Angiogenesis Highlights 2021

Roche Analyst Webcast

South San Francisco, 16 Feb 2021

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1 pricing and product initiatives of competitors;
2 legislative and regulatory developments and economic conditions;
3 delay or inability in obtaining regulatory approvals or bringing products to market;
4 fluctuations in currency exchange rates and general financial market conditions;
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Welcome

Karl Mahler

Head of Investor Relations and Group Planning

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Karl Mahler, Head of Investor Relations and Group Planning

Ophthalmology Strategy Update
Atul Dandekar, Vice President and Global Franchise Head, Ophthalmology

Ophthalmology Pipeline Update
Chris Brittain, Vice President and Global Head of Ophthalmology Product Development

Faricimab in DME and nAMD: – Phase III results
Nancy Holekamp, M.D., Retina Specialist and Faricimab Clinical Investigator

Q&A
Karl Mahler, Head of Investor Relations and Group Planning

Strong short- and mid-term news flow

Diversifying the late stage pipeline and setting new standards of care

Product	Indication	Filing/Data	
tominersen	Huntington's	2022	
gantenerumab	Alzheimer's	2022	
SRP-9001	DMD	latest 2023	
etrolizumab	Crohn's	2022	
PDS	nAMD DME	2020/21 2022	✓
faricimab	DME nAMD	2021	✓ ✓
Actemra +/- remdesivir	COVID-19 related pneumonia	2021	
casirivimab/ imdevimab	SARS-CoV-2	2021	
AT-527	SARS-CoV-2	2021/22	
crovalimab	PNH	2022	

Product	Indication	Filing/Data
Tecentriq	Adj SCCHN	2021
	(Neo)Adj NSCLC	2021/22
	Adj RCC	2022
	Adj HCC	2022
Tecentriq + P+H	NeoAdj HER2+ BC	2021
ipatasertib	1L mCRPC	2022
Polivy	1L DLBCL	2021
tiragolumab + T	1L SCLC	2022
mosunetuzumab	R/R FL	2021
glofitamab	R/R DLBCL	2022
Venclexta	R/R MM t(11;14)	2022
giredestrant	2L/3L mBC	2022
inavolisib	1L HR+ BC	2022/23

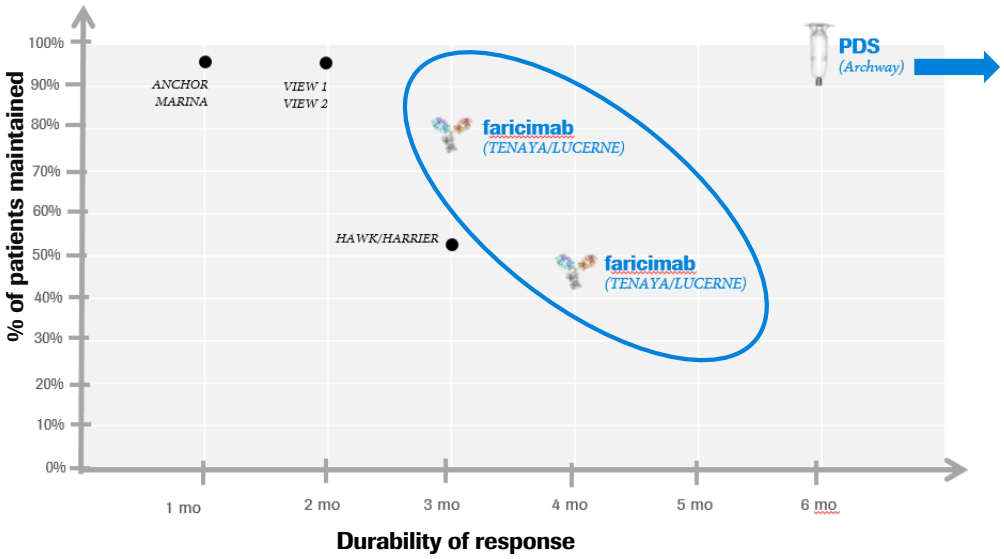
✓ Positive top-line announced Neuroscience Immunology Ophthalmology Infectious diseases Oncology/Hematology

Source: DMD=duchenne muscular dystrophy; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; PNH=paroxysmal nocturnal hemoglobinuria; SCCHN=squamous cell carcinoma of the head and neck; RCC=renal cell carcinoma; NSCLC=non-small cell lung cancer; HCC=hepatocellular carcinoma; mCRPC=metastatic castration resistant prostate cancer; DLBCL=diffuse large B-cell lymphoma; SCLC=small cell lung cancer; FL=follicular lymphoma; MM=multiple myeloma

Roche Ophthalmology Franchise

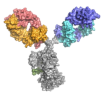
Addressing key unmet medical needs

Offering substantially improved patient benefits



PDS and faricimab have the potential to improve outcomes with longer durability

- **Port Delivery System (PDS):** permanent, refillable intraocular implant. One-time ~30 min outpatient surgical procedure. Refill twice yearly in-office



- **Faricimab:** in DME and wAMD: met primary endpoint, strong durability across all studies (~50% for 16 weeks)

Lucentis USPI, Eylea USPI and Beovu USPI; faricimab data presented at Angiogenesis 2021
Comparisons meant for illustrative purposes only

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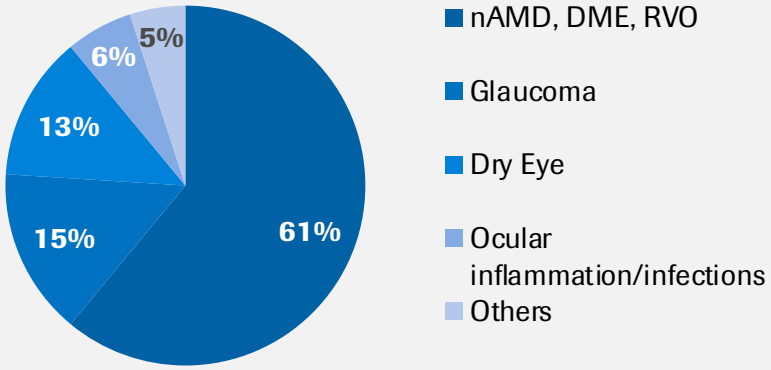
Retinal diseases are the fastest growing segment of the Ophthalmology market

Ophthalmology market

Retinal vascular diseases remain leading causes of vision loss

Total Market (2020) – $20.7 Billion



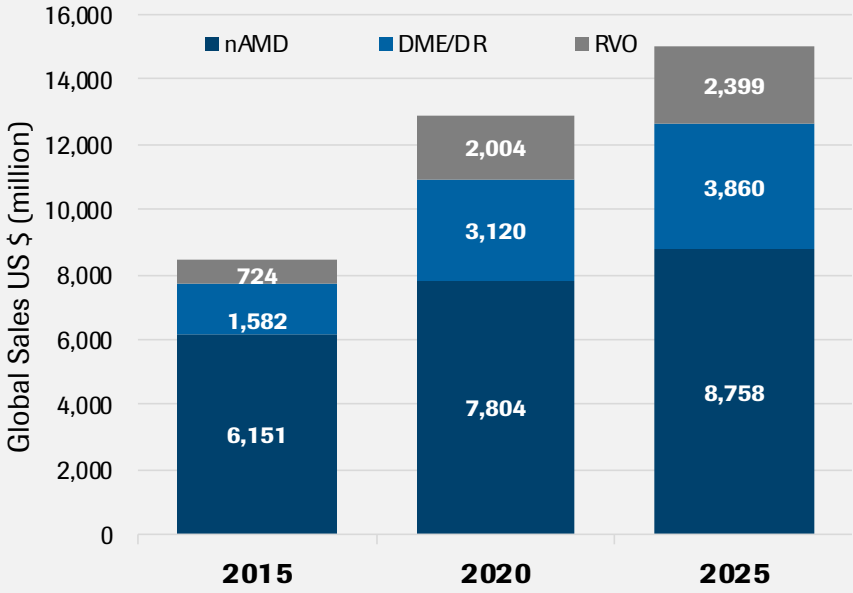
Leading causes of vision loss in US, Europe:

- Working-age people: **Diabetic eye disease (DME, DR)**
- Elderly people: **Neovascular AMD**

Source: Evaluate Pharma (January 2021)

Global Retinal Disease Landscape

Market growth driven by aging population and product innovation



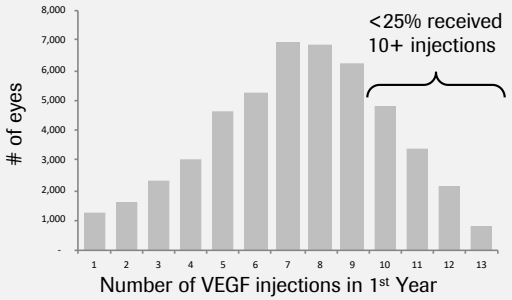
Source: Evaluate Pharma (January 2021)

DME: diabetic macular edema, DR: diabetic retinopathy, nAMD: neovascular age-related macular degeneration, RVO: retinal vein occlusion

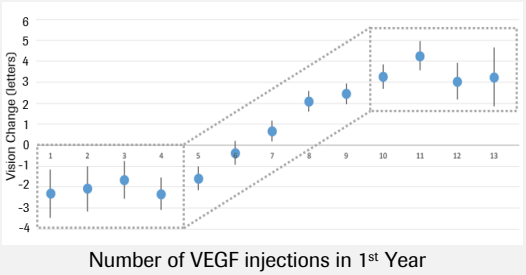
Reduction in treatment burden is a key unmet medical need

Real world vision outcomes are suboptimal

Adherence to IVT therapies is low and infrequent dosing in the real world correlates with vision loss

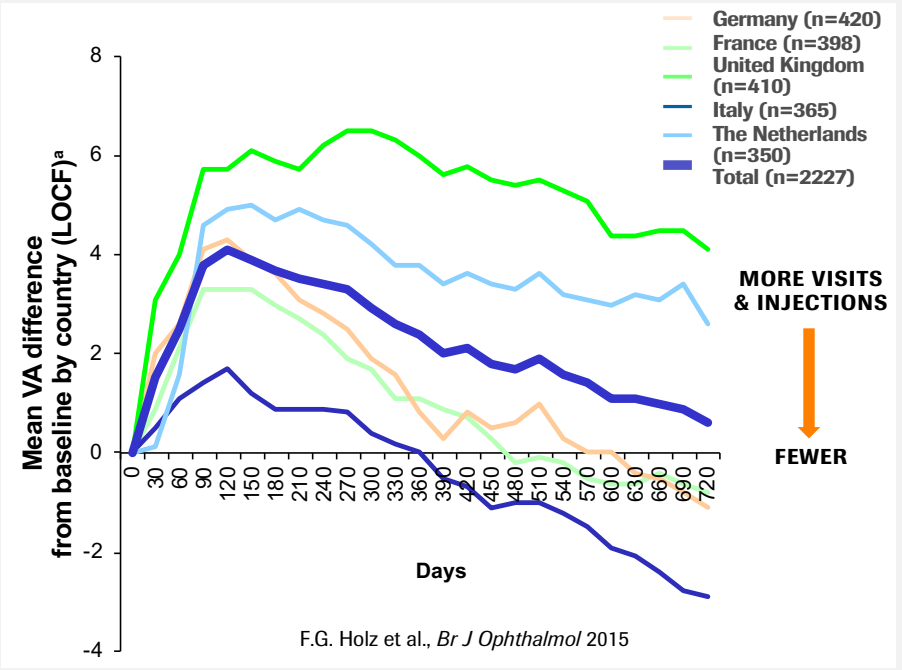


Real world treatment frequency for nAMD[1]



Number of anti-VEGF injections correlates with vision improvement[1]

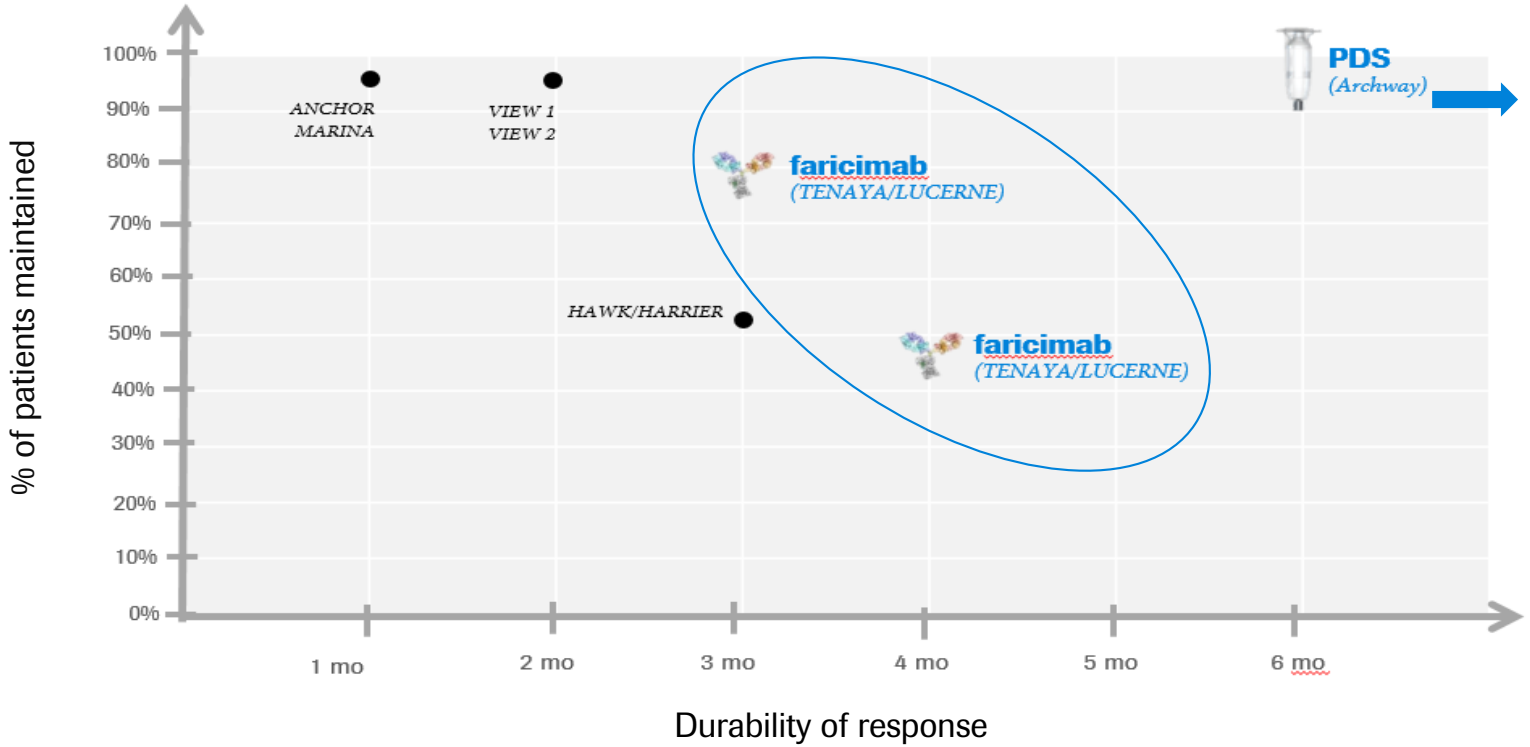
Lower frequency of injections associated with worse outcomes



[1] Courtesy of T. Brogan/Vestrum Health, presented by Dr. D. Williams at ASRS 2018;
Source: Evaluate Pharma; DME=diabetic macular edema; nAMD=neovascular AMD; IVT=intravitreal

