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- 6 increased government pricing pressures;
- 7 interruptions in production;
- 8 loss of or inability to obtain adequate protection for intellectual property rights;
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- 10 loss of key executives or other employees; and
- 11 adverse publicity and news coverage.

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ASRS 2024

Virtual IR Event

July 23 2024

Welcome

Bruno Eschli

Head of Investor Relations

Agenda

Welcome

Bruno Eschli, Head of Investor Relations

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Ophthalmology franchise update

Nilesh Mehta, Franchise Head Ophthalmology, Global Product Strategy

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Ophthalmology pipeline

Christopher Brittain, Global Head of Ophthalmology, Product Development

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RHONE-X - Vabysmo 4 year follow-up data in DME

TRUCKEE - Vabysmo updated real-world data in nAMD

SUMMIT - Susvimo real-world data in nAMD

Arshad M. Khanani MD, MA, FASRS, Retina Specialist and Clinical Investigator

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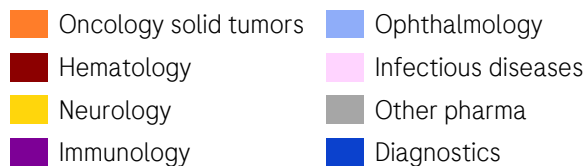
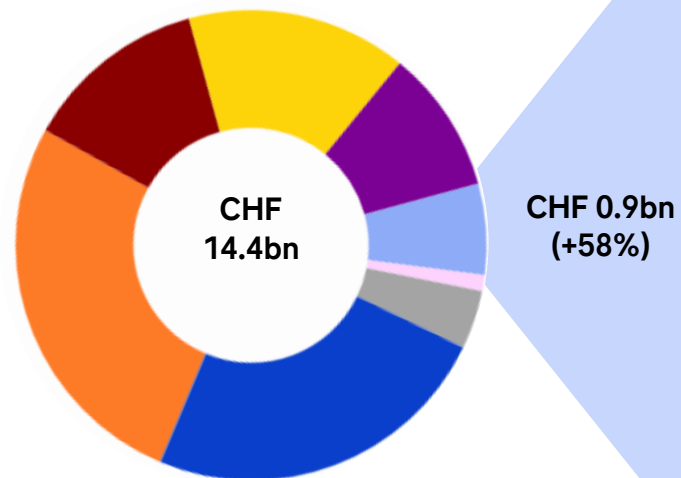
Q&A



Roche establishing leadership in Ophthalmology

Susvimo relaunch in the US has generated excitement among patients and physicians

Q1 2024 sales
(YoY CER growth)



Vabysmo:

- Approved in 98 countries, reimbursed in 35 countries (including EU5)
- US market share* reached 27% in nAMD, 19% in DME, and 15% in RVO; naïve patients >40%
- >20% market-share in UK, Switzerland within 1 year of launch; Double-digit market shares achieved in Japan, Germany, and France
- US: Pre-filled syringe approved, launch in coming months
- Rapidly growing body of RWD confirming drying effect and durability

Susvimo:

- US: Commercial relaunch in nAMD ongoing; filing for DME/DR completed

*Claims data based on Verana Shares through May 2024; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; RVO=retinal vein occlusion; RWD=real-world data; DR=diabetic retinopathy

Key growth drivers beyond 2025

Intense news flow remaining in 2024; ASO factor B discontinued in GA, Ph III (IMAGINATION) in IgAN continues

Pharmaceuticals				
	NME	Indication	Newsflow	Timing
 Oncology / Hematology	tiragolumab	NSCLC	Final Ph III data	H2 2024
	inavolisib	BC	US/EU filing	2024
	divarasib	NSCLC	Ph I/II readout	2024/25
	giredestrant	BC	Ph III readout	2025
 Neurology	Elevidys	DMD	Ph III readout	2024/25
	prasinezumab	PD	Ph IIb readout	2024
	Evrysdi + GYM329	SMA	Ph II readout	2024
	trontinemab	AD	Ph I/II readout	2024
	fenebrutinib	MS	Ph III readout	2025
 Immunology	Gazyva	LN	Ph III readout	2024
	anti-TL1A	IBD	Ph III initiation	2024
	astegolimab	COPD	Ph III readout	2025
 Ophthalmology	vamikibart (anti-IL6)	DME/UME	Ph II/III readout	2024/25
	ASO X factor B	GA	Ph II readout	2024
 Cardiovascular & Metabolism	zilebesiran	HT	Ph II readout	2024
	CT-388/368/996 (GLP-1/GIP)	Obesity	Ph I/II readout	2024

Diagnostics			
	Product	Description	Launch
 Core Lab	i601 mass spec	Total solution for clinical mass spectrometry and first reagent ipack	2024
	cobas pro serology solution	Roche blood safety solution for the US donor screening market	2024
	cobas c703 & ISE neo	High-throughput clinical chemistry and ISE testing on cobas pro	2024
	Elecsys Amyloid Plasma Panel	Rule-out blood-based test for amyloid pathology detection in AD	2025
 Molecular Lab	cobas 6800/8800 v2.0	Upgrade with increased testing flexibility, throughput and automation	2024
	cobas Respiratory flex	Novel TAGS® multiplex technology for respiratory testing on cobas x800	2024
	Next generation sequencing	Nanopore sequencer with unique sequencing by expansion technology	2025+
 Near Patient Care	Accu-Chek SmartGuide	Roche's first generation continuous glucose monitoring solution	2024
	cobas Liat Resp. panel	Detection & differentiation of four most prevalent respiratory targets	2024
	LumiraDx deal closing	Potentially disruptive solution for the Point of Care setting	2024

Upcoming Roche IR events 2024

Additional events driven by readouts

 CVM/EASD Sep 13	 Pharma Day Sep 30	 Neurology/CTAD Oct/Nov	 Digitalization Day Nov/Dec
• Key data presented at EASD: • CT-388 (Ph I cohort 11 & 12 in obese patients without T2D) • CT-996 (Ph I 4 week data in obese patients without T2D)	• Group & Pharma strategy update • R&D excellence update • Pharma commercial portfolio update • Late stage pipeline and therapeutic area updates	• Key data presented at CTAD: trontinemab Ph I/IIb expansion cohort data • Update on the Neurology franchise	• Roche digital efforts in Pharma and Diagnostics • Highlighting use cases across the value chain
Neurology Update ✓ Virtual Mon, 11 Mar 15:00-16:30 CET Diagnostic Day ✓ London & virtual Wed, 22 May 13:00-15:30 BST Oncology/ASCO ✓ Virtual Fri, 31 May 16:00-17:30 CEST Hematology/EHA ✓ Virtual Sun, 16 June 13:00-14:00 CEST Ophtha/ASRS ✓ Virtual Tue, 23 Jul 16:30-17:30 CEST EASD Virtual Fri, 13 Sep tbd Pharma Day London & virtual Mon, 30 Sep 9:00-15:00 BST CTAD Virtual Oct/Nov tbd Digitalization Day Virtual Nov/Dec tbd			

EASD=European Association for the Study of Diabetes; CTAD=Clinical Trials on Alzheimer's Disease; T2D=type 2 diabetes

Ophthalmology franchise update

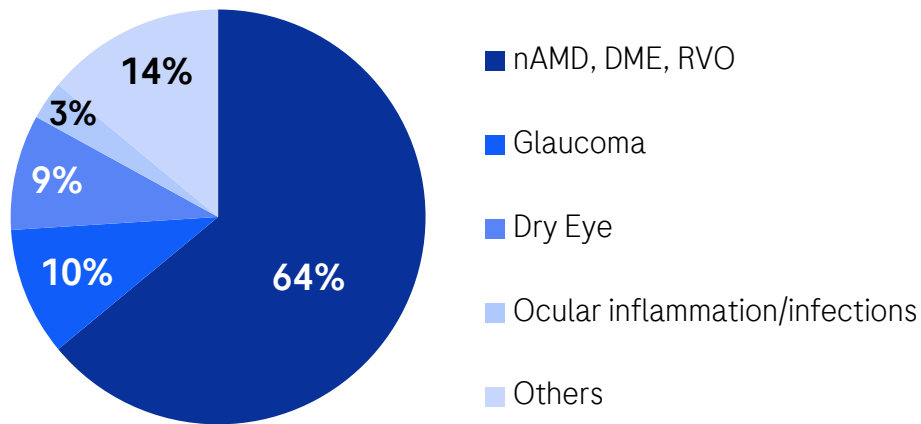
Nilesh Mehta

Franchise Head Ophthalmology, Global Product Strategy

Retinal diseases are the fastest growing segment of the ophthalmology market

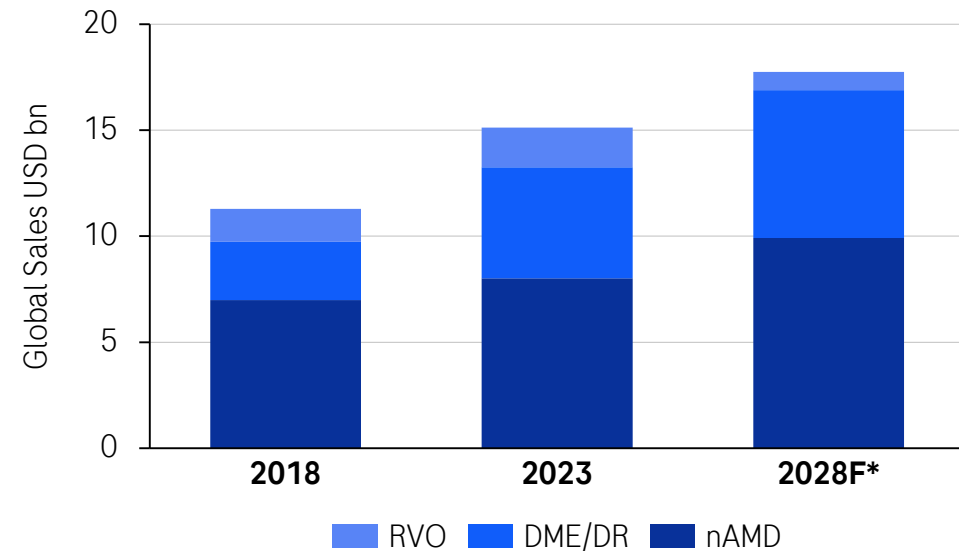
Ophthalmology market¹

Total Market (2023) ~\$24 Billion



- Retinal vascular diseases remain leading causes of vision loss

Global retina market >15 bn USD and growing¹

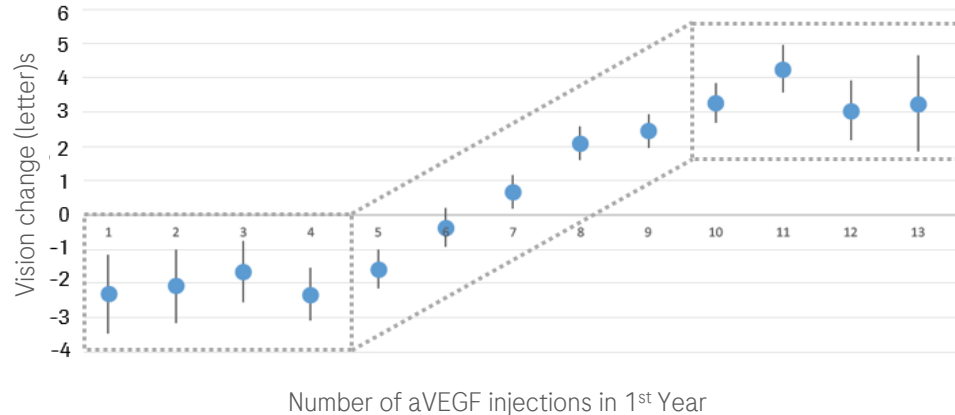


- Incidence and prevalence of common retinal diseases are increasing due to ageing and Type 2 Diabetes²

1. Evaluate Pharma 2024; 2. Rosenblatt T et al., Ophthalmic Surg Lasers Imaging Retina. 2021 Jan 1;52(1):29-36, National Eye Institute. Facts About Diabetic Eye Disease; *2028 Evaluate forecast, Eylea LOE impacting 2028; DME=diabetic macular edema; DR=diabetic retinopathy; nAMD=neovascular age-related macular degeneration; RVO=retinal vein occlusion

Optimal outcomes can be further achieved with longer treatment intervals and improved anatomic control

Infrequent dosing with aVEGF monotherapy correlates with poor vision gains in real-world¹

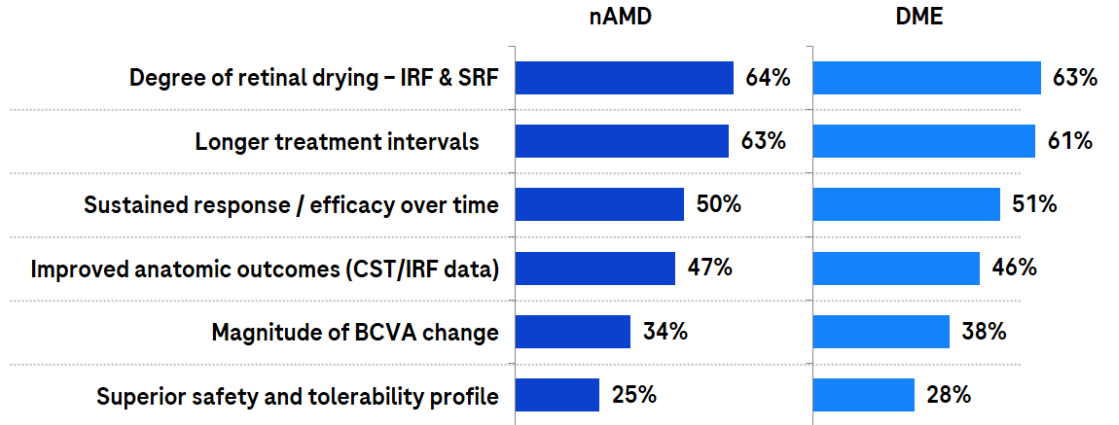


- RWD show patients receive as few as 3-7 aVEGF treatments in the first year, with consistently suboptimal visual outcomes³
- Even in long term follow-up of aVEGF treatment studies, only half of patients achieve 20/40 vision, resulting in a remaining patient need for superior vision outcomes⁴

Drying and longer treatment intervals are the most important drivers in retinal disease for HCPs²

Drivers for aVEGF use in nAMD and DME

(% of HCPs ranking Top-3 either for Vabysmo and/or Eylea HD)



- Drying is a key indicator for physicians to assess potential to extend treatment intervals in the real-world setting
- Sustained efficacy is another important driver for aVEGF use for improving visual outcomes and anatomy for longer, which can also potentially prolong treatment intervals

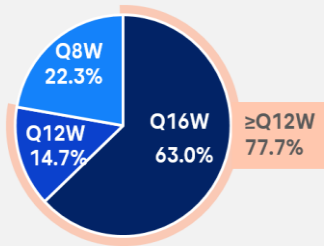
1. Courtesy of T. Brogan/Vestrum Health, presented by Dr. D. Williams at ASRS 2018; 2. Awareness Trial and Usage (ATU), ZS Associates, June 2024; 3. Blinder KJ et al., Clin Ophthalmol 2017;11:393-401; Hølekamp NM et al., Am J Ophthalmol 2018;191:83-91; Cantrell R et al., Ophthalmology 2019; 4. Maguire M, Ophthalmology. 2016 Aug; 123(8): 1751-1761; DME=diabetic macular edema; nAMD=neovascular age-related macular degeneration, IVT=intravitreal; VEGF=vascular endothelial growth factor; HCP=healthcare professional; aVEGF=anti-vascular endothelial growth factor; HD=high dose; BCVA=best-corrected visual acuity; IRF=intraretinal fluid; SRF=subretinal fluid; CST=central subfield thickness; RWD=real-world data

Vabysmo and Susvimo offer options for patients to achieve optimal vision improvements with fewer treatments

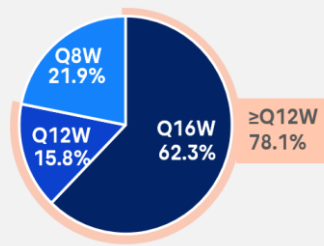


First and only dual-pathway inhibition in retina, targeting VEGF-A and Ang-2

nAMD
TENAYA/LUCERNE



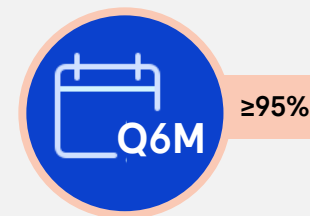
DME
YOSEMITE/RHINE



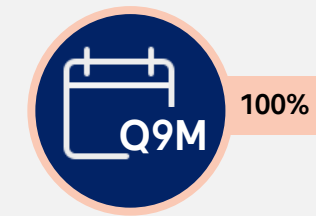
- ~80% of patients reaching Q12W dosing or longer and >60% Q16W dosing in both DME and AMD
- Drying and anatomic improvements vs. 2 mg aflibercept*
- Suitable for newly diagnosed or switch patients

