ASRS Highlights 2020

Roche Analyst Webcast

South San Francisco, 27 July 2020

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2 legislative and regulatory developments and economic conditions;
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4 fluctuations in currency exchange rates and general financial market conditions;
5 uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products;
6 increased government pricing pressures;
7 interruptions in production;
8 loss of or inability to obtain adequate protection for intellectual property rights;
9 litigation;
10 loss of key executives or other employees; and
11 adverse publicity and news coverage.

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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
Atul Dandekar, Vice President and Global Franchise Head, Ophthalmology

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

PDS: Archway – Phase III topline results
Dante Pieramici, M.D., Retina Specialist and PDS Clinical Investigator

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

Roche significantly advancing patient care

Pivotal trials on track despite difficult environment

34 *Breakthrough Therapy Designations (BTD) since 2013*

Year	Molecule	Indication
2020	mosunetuzumab	3L+ FL
	Tecentriq	unresectable or metastatic ASPS
	Esbriet	uILD
2019	Cotellic	Histiocytic neoplasms
	Gazyva	Lupus nephritis
	PRM-151	IPF
	Venclexta + Gazyva	1L unfit CLL
	Kadcyla	Adjuvant HER2+ BC
2018	SPK-8011	Hemophilia A
	satralizumab	NMOSD
	Xolair	Food allergies
	Tecentriq + Avastin	1L HCC
	Hemlibra	Hemophilia A non-inhibitors
	Rozlytrek	NTRK+ solid tumors
2017	Polivy + BR	R/R DLBCL
	Venclexta + LDAC	1L unfit AML
	Zelboraf	BRAF-mutated ECD
	Rituxan	Pemphigus vulgaris

8 *Breakthrough Device Designations (BDD) since 2018*

Year	Device	Intended use
2020	Elecsys GALAD score	early stage HCC
2018	Elecsys β-Amyloid + p-Tau Cerebro Spinal Fluid assays	AD: PET concordance AD: Progression
	sFlt + PLGF	Preeclampsia: rule-out within 1w
	FACT CDx (liquid biopsy assay)	70 oncogenes + MSI + bTMB
	cobas EBV	EBV in transplant patients
	cobas BKV	BKV in transplant patients
	CoaguChek Direct-X	Patients on Factor Xa

Pivotal trial recruitment finished in HY1 2020

ipatasertib	1L TNBC (Ph III: IPATunity130)
risdiplam	SMA type 1/2/3 (Ph II: JEWELFISH)
gantenerumab	Alzheimer's disease (Ph III: GRADUATE 1 & 2)
tominersen	Huntington's disease (Ph III: Generation HD1)

New pivotal study starts in HY1 2020

tiragolumab	mNSCLC (Ph III: SKYSCRAPER-01), ES-SCLC (Ph III: SKYSCRAPER-02) Cervical cancer (Ph II: SKYSCRAPER-04)
PI3Ki	HR+ mBC (Ph III: INAVO120)
Venclexta+Gazyva	1L fit CLL (Ph III: CristaLLo)
Actemra	severe COVID-19 pneumonia (Ph III: COVACTA, REMDACTA, EMPACTA)

Oncology Neuroscience Immunology

Key Diagnostics news flow in HY1 2020

Instruments/Devices	Launch of cobas® prime pre-analytical system
Tests/Assays	Launch of SARS-CoV-2 antibody & PCR tests
Software	Launch of v-TAC digital algorithm for blood-gas monitoring

Major pipeline advances and upcoming launches in HY2 2020

Pharma

3 Upcoming NME launches

- **risdiplam** in SMA
- **Enspryng (satralizumab)** in NMOSD
- **pralsetinib*** in RET+ NSCLC; Thyroid cancer

7 Upcoming pivotal trial starts

- **SERDi** (Ph III 1L HR+ mBC)
- **glofitamab** (Ph III r/r DLBCL)
- **PRM-151/pentraxin-2** (Ph III IPF)
- **Gazyva** (Ph III Lupus Nephritis)
- **crovalimab** (Ph III PNH in patients switching from a C5 inhibitor; Ph III PNH in C5 inhibitor-naive patients)
- **SRP-9001** (Ph III DMD; run by Sarepta)

Diagnostics

4 Upcoming key launches

- **cobas®** SARS-CoV-2 & Influenza A/B for use on the **cobas®** Liat® System
- **cobas®** SARS-CoV-2 & Influenza A/B for use on the **cobas®** 6800/8800 Systems
- SARS-CoV-2 Rapid Antibody test
- Elecsys® Anti-SARS-CoV-2 S

* subject to the expiration or termination of the waiting period under the HSR Act

Replace and extend the business: Further milestones achieved

Replace/extend existing businesses		Entering new franchises
MabThera/Rituxan	Gazyva, Venclexta, Polivy, mosunetuzumab, glofitamab	**Oncology:** Tecentriq (mUC, TNBC, SCLC, HCC, mM), ipatasertib (mCRPC), SERD (HR+ BC)
Herceptin	Perjeta, Kadcyla, Phesgo	**MS:** Ocrevus
Avastin	Tecentriq, Alecensa, Rozlytrek, tiragolumab	**Hemophilia A:** Hemlibra
Lucentis	Port delivery system (PDS) faricimab	**CNS:** Enspryng (NMOSD), risdiplam (SMA), tominersen (Huntington), gantenerumab (AD), SRP-9001 (DMD)
Tamiflu	Xofluza	**Immunology:** etrolizumab (UC, CD), Gazyva (lupus nephritis)

Achievements Q2 2020

Entering new franchises

Tecentriq: US approval in 1L HCC (with Avastin)

ipatasertib: Positive Ph III (IPATential150) results in patients with PTEN loss tumors in mCRPC

Enspryng: First approvals in Canada, Japan, CH in NMOSD

risdiplam: FIREFISH (SMA) part 2 results in Type 1 patients presented at AAN

SPARK: 2 to 3.3 year follow up efficacy/safety data for SPK-8011 hem A gene therapy presented at ISTH

Replace/extend existing businesses

Phesgo: US approval for P+H FDC-SC

tiragolumab: Randomized Ph II data presented at ASCO; Ph III trials in 1L NSCLC and 1L SCLC initiated

SERD: Clinical data showing excellent efficacy /safety profile presented at ASCO

glofitamab: Ph Ib data presented at EHA; Ph III in 2L+ DLBCL initiated

mosunetuzumab: BTD designation in 3L+ FL awarded

PDS: Positive Ph III (ARCHWAY) results in nAMD

mUC=metastatic urothelial carcinoma; TNBC=triple negative breast cancer; SCLC=small cell lung cancer; HCC=hepatocellular carcinoma; mM=metastatic melanoma; mCRPC=metastatic castration resistant prostate cancer; BC=breast cancer; NMOSD=neuromyelitis optica spectrum disorder; SMA=spinal muscular atrophy; AD=Alzheimer's disease; DMD=duchenne muscular dystrophy; UC=ulcerative colitis; CD=Crohn's disease; NSCLC=non-small cell lung cancer; FDC=fixed dose combination; NSCLC=non-small cell lung cancer; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; nAMD=neovascular age-related macular degeneration

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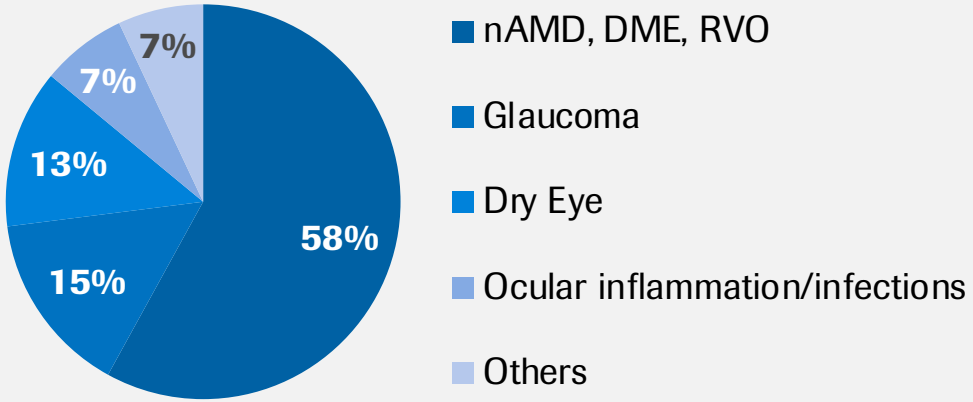
Retina is the fastest growing segment of the Ophthalmology market