Improved durability will help improve real world outcomes

Faricimab and PDS are potential new standards of care

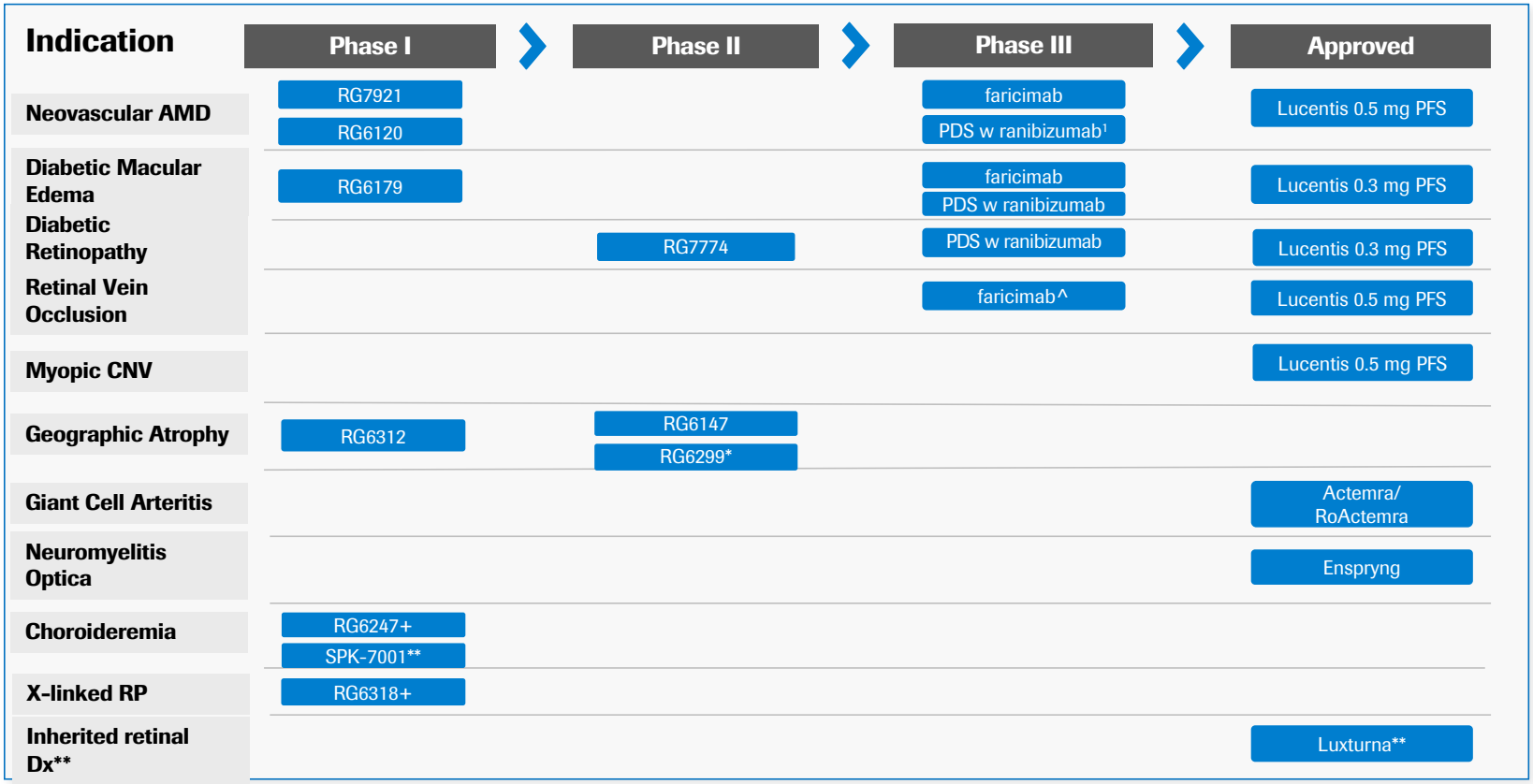


Comparisons meant for illustrative purposes only

Lucentis USPI, Eylea USPI and Beovu USPI; Faricimab data presented at Angiogenesis 2021

Roche's industry leading retina pipeline

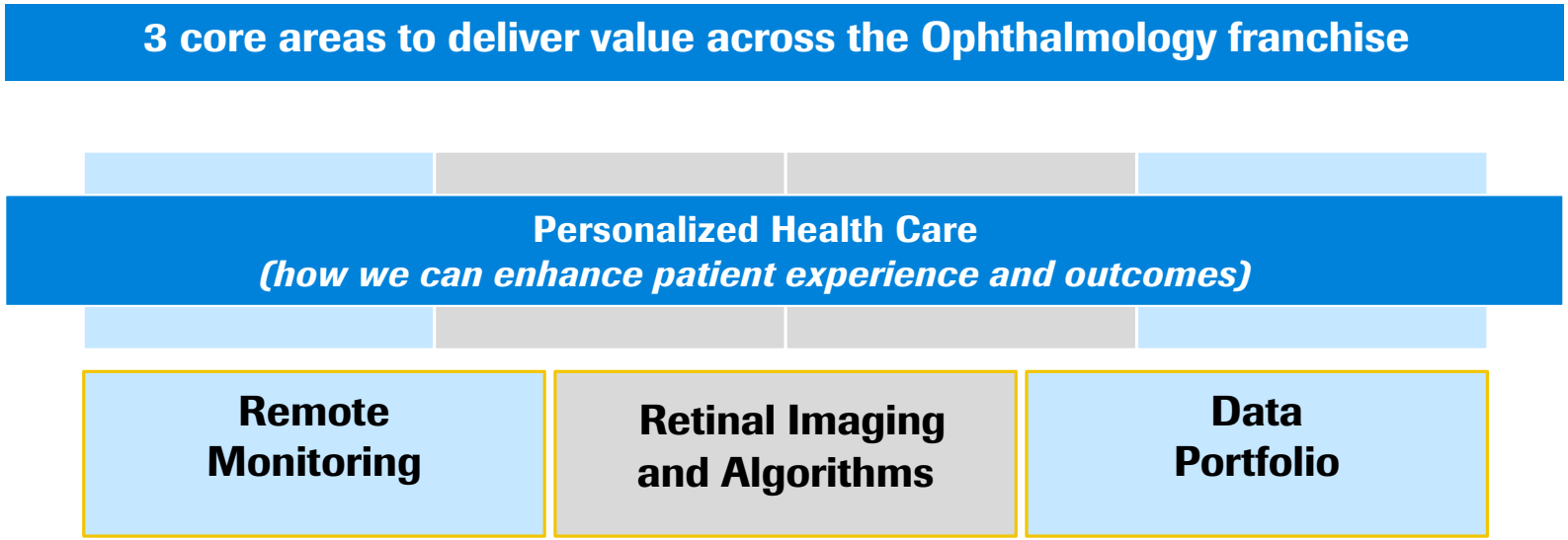
Focus on nAMD, DME/DR and GA



Status as of Feb 2021. PDS (Port Delivery System); PFS (Pre-filled Syringe); RP (retinitis pigmentosa); Lucentis PFS is marketed by Novartis outside the U.S.;
* Study conducted by Ionis, Roche option to in-license; + Study conducted by 4DMT, Roche option to in-license; **with Spark Therapeutics, approved for patients with biallelic *RPE65* mutation-associated retinal dystrophy;
[1]US submission initiated; ^ study planned; GA – Geographic Atrophy

Ophthalmology Personalized Healthcare

Remote monitoring & advanced analytics to help treat vision loss early

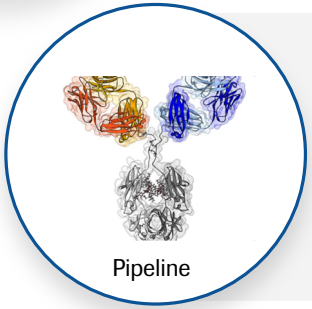


Objective: TREAT VISION LOSS and PRESERVE VISION

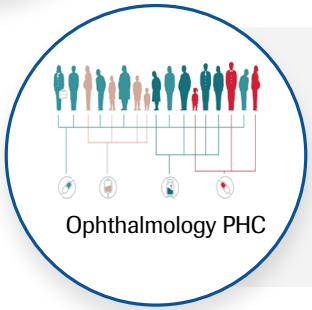
Roche Ophthalmology strategy execution is on track

Faricimab nAMD / DME joint filing planned for H1 2021

- Positive faricimab nAMD and DME Ph3 data – 1st therapy with Q4M dosing in Ph3
- Positive PDS nAMD Ph3 study – US approval anticipated in Q4 21, additional ex-US studies planned
- PDS DME & DR Ph3 studies enrolling rapidly; faricimab RVO phase 3 studies planned



- 3 NMEs in Ph2 clinical development, 7 NMEs in Ph1 studies including gene therapies
- Positive PDS Ph3 has enabled acceleration of DutaFabs in PDS platform
- Partnering - Extensive partnering effort focused on strategic indications and platforms



- Demonstrated PoC utilizing internal algorithms in disease detection, prediction of progression and response to treatment
- Focus on Remote Monitoring, Retinal Imaging & Algorithms, Data Portfolio
- Ongoing Home Vision Monitoring pilot to support patients during COVID-19

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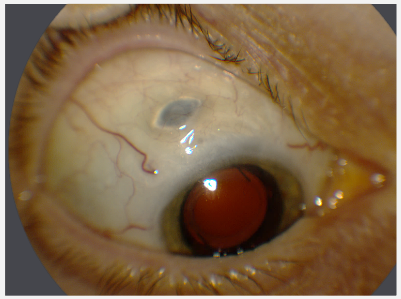
Archway phase 3 trial design

Evaluate the efficacy and safety of the PDS Q24W for nAMD

The Port Delivery System with Ranibizumab



- Innovative, investigational drug delivery system
- Permanent, refillable ocular implant
- Implant surgically placed at the pars plana
- In-office refill-exchange procedures

Archway

Patients with nAMD responsive to any anti-VEG treatment[a]
N = 415[b]

Randomized 3:2

PDS with ranibizumab 100 mg/mL Q24W n = 248	Intravitreal ranibizumab 0.5 mg Q4W n = 167

Weeks 36 and 40: primary endpoint

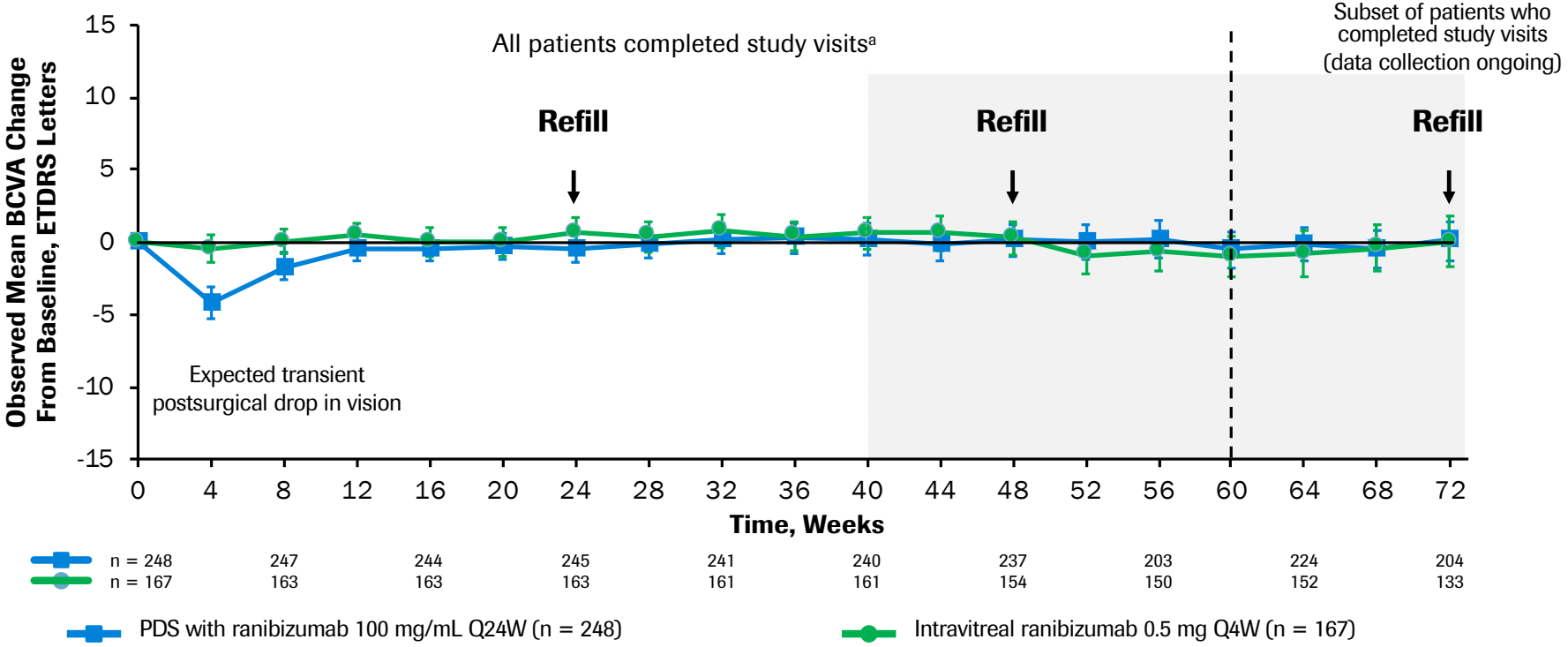
Week 96: final visit

[a] nAMD in study eye diagnosed within 9 months of screening; ≥ 3 intravitreal injections of any anti-VEGF agent within previous 6 months. [b] Efficacy- and safety-evaluable population. 418 total patients were enrolled, with 251 and 167 patients randomized to the PDS 100 mg/mL Q24W and intravitreal ranibizumab 0.5 mg Q4W arms, respectively; 3 patients in the PDS arm did not receive study treatment and were excluded from the efficacy- and safety-evaluable population.

Archway, NCT03677934; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

Archway phase 3: PDS maintained vision through week 72

Observed mean BCVA change from baseline

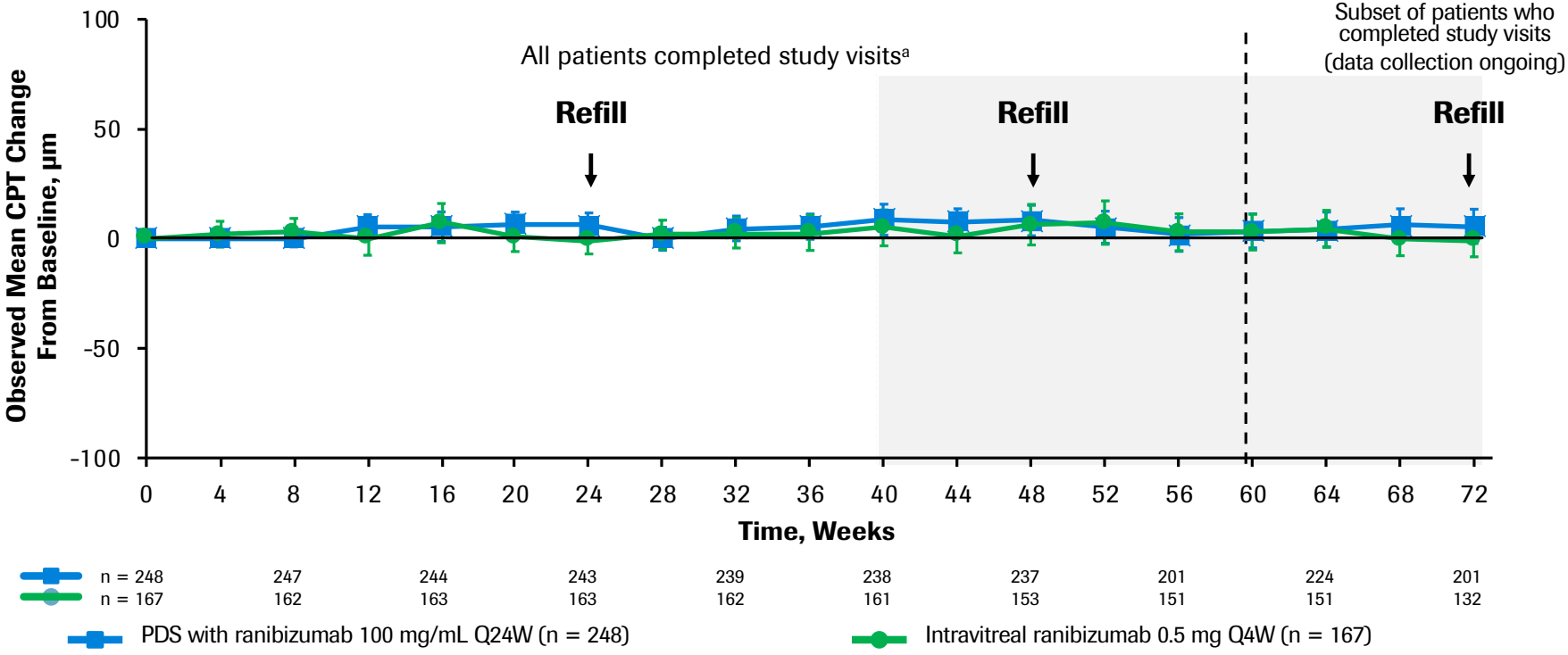


[a] All patients have passed their week 60 scheduled visit date or have discontinued the study early.