First and only continuous drug delivery treatment** as an alternative to regular IVT injections

nAMD & DME
ARCHWAY/PAGODA



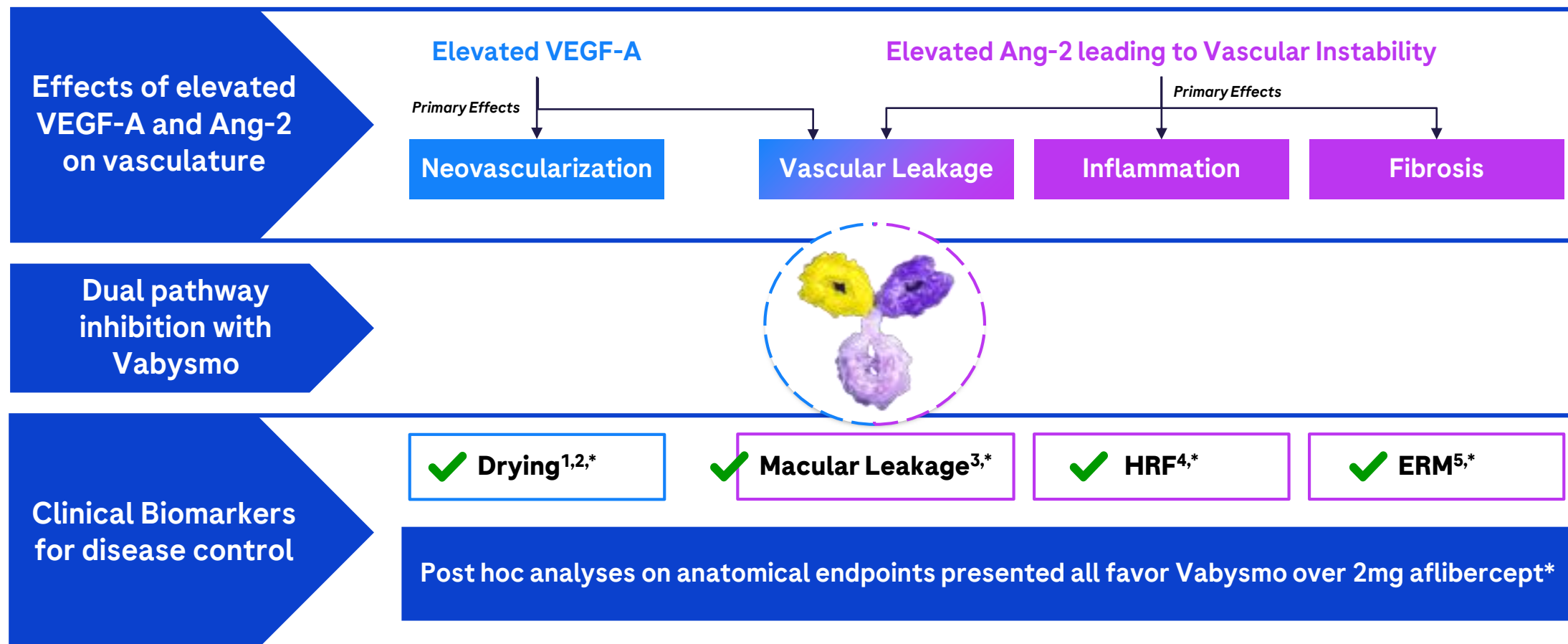
DR
PAVILION



- ≥95% of nAMD pts received Q6M and 100% of DR pts received Q9M without the need for any supplemental IVT injections
- Suitable for patients who have responded to aVEGF therapy and wish to reduce their treatment burden

Vabysmo: Benefits of dual pathway supported by anatomic results

Comprehensive disease control and extended durability



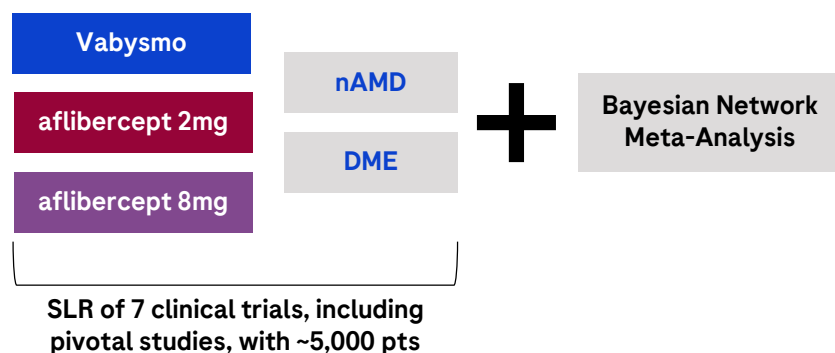
1. Dhoot et al. Macula Society 2023 Annual Meeting; 2. Csaky et al. Angiogenesis 2023 Annual Meeting; 3. Goldberg et al. ARVO 2023 Annual Meeting; 4. Maunz et al. ARVO 2023; 5. Jaffe et al. ASRS 2023 Annual Meeting; *based on post-hoc, exploratory analysis with nominal p-value statistical analysis not adjusted for multiple testing, no formal statistical conclusions can be drawn; Ang-2=angiopoietin-2; VEGF-A=vascular endothelial growth factor A; HRF=hyper-reflective foci; ERM=epiretinal membrane; Eylea (aflibercept) is a registered trademark/product of Regeneron/Bayer

Vabysmo vs. aflibercept: Indirect analysis of CST reductions¹

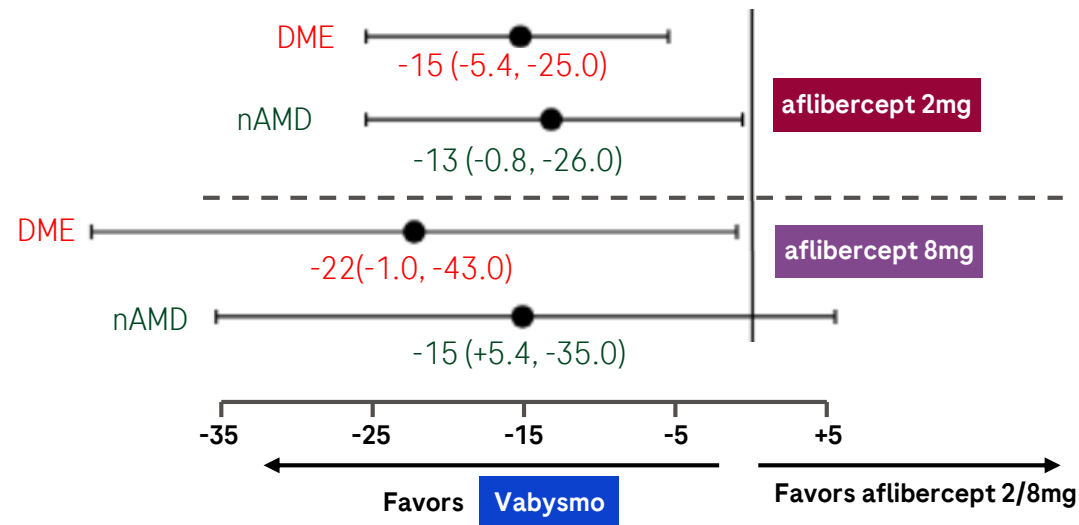
CST improvements vs aflibercept 2mg and 8mg after the monthly loading phase (week 12) favor Vabysmo

Comparative efficacy of Vabysmo: A Systematic Literature Review and Network Meta-Analysis¹

Methodology*



Mean difference in CST change from baseline for Vabysmo vs aflibercept 2mg/8mg at 12 weeks (μm , RE model, 95% CrI)**



- NMA are an established method for cross-trial comparisons between studies despite elevated uncertainty due to the lack of direct evidence²
- NMA shows overall high probability to achieve greater CST reduction compared to aflibercept during the loading phase at week 12
- Analysis insights add to growing body of evidence supporting Vabysmo as the preferred choice for 1L treatment in both nAMD and DME

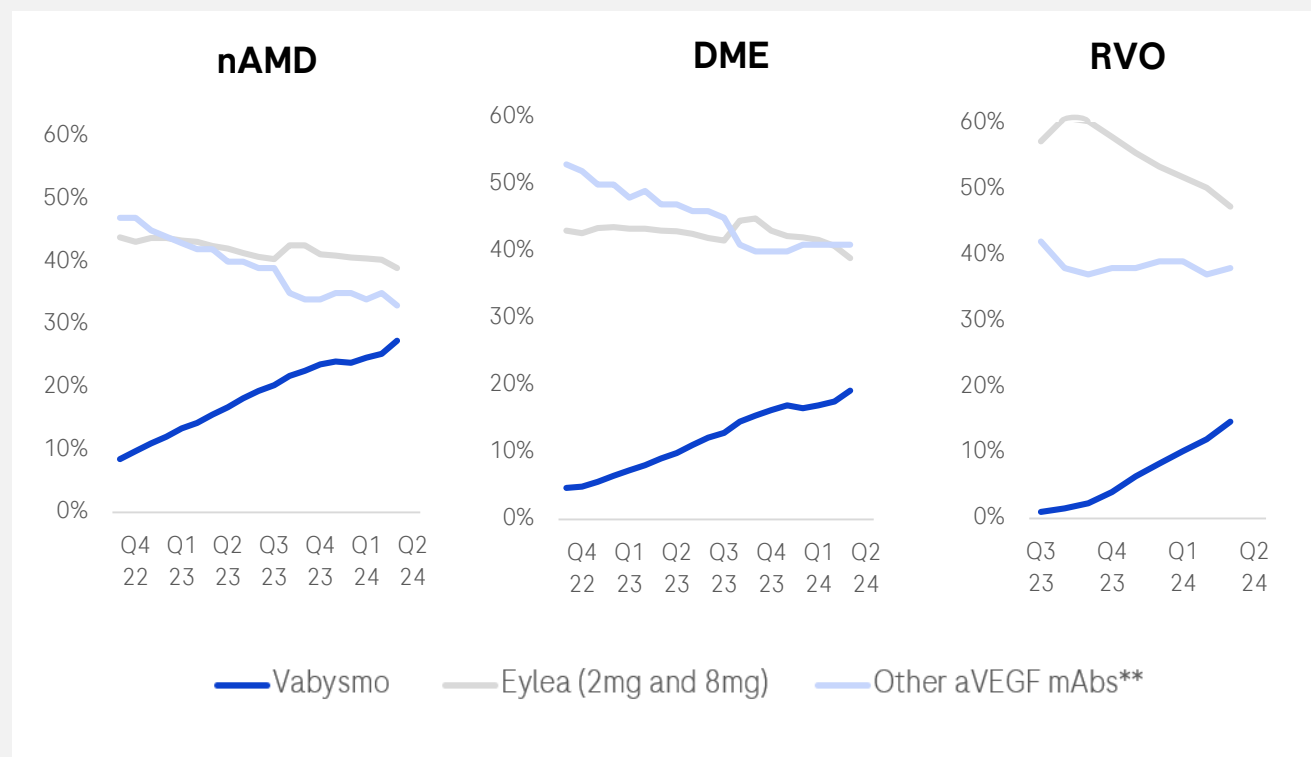
1. Leng, T et al., Macula Society 2024; 2. NICE health technology evaluations: the manual, published: 31 January 2022, last updated: 31 October 2023; to be accessed via: www.nice.org.uk/process/pmg36; *Trials included in the analysis and their respective patient counts: nAMD=TENAYA/LUCERNE (n=671/658), PULSAR (n=1009), CANDELA (n=106); DME=YOSEMITE/RHINE (n=940/951), PHOTON (n=659); Bayesian NMA outcomes of interest=CST change through week 12 and differences & probability of better outcomes with Vabysmo; **For all treatments data of intravitreal Q4W dosing schemes was used for the NMA; The NMA was preceded by a classic feasibility analysis, which confirmed the studies showed no substantial differences with regard to the study populations; SLR=systematic literature review; NMA=network meta-analysis; CST=central subfield thickness; DME=diabetic macular edema; nAMD=neovascular age-related macular degeneration; RE=random effects; CrI=credible interval; Q4W=every 4 weeks



Vabysmo: Continued strong growth momentum

Pre-filled syringe approved by FDA and will become available in the coming months

US patient share continues to expand in nAMD, DME, and RVO*



Vabysmo performance update

- Approved in 98 countries, reimbursed in 35 countries (including EU5)
- US market share reached 27% in nAMD, 19% in DME, and 15% in RVO; naïve patients >40%
 - Label allows for a flexible treatment schedule ranging from 1-4 months in the first year, based on evaluation of the pts anatomy and vision outcomes
- >20% market-share in UK, Switzerland within 1 year of launch; Double-digit market shares achieved in Japan, Germany, and France

Outlook

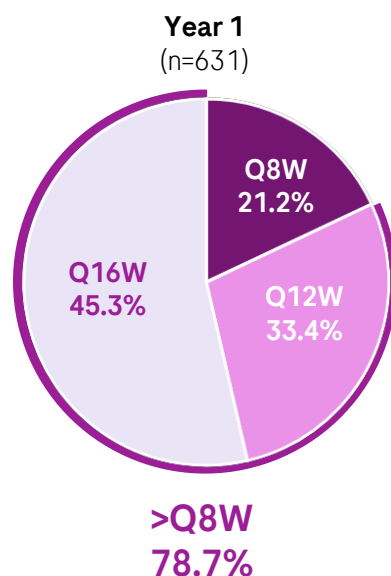
- Vabysmo in RVO received CHMP positive opinion: EU approval expected Q3

*Claims data based on Verana Shares through May 2024; **Avastin, Lucentis and biosimilars; mAb=monoclonal antibody; aVEGF=anti-vascular endothelial growth factor; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; RVO=retinal vein occlusion

Vabysmo: RWD reflects clinical trials in treatment durability

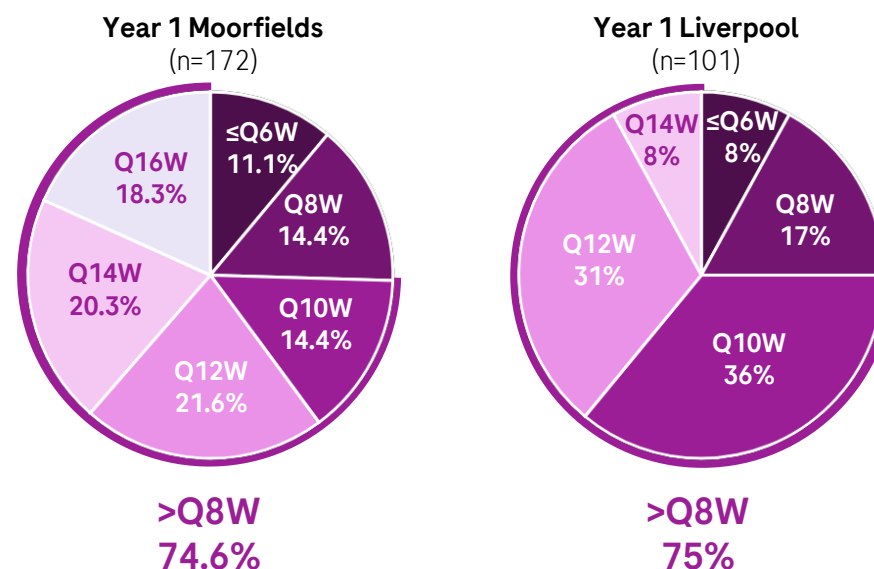
TENAYA/LUCERNE pooled analysis¹

~80% of faricimab treatment-naïve patients achieve **extended intervals** by year 1



Independent UK Real-World Data^{2,3}

~75% of faricimab treatment-naïve patients achieved **extended intervals** in the real world



1. Khanani A et al. Angiogenesis, Exudation, and Degeneration Virtual Congress 2023; 2. Sim SY. ARVO 2024; 3. Babiker S et al. ARVO 2024; QXW=every X weeks; RWD=real-world data