Ophthalmology market
Retinal vascular diseases remain leading causes of vision loss

Total Market (2019) – $21.5 Billion

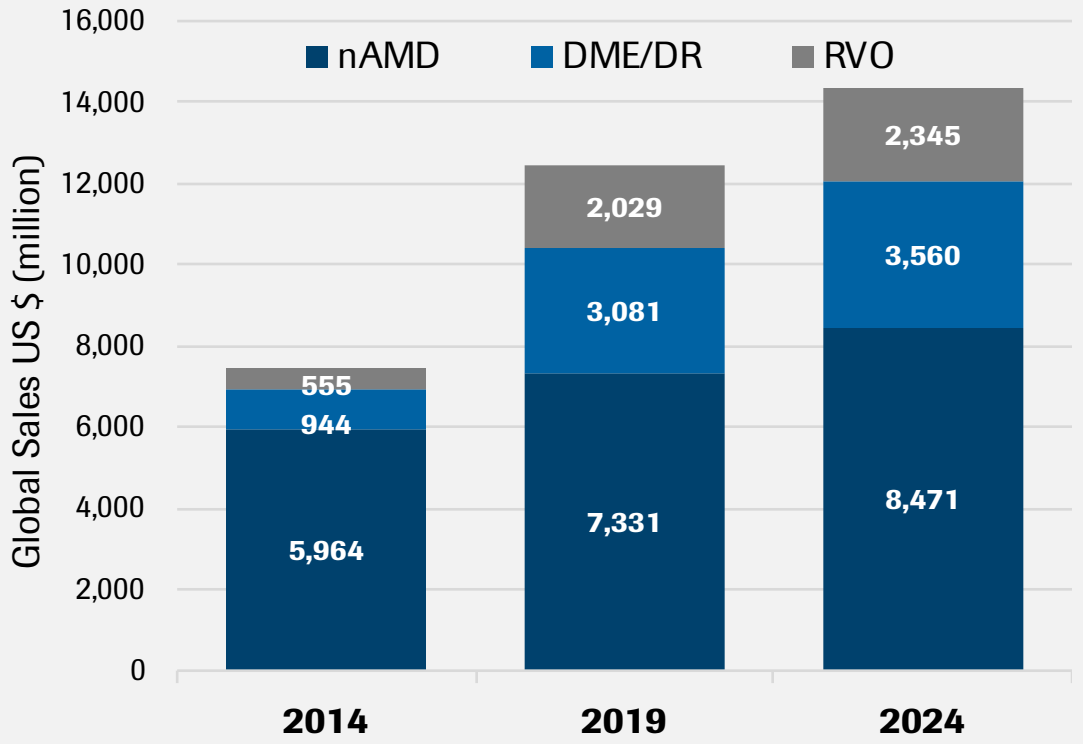


Leading causes of vision loss in US, Europe:

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

Source: Evaluate Pharma (April 2019)

Global Retina Landscape:
Market growth driven by aging population and product innovation

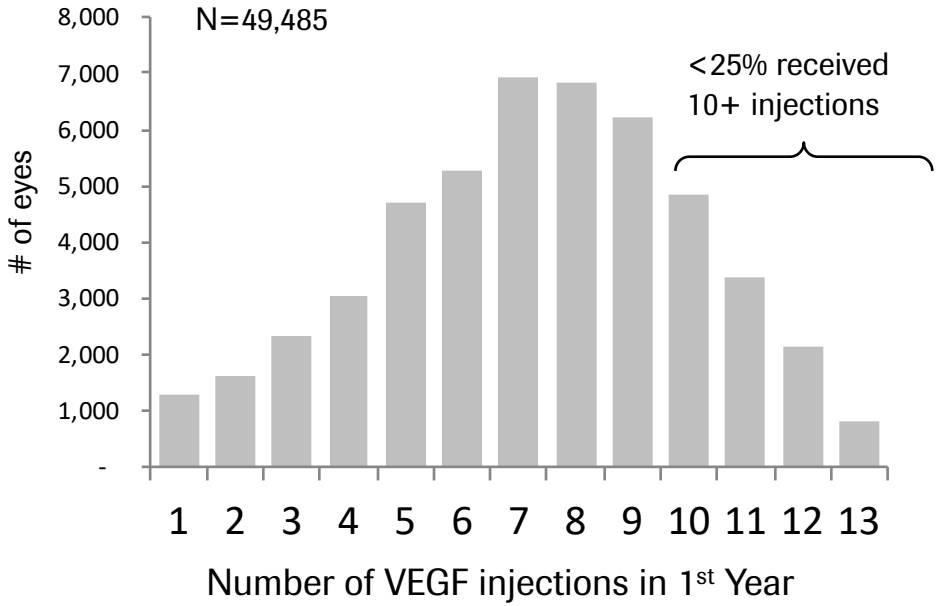


Source: Evaluate Pharma for historic sales and branded forecasts, Decision Resources for biosimilar forecasts (6/2020)

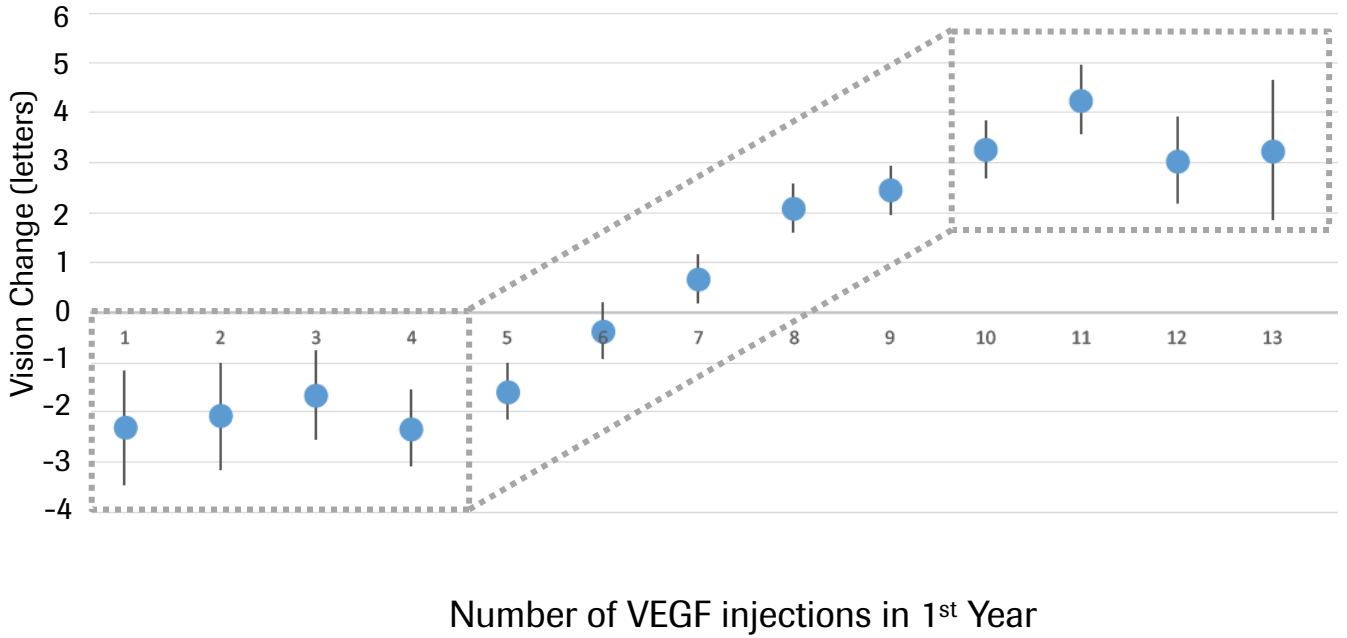
DME: diabetic macular edema, DR: diabetic retinopathy, nAMD: neovascular age-related macular degeneration, RVO: retinal vein occlusion

Real world outcomes with anti-VEGF intravitreal injections have significant room for improvement

nAMD treatment frequency in real world[1]