Observed data through the September 11, 2020 clinical cutoff date; data collection ongoing. Vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

PDS controlled retinal thickness through week 72

Observed mean CPT change from baseline

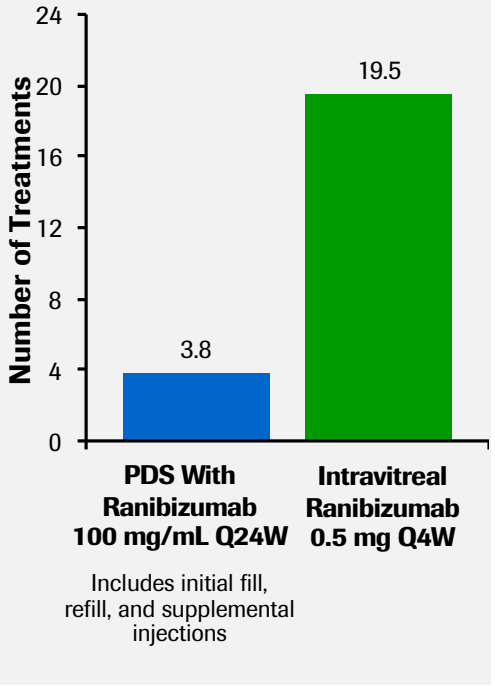


[a] All patients have passed their week 60 scheduled visit date or have discontinued the study early.
Observed data through the September 11, 2020 clinical cutoff date; data collection ongoing. Vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring.
CPT defined as retinal thickness in the center of the fovea measured between the inner limiting membrane and the inner third of the retinal pigment epithelium layer.
CPT, center point thickness; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

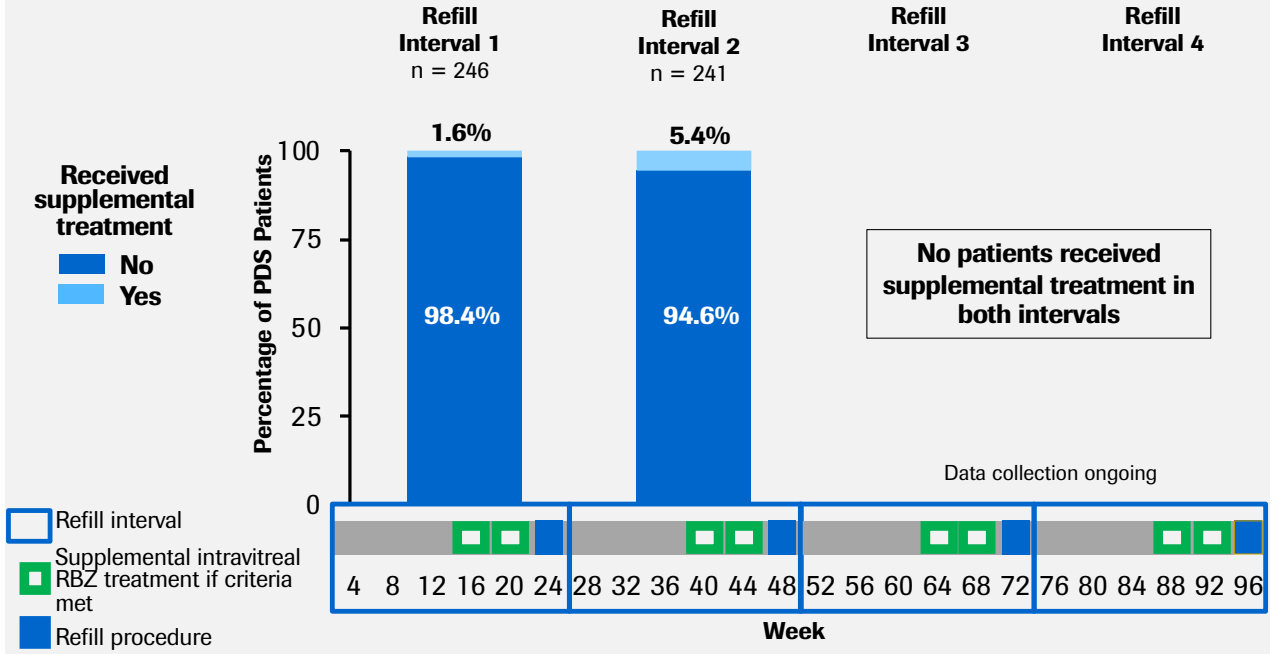
Treatment burden and supplemental treatment

~5x fewer treatments in PDS patients over a mean duration of 80 weeks

Total mean number of Ranibizumab treatments[a,b]



> 90% of patients did not receive supplemental treatment before each refill-exchange procedure



Data through September 11, 2020 clinical cutoff date; data collection ongoing. [a] Total number of ranibizumab treatments includes initial fill, refill-exchanges, and supplemental intravitreal ranibizumab 0.5 mg injections in PDS-treated patients and all intravitreal ranibizumab 0.5 mg injections in patients in the intravitreal ranibizumab 0.5 mg Q4W arm. [b] Includes PDS patients who received supplemental treatment. For each interval, percentages of patients who did/did not receive supplemental treatment were calculated out of the number of patients who were on treatment and assessed for supplemental treatment for ≥ 1 visit (interval 1, week 16 or 20; interval 2, week 40 or 44); PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

PDS insertion and refill procedures generally well tolerated

MedDRA Preferred Term, n (%)[b]	PDS with Ranibizumab 100 mg/mL Q24W (n = 248)		Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)	
	Onset After Week 40	Overall[c]	Onset After Week 40	Overall[c]
Cataract[d]	11 (4.4%)	20 (8.1%)	2 (1.2%)	8 (4.8%)
Conjunctival bleb/ conjunctival filtering bleb leak	1 (0.4%)	17 (6.9%)	0	0
Conjunctival erosion	1 (0.4%)	6 (2.4%)	0	0
Conjunctival retraction	0	5 (2.0%)	0	0
Endophthalmitis	1 (0.4%)	4 (1.6%)	1 (0.6%)	1 (0.6%)
Hyphema	0	1 (0.4%)	0	0
Rhegmatogenous retinal detachment	0	2 (0.8%)	0	0
Tractional retinal detachment	0	0	0	0
Vitreous hemorrhage	2 (0.8%)	15 (6.0%)	2 (1.2%)	6 (3.6%)

- 3 PDS patients experienced implant dislocation; 2 had onset after week 40
- 1 of 248 PDS-treated patients had irreversible vision loss due to an adverse event (*E. faecalis* endophthalmitis); no new events after week 40
- Systemic safety of PDS Q24W was generally comparable with monthly ranibizumab

[a] Protocol-defined ocular adverse events of special interest potentially related to the PDS implant or implant insertion procedure. [b] Frequency counts by Preferred Term. Multiple occurrences of the same adverse event in an individual are counted only once for each column. [c] All data through the September 11, 2020 clinical cutoff date. [d] Includes the following terms: cataract, cataract nuclear, cataract cortical, cataract subcapsular. Observed data, all treated patients who received ≥ 1 dose of study drug according to the actual treatment. Month 1 visit includes data up to 37 days (monthly study visit + 7 days).

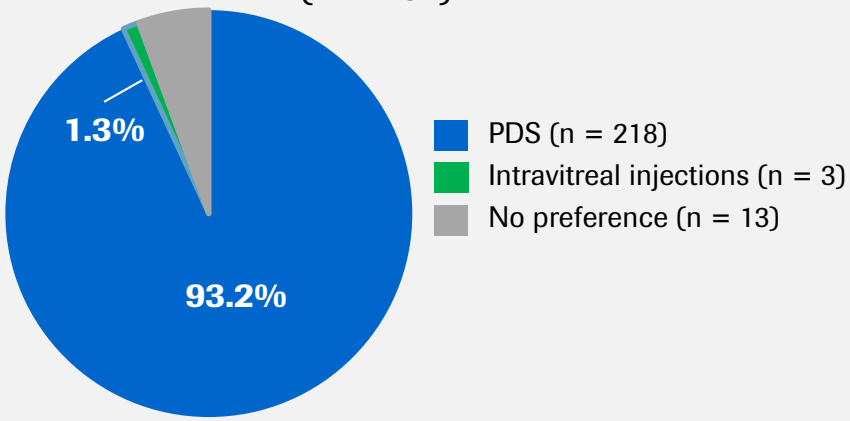
HLA-B27, human leukocyte antigen B27; MedDRA, Medical Dictionary for Regulatory Activities; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

Patient preference: 93% preferred PDS over intravitreal injections

PDS Patient Preference Questionnaire (PPPQ)

The PPPQ was administered to all patients in the PDS arm at week 40[a]

Preference Among PDS Patients (n = 234)[b]



Next for PDS with Ranibizumab

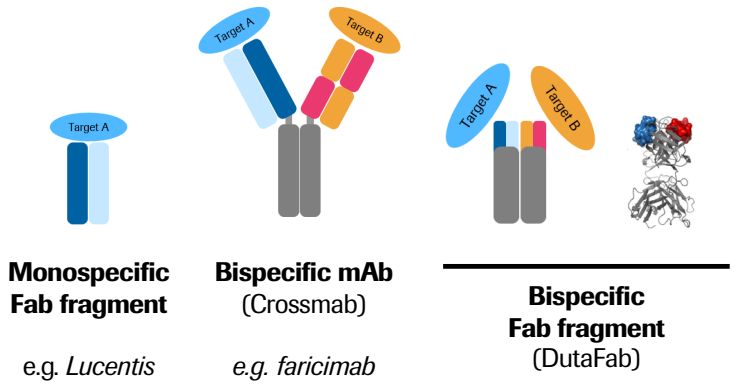
- Ph III trials in DME (PAGODA) and DR (PAVILION) enrolling rapidly
- Ex-US studies to be initiated in nAMD
- Additional Ph III (ARCHWAY) recently presented at Angiogenesis
- US approval expected in 2021

[a] For patients with missing week 40 values the last post-baseline observation was imputed. [b] Percentages are based on total number of patients who completed the measure.
PDS, Port Delivery System with ranibizumab.; PPPQ, PDS Patient Preference Questionnaire.

Port Delivery System is a Platform Technology

DutaFabs are next generation bispecifics designed for increased efficacy & durability*

New bispecific format (DutaFabs)

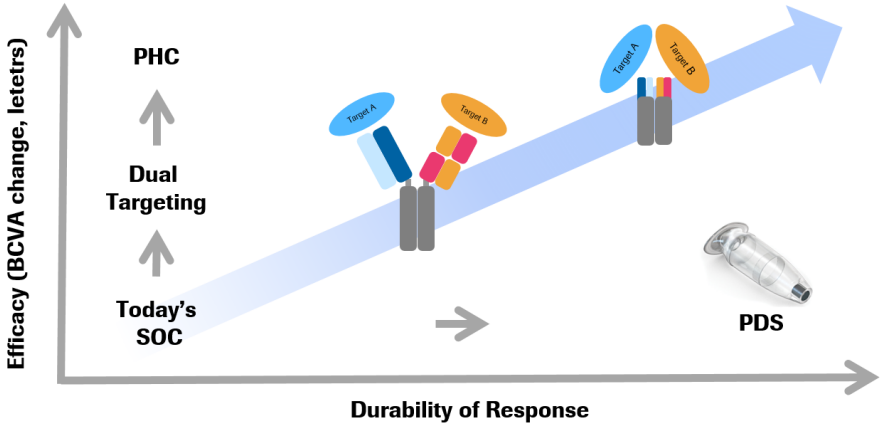


Monospecific Fab fragment
e.g. *Lucentis*

Bispecific mAb (Crossmab)
e.g. faricimab

Bispecific Fab fragment (DutaFab)

Further improving the standard of care

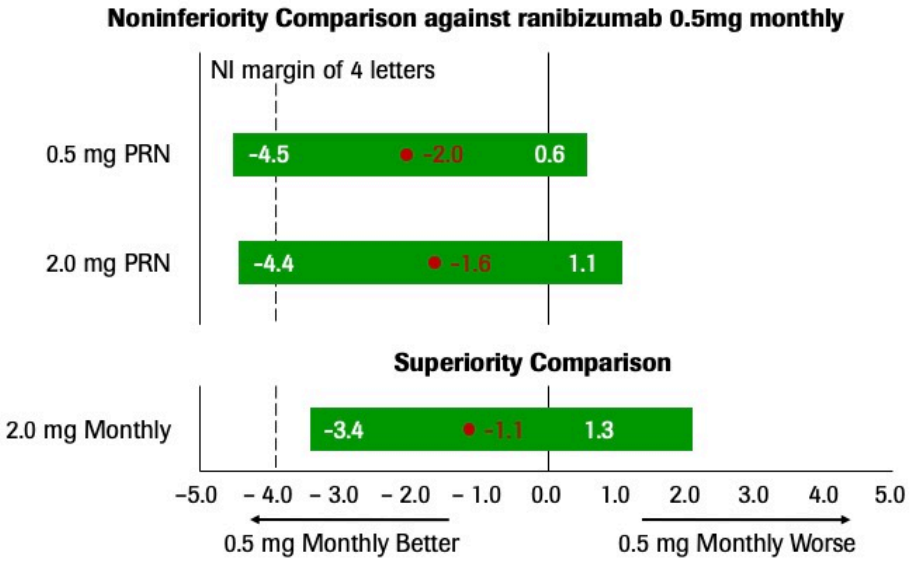


- DutaFabs are a novel bispecific Fab format significantly smaller than bispecific antibodies
- DutaFabs are compatible with the Port Delivery System enabling increased durability beyond Q6M
- 2 DutaFabs are in clinical development targeting different MOAs

*Nature Communications, volume 12, Article number: 708 (2021); SOC=standard of care; PHC=personalized health care; Q6M=every six months dosing; MOA=mechanism of action; PHC=personalized healthcare

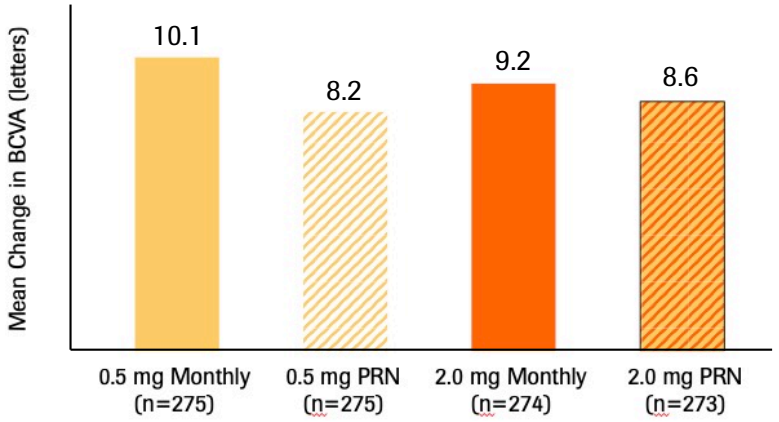
Higher molar doses of anti-VEGF do not lead to greater efficacy or durability

0.5mg ranibizumab at top of dose-response curve



*Pre-specified in HARBOR SAP

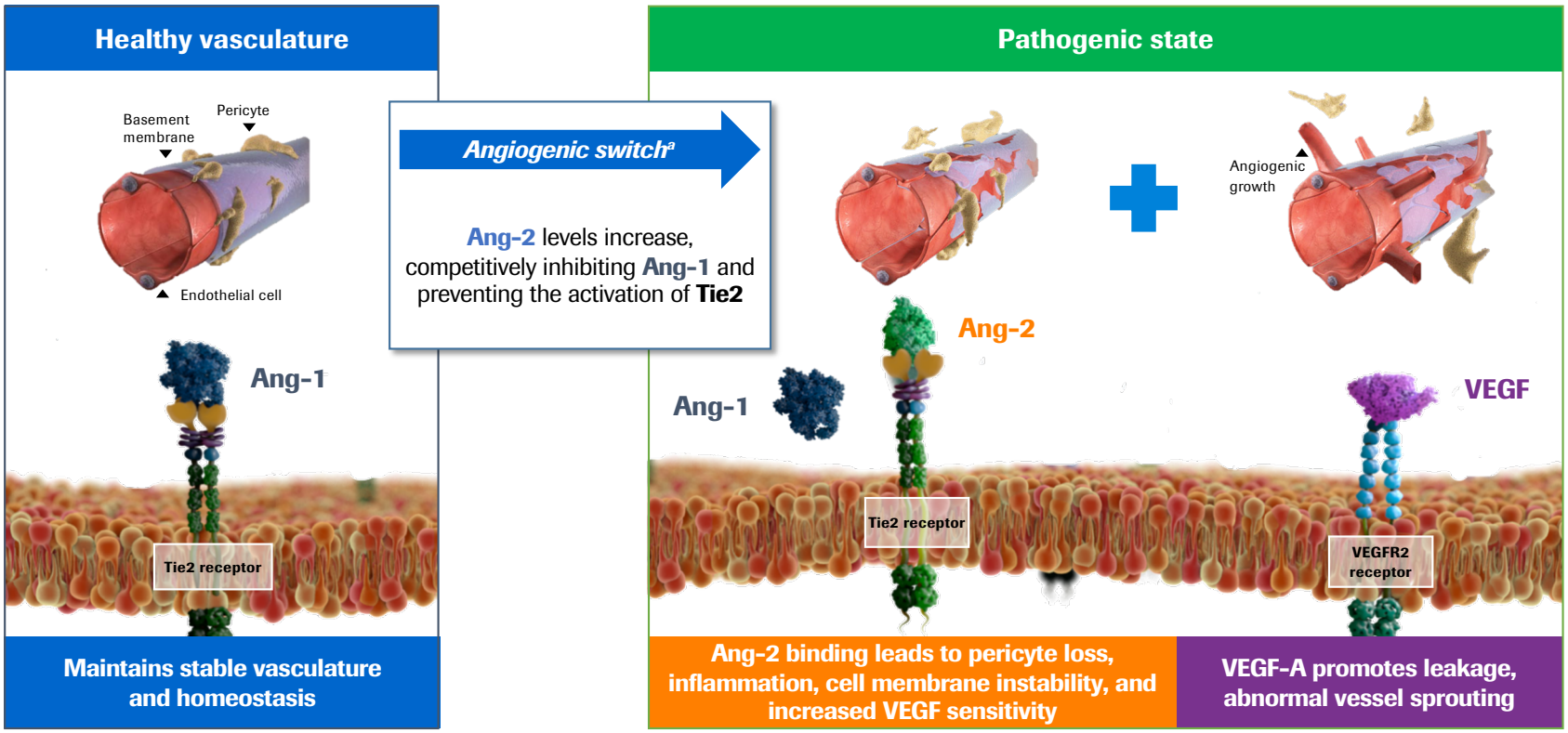
Mean change in BCVA at month 12 in HARBOR