Susvimo: Blockbuster potential with relaunch ongoing

The first and only approved nAMD treatment shown to maintain vision with x2 treatments/yr in the vast majority of patients

Stronger vision outcomes with potential for extended $\geq$ Q6M dosing

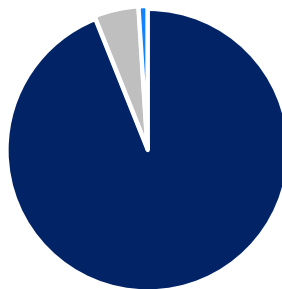


Continuous
delivery of aVEGF
via PD implant



1-2
refill exchanges
per year

93% of patients prefer PDS to IVT injections¹



- Prefer PDS
- No Preference
- Prefer IVT

nAMD relaunch in the US

- FDA has approved updates to the Susvimo implant and refill needle
- Reintroduction to the US market is underway with excitement from patients and physicians
 - PORTAL extension study interim data shows long term maintenance of vision for 5 years
 - Real-world studies including SUMMIT mirror data from clinical trials

Outlook

- Ex-US nAMD approvals expected in 2025+
- Filed in the US for DME (PAGODA) and DR (PAVILION), approval expected in Q1 2025
- Ph IIIb (VELODRONE) extended Q9M refill study in nAMD ongoing
- Continuing to innovate on Port Delivery Platform:
 - Ph I/II (BURGUNDY) zifibancimig (VEGF-Ang2 bispecific) in nAMD ongoing, data expected 2026

1. Holekamp N et al. Archway Ph III Trial of the PDS for nAMD, American Academy of Ophthalmology, 129(3), 2022; IVT=intravitreal; PD=port delivery; PDS=port delivery system; aVEGF=anti-vascular endothelial growth factor; Q6M=every 6 months; DME=diabetic macular edema; DR=diabetic retinopathy; nAMD=neovascular age-related macular degeneration; DutaFabs=dual targeting fragment antigen-binding; Q9M=every 9 months

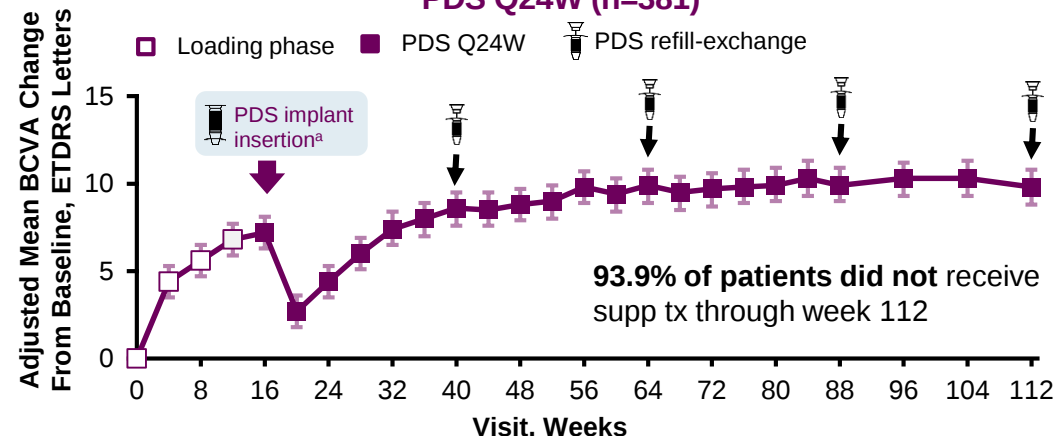
Susvimo in DME and DR: Efficacy maintained at year 2

DME and DR filed with FDA; approval expected in Q1 2025

Ph III (PAGODA) in DME¹

Change in BCVA Over 112 Weeks

PDS Q24W (n=381)

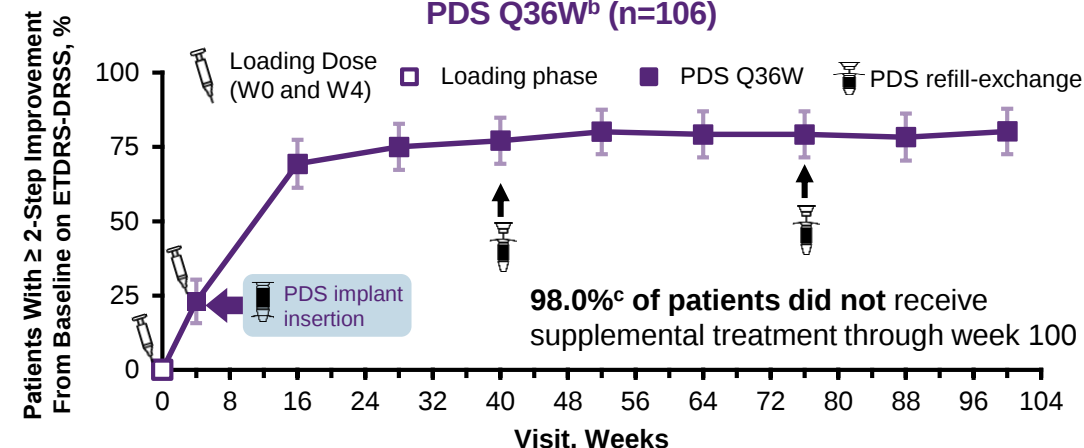


- PDS Q24W resulted in visual and anatomic outcomes comparable to ranibizumab 0.5mg Q4W injections at year 1 (week 64) which were maintained through year 2 with 4 refill-exchanges
- Well tolerated; no cases of endophthalmitis or retinal detachment through week 64; no new safety signals observed in updated analysis

Ph III (PAVILION) in DR²

≥2-Step DRSS Improvement Over 100 Weeks

PDS Q36W^b (n=106)



- PDS Q36W achieved DRSS improvements at year 1 (week 52) which were maintained through 100 weeks with 2 refill-exchanges
- Well tolerated; no cases of endophthalmitis or implant dislocation through week 52; updated safety consistent with primary analysis



1. Aw C et al, ASRS 2024; 2. Chang M et al. ASRS 2024; ^aDue to extenuating circumstances, implant insertion may be delayed beyond week 16; implant insertion procedure must happen within 28 ± 7 days since last intravitreal injection; ^bPatients who receive supplemental treatments, prohibited therapy, or PRP are considered nonresponders regardless of their observed outcome after the corresponding visit. Missing values not preceded by these intercurrent events are imputed using the last observation carried forward method. Patients with missing baseline values are excluded; ^cThis is calculated on the number of patients that were implanted (n = 99); DME=diabetic macular edema; DR=diabetic retinopathy; PDS=Port Delivery System; BCVA=best-corrected visual acuity; ETDRS=Early Treatment Diabetic Retinopathy Study; Tx=treatment; Q24W=every 24 weeks; DRSS=diabetic retinopathy severity scale; Q36W=every 36 weeks

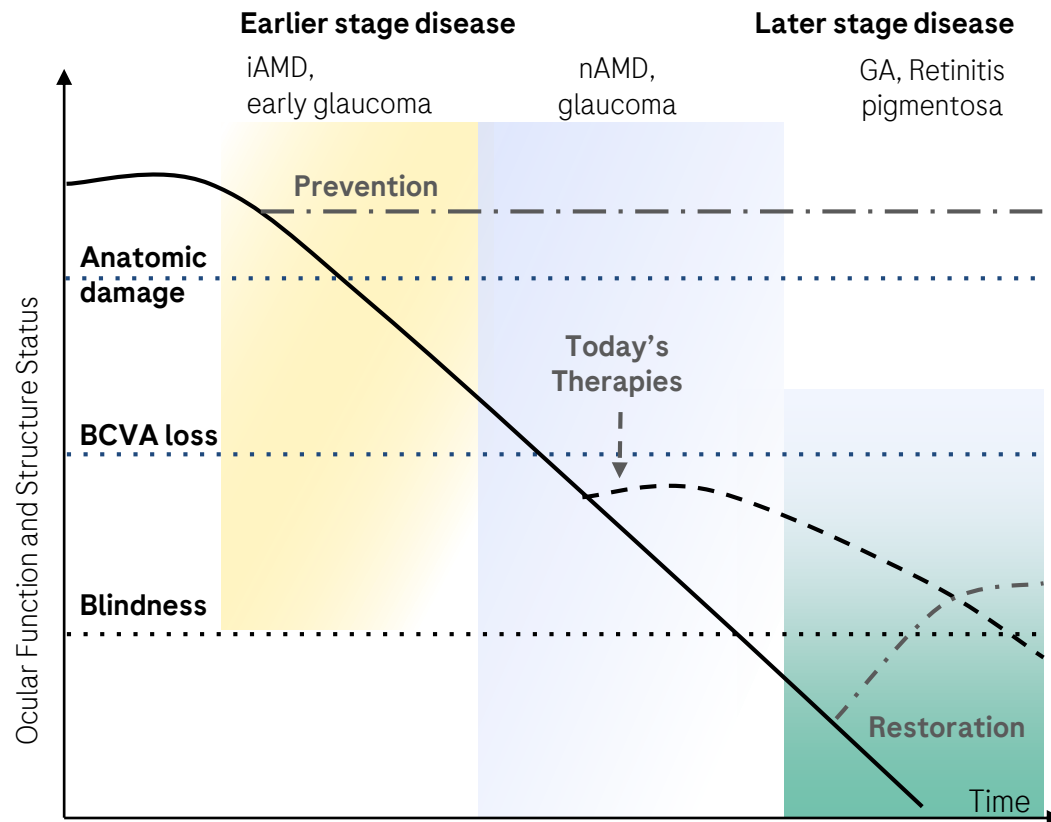
Ophthalmology pipeline

Christopher Brittain

*Senior Vice President and Global Head of Ophthalmology,
Product Development*

Ophthalmology pipeline

Aiming to alter the trajectory of vision loss as experienced today



Improve outcome across all stages of ocular diseases

Earlier stage disease: vision preservation

- Supplement current target approaches: inhibit inflammation & neo-angiogenesis
- Explore clinically useful biomarkers predicting rapid vision loss
- Protect key retinal lineages

Later stage disease: vision restoration

- Replace photosensitive cells once vision is lost
- Continue investment in new therapeutic modalities e.g. cell therapy and gene therapy/optogenetics

Ophthalmology R&D focus areas

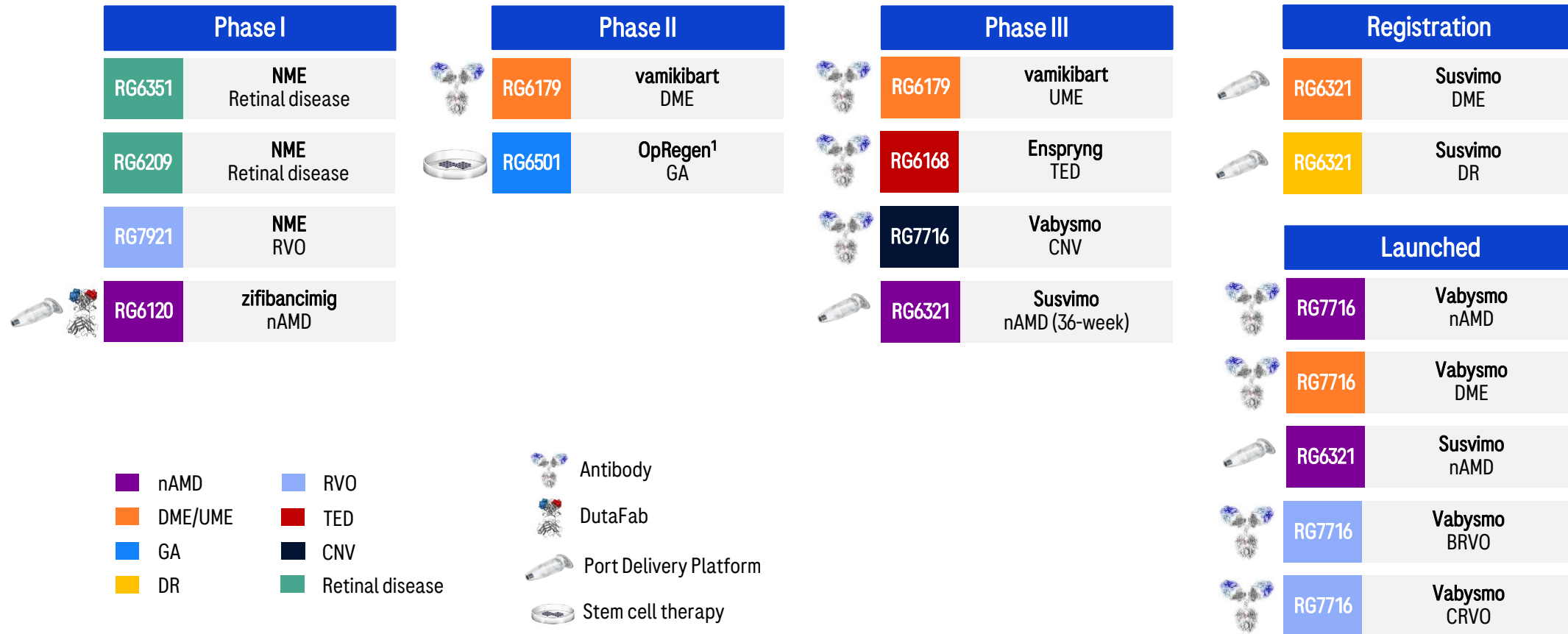
Improving patient outcomes and reducing treatment burden

 Extended durability, Future technologies	 Novel MOAs, New Indications	 Digital capabilities and PHC
Long acting delivery - Port Delivery Platform - DutaFabs  Cell therapy  - Retinal pigment epithelium cell therapy for patients with GA - Ph I/II study ongoing, with FDA Fast Track Designation granted Gene therapy  - AAV engineering platform technology to target specific cell types - Development of AAV capsids for intravitreal targets	Novel MOAs - Vabysmo first dual pathway inhibitor (VEGF/Ang-2) - Addressing retinal inflammation (IL-6) - Semaphorin-3A  New indications - UME, GA, DR, Glaucoma Potential for combination therapies - Characterizing disease pathways, e.g. angiogenesis, inflammation, fibrosis and ischemia	Biomarker and data analytics - Integration of omics, clinical and imaging data - Real world data and natural history - Improved disease understanding    Remote vision monitoring tools - Accessible, effective and low cost tracking of disease activity - Flexibility/compliance with longer duration treatments AI: support clinical decision - e.g. automatic image segmentation algorithms and treatment response prediction algorithms for personalized management of disease     

PHC=personalized healthcare; AI=artificial intelligence; MOA=mode of action; Ang-2=angiopoietin-2; VEGF=Vascular endothelial growth factor; DutaFab=dual targeting fragment antigen-binding; IL-6=inter-leukin 6; AAV=adeno-associated virus; DR: diabetic retinopathy; GA=geographic atrophy; UME=uveitic macular edema

Ophthalmology pipeline gaining momentum

Further improving the standard of care and expanding in new indications



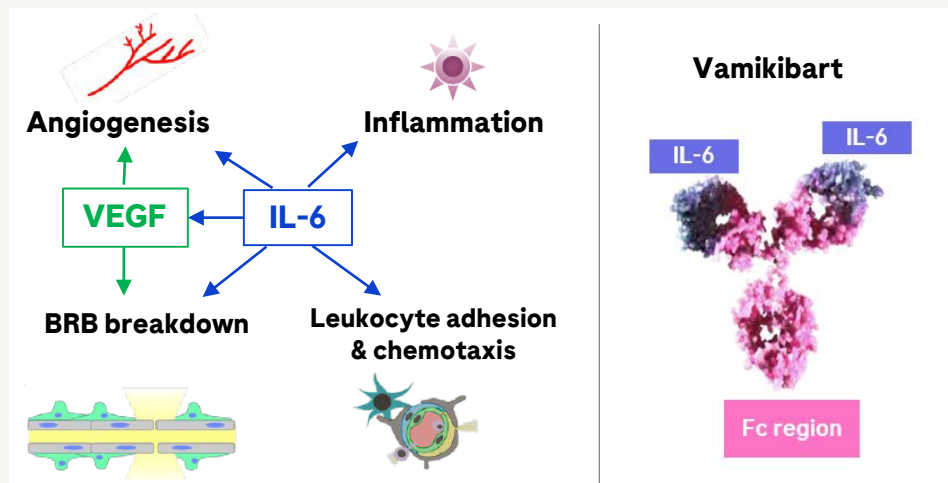
1. In collaboration with Lineage Cell Therapeutics (LCTX); NME=new molecular entity; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; UME=Uveitic macular edema; DR=diabetic retinopathy; BRVO=branch retinal vein occlusion; CRVO=central retinal vein occlusion; DutaFab=dual targeting fragment antigen-binding; TED=Thyroid eye disease; GA=geographic atrophy; CNV=myopic choroidal neovascularization