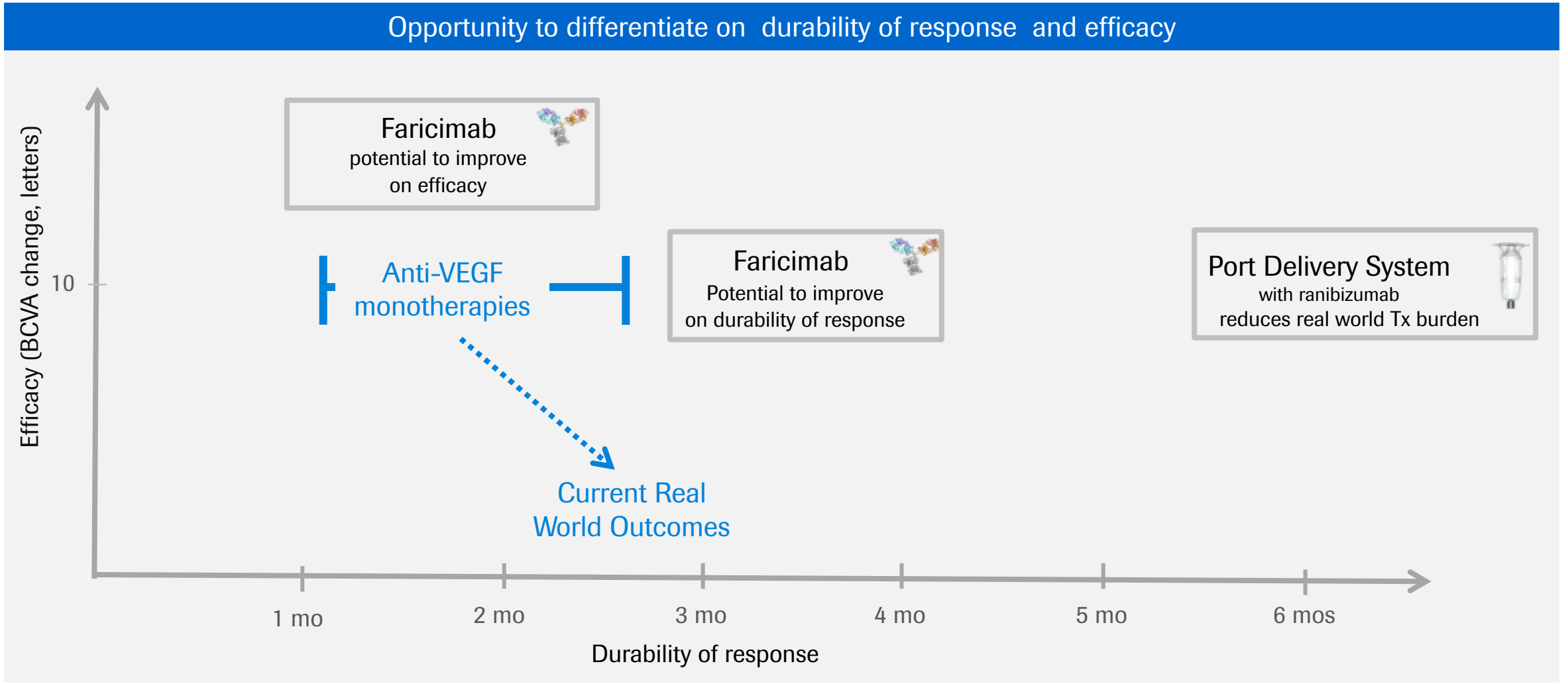


Number of aVEGF injections correlates with vision improvement[1]



[1] Courtesy of T. Brogan/Vestrum Health, presented by Dr. D. Williams at ASRS 2018; Ophthalmology Retina; nAMD=neovascular age-related macular degeneration

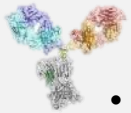
PDS and Faricimab potentially address key unmet needs



For illustrative purposes only

Roche Ophthalmology strategy has four strategic levers

1 Improved Efficacy via novel MOAs



- anti-VEGF/Ang-2
- New MOAs utilizing Duta-Fab platform

2 Long-Acting Delivery technologies

- Port Delivery System Platform
- Injectable LADs
- Gene therapy bio-factory approach

3 Internal innovation complemented by external partnering

- pRED
- gRED

Spark THERAPEUTICS

4DMT

IONIS™

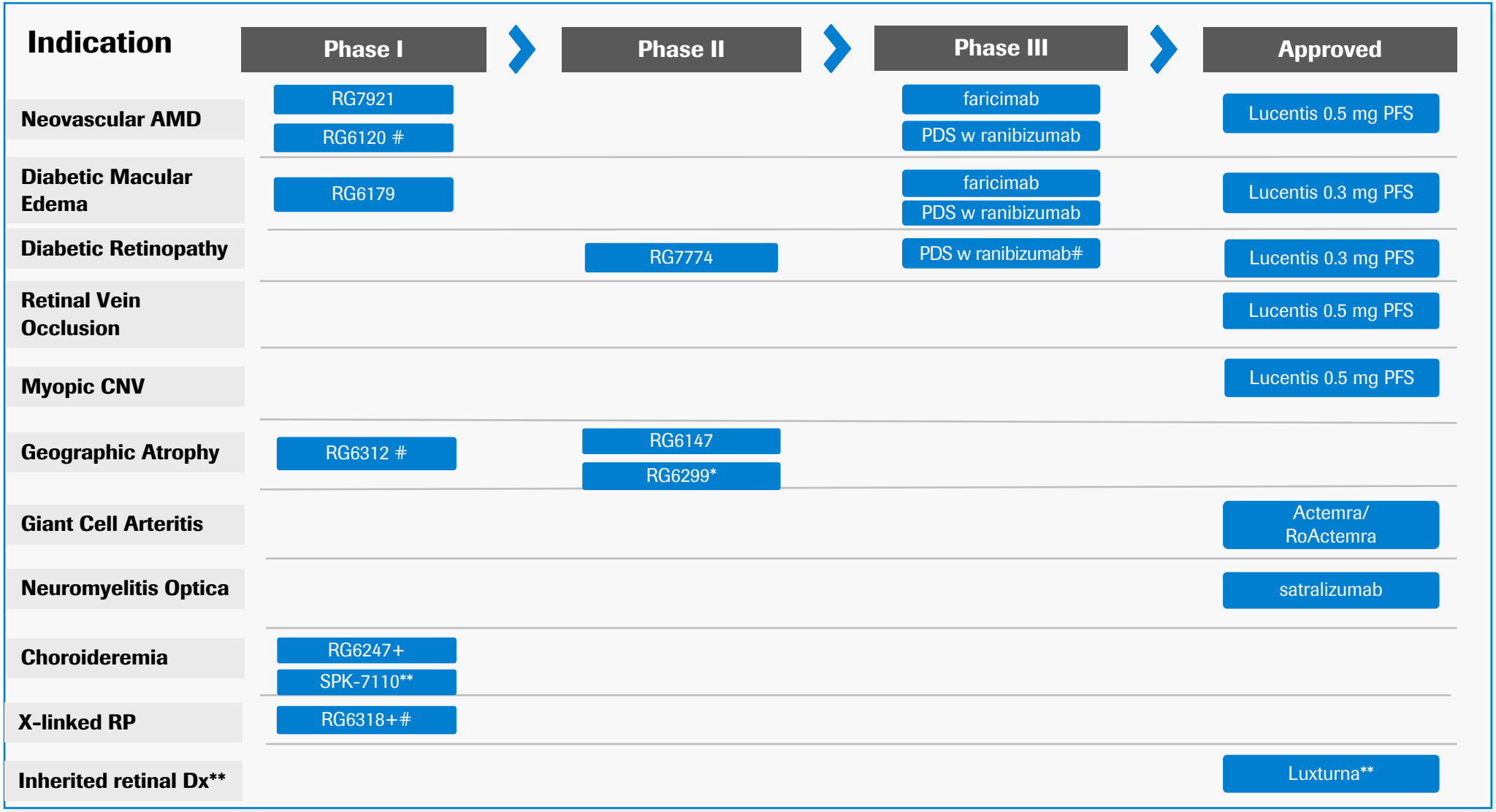
4 Personalized Healthcare

- Vision loss prevention and treatment algorithms leveraging AI and machine learning
- Remote vision monitoring