	0.5 mg Monthly (n=275)	0.5 mg PRN (n=275)	2.0 mg Monthly (n=274)	2.0 mg PRN (n=273)
Mean Number of injections*	11.3	7.7	11.2	6.9

Injection frequency similar in 0.5mg and 2mg prn arms

Ang-2 and VEGF-A are key drivers of angiogenesis, inflammation, vascular instability, and leakage



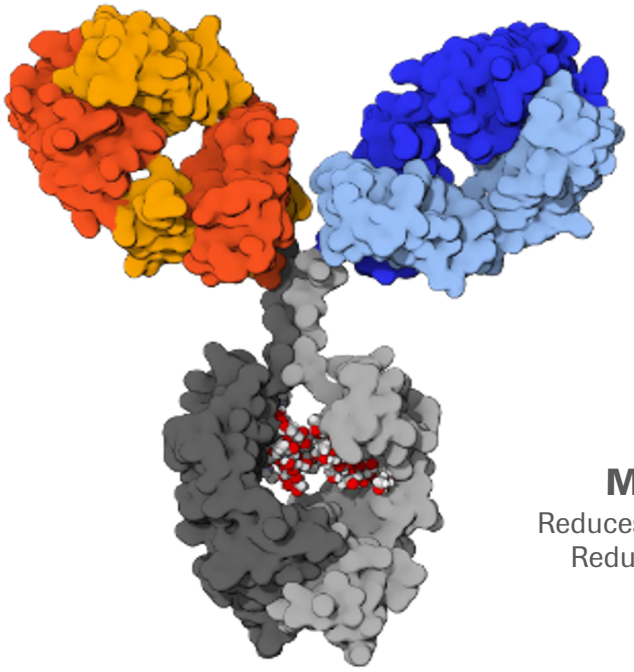
[a] Retinal ischemia and hypoxia lead to an overexpression of growth factors (VEGF, fibroblast growth factor) and cytokines; this includes the upregulation of Ang-2, which subsequently reduces Ang-1 binding to the Tie2 receptor. Saharinen P et al. *Nat Rev Drug Discov*. 2017;16(9):635-661. Ang-1, angiopoietin-1; Ang-2, angiopoietin-2; Tie, tyrosine kinase with immunoglobulin-like domains; VEGF-A, vascular endothelial growth factor-A; VEGFR, vascular endothelial growth factor receptor.

Faricimab – Beyond anti-VEGF monotherapy

The first bispecific antibody designed for intraocular use

One molecule – Two targets

Anti–Ang-2 Fab
Enhances vascular stability
Reduces inflammation and vascular leakage



Anti–VEGF-A Fab
Inhibits vascular leakage and neovascularization

Modified Fc
Reduces systemic exposure
Reduces inflammatory potential

CrossMAb molecule representative of faricimab
Regula JT et al. *EMBO Mol Med*. 2016;8(11):1265-1288, with correction in Regula JT et al. *EMBO Mol Med*. 2019;11(5):e10666
Ang-2, angiopoietin-2; Fab, fragment antigen binding; Fc, fragment crystallizable; VEGF-A, vascular endothelial growth factor-A

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Faricimab: 4 global phase III studies for DME and nAMD

Diabetic Macular Edema	Neovascular Age-Related Macular Degeneration
YOSEMITE and RHINE	**TENAYA and LUCERNE**
Phase III, multicenter, randomized, double-masked, active comparator-controlled studies to evaluate the efficacy and safety of faricimab in patients with diabetic macular edema	Phase III, multicenter, randomized, double masked, active comparator-controlled studies to evaluate the efficacy and safety of faricimab in patients with neovascular age-related macular degeneration

First study results presented at the Annual Angiogenesis, Exudation and Degeneration 2021 Virtual Meeting on February 13, 2021

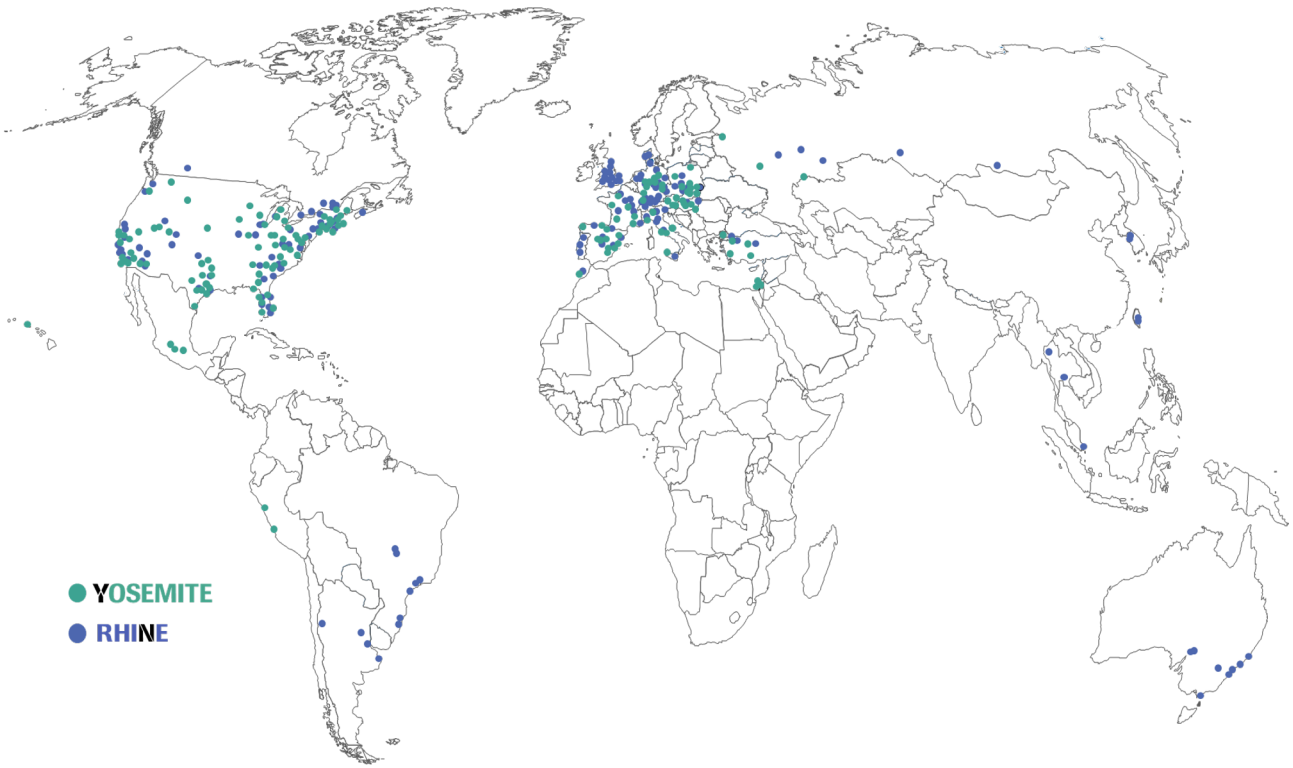
The first time that pivotal ph3 study data has been released simultaneously for two major retinal diseases; nAMD and DME

	DME YOSEMITE / RHINE	nAMD TENAYA / LUCERNE
Primary endpoint	**BCVA change from baseline[1] :** • Non-inferiority achieved for faricimab up to Q16W, over aflibercept dosed Q8W	**BCVA change from baseline[2]:** • Non-inferiority achieved for faricimab up to Q16W, over aflibercept dosed Q8W
	• Consistent results between both sets of studies - YOSEMITE & RHINE and TENAYA & LUCERNE • Secondary analysis results consistent with main analysis	
Secondary endpoint: Durability	• ~ 50% PTI* patients on Q16W • ~ 70% PTI* patients on at ≥Q12W	• ~ 45% patients on Q16W dosing interval • ~ 80% patients on ≥Q12W dosing interval
Safety	• Faricimab was generally well-tolerated, with no new or unexpected safety signals identified • No intraocular inflammation associated with retinal vasculitis or retinal occlusive events	

[1]averaged over Weeks 48, 52, 56; [2]averaged over Weeks 40, 44, 48; *= PTI, Personalized Treatment Internval; Data quality and integrity of acceptable standard for filing in spite of the COVID-19 pandemic

YOSEMITE and RHINE for Diabetic Macular Edema (DME)

Global studies with ~2000 patients across 353 study sites



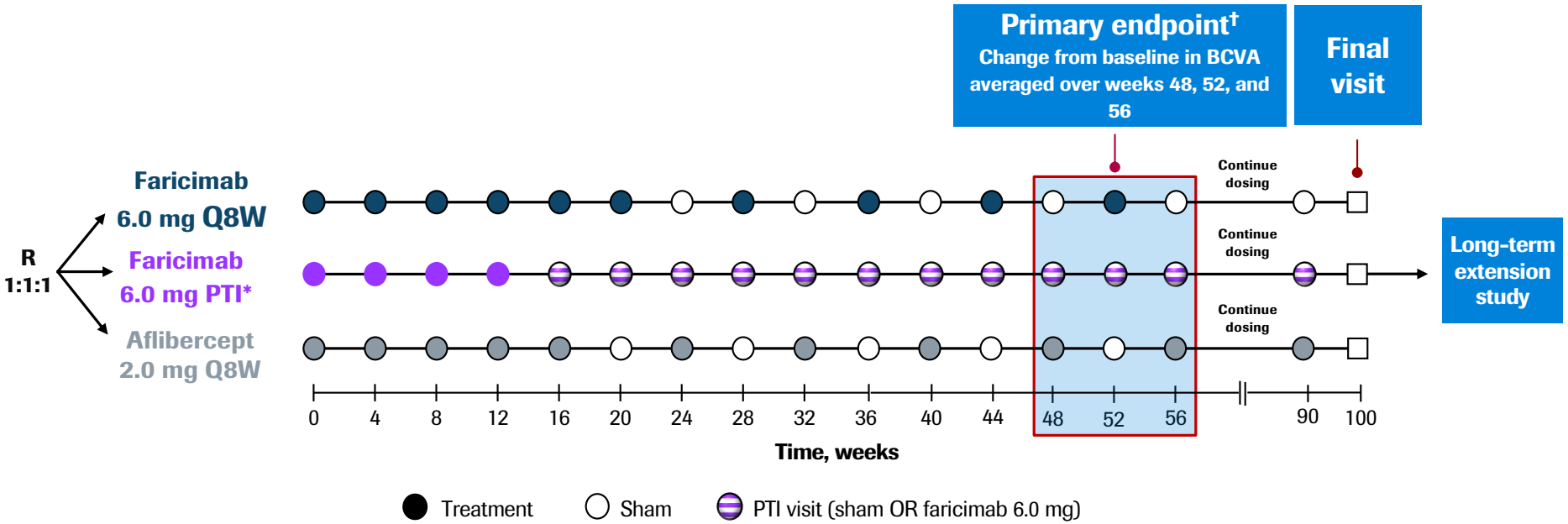
Study Details

- Baseline demographics and ocular characteristics similar between treatment arms and across studies
- Baseline DR severity well-balanced across treatment arms
- Missed doses due to the COVID-19 pandemic, but overall results consistent with primary analysis
- Discontinuation rates low and similar to other Phase III DME studies

Clinical trial registration numbers: NCT03622580 (YOSEMITE); NCT03622593 (RHINE); DR=Diabetic retinopathy

YOSEMITE and RHINE in DME

Evaluating efficacy and safety of faricimab versus aflibercept



Treatment Naive (TN) and **Previously treated with anti-VEGF** agents (cap of 25% at enrolment)

* The Personalized Treatment Arm (PTI) algorithm is a protocol-driven regimen based on the treat-and-extend concept. † BCVA was measured using the Early Treatment Diabetic Retinopathy Study visual acuity chart at a starting distance of 4 m. Clinical trial registration numbers: YOSEMITE: NCT03622580; RHINE: NCT03622593.
BCVA, best-corrected visual acuity; PTI, personalized treatment interval; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor

Personalized treatment interval (PTI) in DME

Based on the treat-and-extend concept to individualize dosing interval

Initiation phase

- Minimum of four initial Q4W doses through week 12

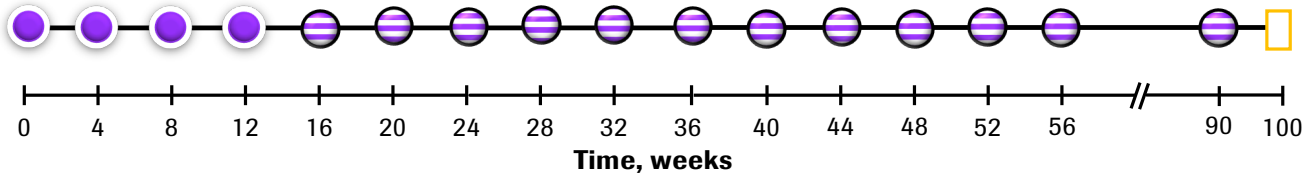
Personalized Treatment Interval – automated, standardized & objective

- BCVA and reading center CST was used for standardization and maintaining study masking
- Intervals automatically calculated based on CST and BCVA compared with the reference value* (min = Q4W, max = Q16W)
- Extend treatment intervals (*in increments of 4 weeks*) if reference CST value reaches < 325 µm on SD-OCT; otherwise continue monthly

Extended by 4 weeks
Stable CST (reference CST ± ≤10%)*

Maintained
Improved CST (reference CST decreased by >10%)*

Reduced by 4 or 8 weeks†
Worsened CST (reference CST increased by >10%)*
(†*depending on severity of BCVA change*)

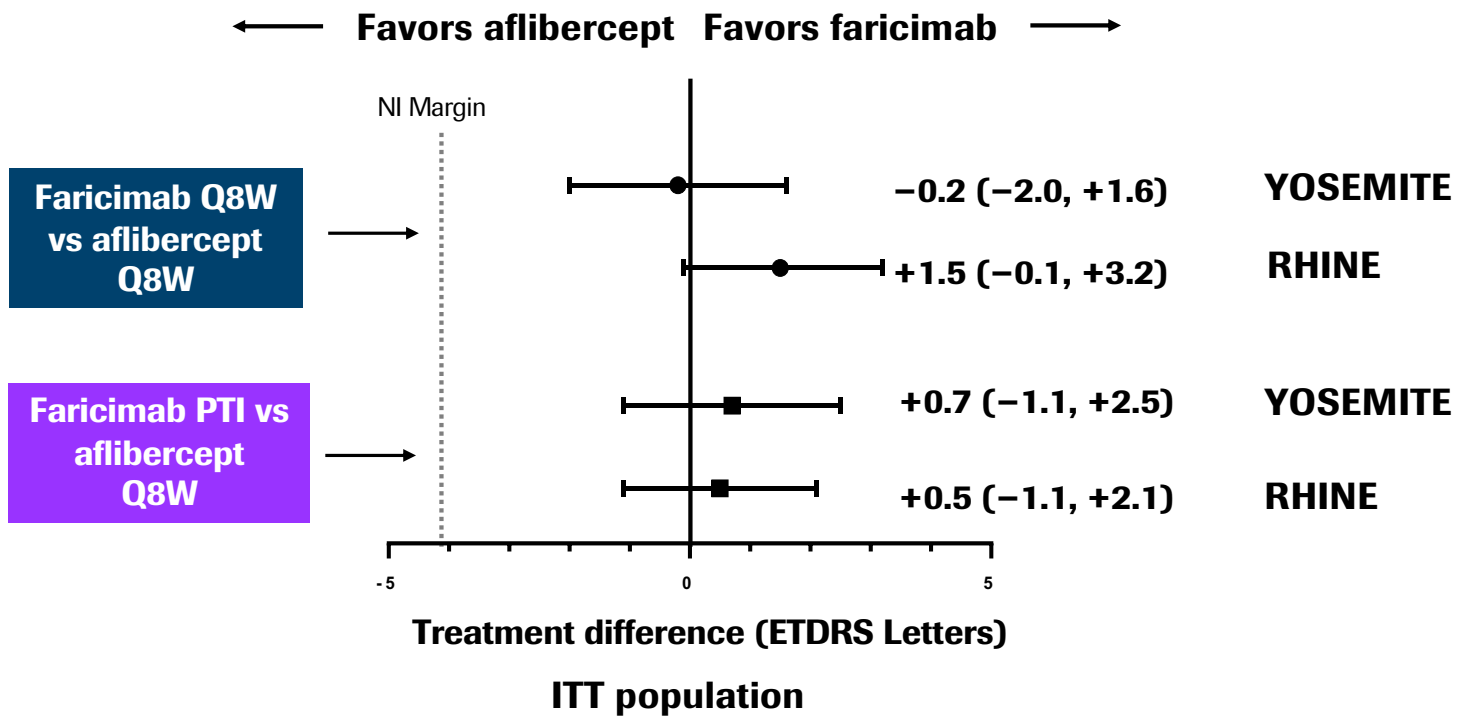


Mandatory initial doses
Masked PTI injection‡ (Sham OR faricimab 6.0 mg)

* Reference CST was defined as the CST value when the original reference value (CST < 325 µm on Spectralis SD-OCT, or < 315 µm on Cirrus SD-OCT or Topcon SD-OCT) were met. Reference CST was adjusted if CST decreased by >10% from the previous reference CST for two consecutive study drug dosing visits and the values obtained were within 30 µm. The CST value obtained at the latter visit served as the new reference CST. Reference BCVA was defined as the mean of the 3 best BCVA scores obtained at any prior study drug dosing visit. ‡ Assessments at sham injection visits were not considered by the IxRS for determination of PTI dosing intervals.
BCVA, best-corrected visual acuity; CST, central subfield thickness; IxRS, interactive voice or web-based response system; PTI, personalized treatment interval; SD-OCT, spectral-domain optical coherence tomography.