Vamikibart in UME and DME

Addressing the inflammatory component (IL-6) in macular edema

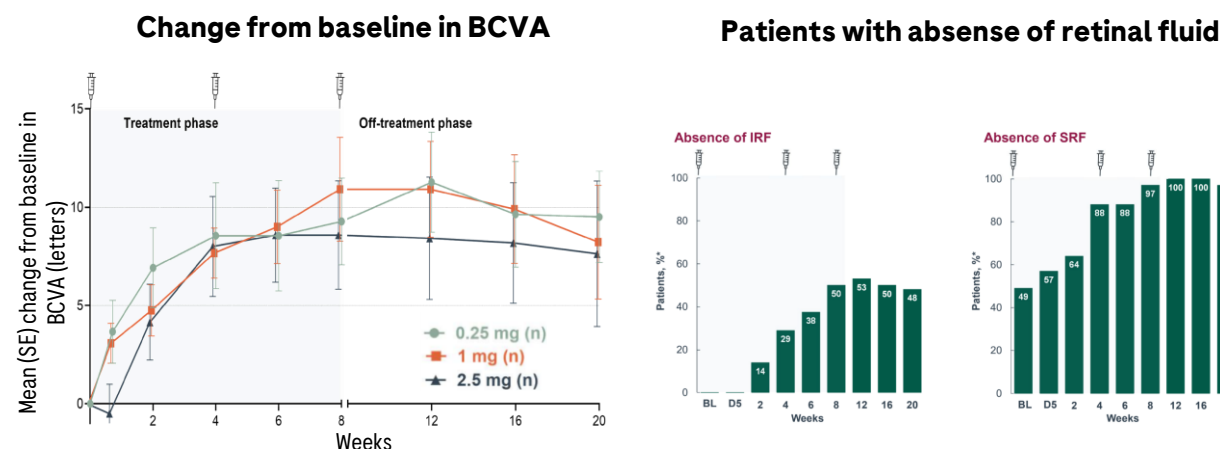
ARVO
2023

IL-6 is involved in many pathways, including inflammation



- Inflammation is a currently sub-optimally treated pathway in a number of ocular diseases
- IL-6 is upregulated in retinal diseases
- Vamikibart inhibits all known forms of IL-6 signaling; specifically designed for intraocular use and optimized for a rapid systemic clearance

Ph I (DOVETAIL) data in UME: Improved vision and retinal thickness in all dosing cohort ¹



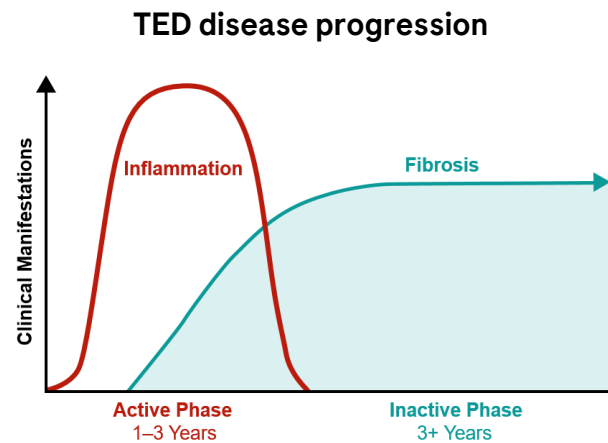
- 25-36% of patients gained 15 letters or more at week 12
- All doses of vamikibart were well tolerated across all patients, with no treatment-related serious AEs, sustained IOP increase, or new cataracts
- Ph III (SANDCAT/MEERKAT) trials in UME ongoing, data expected 2025
- Ph II (BARDENAS/ALLUVIUM) trials in DME ongoing, data expected H2 2024

1. Sharma et al. ARVO 2023; UME=uveitic macular edema; DME=diabetic macular edema; BRB=blood-reintal barrier; IOP=intraocular pressure; IL-6=interleukin-6; VEGF=Vascular endothelial growth factor; AE=Adverse event; BCVA=Best-corrected visual acuity; SE=standard error; IRF=intraretinal fluid; SFR=subretinal fluid

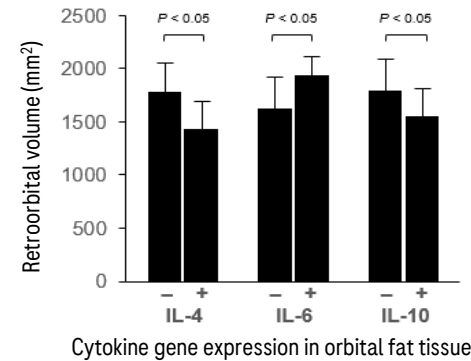
Enspryng in thyroid eye disease

Potential to be the first SC therapy in TED with a well-established safety profile

IL-6 and IL-6R play a key role in the pathogenesis of thyroid eye disease¹



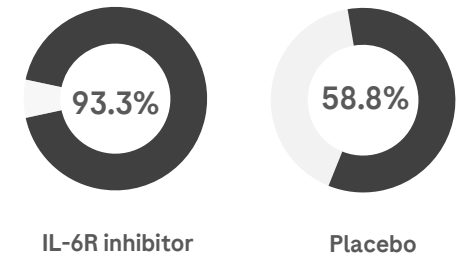
In TED, IL-6 expression correlates with orbital tissue expansion²



- TED is a complex orbital inflammatory autoimmune disease; current treatment options are limited. Faster & durable systemic disease modification needed to prevent downstream fibrosis with minimum or acceptable side effects
- IL-6 is a key mediator of inflammation and drives fibrosis in TED; blocking IL-6R signaling has the potential to reverse the manifestation of the disease
- Enspryng is designed to enable maximal sustained suppression of IL-6 signaling and allow practical dosing with favorable safety profile (9 years of exposure data in NMOSD)

Clinical evidence supports IL-6 signaling inhibition in TED³

Proportion of patients with ≥ 2 points CAS reduction from baseline, week 16

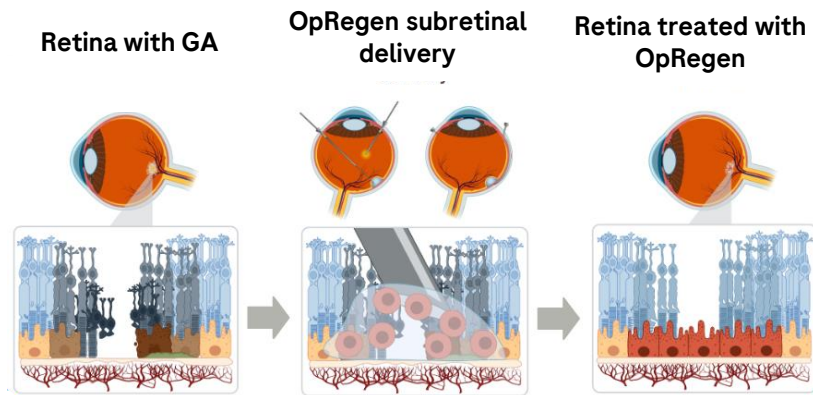


- In a placebo-controlled randomized trial, CAS reduction of ≥ 2 point and proptosis reduction were achieved with IL-6R inhibition
- Ph III (SatraGO-1/SatraGO-2) trials in TED ongoing, data expected 2025

OpRegen in GA: Replenishing the retinal pigment epithelium

Potential to slow, stop, or reverse GA disease progression

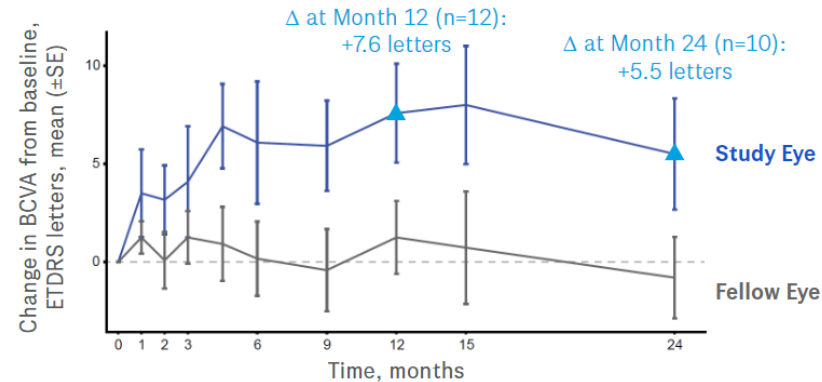
Potential to counteract RPE loss in GA



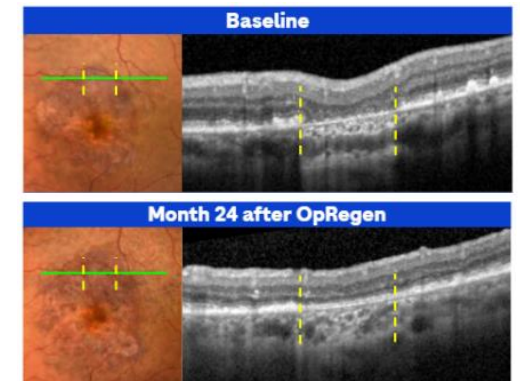
- OpRegen is a suspension of human allogenic RPE cells with the potential to counteract RPE cell loss in areas of GA by supporting retinal cell health
- Ph IIa study to optimize subretinal surgical delivery ongoing

Ph I/IIa data: Visual function and retinal structure improvements sustained through month 24¹⁻²

Cohort 4 (n=12) Patients with impaired vision
(BCVA $\geq$ 20/250 and $\leq$ 20/64)¹



Case 14²

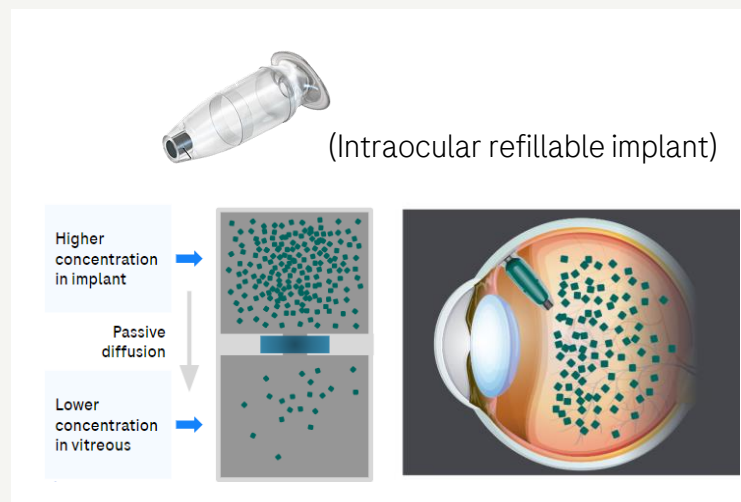


- BCVA gains in patients in Cohort 4 (less advanced GA) measured at month 12 remain evident at month 24, with an average 5.5 letter gain
- Preliminary evidence of maintenance of structural improvement 24 months following OpRegen delivery
- With extended follow-up, OpRegen continues to show an acceptable safety profile

Continuing to innovate on Port Delivery Platform

Ph I/II (BURGUNDY) zifibancimig (VEGF-Ang-2 DutaFab) in nAMD ongoing, data expected 2026

Port Delivery Platform



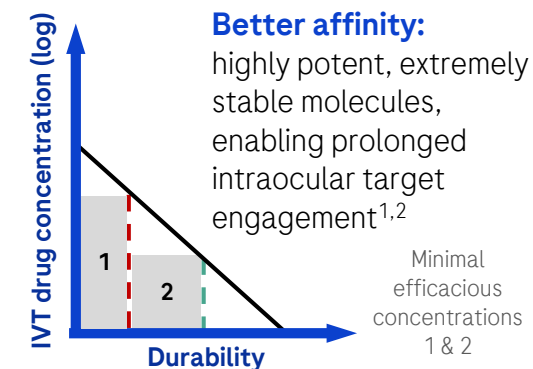
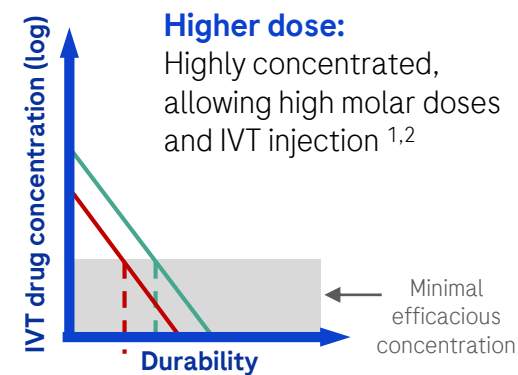
- Port Delivery Platform is designed for continuous delivery of customized molecules through passive diffusion
- Assets in development with Port Delivery Platform: 3 DutaFab molecules (including zifibancimig) and 2 preclinical molecules

DutaFabs: Next generation bispecifics compatible with Port Delivery Platform, designed for increased durability

DutaFab bispecific Fab
e.g. zifibancimig



Single antigen-binding fragment binding two targets



- DutaFabs are a novel bispecific Fab format significantly smaller than bispecific antibodies, size similar to Fabs e.g. Lucentis
- DutaFabs are compatible with the Port Delivery Platform owing to their size and ability to be highly concentrated, enabling increased durability beyond Q6M²

1. Roche. Data on file. Bispecific Antibody Technologies to improve Clinical Efficacy and Duration of Action for Ophthalmology. I2O Summit 2019; 2. Roche. Data on file. 2020; DutaFabs=dual targeting fragment antigen-binding; VEGF=vascular endothelial growth factor; Ang-2=angiopoietin-2; mAb=monoclonal antibody; IVT=Intravitreal; Q6M=every 6 months; nAMD=neovascular age-related macular degeneration

RHONE-X - Vabysmo 4 year follow-up data in DME
TRUCKEE - Vabysmo updated real-world data in nAMD
SUMMIT - Susvimo real-world data in nAMD

Arshad M. Khanani MD, MA, FASRS
Retina Specialist and Clinical Investigator



FOUR-YEAR OUTCOMES OF FARICIMAB IN DME: FIRST TIME SAFETY AND EFFICACY RESULTS FROM THE RHONE-X LONG-TERM EXTENSION TRIAL

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Financial Disclosures

- AMK: Consultant: 4D Molecular Therapeutics, AbbVie, Adverum, Alcon, Amgen, Annexin, Annexon, Apellis, Aviceda, Beacon Therapeutics, Boehringer Ingelheim, Clearside, Complement Therapeutics, Exegensis Bio, EyePoint, Frontera, Genentech, Inc., Gyroscope, iLumen, Iveric Bio, Janssen, Kodiak Sciences, Kriya, Kyowa Kirin, Nanoscope, Novartis, Ocular Therapeutix, Oculis, Ocuphire, OcuTerra, Olives Bio, Opthea, Oxular, Oxurion, Perfuse, Ray Therapeutics, RecensMedical, Regeneron, Regenxbio, Revive, RevOpsis, Roche, Sanofi, Stealth, Thea, Unity, Vanotech, Vial; Research Support: 4D Molecular Therapeutics, Aviceda, Adverum, Alexion, Annexon, Apellis, Aviceda, Eluminex, EyePoint, Exegensis, Genentech, Inc., Gyroscope, Iveric Bio, Janssen, Kodiak Sciences, Kyowa Kirin, Neurotech, Ocular Therapeutix, Oxular, Regenxbio; Stock options: Aviceda, Oculis, Opthea, PolyPhotonix, RecensMedical, Perfuse, RevOpsis, Vial; Board of Directors: Oculis

Study and Product Disclosures

- Faricimab is approved for the treatment of neovascular age-related macular degeneration, diabetic macular edema, and retinal vein occlusion in multiple countries worldwide. Faricimab is not currently approved for use outside these indications
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by F. Hoffmann-La Roche Ltd. for the study and third-party writing assistance, which was provided by Trishan Gajanand, PhD, of Envision Pharma Group