MOA=mechanism of action; LAD= Long-acting delivery; AI=artificial intelligence

Roche Ophthalmology pipeline

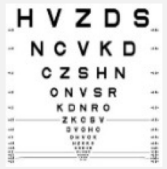
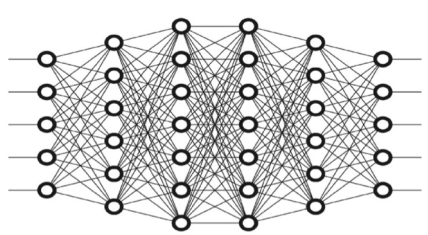
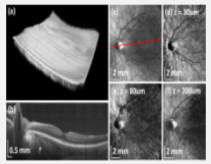
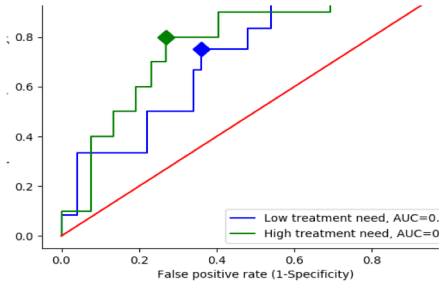
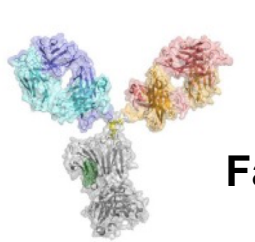
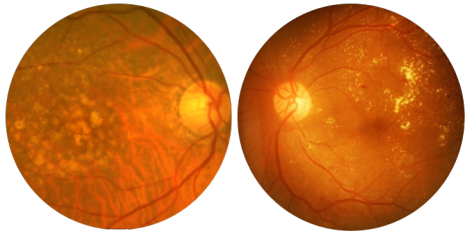
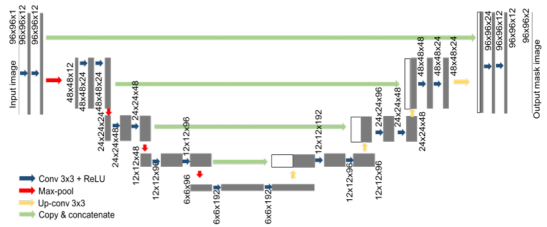
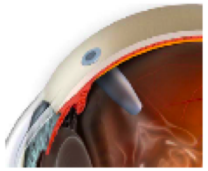
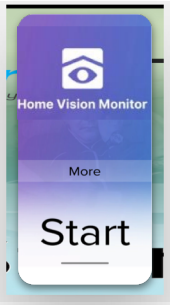
Focus on retinal disorders: nAMD, DME/DR and GA



Status as of July 2020. PFS, Prefilled Syringe; Lucentis PFS is marketed by Novartis outside the U.S.; RP= retinitis pigmentosa; * Study conducted by Ionis, Roche has option to in-license; + Study conducted by 4DMT, Roche has option to in-license; #Studies planned to start in 2020 subject to the COVID situation; **with Spark Therapeutics, approved for patients with biallelic *RPE65* mutation-associated retinal dystrophy

Preservation of vision with Personalized Healthcare (PHC)

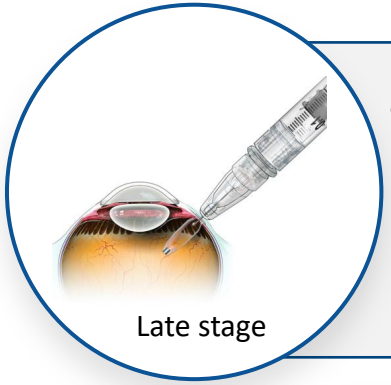
Remote monitoring & advanced analytics to help treat vision loss early

Meaningful Data at Scale	Advanced Analytics	Insights on Key Drivers of Unmet Need	Impact on Personalized Treatments
 Clinical		 Lucentis	Treat intermediate disease early…
 Imaging		 Faricimab	
INSIGHT Health Data Research Hub Real World Data		 PDS	…to avoid irreversible vision loss
 Home Vision Monitoring			

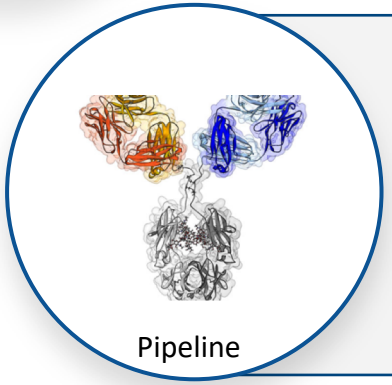
Ultimate Goal to TREAT VISION LOSS and PRESERVE VISION

Roche Ophthalmology strategy execution is on track

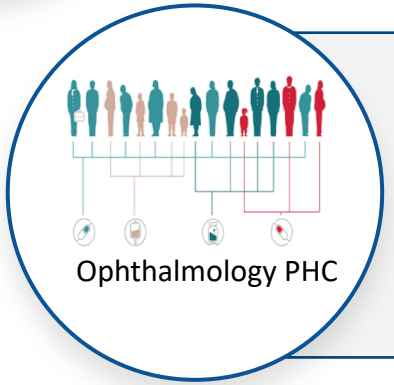
Pivotal readouts in 2020



- Faricimab DME and nAMD data anticipated Dec 2020 / Jan 2021
- PDS nAMD Ph3 study met primary endpoint – Non-inferior and equivalent to monthly Lucentis
- PDS DME study underway, DR study planned



- 3 NMEs in Ph2 clinical development
- 7 Ph1 programs underway including gene therapies
- Positive PDS Ph3 has enabled acceleration of Dutafab platform and early pipeline
- 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, Digital Vision tools & Algorithm Validation
- Home Vision Monitoring pilot with Moorfields to support patients during COVID-19

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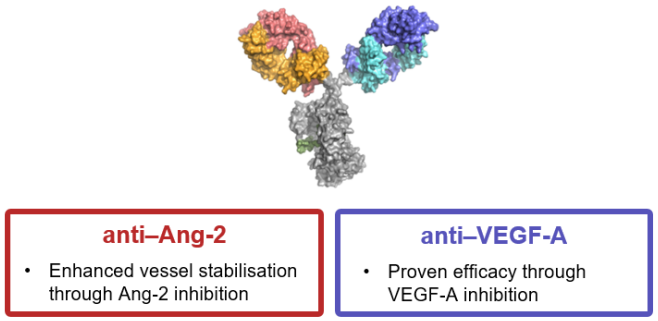
Faricimab in nAMD

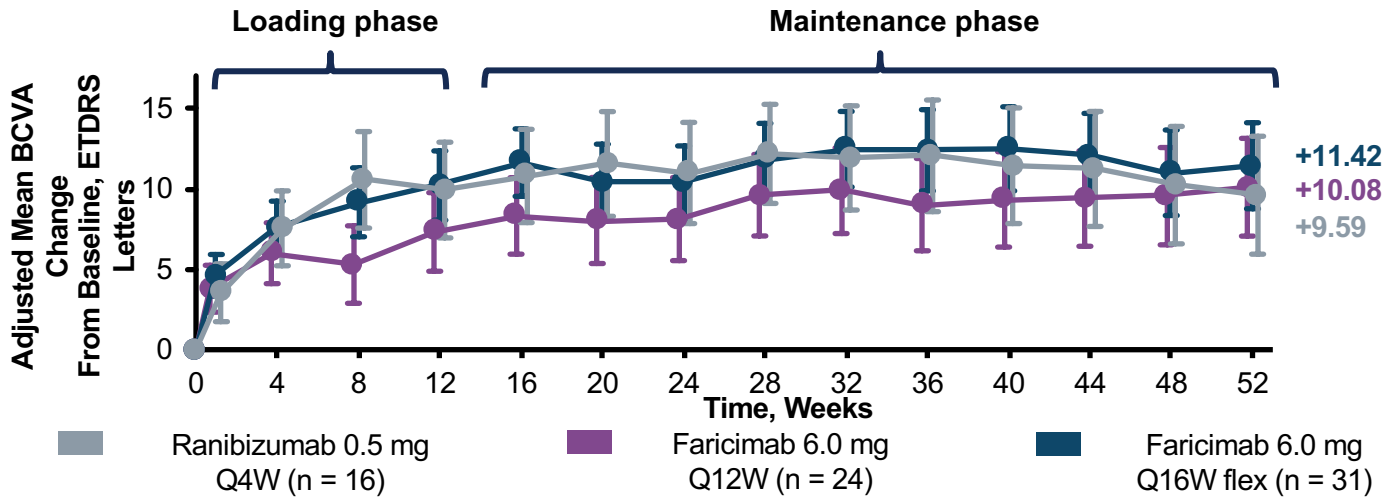
Potential to stabilize retinal vasculature and improve treatment durability

Anti-VEGF/Ang2 Bispecific mAb



- First bispecific antibody in ophthalmology binding simultaneously to VEGF and Angiopoietin2 (Ang2)
- Ang2 inhibition could improve vascular stability and reduce retinal inflammation

