12 (5.4%)
Retinal pigment epithelial tear	1 (0.4%)	2 (0.9%)
Intraocular inflammation	1 (0.4%)	0
Eye Pain	0	5 (2.2%)
Elevated IOP	0	2 (0.9%)
Cataract ^c	0	2 (0.9%)
Occlusive retinal vasculitis	0	0
Endophthalmitis	0	0

Results presented for the Safety Population. Events are investigator reported. Adverse events (start date ≥ first study drug date and ≤ last study drug date + 28 days).

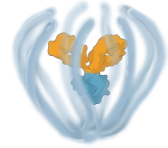
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b. Total number of patients with one or more adverse event. A patient with multiple events of the same AE term reported are only counted once.

c. Includes the following cataract AE terms: cataract, cataract cortical, cataract nuclear, posterior subcapsular cataract and lenticular opacities.

Tarcocimab & tabirafusp-ted met their independent primary endpoints in DAYBREAK: Equivalence in BCVA compared to Q8W aflibercept

Tarcocimab



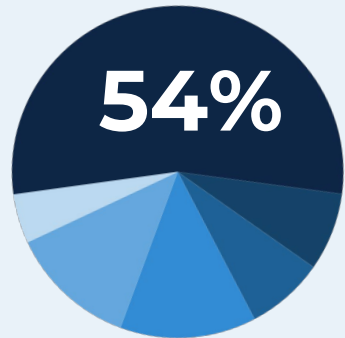
Strong vision gains

Noninferior vs aflibercept Q8W ($p=0.0007$)

Rapid and sustained reduction in CST

Maintained through Week 48 (nominal $p<0.0001$)

New benchmark in durability



6-month durability

At the primary endpoint, using a strict fluid-based retreatment criteria

Multi-indication BLA in wAMD, DR and RVO on track for submission in 2026

Tabirafusp-ted



Equivalent vision gains

Versus aflibercept Q8W ($p=0.0036$)

Equivalent retinal drying

Versus aflibercept Q8W ($p<0.0001$)

Exploring additional benefits

Planned post hoc analyses will evaluate which specific subgroups of wAMD patients may have added benefit from dual VEGF and IL-6 inhibition

Phase 3 ALTO study is actively enrolling in DME, a disease in which IL-6 driven inflammation plays an important role

With DAYBREAK, tarcocimab has completed 5 positive Phase 3 studies across three indications and is BLA-ready

Wet AMD



DAYBREAK



DAYLIGHT

- 54% of patients on **6-month dosing**
- Rapid and sustained disease control
- Monthly dosing enabled

Diabetic Retinopathy



GLOW1



GLOW2

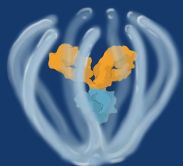
- 100% of patients on **6-month dosing**
- Proliferative disease and mild DME included in trial
- Dosing flexibility

Retinal Vein Occlusion



BEACON

- 75% of patients on **6-month dosing¹**
- Doubled treatment interval (Q8W) at 6 months



Setting a new standard of care in durability

Multi-indication BLA submission in 2026