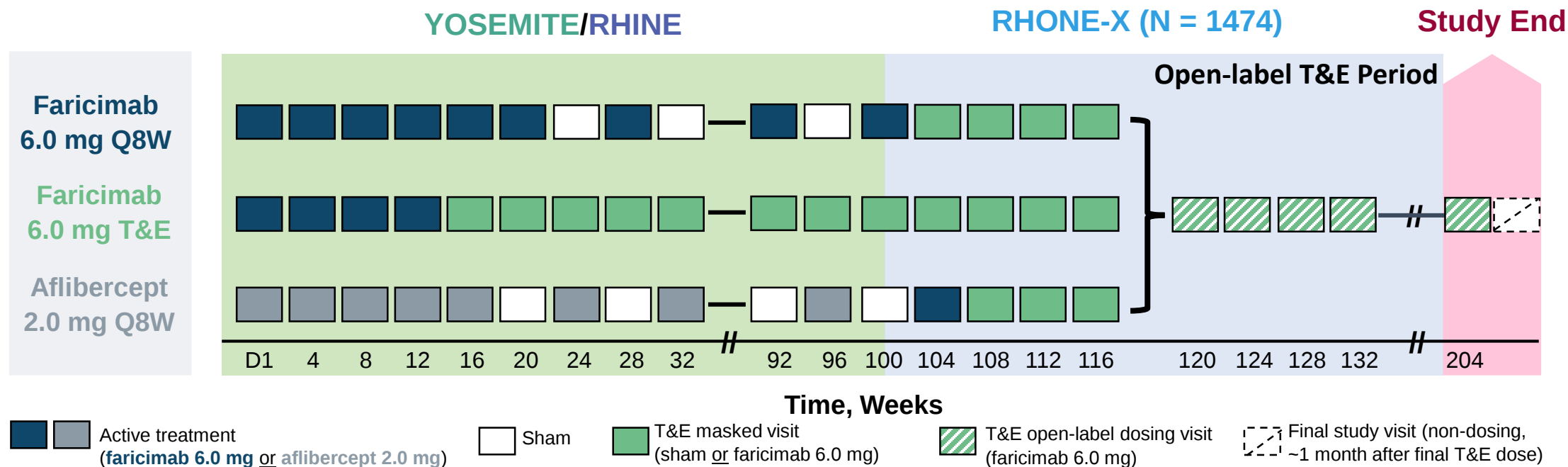
METHODS: RHONE-X Extension Trial Assessed the Long-Term Safety and Efficacy of Faricimab Treat & Extend in Patients With DME

Phase 3, multicenter, open-label, long-term extension trial

- Patients with DME who completed either the YOSEMITE or RHINE clinical trials without discontinuation of study treatment were included
- Patients were followed for an additional two years to assess the safety and efficacy of faricimab over 4 years

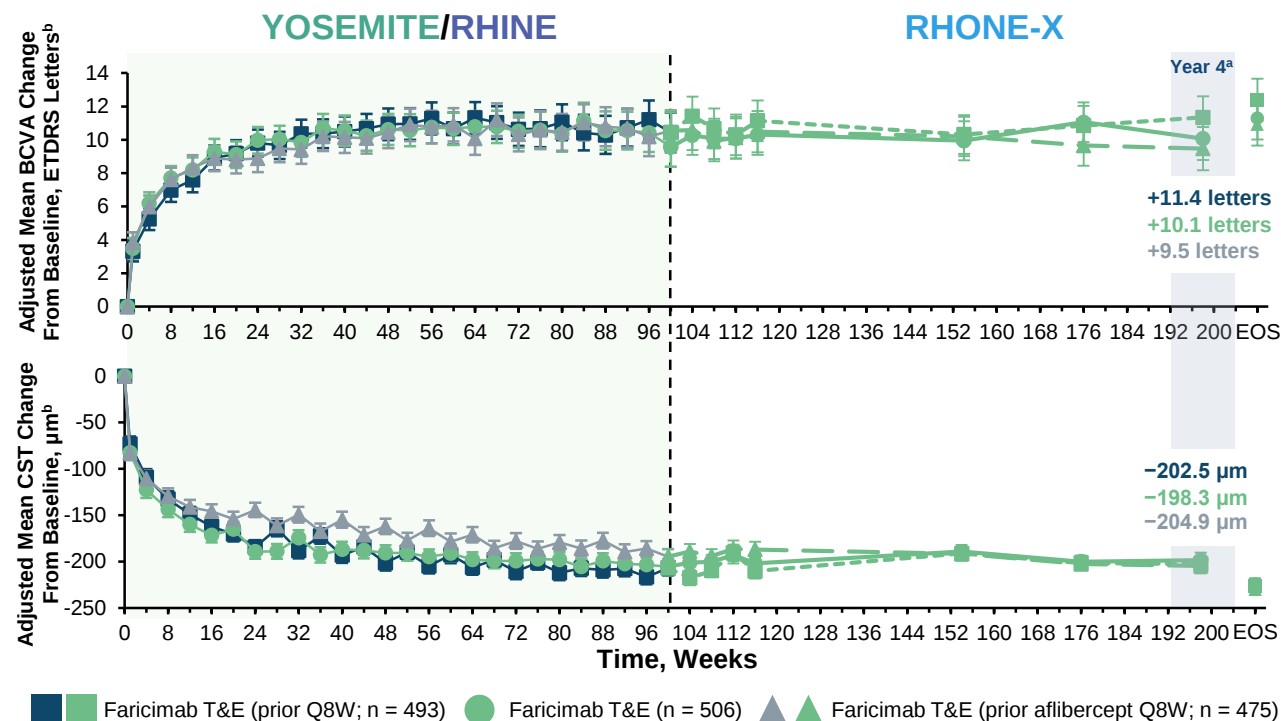
Faricimab treat & extend in RHONE-X

- Patients in RHONE-X attended monthly visits during the first 16 weeks (masked period) and subsequently only attended at T&E dosing visits (open label period)
- All patients received faricimab T&E up to Q16W

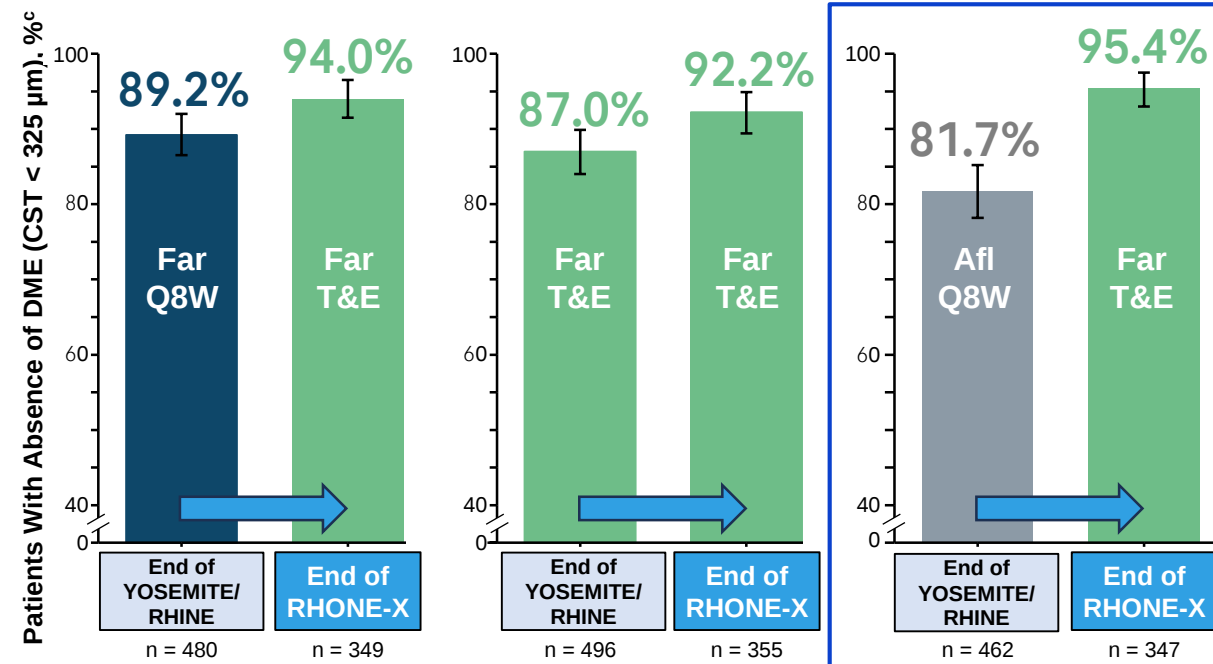


RESULTS: Robust Vision and CST Improvements Were Maintained in RHONE-X With >90% of Patients Achieving Absence of DME (CST < 325 μ m) with Faricimab up to Q16W by End of Study

Safety: Faricimab was well tolerated through years 3 and 4 of RHONE-X with the nature of AEs consistent with the YOSEMITE/RHINE parent trials



Absence of DME was achieved by >90% of patients by the end of RHONE-X regardless of prior treatment arm



~80% of patients achieved $\geq$ Q12W dosing at the end of RHONE-X

Faricimab T&E regimen started at week 100/day 1 of RHONE-X for faricimab Q8W and aflibercept Q8W but not all patients received faricimab at week 100. Estimates for year 3 and 3.5 are averaged over weeks 144 to 164 and 168 to 188, respectively. ^aAdjusted mean change from baseline at year 4 of RHONE-X, averaged over weeks 192 to 204. EOS minimum of 28 days after the final faricimab dose. ^bAnalysis of Covariance model was adjusted for parent study treatment group, visit, visit-by-treatment group interaction, baseline BCVA (continuous) or baseline CST (continuous) as applicable, baseline BCVA (< 64 vs $\geq$ 64 ETDRS letters), prior intravitreal anti-VEGF therapy (yes vs no), region (US and Canada, and the rest of the world). ^cWeighted estimates were based on CMH test stratified by baseline BCVA score (< 64 letters vs. $\geq$ 64 letters), prior intravitreal anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. the rest of the world). Missing data were not imputed. Estimates < 0% or > 100% were imputed as 0% or 100% respectively. 95% CI error bars are shown.

AE, adverse event; Afl, aflibercept 2 mg; BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; CST, central subfield thickness; DME, diabetic macular edema; EOS, end of study; ETDRS, Early Treatment Diabetic Retinopathy Study; Far, faricimab; Q8W, every 8 weeks; Q16W, every 16 weeks; T&E, treat & extend; VEGF, vascular endothelial growth factor.

DISCUSSION: Long-term Safety and Efficacy Outcomes in DME With Faricimab

- ▶ RHONE-X is the **largest DME long-term extension study** to date and had **excellent patient retention (81.7%)**
- ▶ Faricimab was **well tolerated** with a safety profile that was **consistent** with the YOSEMITE/RHINE parent trials
- ▶ BCVA and CST **improvements** achieved in the YOSEMITE/RHINE trials were **maintained** with ~80% of patients on $\geq$ Q12W dosing intervals at the end of study
- ▶ **Absence of DME** (CST <325 μ m) was achieved in **over 90% of patients** by the end of the study
- ▶ RHONE-X demonstrated the long-term safety and efficacy of **dual Ang-2/VEGF-A inhibition** with faricimab in DME

Backup: Faricimab Was Well Tolerated Through Years 3 and 4 of RHONE-X With the Nature of AEs Consistent With the YOSEMITE/RHINE Parent Trials

AEs Through Study End, Patients With ≥ 1 AE, n (%) ^a	Faricimab T&E (prior Q8W) n = 491	Faricimab T&E n = 500	Faricimab T&E (prior aflibercept) n = 473
Ocular AEs^b	219 (44.6%)	188 (37.6%)	197 (41.6%)
Serious ocular AEs^b	31 (6.3%)	15 (3.0%)	26 (5.5%)
Ocular AEs of special interest^c	30 (6.1%)	14 (2.8%)	24 (5.1%)
Intraocular inflammation events^d	7 (1.4%)	7 (1.4%)	5 (1.1%)
Uveitis	3 (0.6%)	1 (0.2%)	0
Iritis	2 (0.4%)	4 (0.8%)	1 (0.2%)
Iridocyclitis	0	2 (0.4%)	3 (0.6%)
Vitritis	1 (0.2%)	1 (0.2%)	2 (0.4%)
Post-procedural inflammation	1 (0.2%)	0	0
Endophthalmitis events	2 (0.4%)	0	1 (0.2%)
Retinal vasculitis/retinal occlusive vasculitis events	0	0	0
Retinal vascular occlusion events (not associated with inflammation)			
Retinal vein occlusion	4 (0.8%)	4 (0.8%)	1 (0.2%)
Retinal artery occlusion	0	1 (0.2%)	2 (0.4%)
Retinal artery embolism	0	0	0
Arterial occlusive disease	0	0	0
Serious non-ocular AEs	122 (24.8%)	100 (20.0%)	112 (23.7%)
APTC events^e	27 (5.5%)	24 (4.8%)	26 (5.5%)

Safety data are presented only for the safety evaluation population from RHONE-X who are defined as patients who received at least one dose of faricimab in the RHONE-X long-term extension study. Includes AEs with onset from the first dose of study drug through study end. ^a Percentages are based on n values in the column headings; multiple occurrences of the same AE in an individual are counted only once. ^b Ocular AEs in the study eye only are presented. ^c Ocular AEs of special interest were defined as events associated with severe intraocular inflammation, events requiring surgical or medical intervention to prevent permanent loss of sight or events associated with BCVA loss of ≥ 30 letters for > 1 hour. ^d Excluding endophthalmitis. ^e APTC events were adjudicated by an external independent committee; all other events were investigator reported.

AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; BCVA, best-corrected visual acuity; T&E, treat-and-extend; Q8W, every 8 weeks.

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The Real-World Efficacy and Safety of Faricimab in Neovascular Age- Related Macular Degeneration: The TRUCKEE Study – 2 Year Results

Arshad M. Khanani, MD, MA, FASRS

Sierra Eye Associates, Reno, NV



The TRUCKEE and SUMMIT Studies are a collaborative clinician directed and organized study with no industry sponsor across multiple sites in the US.

TRUCKEE Study: Design

Evaluating efficacy and safety of faricimab in real-world patients with nAMD

Target Patient Population

- Treatment-naïve AND previously-treated patients

Ongoing Data Collection

- Demographics
- Prior treatment history
- Efficacy (vision, central subfield thickness, retinal fluid status)
- Durability
- Safety

TRUCKEE Results: Demographics

Population (N = 2756 patients, 3412 eyes)

Variable	Mean	Range
Age (years)	80.24	47 - 100
Variable	Groups	N (%)
Gender (patients)	Female	1521 (55.2%)
	Male	1087 (39.4%)
	Not Reported	148 (5.4%)
Last anti-VEGF injection (eyes)	Aflibercept	1461 (42.8%)
	Bevacizumab	391 (11.5%)
	Brolucizumab	134 (3.9%)
	Ranibizumab	621 (18.2%)
	Treatment Naïve	330 (9.7%)
	Not known	475 (13.9%)

Efficacy After Three Injections of Faricimab in All-Switched Patients

Population with Follow-up (N = 1735 eyes)

Previous Interval: 45.5 days

Current Interval: 54.5 days

Increase in interval post-faricimab: + 9.0 days

	Baseline	Follow-Up	Change	P-Value
Variable	Mean (SEM)	Mean (SEM)		
ETDRS (letters)*	61.92 (0.01)	62.27 (0.01)	+0.35 letters	0.653
CST (μ M)	304.70 (0.13)	277.71 (0.11)	-26.99 μ M	< 0.0001
PED Height	270.57 (0.88)	236.28 (0.61)	-34.29 μ M	0.326

*Based on Snellen to ETDRS conversion

Efficacy After Three Injections of Faricimab in Aflibercept-Switched Patients

Population with Follow-up (N = 1005 eyes)

Previous Interval: 44.4 days

Current Interval: 52.8 days

Increase in interval post-faricimab: + 8.4 days

	Baseline	Follow-Up	Change	P-Value
Variable	Mean (SEM)	Mean (SEM)		
ETDRS (letters)*	63.89 (0.02)	64.14 (0.02)	+0.25 letters	0.488
CST (μ M)	303.52 (0.2)	278.58 (0.16)	-24.94 μ M	< 0.0001
PED Height	262.1 (1.25)	232.34 (0.98)	-29.76 μ M	0.25