Phase II (STAIRWAY) results in nAMD



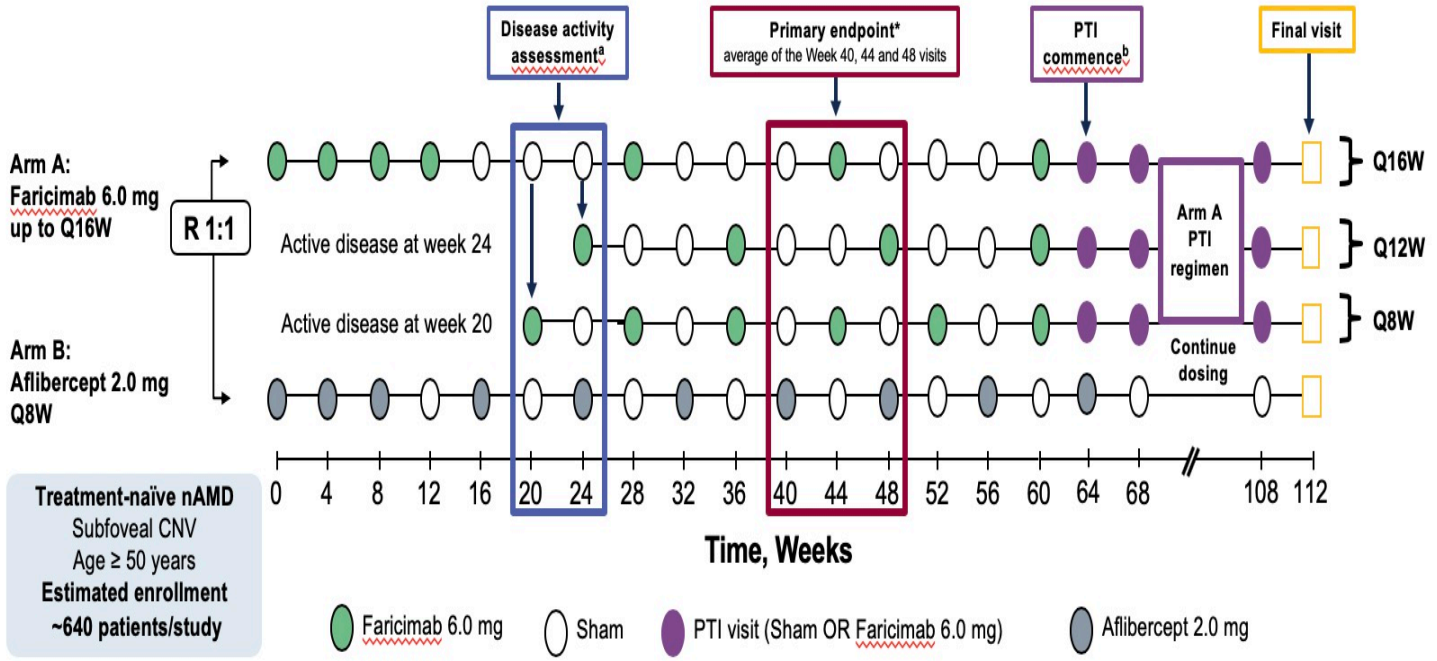
- BCVA Gains With Faricimab Q16W Flex and Q12W Comparable With Ranibizumab Q4W
- 12 Weeks After Last Faricimab Loading Dose, 65% of Patients Had No Disease Activity, and Could Potentially Benefit From Q16W Dosing
- Phase III nAMD data expected Jan 2021

Sahni et al, Ophthalmology 2019;126:1155-1170; DME=diabetic macular edema; nAMD=neovascular age-related macular degeneration; BCVA= best-corrected visual acuity; *Linear model adjusted for baseline BCVA, previous macular laser treatment status, BCVA category (≥ 64 letters vs ≤ 63 letters)

Phase 3 faricimab development program in nAMD
Robust global studies to assess efficacy, safety and durability

TENAYA and LUCERNE

- 2 randomized, global, multicenter, phase 3 trials
- N = 640 per study
- **Primary Study Objective:** Mean BCVA change from baseline at Week 48 as an average of Weeks 40, 44 and 48
- **Key Secondary Objective:** Proportion of patients on a Q8W, Q12W, or Q16W treatment interval
- Personalized treatment arm to assess durability of response



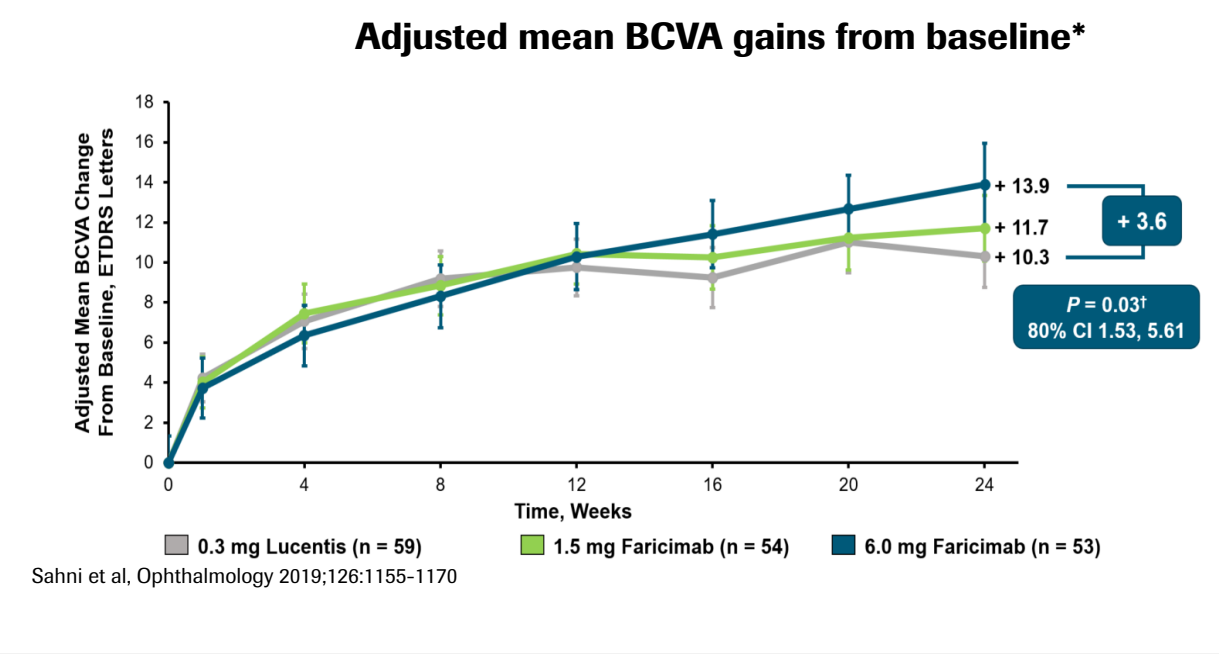
*Change from baseline in BCVA, as measured on the ETDRS chart at a starting distance of 4 meters, based on an average of the Week 40, 44, and 48 visits. [a] Protocol-defined assessment of disease activity at week 20 and 24. Patients with anatomic or functional signs of disease activity at these timepoints will receive Q8W or Q12W, respectively. [b] PTI: IxRS-guided flexible dosing in faricimab arms starting at Week 60. From Week 60 onward, patients in Arm A will be treated according to a PTI dosing regimen between Q8W and Q16W. ClinicalTrials.gov. TENAYA study information. https://clinicaltrials.gov/ct2/show/NCT03823287 [last accessed Feb 2020]; ClinicalTrials.gov. LUCERNE study information. https://clinicaltrials.gov/ct2/show/NCT03823300 [last accessed Feb 2020].

BCVA, best-corrected visual acuity; CNV, choroidal neovascularization; 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.