YOSEMITE and RHINE met primary endpoint in DME

BCVA gains with faricimab Q8W or up to Q16W non-inferior to aflibercept Q8W

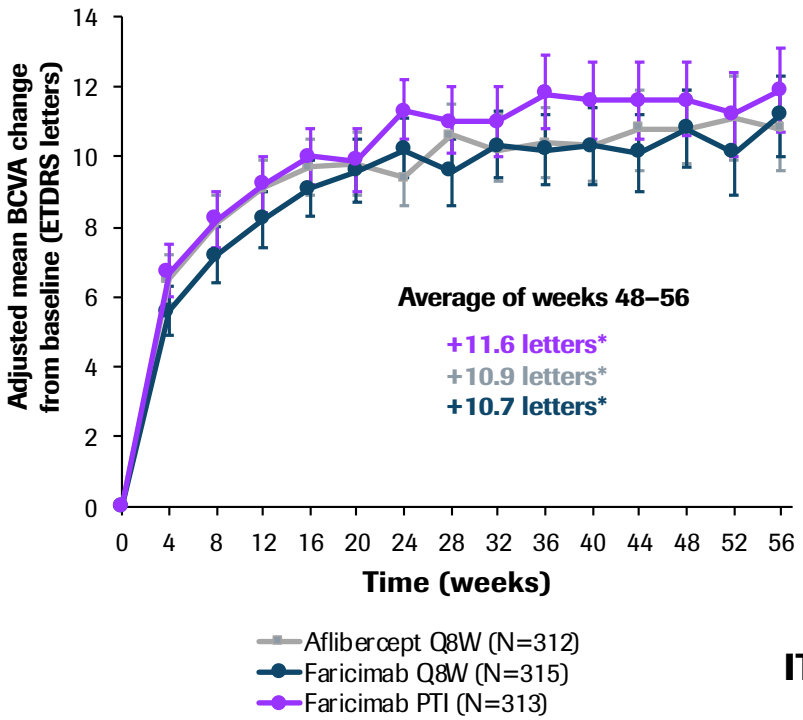


ITT population

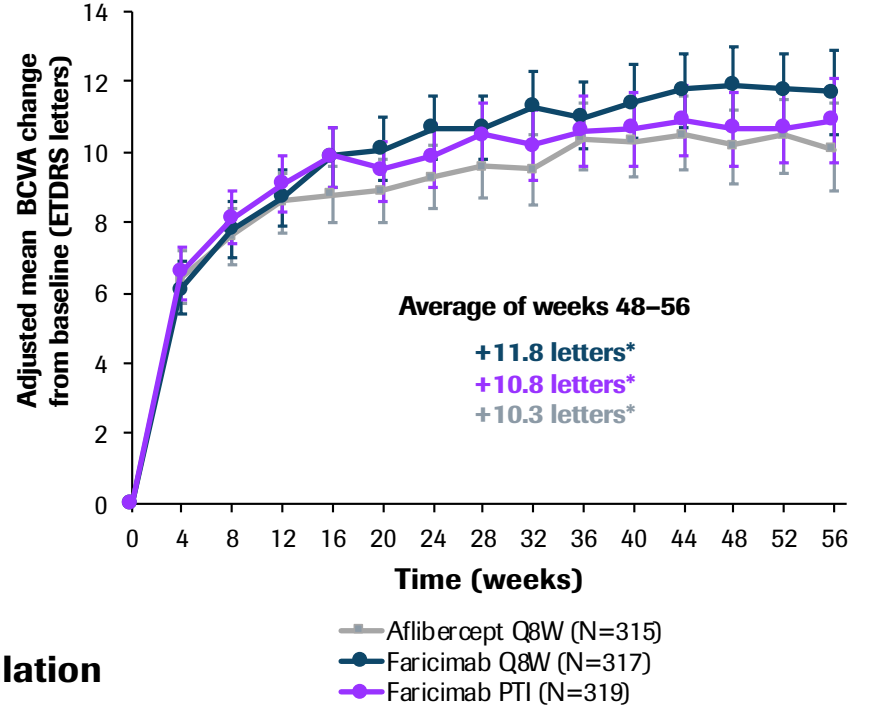
Results are based on a Mixed-Model Repeated-Measures (MMRM) analysis. 97.5% confidence intervals are shown. Primary endpoint: BCVA change from baseline at 1 year, averaged over weeks 48, 52, and 56.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intention-to-treat; NI, non-inferiority; PTI, personalized treatment interval, Q8W, every 8 weeks.

Consistent improvement in BCVA with faricimab in DME

YOSEMITE



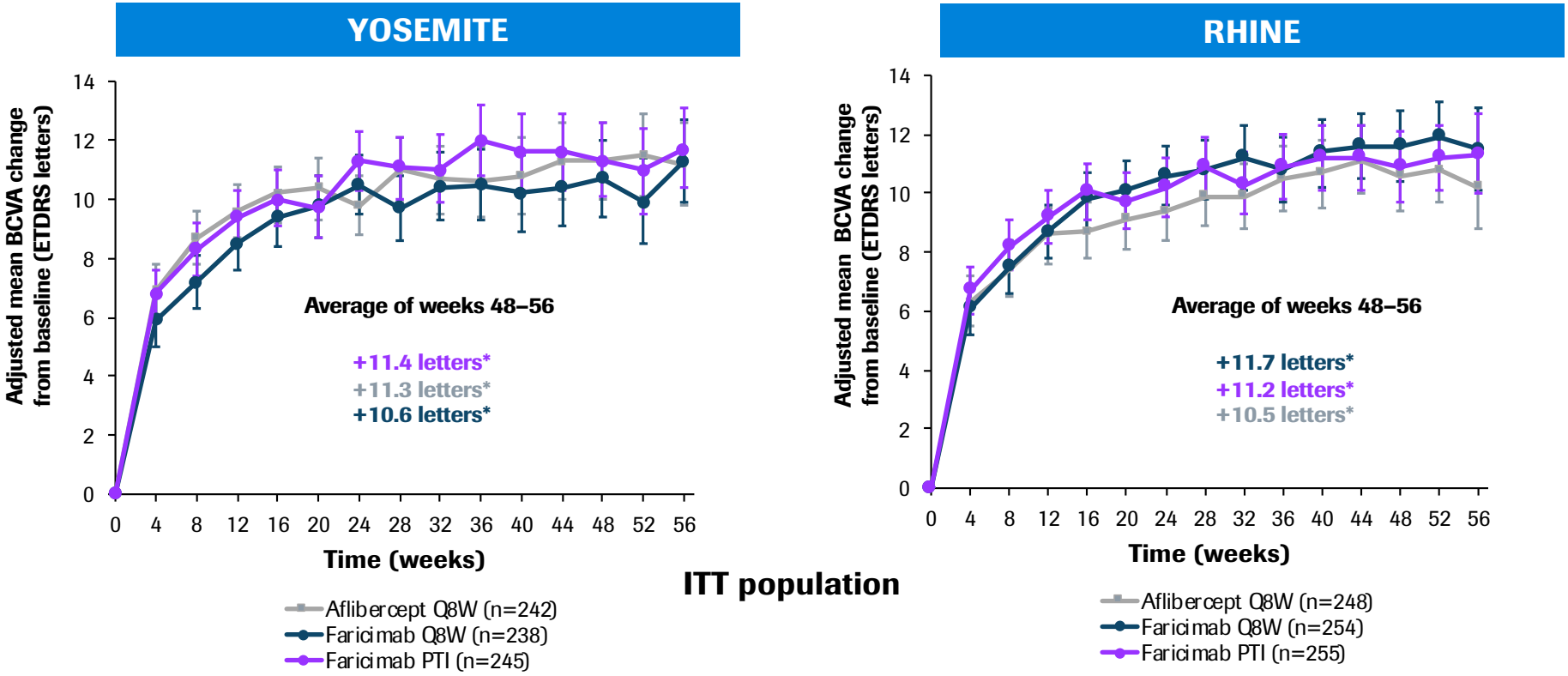
RHINE



ITT population

*Adjusted mean BCVA change from baseline at 1 year, averaged over weeks 48, 52, and 56. Results are based on a Mixed-Model Repeated-Measures (MMRM) analysis. 95% confidence intervals are shown.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intention-to-treat; PTI, personalized treatment interval; Q8W, every 8 weeks.

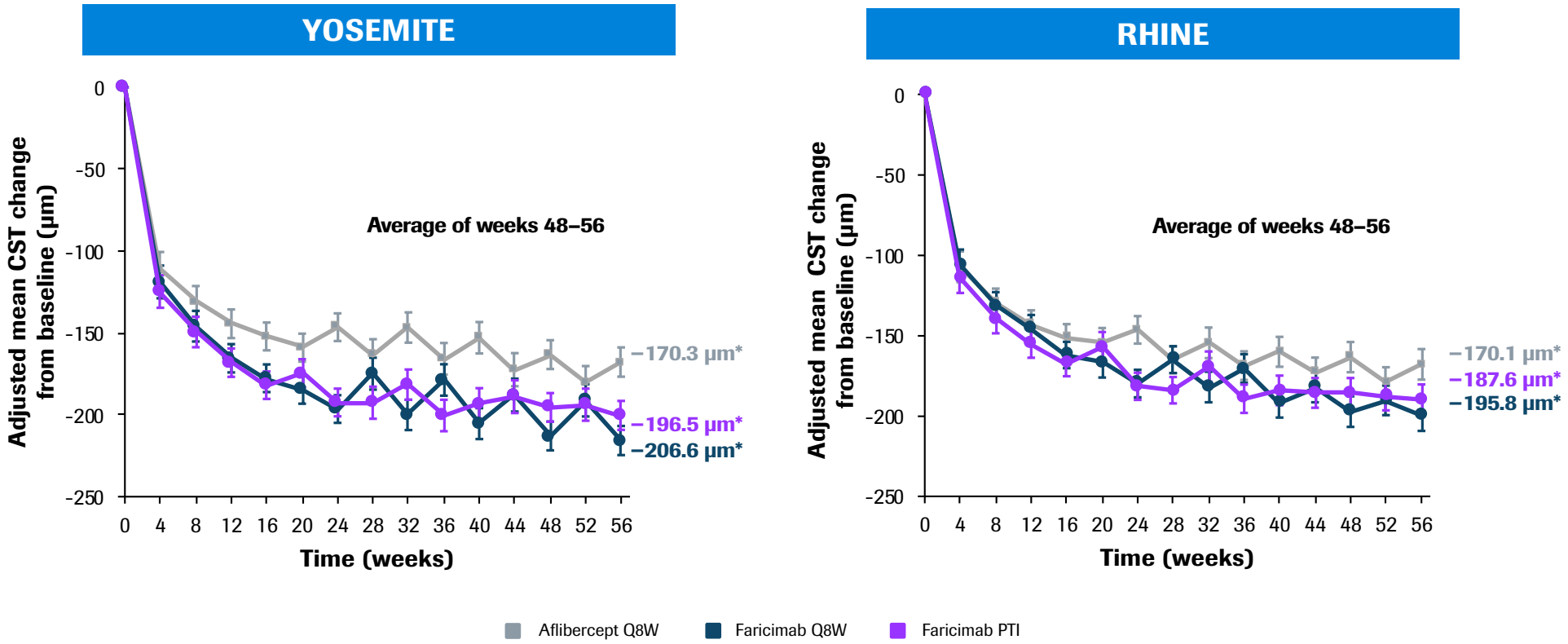
In treatment-naïve DME patients, improvement in BCVA from baseline with faricimab was similar to aflibercept



ITT population

*Adjusted mean BCVA change from baseline at 1 year, averaged over weeks 48, 52, and 56. Results are based on a Mixed-Model Repeated-Measures (MMRM) analysis. 95% confidence intervals are shown
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q8W, every 8 weeks.

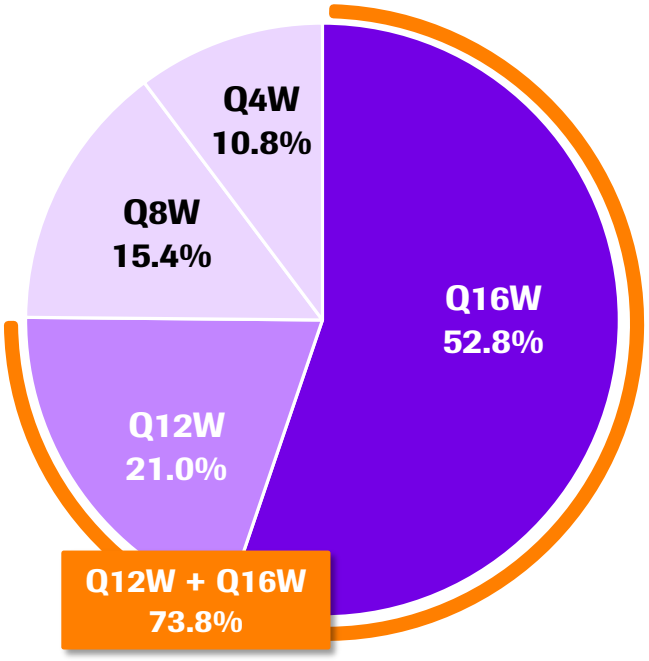
Change in central subfield thickness (CST) from baseline through week 56 consistently favored faricimab



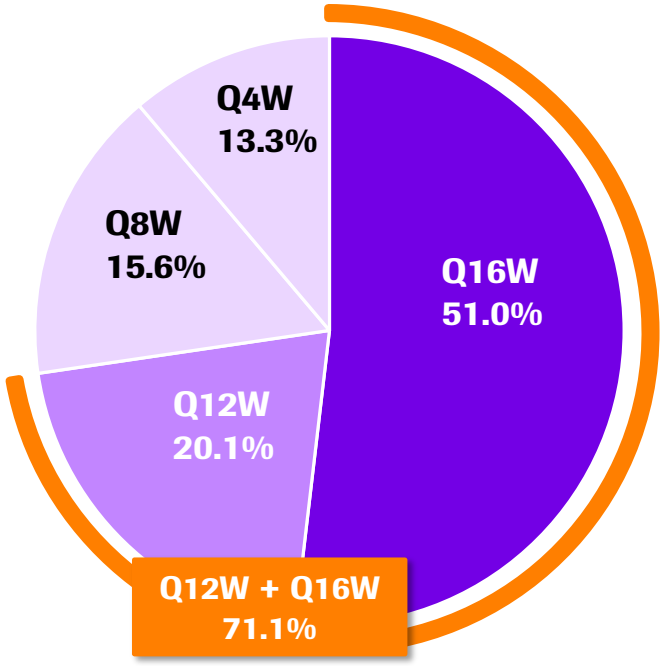
* Adjusted mean CST change from baseline at 1 year, averaged over weeks 48, 52, and 56. Results are based on a Mixed-Model Repeated-Measures (MMRM) analysis.
PTI, personalized treatment interval; Q8W, every 8 weeks.