*Based on Snellen to ETDRS conversion

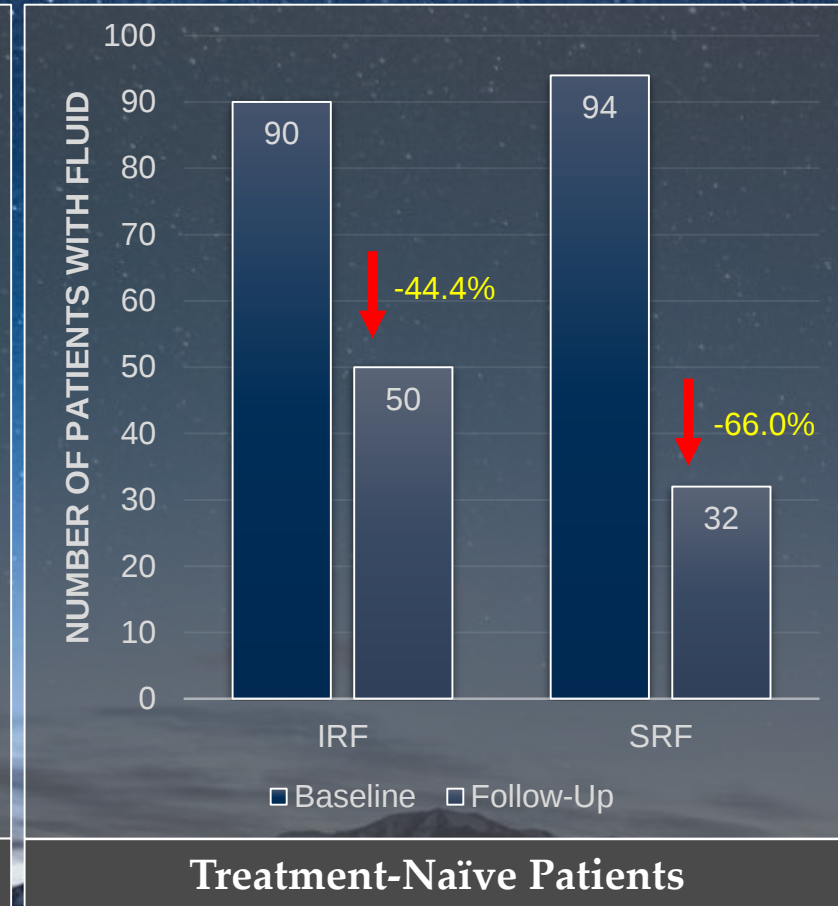
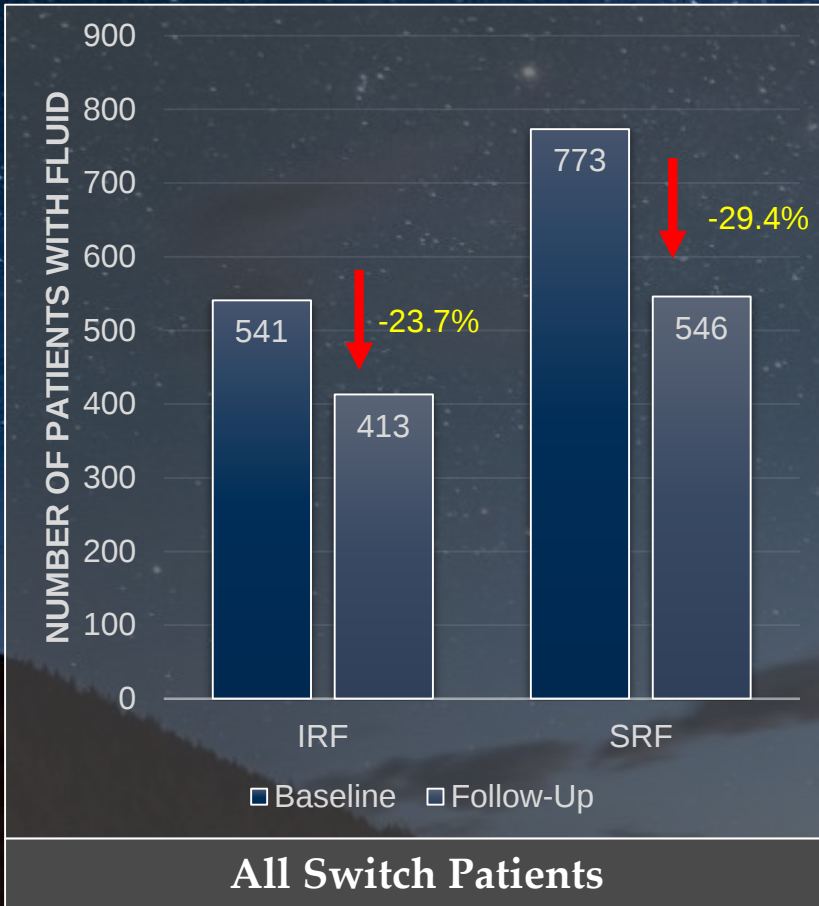
Efficacy After Three Injections of Faricimab in Treatment-Naïve Patients

Population with Follow-up (N = 186 eyes)

	Baseline	Follow-Up	Change	P-Value
Variable	Mean (SEM)	Mean (SEM)		
ETDRS (letters)*	60.02 (0.13)	62.78 (0.12)	+2.76 letters	0.003
CST (μ M)	381.83 (0.87)	297.85 (0.75)	-83.98 μ M	< 0.0001
PED Height	263.09 (2.96)	226.64 (2.46)	-36.45 μ M	0.18

*Based on Snellen to ETDRS conversion

Resolution of Fluid After Three Injections of Faricimab



Efficacy After Six Injections of Faricimab in All-Switched Patients

Population with Follow-up (N = 771 eyes)

Previous Interval: 43.9 days

Current Interval: 56.5 days

Increase in interval post-faricimab: + 12.6 days

	Baseline	Follow-Up	Change	P-Value
Variable	Mean (SEM)	Mean (SEM)		
ETDRS (letters)*	60.44 (0.03)	61.45 (0.03)	+1.01 letters	0.386
CST (μ M)	322.60 (0.28)	284.17 (0.22)	-38.43 μ M	< 0.00001
PED Height	283.86 (1.42)	236.15 (1.08)	-47.71 μ M	0.0004

*Based on Snellen to ETDRS conversion

Efficacy After Six Injections of Faricimab in Aflibercept-Switched Patients

Population with Follow-up (N = 448 eyes)

Previous Interval: 42.0 days

Current Interval: 57.4 days

Increase in interval post-faricimab: + 15.4 days

	Baseline	Follow-Up	Change	P-Value
Variable	Mean (SEM)	Mean (SEM)		
ETDRS (letters)*	62.97 (0.04)	63.78 (0.04)	+0.81 letters	0.19
CST (μ M)	322.90 (0.43)	285.20 (0.37)	-37.7 μ M	< 0.0001
PED Height	281.54 (2.16)	220.56 (29.28)	-60.98 μ M	0.038

*Based on Snellen to ETDRS conversion

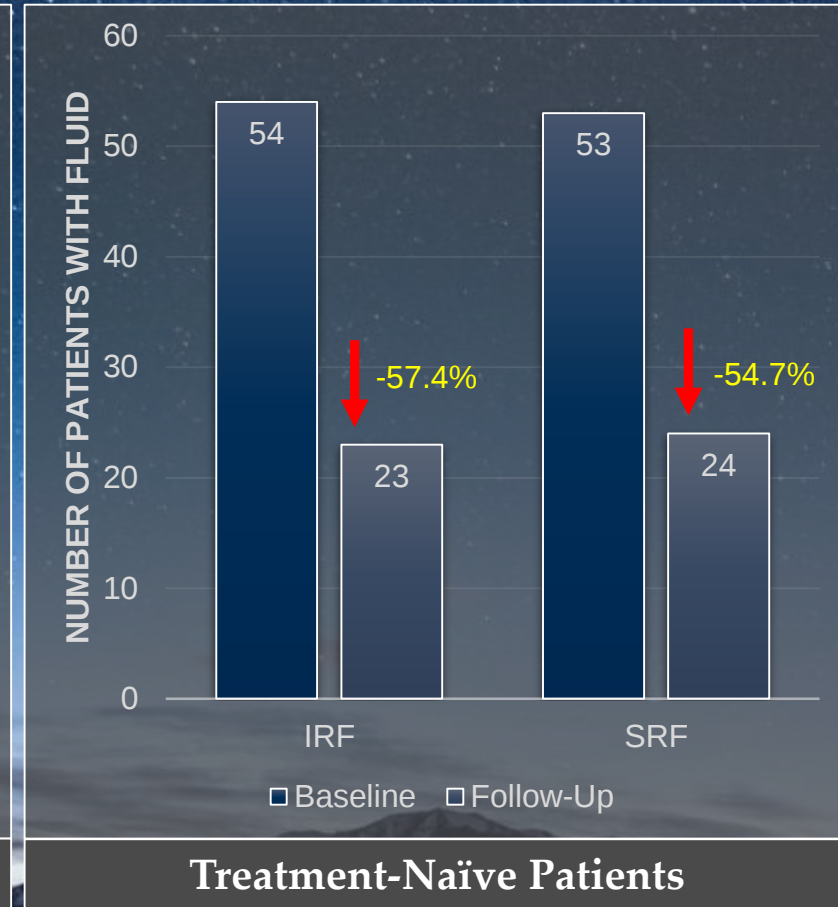
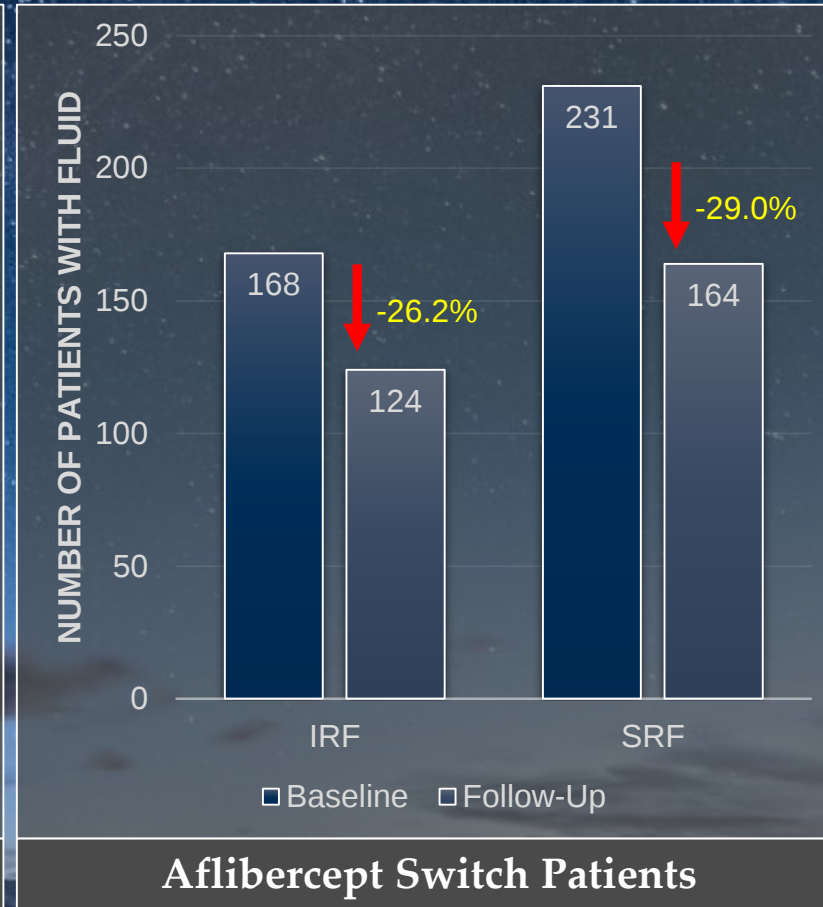
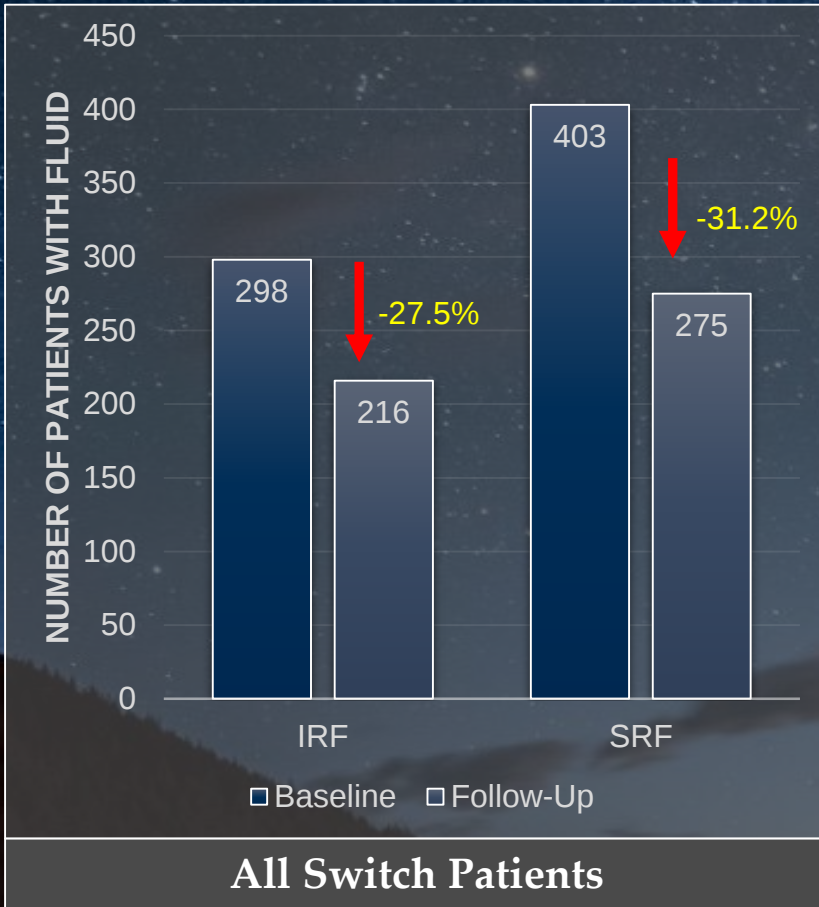
Efficacy After Six Injections of Faricimab in Treatment-Naïve Patients

Population with Follow-up (N = 90 eyes)

	Baseline	Follow-Up	Change	P-Value
Variable	Mean (SEM)	Mean (SEM)		
ETDRS (letters)*	60.13 (0.24)	63.35 (1.94)	+3.22 letters	0.001
CST (μM)	395.50 (1.80)	302.34 (1.78)	-93.16 μM	< 0.0001
PED Height	268.76 (4.73)	228.52 (4.15)	-40.24 μM	0.146

*Based on Snellen to ETDRS conversion

Resolution of Fluid After Six Injections of Faricimab



Efficacy After Nine Injections of Faricimab in All-Switched Patients

Population with Follow-up (N = 349 eyes)

Previous Interval: 40.4 days

Current Interval: 52.6 days

Increase in interval post-faricimab: + 12.2 days

	Baseline	Follow-Up	Change	P-Value
Variable	Mean (SEM)	Mean (SEM)		
ETDRS (letters)*	60.44 (0.06)	59.62 (0.08)	-0.82 letters	0.25
CST (μ M)	337.23 (0.54)	288.85 (0.48)	-48.38 μ M	< 0.0001
PED Height	288.49 (2.27)	235.46 (1.71)	-53.03 μ M	0.11

*Based on Snellen to ETDRS conversion

Efficacy After Nine Injections of Faricimab in Aflibercept-Switched Patients

Population with Follow-up (N = 224 eyes)

Previous Interval: 39.0 days

Current Interval: 55.4 days

Increase in interval post-faricimab: + 16.4 days

	Baseline	Follow-Up	Change	P-Value
Variable	Mean (SEM)	Mean (SEM)		
ETDRS (letters)*	62.74 (0.08)	61.03 (0.12)	-1.71 letters	0.55
CST (μ M)	347.99 (0.83)	293.84 (0.67)	-54.15 μ M	< 0.0001
PED Height	288.20 (3.2)	234.50 (2.75)	-53.7 μ M	0.04