Faricimab in DME

Potential to improve efficacy and durability

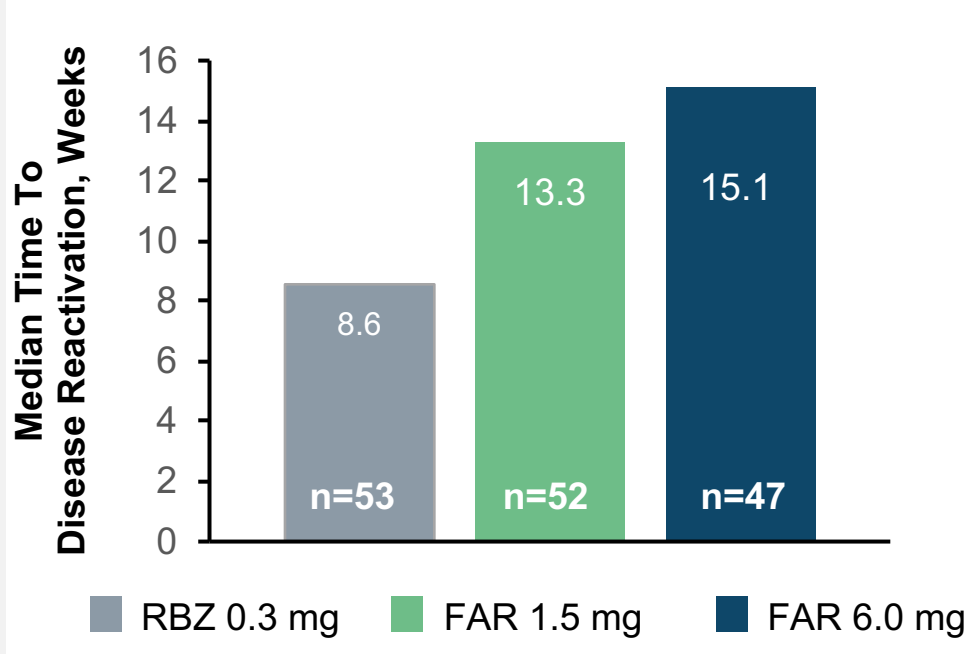
Phase II (BOULEVARD) results in DME: Efficacy



Sahni et al, Ophthalmology 2019;126:1155-1170

- Robust BCVA gains with a mean of +13.9 letters gained from baseline
- In addition, a statistically significant gain of +3.6 letters over Lucentis
- Phase III DME data expected Dec 2020

Phase II (BOULEVARD) in DME: Durability



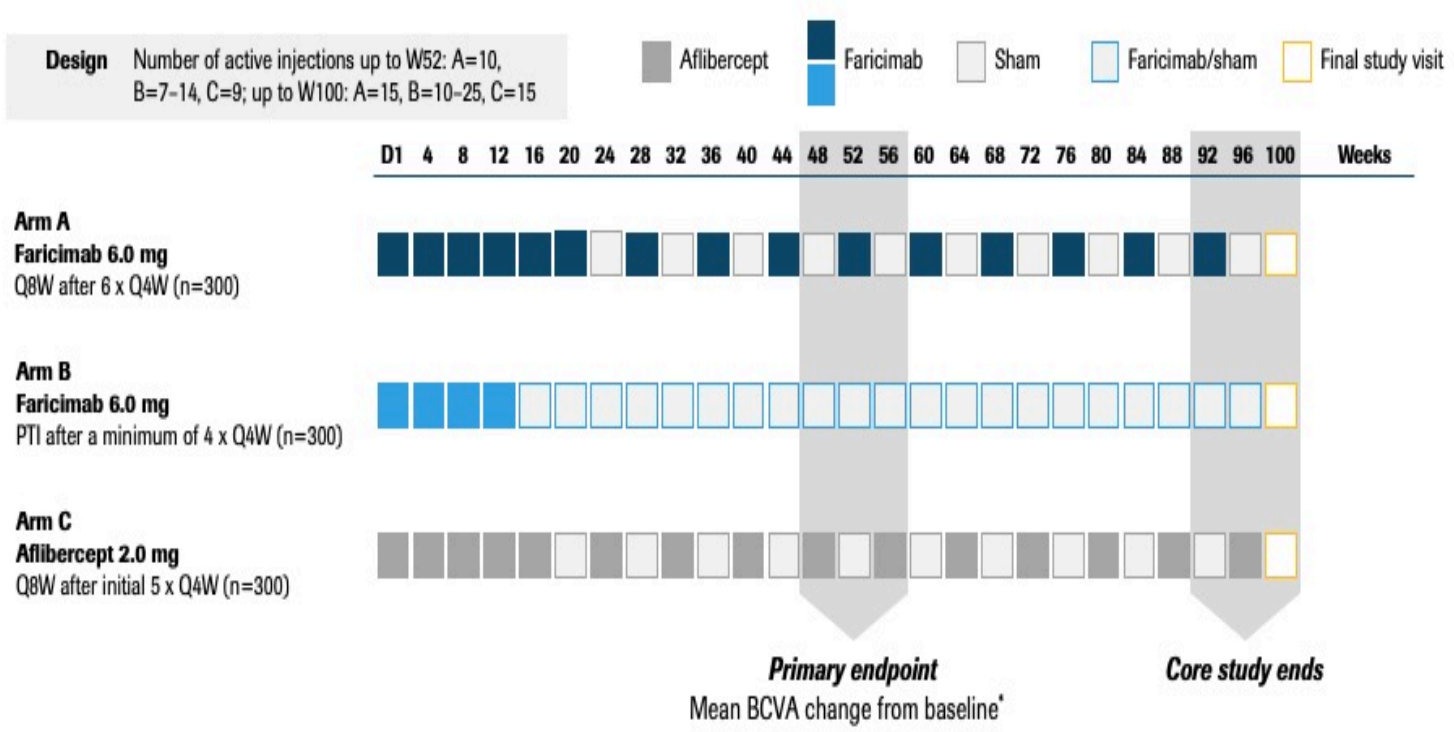
- Durability shown with median time to disease reactivation 15.1 weeks for faricimab vs 8.6 weeks for Lucentis after treatment cessation
- RVO program initiating Q2 2021

Sahni et al, Ophthalmology 2019;126:1155-1170; DME=diabetic macular edema; nAMD=neovascular age-related macular degeneration; BCVA= best-corrected visual acuity; *Linear model adjusted for baseline BCVA, previous macular laser treatment status, BCVA category (≥ 64 letters vs ≤ 63 letters)

Phase 3 faricimab development program in DME
Robust global studies to assess efficacy, safety and durability

YOSEMITE and RHINE

- N = 1800 patients[a] with center-involving DME
- Type 1 or 2 diabetes mellitus with HbA1c ≤ 10%
- Treatment-naïve and previously anti-VEGF–treated patients
- BCVA 20/40–20/320 (73–25 ETDRS letters)
- **Primary study objective:** Mean BCVA change from baseline at 1 year[b]
- **Key secondary endpoints:**
  - Proportion of patients with a ≥2 or ≥3-step improvement in diabetic retinopathy severity
  - Proportion of patients in the PTI arm on a Q12W or Q16W treatment interval

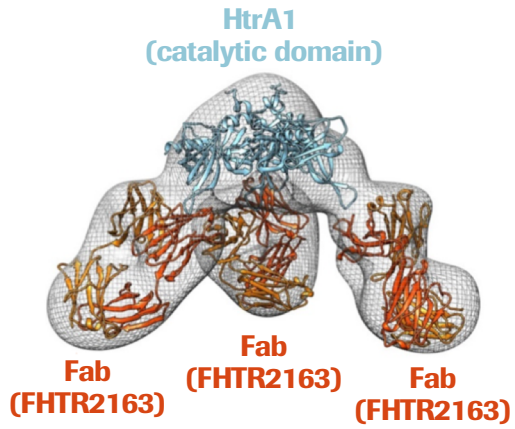


[a] Patients will be randomized 1:1:1 into 3 arms. [b] BCVA at 1 year will be measured on the ETDRS chart at a starting distance of 4 meters. Optical coherence tomography image of baseline DME from BOULEVARD clinical trial (NCT02699450). YOSEMITE clinical trial (NCT03622580); RHINE clinical trial (NCT03622593). BCVA, best-corrected visual acuity; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; HbA1c, glycated hemoglobin; Q8W, every 8 weeks; R, randomized; VEGF, vascular endothelial growth factor. PTI=Personalized Treatment Interval