Strong durability with faricimab in PTI arm
>70% of patients on at least Q12W dosing intervals at Week 52*

YOSEMITE (n=286)



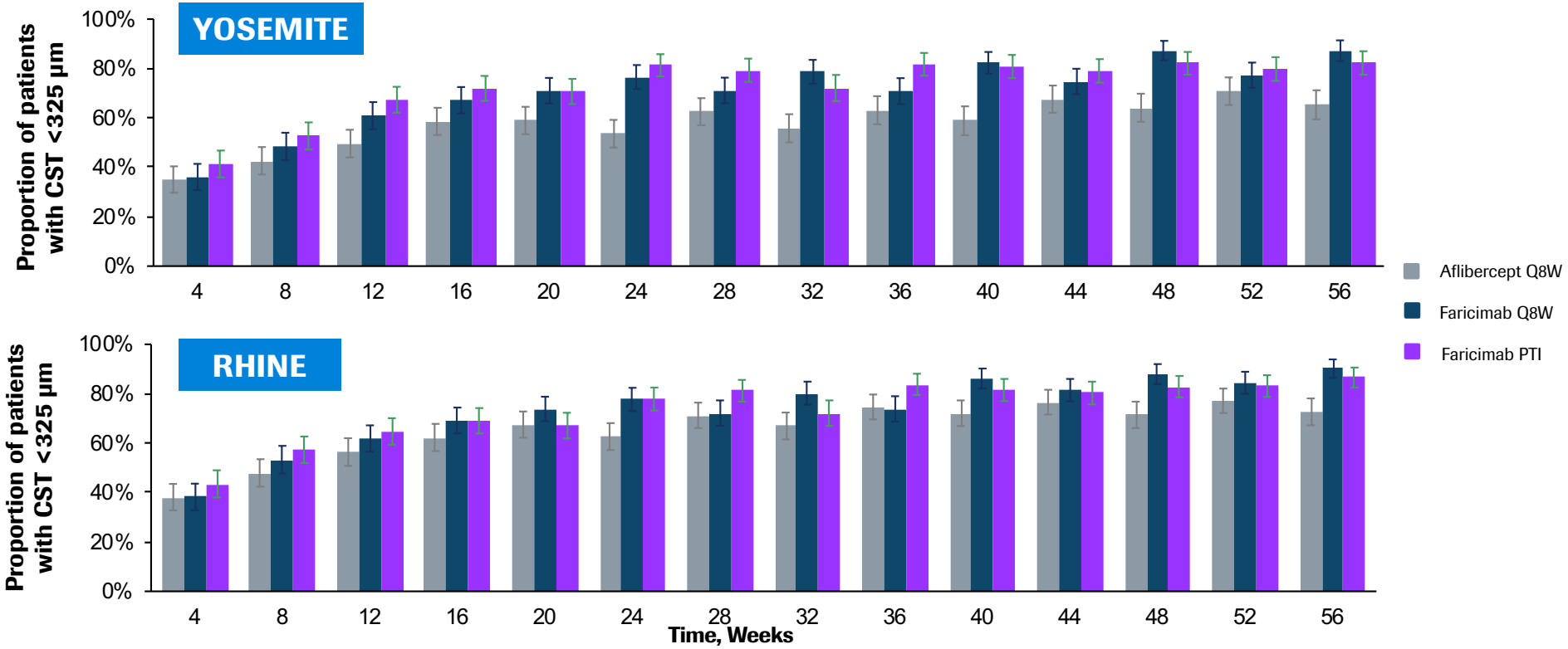
RHINE (n=308)



ITT population

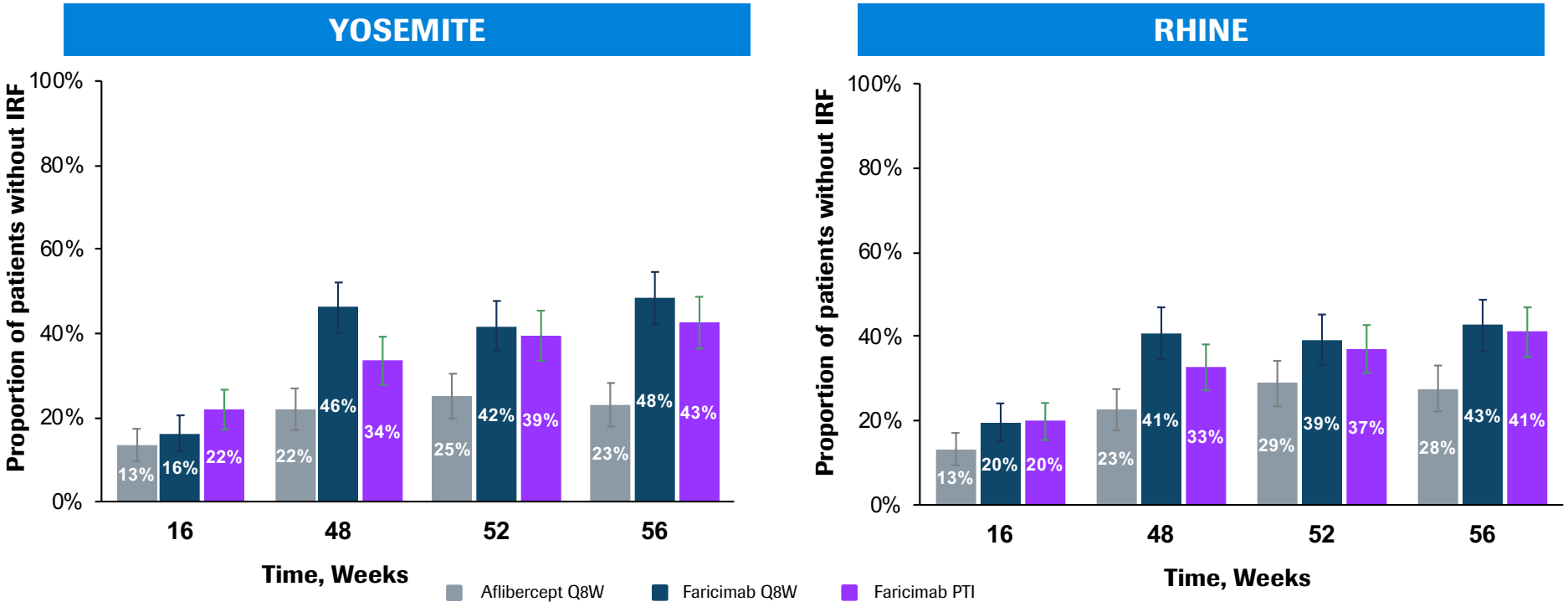
* ITT, intent-to-treat population; N=Number of patients in PTI arm with evaluable data at week 52. Treatment interval at a given visit is defined as the treatment interval decision made at that visit. Percentages are based on the number of patients who have not discontinued the study at the visit;; PTI, personalized treatment interval

More patients treated with faricimab had absence of DME compared with aflibercept through week 56



Absence of DME was defined as CST < 325 µm for Spectralis SD-OCT, or < 315 µm for Cirrus SD-OCT or Topcon SD-OCT. Proportion of patients in each treatment group was estimated using the CMH method. Adjusted for baseline characteristics. The weighted estimate is based on CMH test stratified by baseline BCVA score (< 64 vs ≥ 64 letters), prior intravitreal anti-VEGF therapy (yes vs no), and region (United States and Canada vs the rest of the world). Asia and rest of the world regions are combined due to a small number of enrolled patients. Weighted % for aflibercept arm presented for the faricimab Q8W versus aflibercept comparison. 95% CIs are shown. BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; CST, central subfield thickness; DME, diabetic macular edema; ITT, intent-to-treat; PTI, personalized treatment interval; Q8W, every 8 weeks; SD-OCT, spectral-domain optical coherence tomography; VEGF, vascular endothelial growth factor.

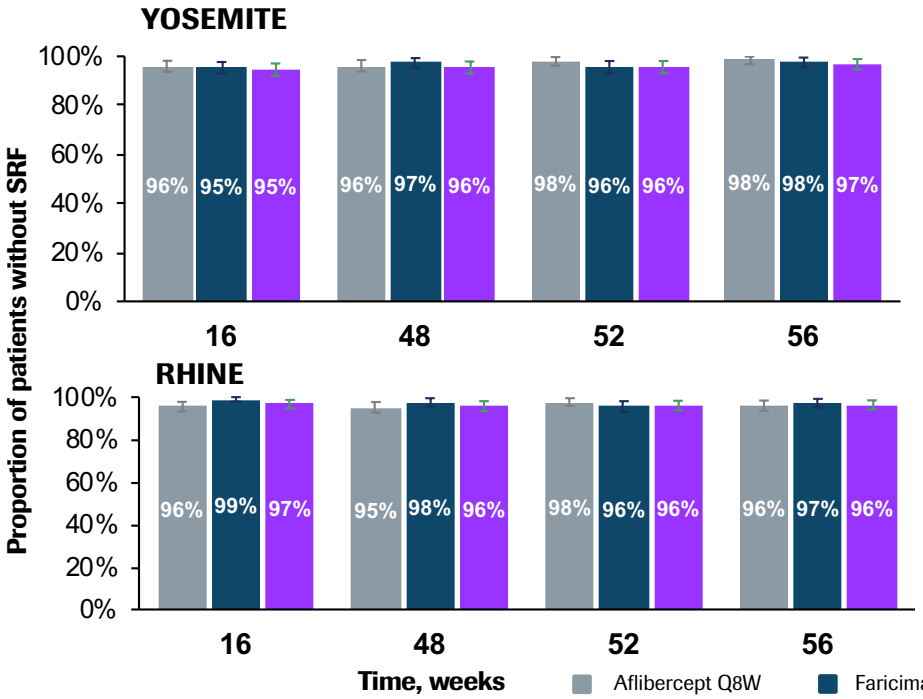
More patients treated with faricimab had absence of intraretinal fluid (IRF) versus aflibercept through Week 56



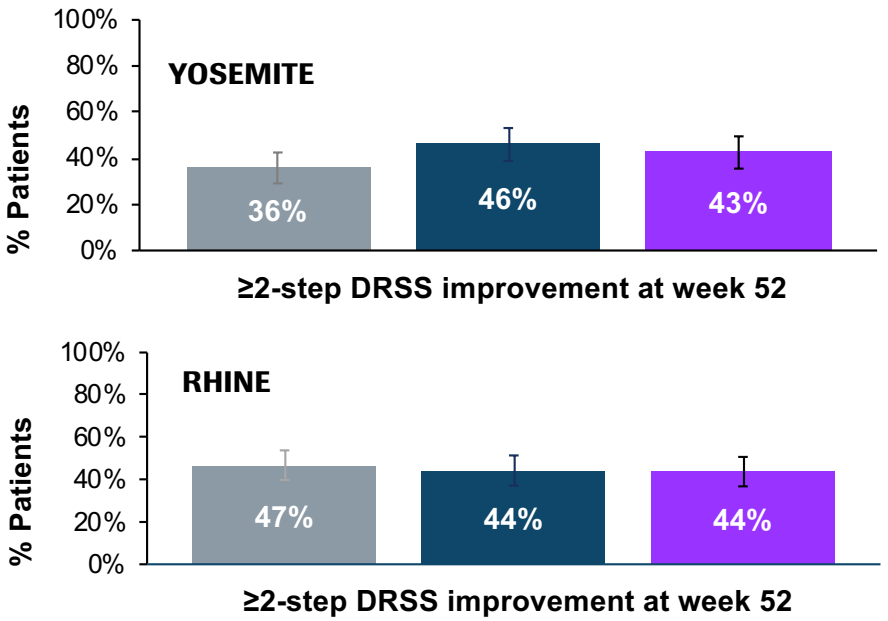
Proportion of patients in each treatment group after baseline was estimated using the CMH method. Adjusted for baseline characteristics. The weighted estimate is based on CMH test stratified by baseline BCVA score (< 64 vs ≥ 64 letters), prior intravitreal anti-VEGF therapy (yes vs no), and region (United States and Canada vs the rest of the world). Asia and rest of the world regions are combined due to a small number of enrolled patients. Weighted % for aflibercept arm presented for the faricimab Q8W versus aflibercept comparison. 95% CIs are shown. BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; IRF, intraretinal fluid; ITT, intent-to-treat population; PTI, personalized treatment interval; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor.

Absence of subretinal fluid (SRF) was high and comparable between faricimab and aflibercept; Improvement in DR severity similar

Absence of SRF[a]



≥ 2-step improvement in DRSS at week 52[b]



[a] The proportion of patients in each treatment group was estimated using the CMH method. Adjusted for baseline characteristics; The weighted estimate is based on CMH test stratified by baseline BCVA score (< 64 vs ≥ 64 letters), prior intravitreal anti-VEGF therapy (yes vs no), and region (United States and Canada vs the rest of the world). Asia and rest of the world regions are combined due to a small number of enrolled patients. Weighted % for the aflibercept arm presented for the faricimab Q8W versus aflibercept comparison. 95% CIs are shown. BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; ITT, intent-to-treat; PTI, personalized treatment interval; Q8W, every 8 weeks; SRF, subretinal fluid; VEGF, vascular endothelial growth factor; [b] Includes patients with evaluable color fundus photograph images at baseline and week 52. 97.5% CIs are shown. DRSS, Diabetic Retinopathy Severity Scale

Adverse events of intraocular inflammation (IOI) were low and consistent with other DME studies

Intraocular inflammation through week 56	YOSEMITE			RHINE		
	Faricimab Q8W (N=313)	Faricimab PTI (N=313)	Aflibercept Q8W (N=311)	Faricimab Q8W (N=317)	Faricimab PTI (N=319)	Aflibercept Q8W (N=314)
Patients with any adverse events of IOI (excluding endophthalmitis)*	5 (1.6%)	7 (2.24%)	3 (0.96%)	3 (0.95%)	2 (0.63%)	1 (0.32%)
Total number of events†	6	13	5	4	2	1
Uveitis	2 (0.64%)	3 (0.96%) **2 severe**	0	0	1 (0.31%)	0
Vitritis	2 (0.64%) **1 severe**	1 (0.32%)	2 (0.64%)	1 (0.32%)	0	0
Iritis	0	3 (0.96%)	1 (0.32%)	2 (0.63%)	0	1 (0.32%)
Iridocyclitis	2 (0.64%)	1 (0.32%)	0	0	1 (0.31%)	0
Anterior chamber inflammation	0	1 (0.32%)	0	0	0	0
Chorioretinitis	0	1 (0.32%)	0	0	0	0
Keratic precipitates	0	1 (0.32%)	0	0	0	0
Keratouveitis	0	1 (0.32%)	0	0	0	0
Post-procedural inflammation	0	0	0	0	0	0
Endophthalmitis	0	2 (0.6%)	0	2 (0.6%)	0	1 (0.3%)

IOI event rates were on average reported in 1.3% and 0.6% for faricimab and aflibercept, respectively

Results are presented based on the Safety Evaluable Population For frequency counts by PT, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Includes AEs with onset up to Day 405 (last day of week 56 analysis window).
Severe events are called out; all other events were mild or moderate.

No cases of retinal vasculitis in either study

Retinal vasculitis through week 56	YOSEMITE			RHINE		
	Faricimab Q8W (n = 313)	Faricimab PTI (n = 313)	Aflibercept Q8W (n = 311)	Faricimab Q8W (n = 317)	Faricimab PTI (n = 319)	Aflibercept Q8W (n = 314)
Number of patients with events	0	0	0	0	0	0

Retinal occlusive events through week 56	YOSEMITE			RHINE		
	Faricimab Q8W (n = 313)	Faricimab PTI (n = 313)	Aflibercept Q8W (n = 311)	Faricimab Q8W (n = 317)	Faricimab PTI (n = 319)	Aflibercept Q8W (n = 314)
Patients with any events, n (%)	1 (0.32%)	1 (0.32%)	1 (0.32%)	0	1 (0.31%)	1 (0.32%)
Number of patients with events, n (%)						
Retinal vein occlusion	1 (0.32%)	1 (0.32%)	0	0	1 (0.3%)	0
Retinal artery occlusion	0	0	1 (0.32%)	0	0	0
Retinal artery embolism	0	0	0	0	0	1 (0.32%)

For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. Results are presented based on the safety-evaluable population. All events are investigator-reported. Retinal vein occlusion: 2 moderate (YOSEMITE), 1 severe (RHINE); retinal artery occlusion: severe (YOSEMITE); retinal artery embolism: mild (RHINE).
PTI, personalized treatment interval; Q8W, every 8 weeks.