*Based on Snellen to ETDRS conversion

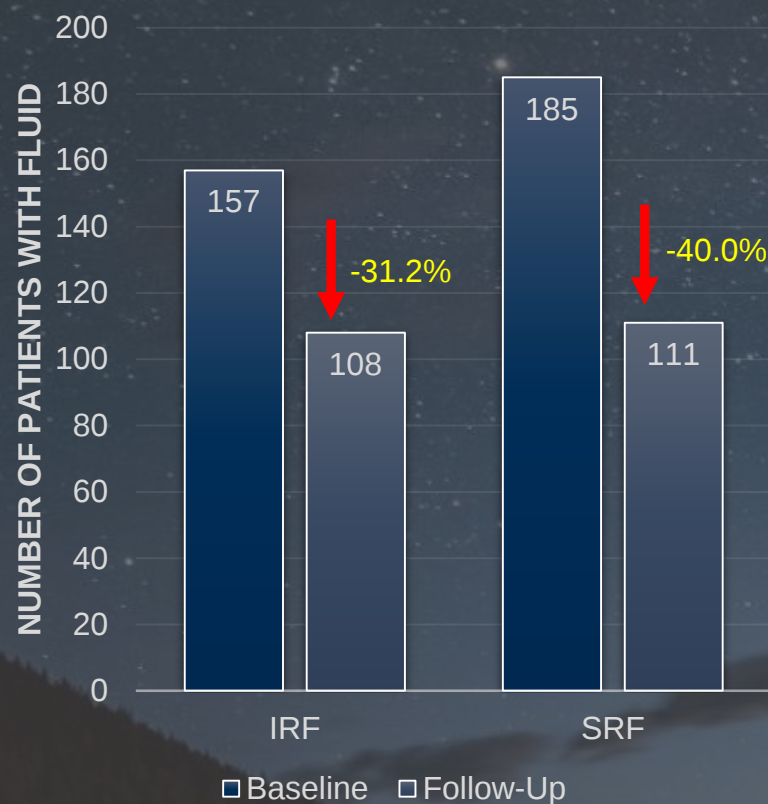
Efficacy After Nine Injections of Faricimab in Treatment-Naïve Patients

Population with Follow-up (N = 28 eyes)

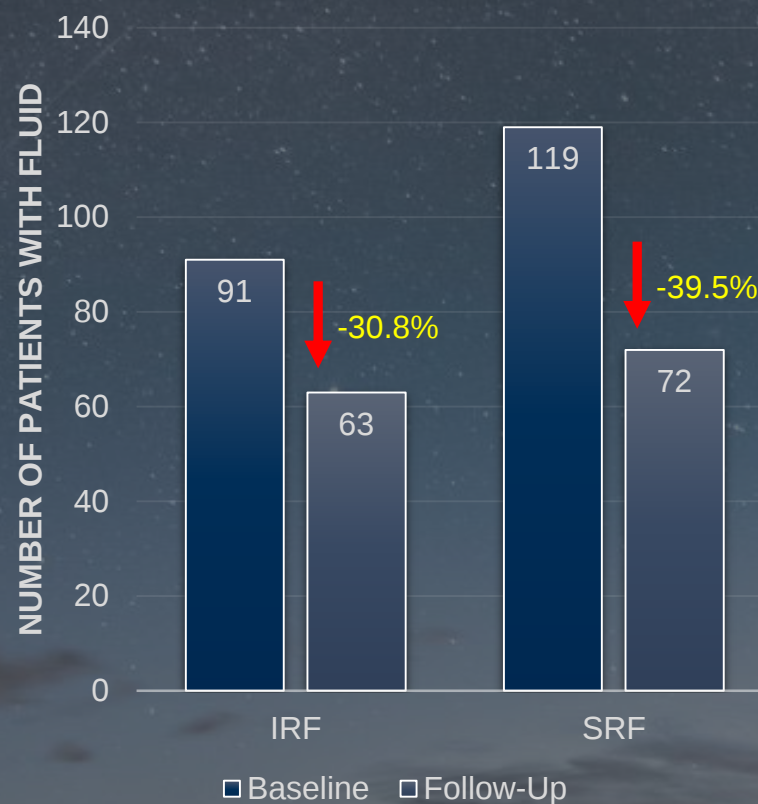
	Baseline	Follow-Up	Change	P-Value
Variable	Mean (SEM)	Mean (SEM)		
ETDRS (letters)*	54.71 (0.87)	63.63 (0.89)	+8.92 letters	0.031
CST (μ M)	428.73 (5.28)	309.81 (7.35)	-118.92 μ M	0.002
PED Height	311.08 (11.15)	216.72 (14.36)	-94.36 μ M	0.04

*Based on Snellen to ETDRS conversion

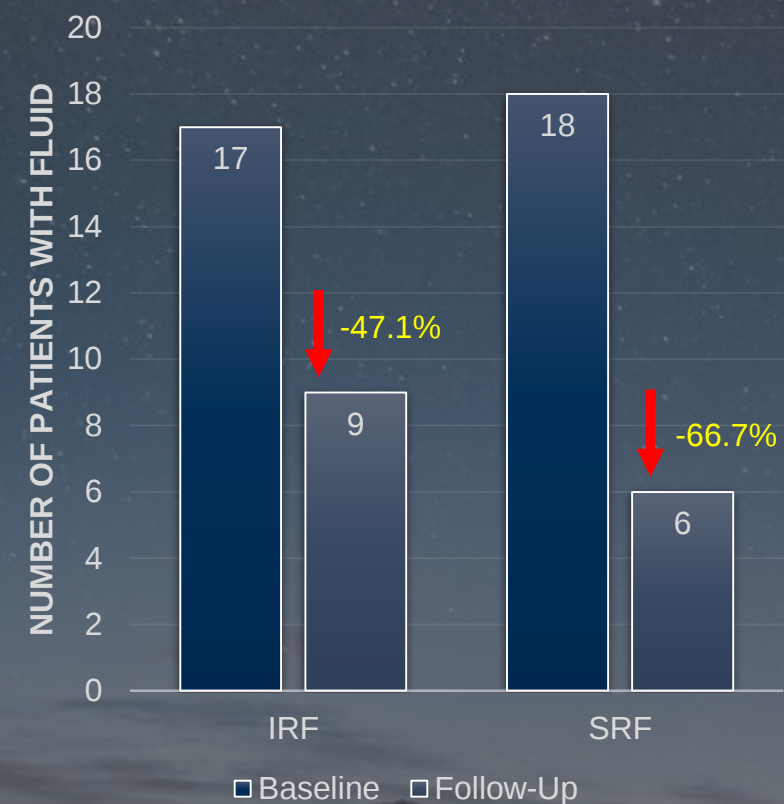
Resolution of Fluid After Nine Injections of Faricimab



All Switch Patients



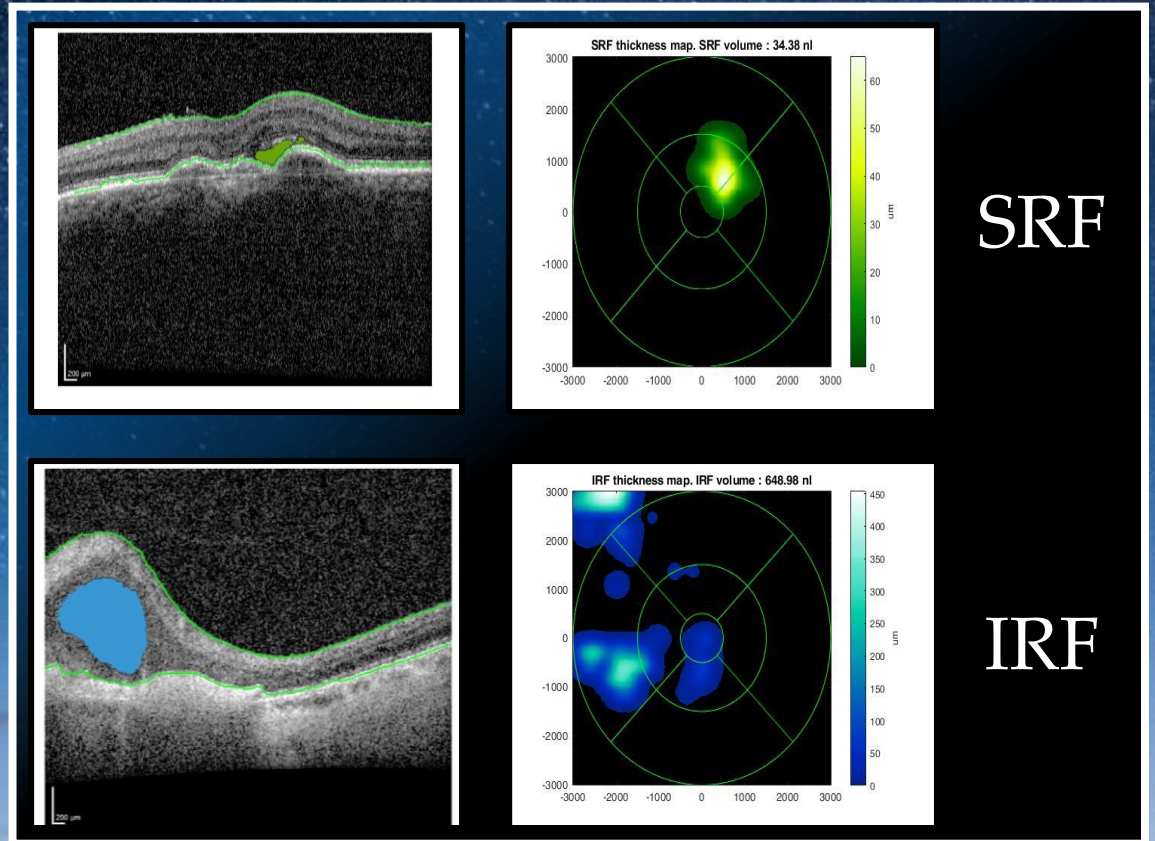
Aflibercept Switch Patients



Treatment-Naïve Patients

TRUCKEE: Fluid Quantification Sub-study

- Spectralis OCT scans acquired during treatment visit were quantified
- Notal OCT Analyzer (NOA)¹ is being used for fluid quantification
- NOA provides separate quantification of IRF and SRF

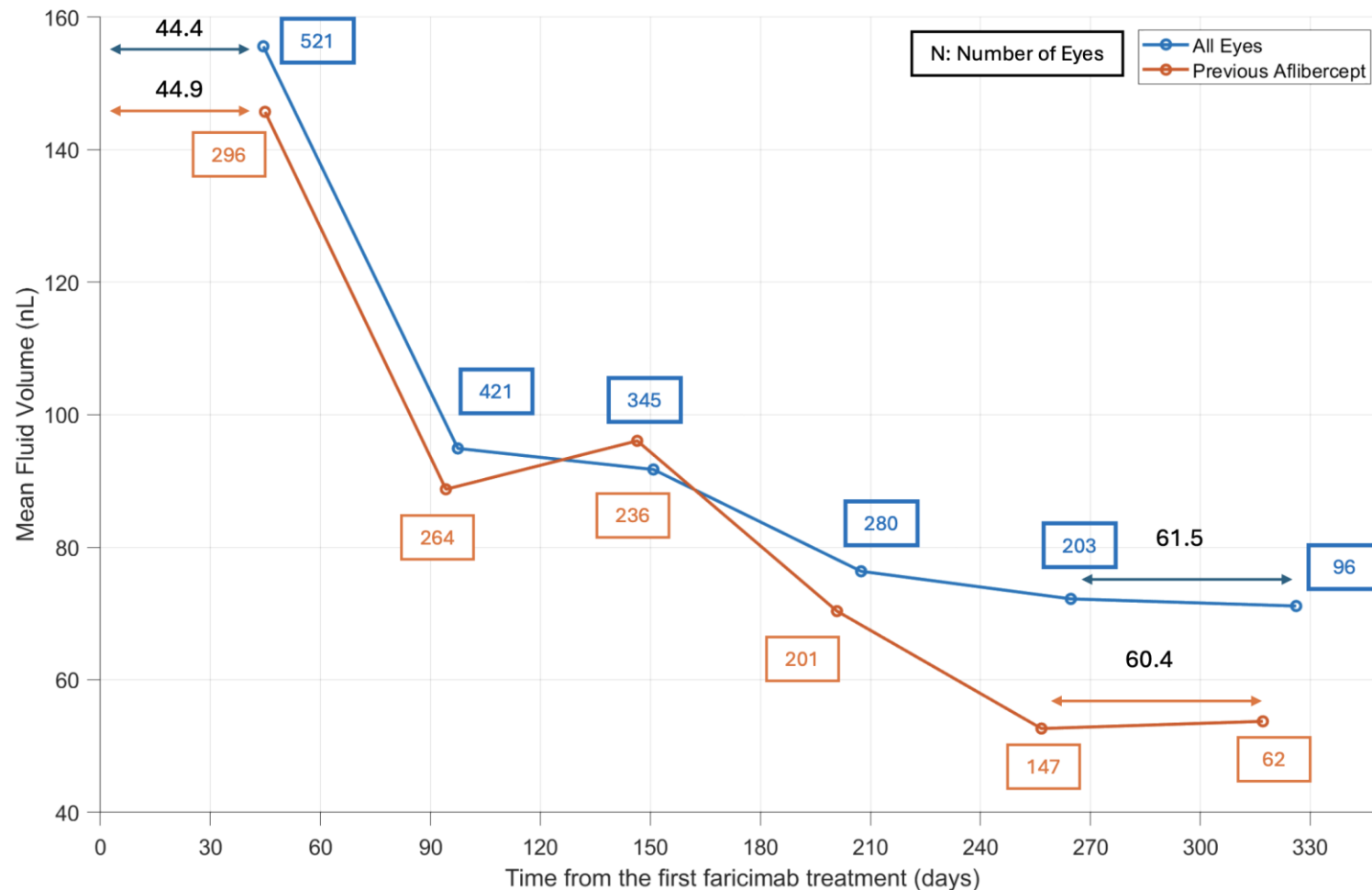


¹Keenan, Tiarnan DL, et al. "Retinal specialist versus artificial intelligence detection of retinal fluid from OCT: age-related eye disease study 2: 10-year follow-on study." *Ophthalmology* 128.1 (2021): 100-109.

Fluid Quantification in Eyes with >5 Injections

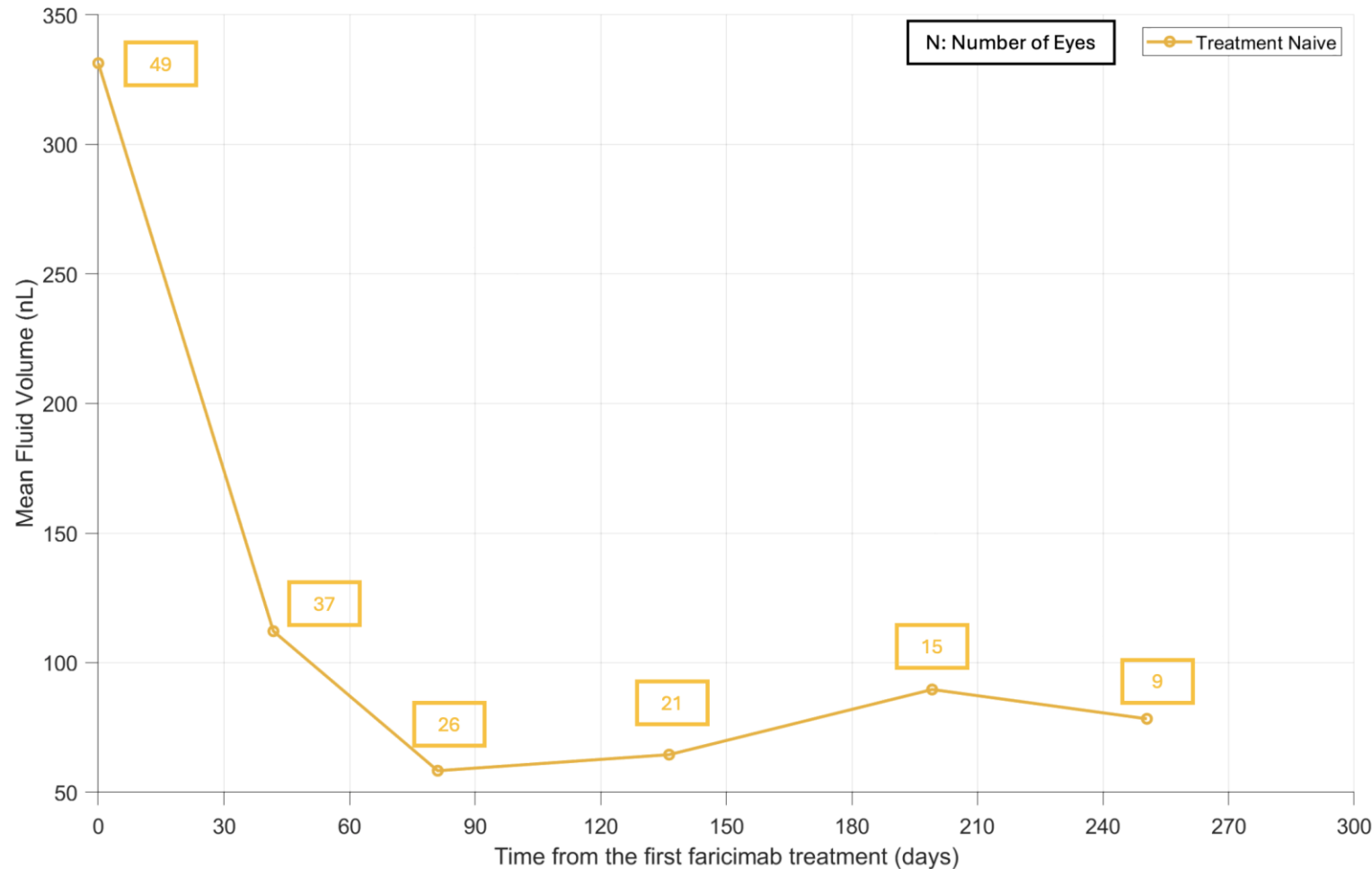
PARAMETERS	All Eyes	Prior Aflibercept	Naïve
Total number of eyes	181	122	13
Mean time between last treatment and 1 st faricimab	35.2 days	37.6 days	N/A
Mean time between 4 th and 5 th faricimab	52.0 days	51.0 days	72.0 days
Mean change in fluid volume	-120.1 nL	-98.54 nL	-189.7 nL
Total Eyes with decrease in fluid	79.0%	78.7%	92.3%
Eyes with full fluid resolution	24.9%	26.2%	53.9%

Total Fluid Reductions over Five Treatments



Total retinal fluid volume reduction in both all eyes and aflibercept-switched patients, demonstrating significant decreases in volume and increases in treatment interval after sustained treatments.