Continuing to Study Treatments for GA Secondary to AMD

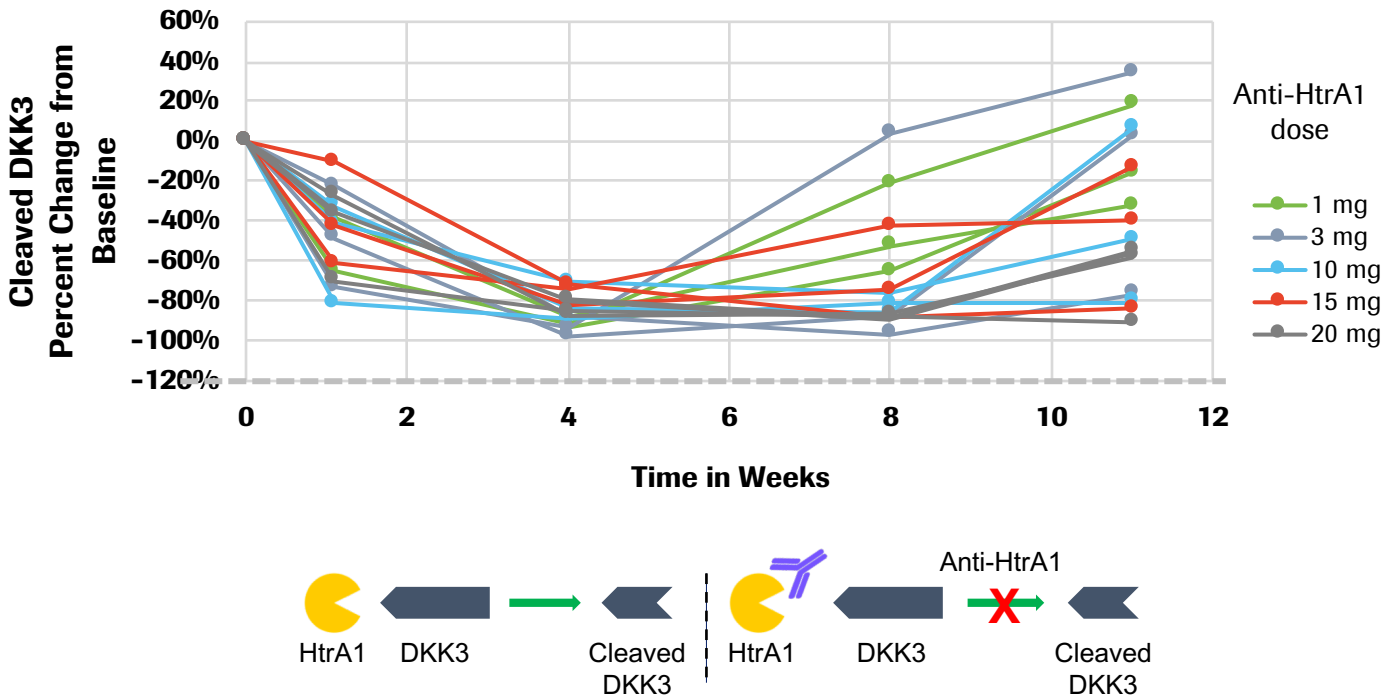
Phase 2 anti-HtrA1 study currently enrolling

Anti High Temperature Requirement A1 (HtrA1)



- ARMS2-HtrA1 is the top genetic locus for AMD risk
- HtrA1, a serine protease, breaks down extracellular matrix protein, resulting in retinal atrophy
- Well tolerated in Phase 1 GA study supporting Q4W and Q8W dosing in Phase 2

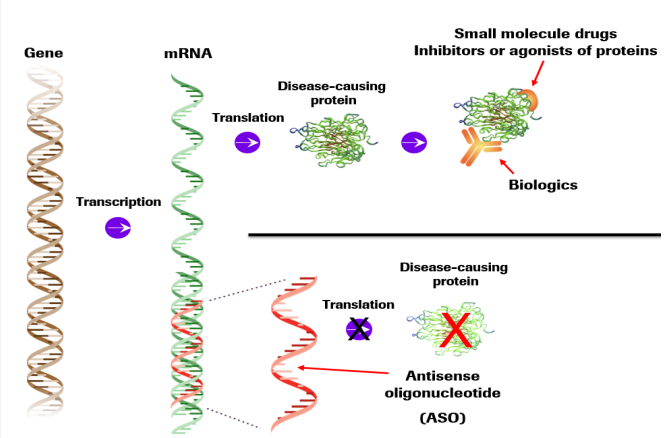
RG6147 - Anti-HtrA1 Fab: Phase 1 results in healthy volunteers



AH50, complement alternative pathway; AMD, age-related macular degeneration; Bb, carboxyl-terminal of factor B after cleavage; CH50, total haemolytic complement; FBL, factor B levels; GA, geographic atrophy; Q4W, every 4 weeks; RPE, retinal pigment epithelium; SEM, standard error of the mean

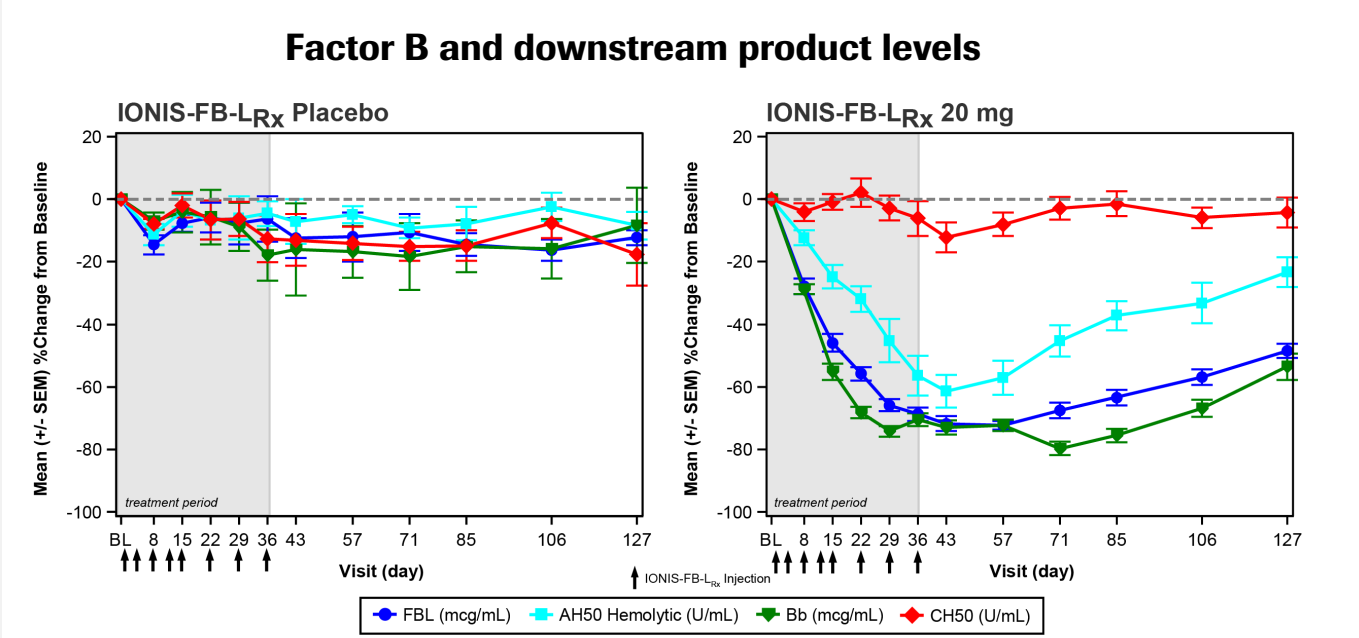
Continuing to Study Treatments for GA Secondary to AMD
Partnering to evaluate novel treatments

IONIS partnership IONIS-FB-LRX



- Antisense oligonucleotide inhibiting complement factor B in the liver (source of complement factor B)
- Modulates complement in RPE, Bruch's membrane, and choriocapillaris
- Q4W SC injection to treat both eyes

IONIS Phase 1 results in healthy volunteers

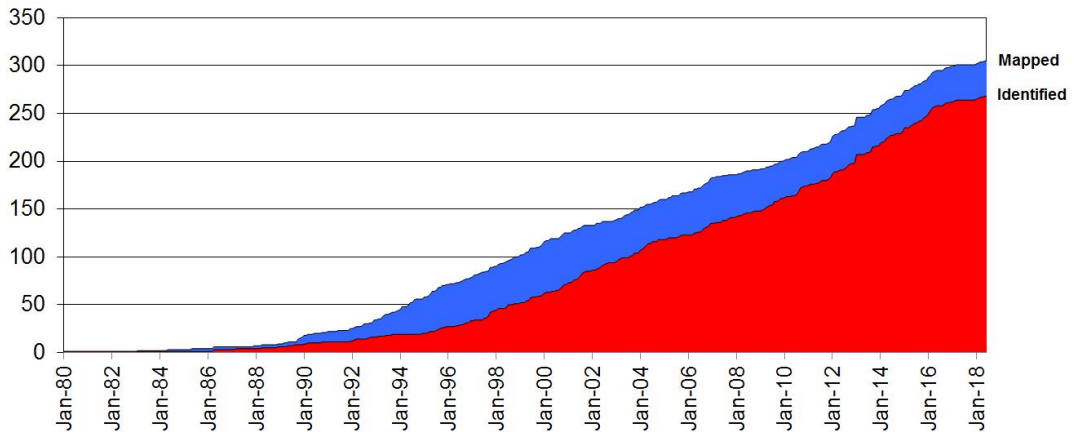


AH50, complement alternative pathway; AMD, age-related macular degeneration; Bb, carboxyl-terminal of factor B after cleavage; CH50, total haemolytic complement; FBL, factor B levels; GA, geographic atrophy; Q4W, every 4 weeks; RPE, retinal pigment epithelium; SEM, standard error of the mean