Other important safety events were infrequent

Serious AEs	YOSEMITE			RHINE		
	Faricimab Q8W (n = 313)	Faricimab PTI (n = 313)	Aflibercept Q8W (n = 311)	Faricimab Q8W (n = 317)	Faricimab PTI (n = 319)	Aflibercept Q8W (n = 314)
Rhegmatogenous retinal detachment, n (%)	1 (0.3%)	0	0	0	0	0
Retinal tear, n (%)	0	1 (0.3%)	0	0	1 (0.3%)	0
Intraocular pressure increased, n (%)	0	0	0	0	1 (0.3%)	0
Traumatic cataract, n (%)	0	0	0	0	0	0

	Faricimab Q8W (n = 313)	Faricimab PTI (n = 313)	Aflibercept Q8W (n = 311)	Faricimab Q8W (n = 317)	Faricimab PTI (n = 319)	Aflibercept Q8W (n = 314)
Patients With Any APTC[a] Events, n (%)	9 (2.9%)	10 (3.2%)	9 (2.9%)	4 (1.3%)	2 (0.6%)	5 (1.6%)
Number of patients with events						
Death, n (%)	2 (0.6%)	6 (1.9%)	2 (0.6%)	3 (0.9%)	0	2 (0.6%)
Non fatal MI, n (%)	4 (1.3%)	2 (0.6%)	4 (1.3%)	0	0	2 (0.6%)
Non-fatal stroke, n (%)	3 (1.0%)	2 (0.6%)	3 (1.0%)	1 (0.3%)	2 (0.6%)	1 (0.3%)

Percentages are based on **n** in the column headings. All events are investigator reported. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. Includes AEs with onset up to Day 405 (last day of Week 56 analysis visit window) [a]APTC events were adjudicated by an external independent committee.
AE, adverse event; APTC, Anti-Platelet Trialists' Collaboration; MI, myocardial infarction; PTI, personalized treatment interval; Q8W, every 8 weeks.

YOSEMITE and RHINE in DME

Demonstrating advantages in durability potential and anatomy

Faricimab improves vascular stability via simultaneous neutralization of both Ang-2 and VEGF-A

YOSEMITE and RHINE met primary endpoint

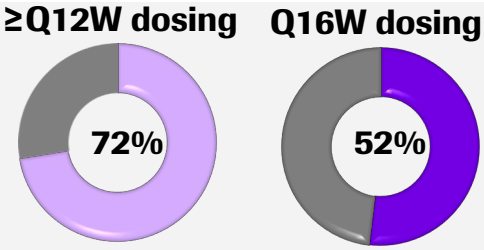
BCVA gains from baseline with **faricimab 6.0mg** dosed at **Q8W** or **up to Q16W** were **non-inferior** to **aflibercept 2.0mg Q8W** in patients with DME

DME disease control with faricimab

Better anatomic outcomes with faricimab vs. aflibercept**:**

- Change in **CST favoring faricimab**
- More patients showing **absence of DME**
- More patients showing **absence of IRF**

Durability up to Q16W at 1 year in the faricimab PTI dosing arm



Results were **reproducible** across the YOSEMITE and RHINE studies in nearly 2000 patients

Safety

- Faricimab was well tolerated. IOI event rates were low and on average reported in 1.3% and 0.6% for faricimab and aflibercept, respectively. There were no cases of **vasculitis or occlusive retinitis** reported

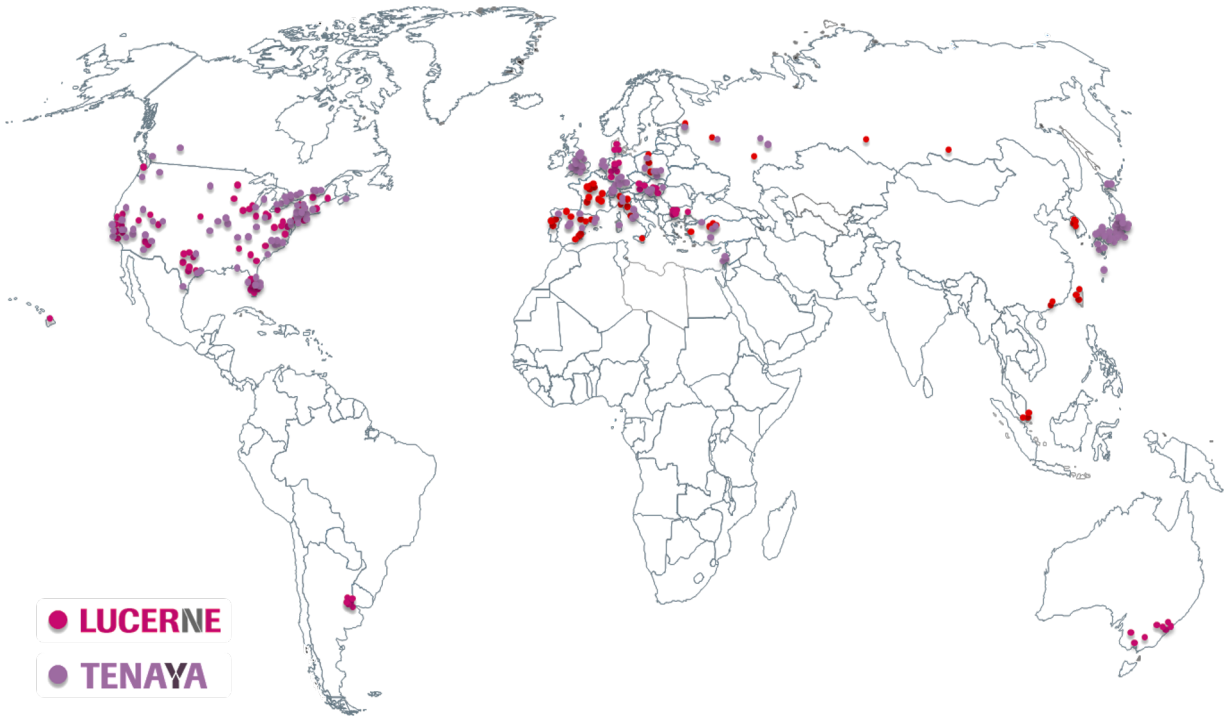
Long-term data

- Year 2 data and long-term studies (RHONE-X) are ongoing

Ang-2, BCVA, DME, IOI, Q8W, Q16W, VEGF-A

TENAYA and LUCERNE for nAMD

Global studies that enrolled 1300+ patients in over 270 study sites



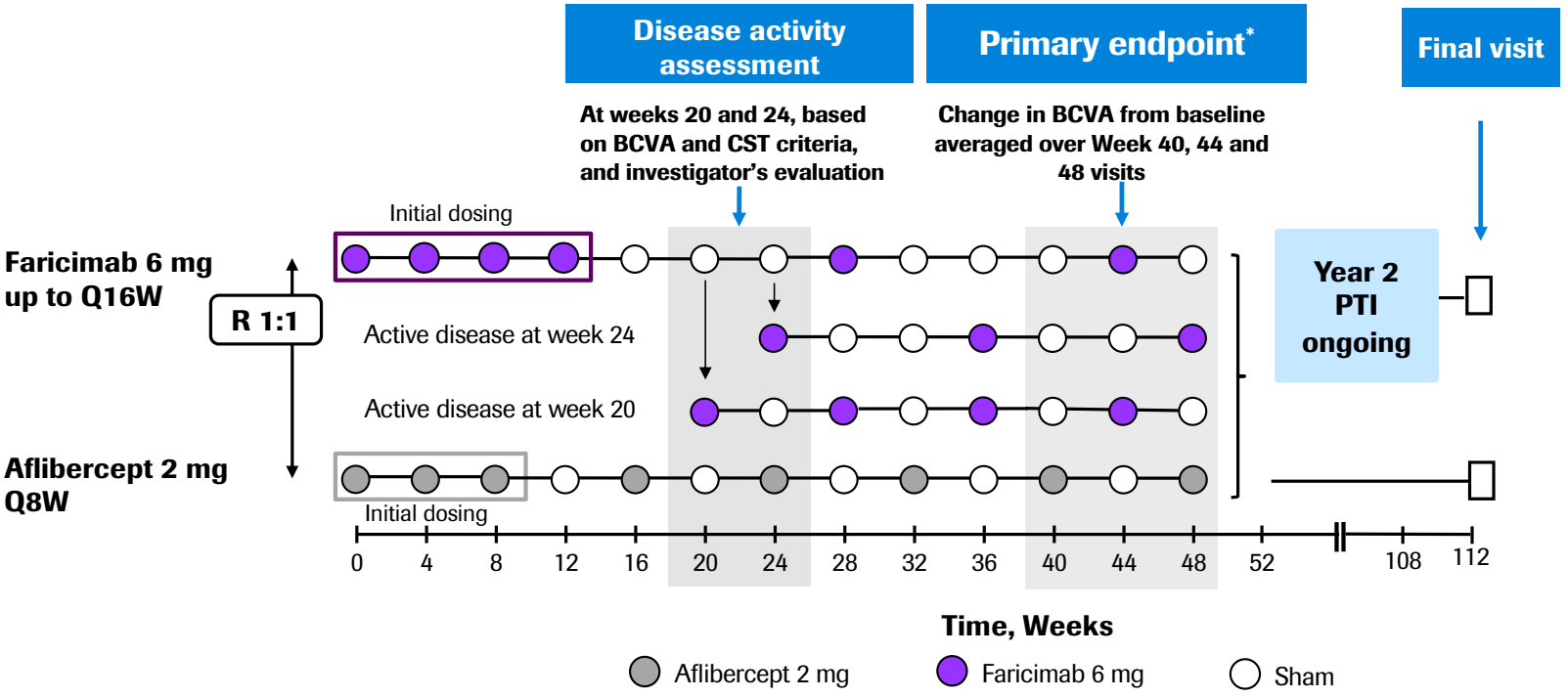
Study Details

- Baseline demographics and ocular characteristics generally well-balanced across treatment arms and studies
- Discontinuation rates low with minimal impact from Covid-19 on overall results
- Robustness of primary analysis assessed through supplemental and sensitivity analyses - all results consistent with primary analysis

Clinical trial registration numbers: NCT03823287 (TENAYA); NCT03823300 (LUCERNE); nAMD=neovascular age-related macular degeneration

TENAYA and LUCERNE in nAMD

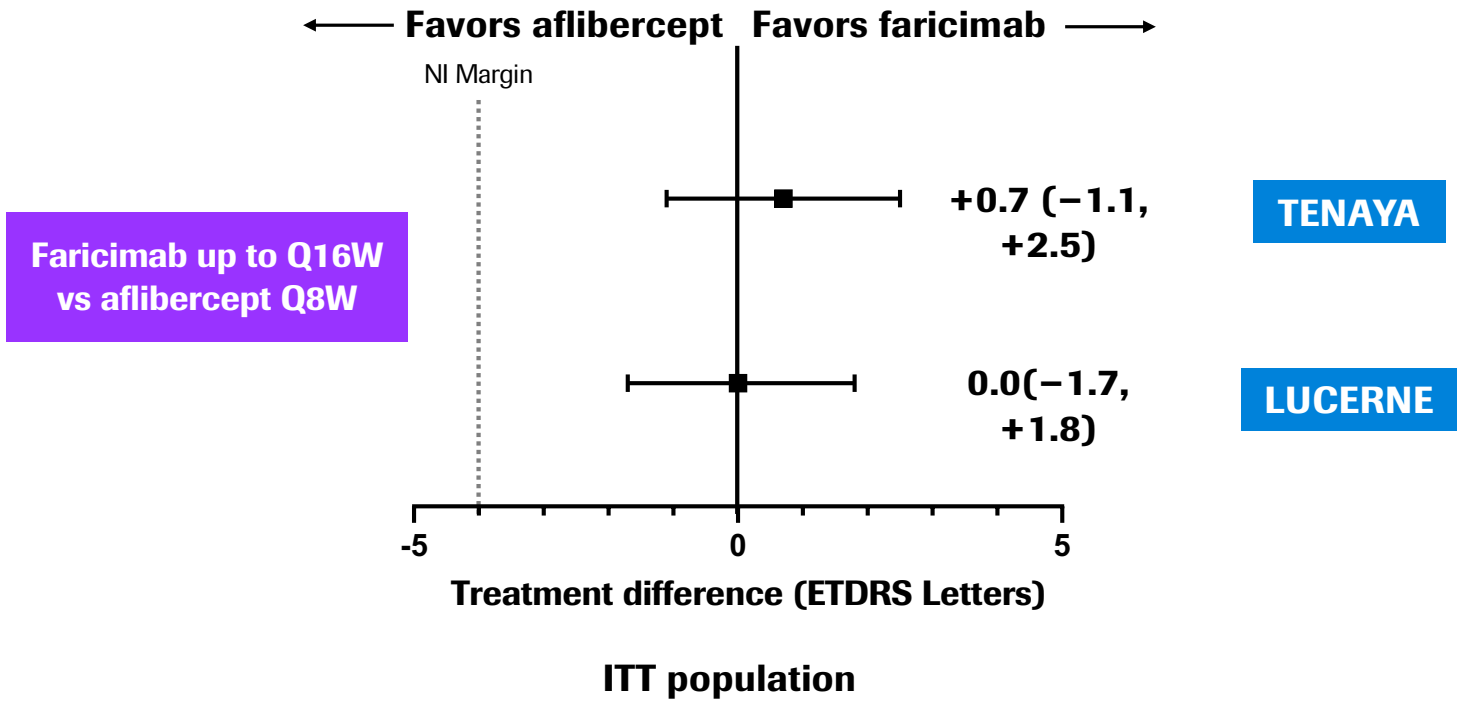
Evaluating efficacy and safety of faricimab versus aflibercept



*BCVA was measured using the Early Treatment Diabetic Retinopathy Study visual acuity chart at a starting distance of 4 m. TENAYA clinical trial (NCT03823287); LUCERNE clinical trial (NCT03823300).
BCVA, best-corrected visual acuity; CNV, choroidal neovascularization; ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; PTI, personalized treatment interval as specified in study protocol; Q4W, every 4 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; R, randomized.

TENAYA and LUCERNE met primary endpoint in nAMD

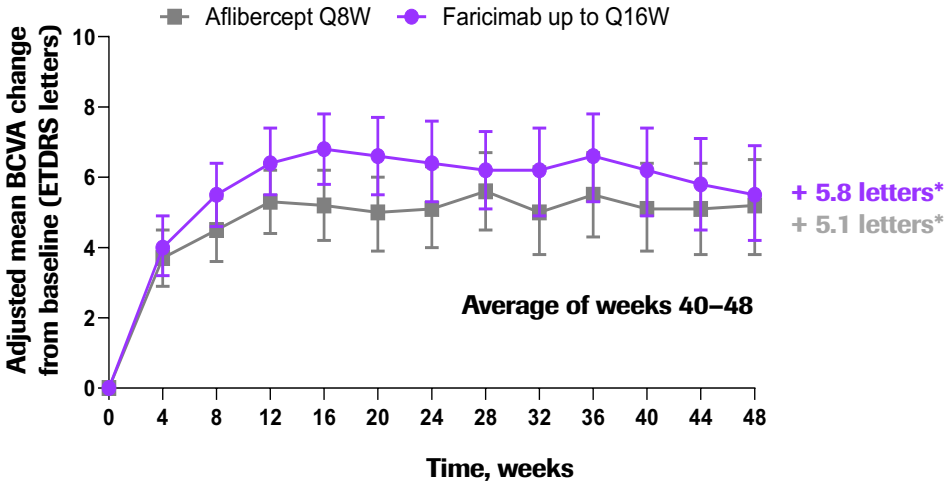
BVCA gains with faricimab dosed up to Q16W non-inferior to aflibercept Q8W



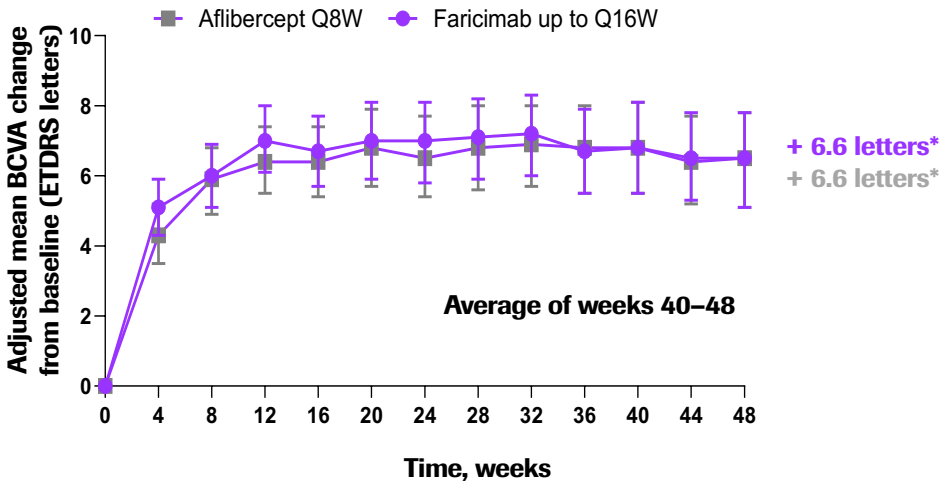
Results are based on a Mixed-Model Repeated-Measures (MMRM) analysis.. 95% confidence interval. Primary endpoint: BCVA change from baseline averaged over Weeks 40, 44, and 48
BCVA, best-corrected visual acuity; CI, confidence interval; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intention-to-treat; NI, non-inferiority.