Total Fluid Reductions over Five Treatments



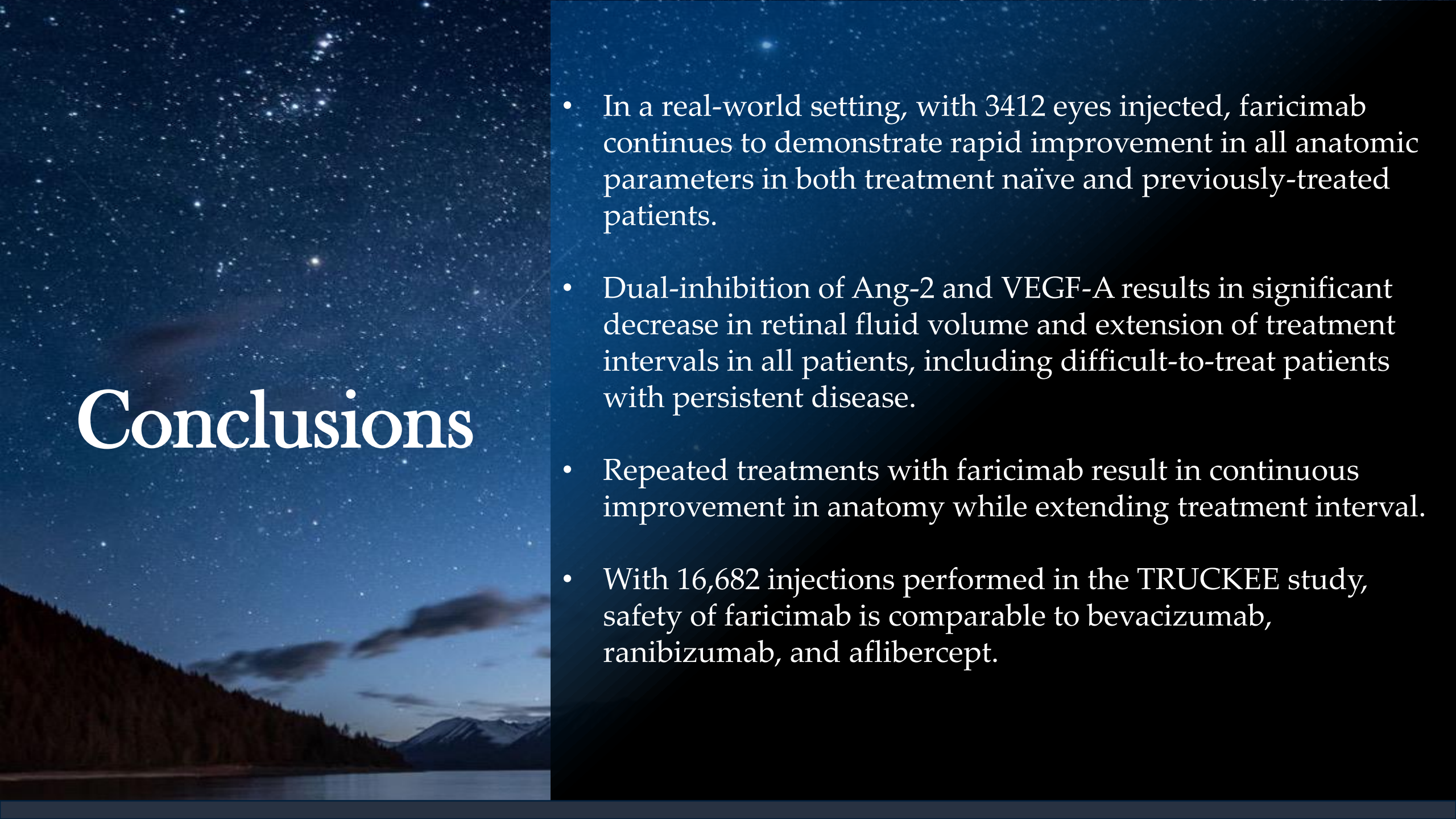
Total retinal fluid volume reduction in treatment-naïve patients, demonstrating significant decreases in total fluid after multiple treatments.

Safety Outcomes

- Number of Patients: 2756
- Number of Eyes: 3412
- Number of Injections: 16,682
 - IOI: 0.08%
 - Endophthalmitis: 0.024%

No cases of retinal vasculitis or retinal artery occlusion have been observed.

Event	Number of Cases	Resolved	VA Returned to Baseline	Retreated with Faricimab
Infectious Endophthalmitis	4	4/4	4/4	4/4
Anterior Chamber Cells	2* *One case had previous inflammation on brolucizumab	2/2	2/2	1/2
Panuveitis	6	4/6	6/6	3/6
Iritis	2* *One case was bilateral; other eye untreated	2/2	2/2	2/2
Vitritis	3* *Two cases had previous inflammation on brolucizumab	3/3	3/3	2/3



Conclusions

- In a real-world setting, with 3412 eyes injected, faricimab continues to demonstrate rapid improvement in all anatomic parameters in both treatment naïve and previously-treated patients.
- Dual-inhibition of Ang-2 and VEGF-A results in significant decrease in retinal fluid volume and extension of treatment intervals in all patients, including difficult-to-treat patients with persistent disease.
- Repeated treatments with faricimab result in continuous improvement in anatomy while extending treatment interval.
- With 16,682 injections performed in the TRUCKEE study, safety of faricimab is comparable to bevacizumab, ranibizumab, and aflibercept.

The SUMMIT Study

Real World Efficacy and Safety of the Ranibizumab Port- Delivery System in Neovascular in AMD

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Nancy Holekamp, MD; John W. Kitchens, MD; Veeral S.
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SUMMIT Study: Design

Real World Efficacy and Safety of the Ranibizumab Port-Delivery System in Neovascular in AMD

Target Patient Population

- Patients following nAMD diagnosis with response to at least two anti-VEGF intravitreal injections

Ongoing Data Collection

- Demographics
- Prior treatment history
- Efficacy (vision, central subfield thickness, retinal fluid status)
- Durability
- Safety
- Need for supplementary injections

Results: Demographics

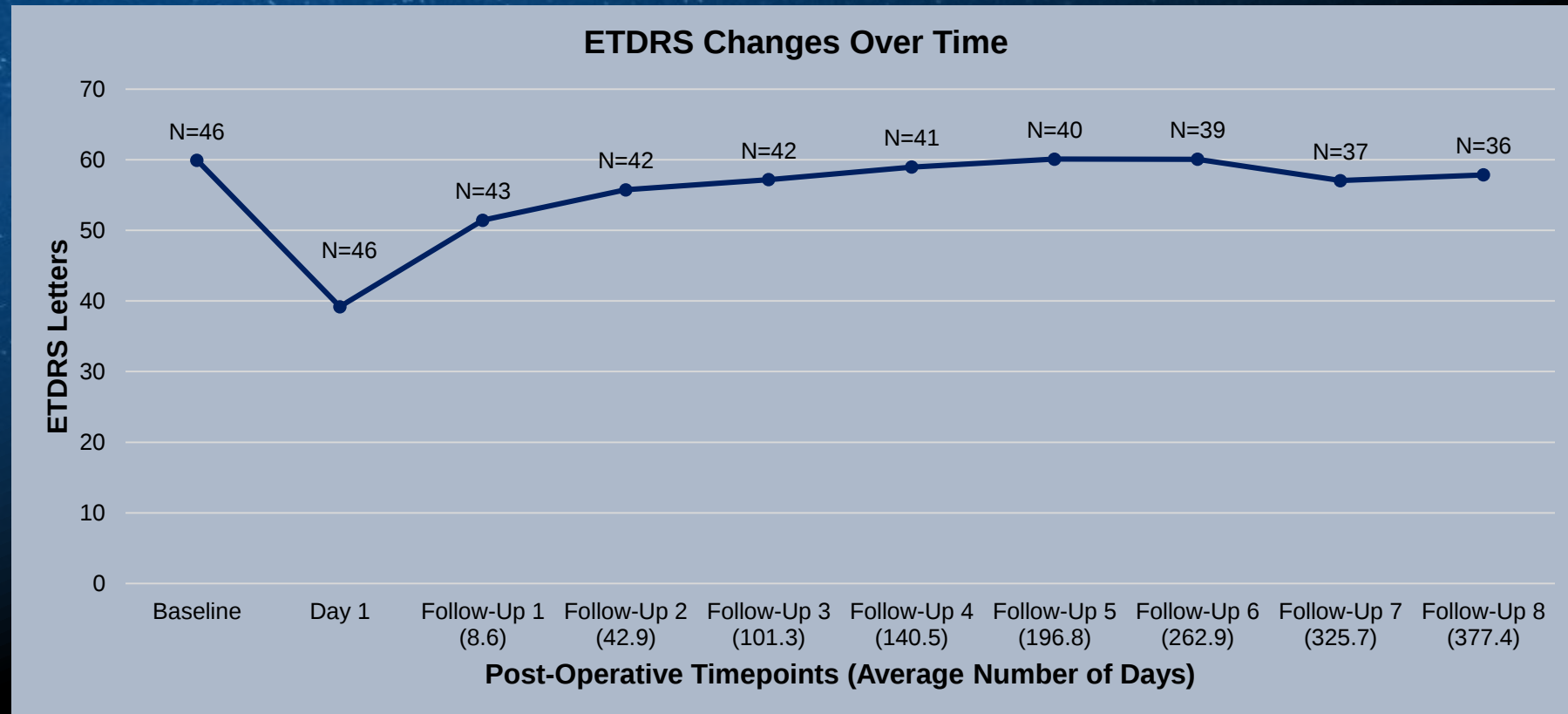
Population (N = 46 patients)

Variable	Mean	Range
Age (years)	79.7	59 - 91

Variable	Groups	N (%)
Gender (patients)	Female	28 (60.8%)
	Male	18 (39.2%)

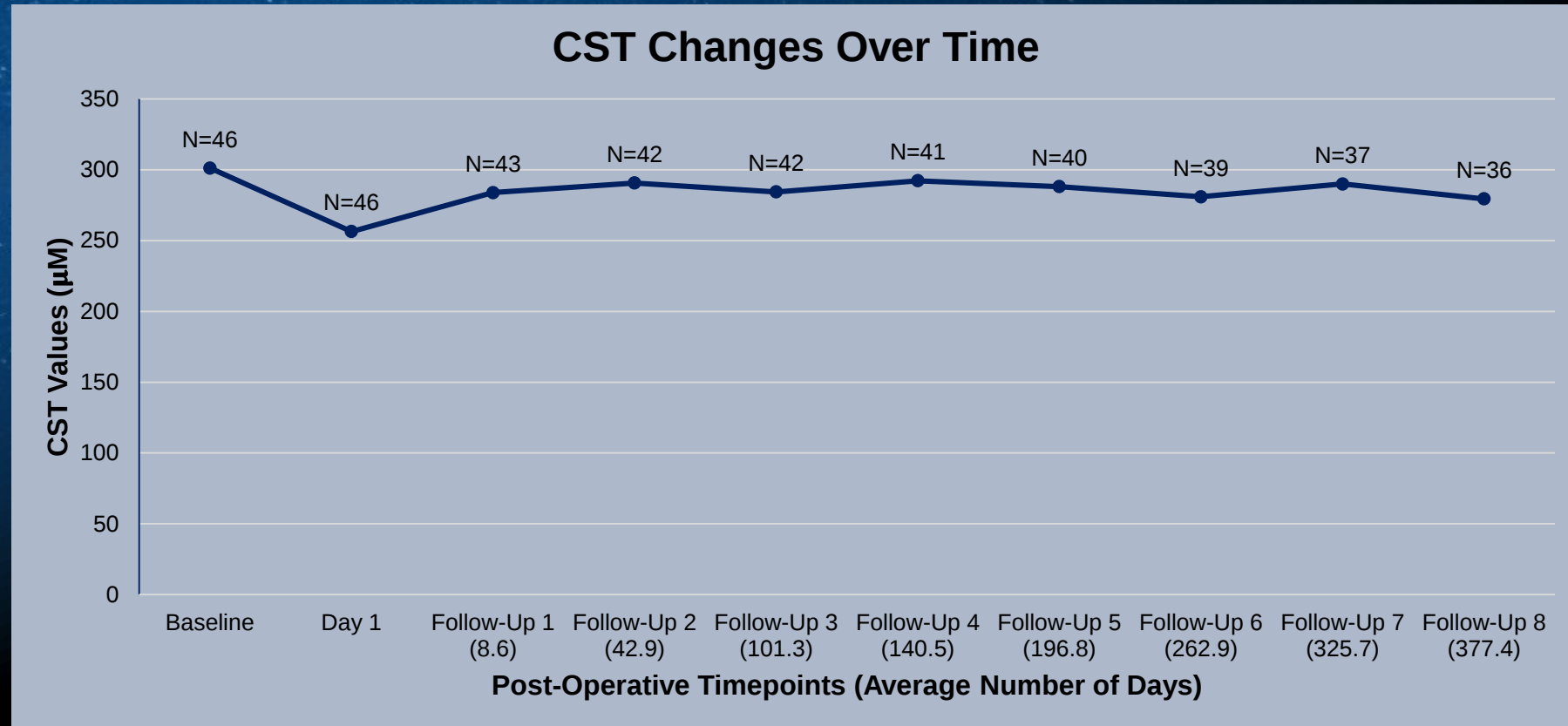
ETDRS Changes Over Time

Vision Maintenance Over 1 Year of Follow-Up



CST Changes Over Time

Retinal Thickness Well-Controlled Over 1 Year Follow-Up



Excellent Durability: Mean Refill Duration 8.6 Months

Time to Refill

Variable	Days (SEM)
Average Days Until First Refill	258.84 (3.27)

Supplemental Injections

Supplemental Injections	N (%)	Description
Aflibercept x1	1/46 (2.2%)	Patient presented with disease activity and was due for a refill-exchange but site did not have refill supply and patient was given aflibercept

Safety Outcomes

N = 46

No cases of endophthalmitis

No cases of conjunctival retraction

Most AEs were post-surgical and resolved over time

Adverse Event	Ongoing (N)	Resolved (N)
Subconjunctival Heme		X (4/4)
Descemet's Folds		X (3/3)
C/S Bleb Formation		X (3/3)
Moderate Low IOP		X (2/2)
Anterior Chamber Cells		X (4/4)
Retinal Detachment		X (1/1)
Conjunctival Erosion		X (1/1)
Ocular Hypertension		X (1/1)

Conclusions

- PDS demonstrated excellent vision and CST maintenance over 1 year
- Average time to first refill was 8.6 months
- Efficacy data from the SUMMIT study is consistent with the data from PDS nAMD trials
- 11/46 patients experienced surgery related AEs, all of which resolved
- No cases of endophthalmitis or conjunctival retraction
- Longer term data will be presented at future meetings

Doing now what patients need next