Initial BCVA gains were sustained with majority of patients in the faricimab arm up to Q16W

TENAYA in nAMD



LUCERNE in nAMD

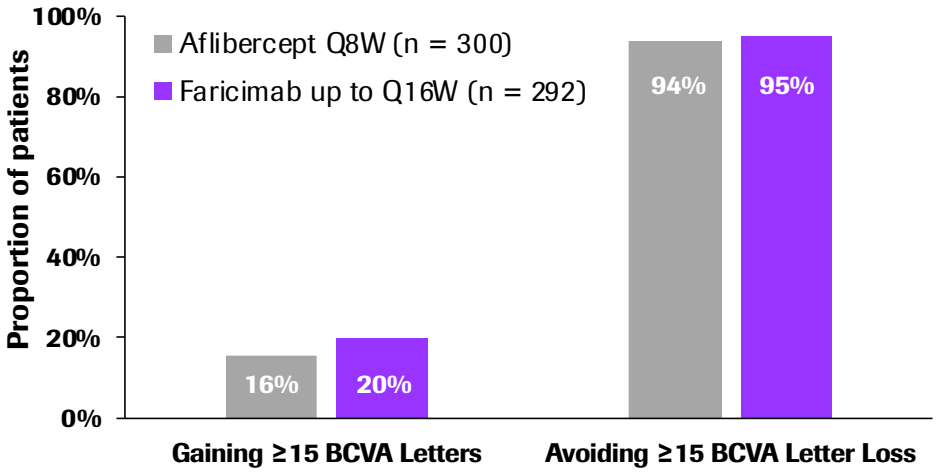


ITT population

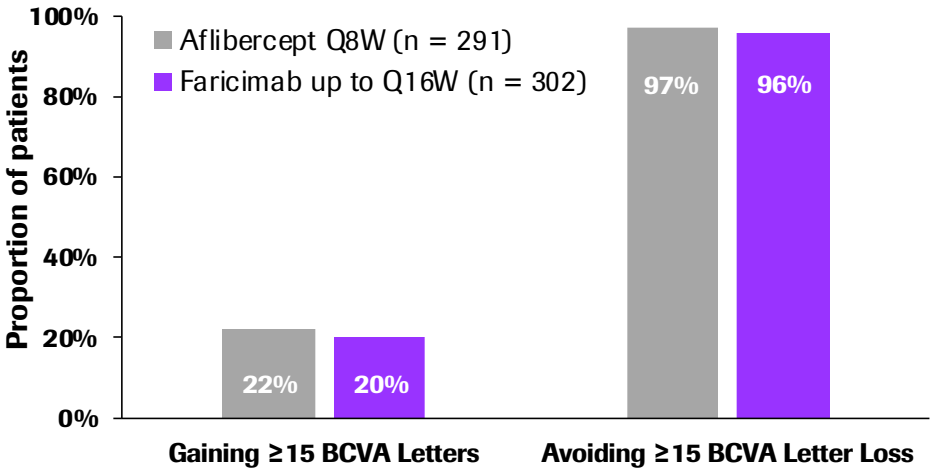
*Adjusted mean BCVA change from baseline at 1 year, averaged over weeks 40, 44, and 48. Results are based on a Mixed-Model Repeated-Measures (MMRM) analysis in the ITT population.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; *ITT population, intention-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks.

Comparable proportion of patients gaining or maintaining vision[a] with faricimab up to Q16W and aflibercept Q8W

TENAYA in nAMD



LUCERNE in nAMD



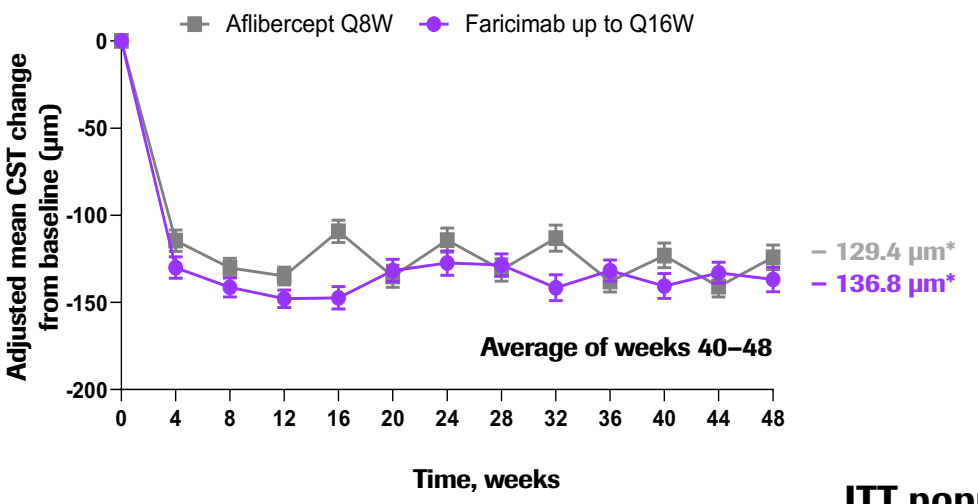
ITT population

[a] BCVA change averaged over weeks 40, 44, and 48

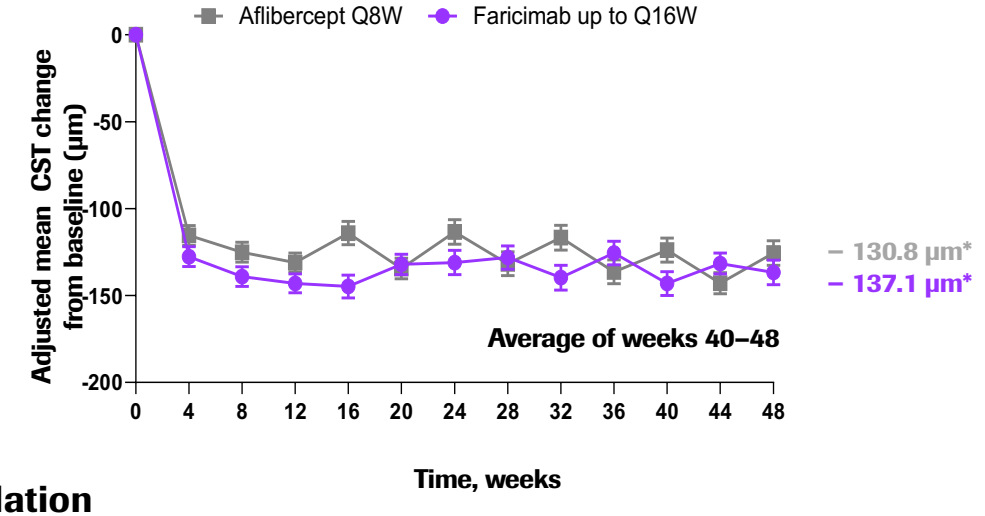
n represents patients with at least one non-missing assessment at Weeks 40, 44, 48. Proportion of patients in each group was estimated using the Cochran-Mantel Haenszel method.
BCVA, best-corrected visual acuity; ITT, intent to treat; Q16W, every 16 weeks.

Meaningful reductions in central subfield thickness (CST) with faricimab up to Q16W

TENAYA in nAMD



LUCERNE in nAMD

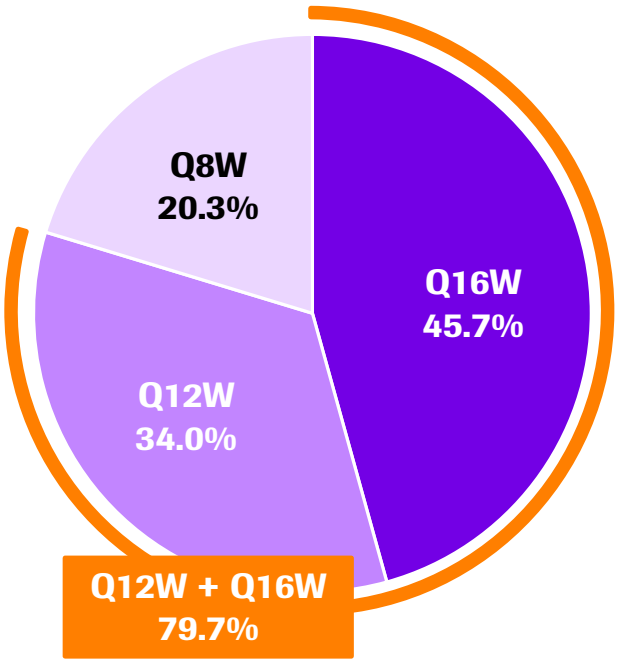


ITT population

*Adjusted mean CST change from baseline at 1 year, averaged over weeks 40, 44, and 48. Results are based on a Mixed-Model Repeated-Measures (MMRM) analysis. CST is measured as ILM-RPE, as graded by central reading center. CST, central subfield thickness; ILM, internal limiting membrane; ITT, intention-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium

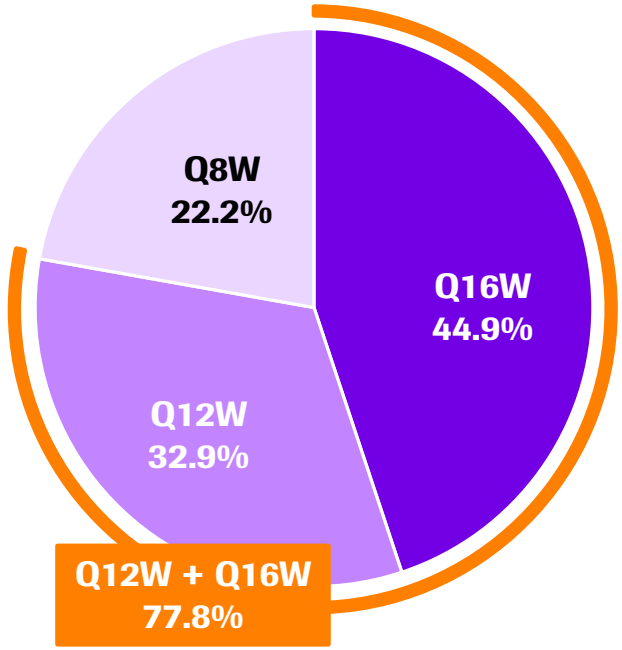
Durability with faricimab: ~ 45% of patients on Q16W and almost 80% on ≥ Q12W dosing at Week 48*

TENAYA (n=334)



Median number of injections:
Faricimab – 6
Aflibercept – 8

LUCERNE (n=331)



Percentages are based on number of patients randomized to the faricimab arm who have not discontinued the study at Week 48. Treatment interval at Week 48 is defined as the treatment interval decision followed at that visit
*ITT intent to treat population; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

Adverse events of intraocular inflammation (IOI) were low

Intraocular Inflammation through week 48	TENAYA		LUCERNE	
	Faricimab up to Q16W (N=333)	Aflibercept Q8W (N=336)	Faricimab up to Q16W (N=331)	Aflibercept Q8W (N=326)
Patients with any events of IOI (excluding endophthalmitis)	5 (1.5%)	2 (0.6%)	8 (2.4%)	6 (1.8%)
Total number of events	6	2	10	7
Iritis	2 (0.6%)	1 (0.3%)	1 (0.3%)	1 (0.3%)
Uveitis	1 (0.3%) **S**	1 (0.3%)	1 (0.3%) **S**	1 (0.3%) **S**
Keratic precipitates	1 (0.3%)	0	0	0
Vitritis	1 (0.3%)	0	2 (0.6%)	1 (0.3%)
Iridocyclitis	0	0	3 (0.9%)	2 (0.6%)
Chorioretinitis	0	0	1 (0.3%) **S**	0
Post procedural inflammation	0	0	0	1 (0.3%)
Endophthalmitis	0	0	0	1 (0.3%)

IOI event rates were on average reported in 2.0% and 1.2% for faricimab and aflibercept, respectively

Results are presented based on the Safety Evaluable Population For frequency counts by patient, multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Includes AEs with onset up to Day 349 (last day of Week 48 analysis visit window).
S = Severe (all other events were moderate or mild). AE, adverse event; Q8W, every 8 weeks; Q16W, every 16 weeks.

No cases of retinal vasculitis in either study

Retinal vasculitis events through week 48	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (n = 326)
Number of patients with events	0	0	0	0

Retinal occlusive events through week 48	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (n = 326)
Patients with any events, n (%)	0	0	1 (0.3%)	0
Number of patients with events, n (%)				
Retinal vein occlusion	0	0	0	0
Retinal artery occlusion	0	0	0	0
Retinal artery embolism	0	0	1 (0.3%)	0

Results are presented based on the Safety Evaluable Population. All events are investigator-reported. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once.
Q8W, every 8 weeks; Q16W, every 16 weeks.

Other Important Safety Events Were Infrequent

Serious AEs	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (N=326)
Rhegmatogenous retinal detachment, n (%)	0	0	0	0
Retinal tear, n (%)	0	0	0	0
Retinal pigment epithelial tear, n (%)	2 (0.6%)	0	2 (0.6%)	0
Intraocular pressure increased, n (%)	0	0	1 (0.3%)	0
Traumatic cataract, n (%)	0	0	0	0

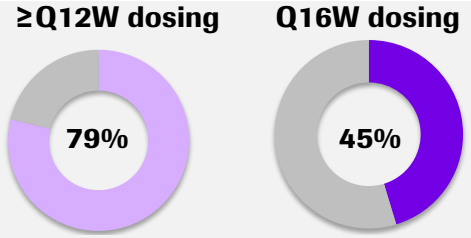
	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (n = 326)
Patients with any APTC[a] events, n (%)	3 (0.9%)	3 (0.9%)	4 (1.2%)	3 (0.9%)
Number of patients with events, n (%)				
Death	2 (0.6%)	1 (0.3%)	0	2 (0.6%)
Nonfatal MI	1 (0.3%)	1 (0.3%)	2 (0.6%)	1 (0.3%)
Nonfatal stroke	0	1 (0.3%)	2 (0.6%)	0

Results are presented based on the Safety Evaluable Population. All safety events are investigator-reported. Percentages are based on n in the column headings. For frequency counts by Preferred Term, multiple occurrences of the same AE in an individual are counted only once. Includes AEs with onset up to day 349 (last day of week 48 analysis visit window). [a] APTC events were adjudicated by an external committee.
AE, adverse event; APTC, Anti-Platelet Trialists' Collaboration; MI, myocardial infarction; Q8W, every 8 weeks; Q16W, every 16 weeks.

TENAYA and LUCERNE conclusions

Faricimab demonstrating ≥Q12W dosing intervals in ~80% of patients in the first year

TENAYA and LUCERNE met primary endpoint	**Non-inferiority** in mean change from baseline in BCVA with **faricimab** dosed **up to Q16W** to **aflibercept Q8W** in patients with nAMD at Week 48
nAMD disease control with faricimab	**Durability up to Q16W** at Week 48 with faricimab Meaningful **reductions in CST** with **faricimab up to Q16W** comparable to **aflibercept Q8W** through Week 48
Safety	Faricimab was well tolerated. IOI events were low and on average reported in 2.0% and 1.2% for faricimab and aflibercept arms, respectively
Long-term data	Ongoing Year 2 and planned long-term (+ 2 years) extension studies (AVONELLE-X)



Results were **reproducible** across the TENAYA and LUCERNE studies in more than 1300 patients

Ang-2, angiopoietin 2; BCVA, best-corrected visual acuity; IOI, intraocular inflammation; VEGF-A; vascular endothelial growth factor-A; Q8W, every 8 weeks; Q16W, every 16 weeks.

Welcome
Karl Mahler, Head of Investor Relations and Group Planning

Ophthalmology Strategy Update
Atul Dandekar, Vice President and Global Franchise Head, Ophthalmology

Ophthalmology Pipeline Update
Chris Brittain, Vice President and Global Head of Ophthalmology Product Development

Faricimab in DME and nAMD: – Phase III results
Nancy Holekamp, M.D., Retina Specialist and Faricimab Clinical Investigator

Q&A
Karl Mahler, Head of Investor Relations and Group Planning

Doing now what patients need next