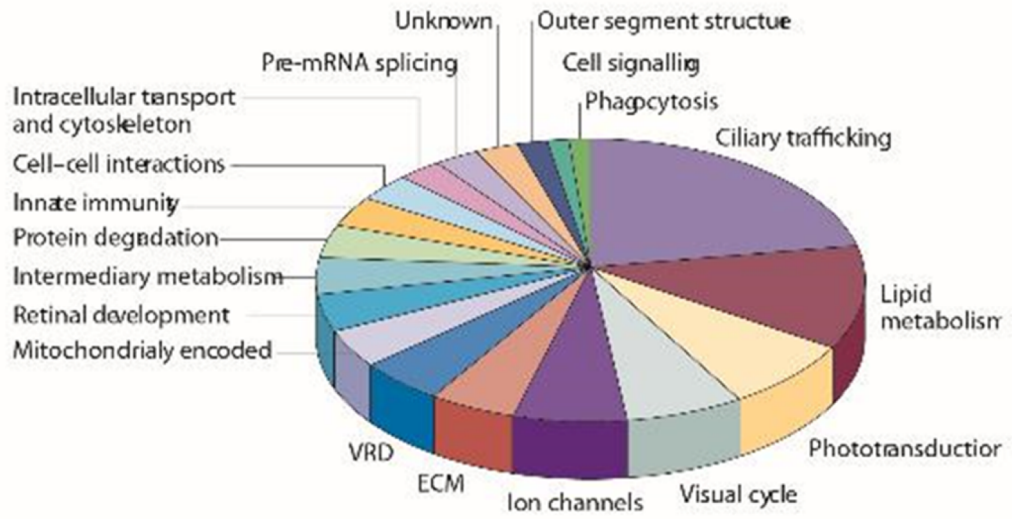
Potential for gene therapy in ophthalmology

To date more than 270 genes causing retinal disease have been identified

Identified disease genes 1980 – 2018



Genes causing retinal degeneration



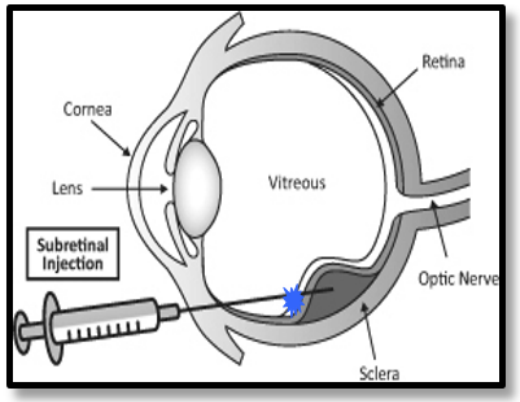
- To date, there over 270 identified genes that cause retinal disease
- Over 95% of the identified gene mutations initially result in death of rod photoreceptors

Source: http://webvision.med.utah.edu

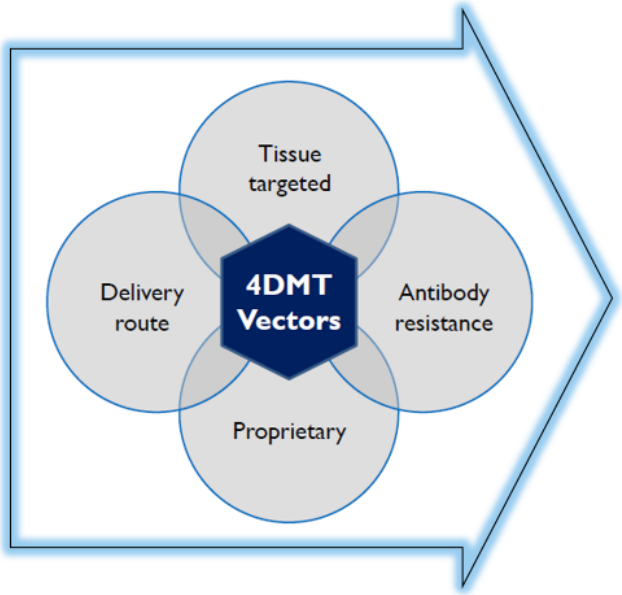
Next generation Retinal Gene Therapy

Safe procedure for transducing across the entire retina

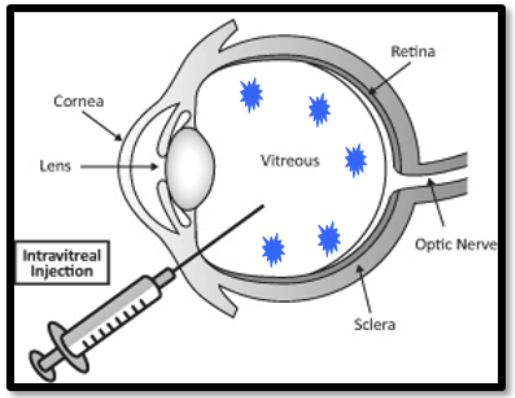
First-Gen Gene Therapy



- Subretinal injection
- Challenging procedure
- Complications include retinal detachment and scarring
- Limited area of transduction



Next-Gen Gene Therapy



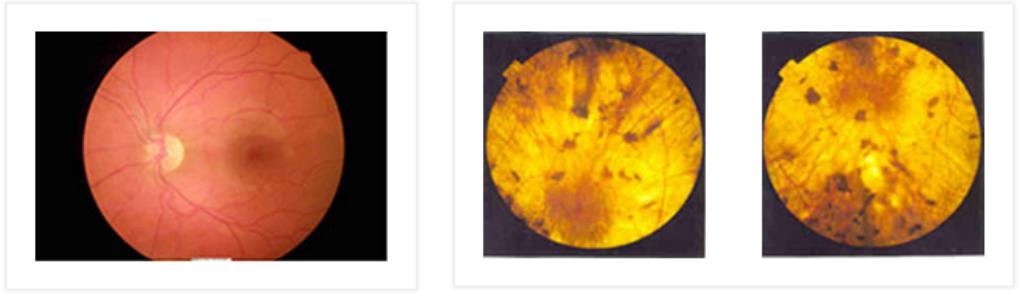
- Intravitreal injection is standard for retinal specialists
- **Safe procedure**
- **Transduction across entire retina**
- **Potential to treat early stage patients**

In collaboration with 4D Molecular Therapeutics

Gene therapy (4D-110) in partnership with 4DMT

Choroideremia - A rare inherited disorder leading to blindness

Retina damage by Choroideremia



Healthy Retina

Retina damaged by Choroideremia

Disease progression

Vision at birth

Vision at age 25

Technology

- 4DMT technology optimized AAV vectors for retinal transfection after intravitreal injection

Disease – Choroideremia

- X-linked recessive disease (incidence rate: 1:50,000 males)
- Loss of function mutation in *CHM* gene which encodes REP1 involved in lipid modification of Rab GTPases
- Cell death & gradual deterioration of retinal pigment epithelium, photoreceptors and choroid leads to loss of peripheral vison then central vision

Clinical development 4D-110

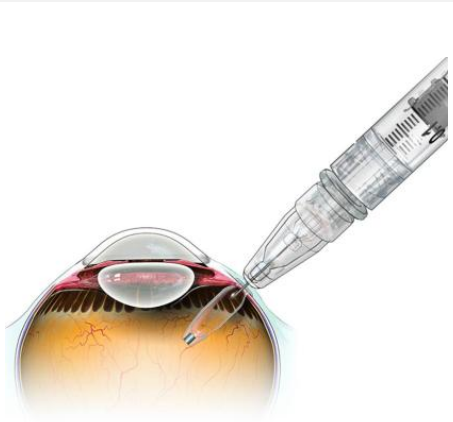
- Ph1 study to be initiated in 2020
- Additional monogenetic diseases targeted

Source: Choroideremia Research Foundation; In collaboration with 4D Molecular Therapeutics (4DMT)

Port Delivery System (PDS) with ranibizumab

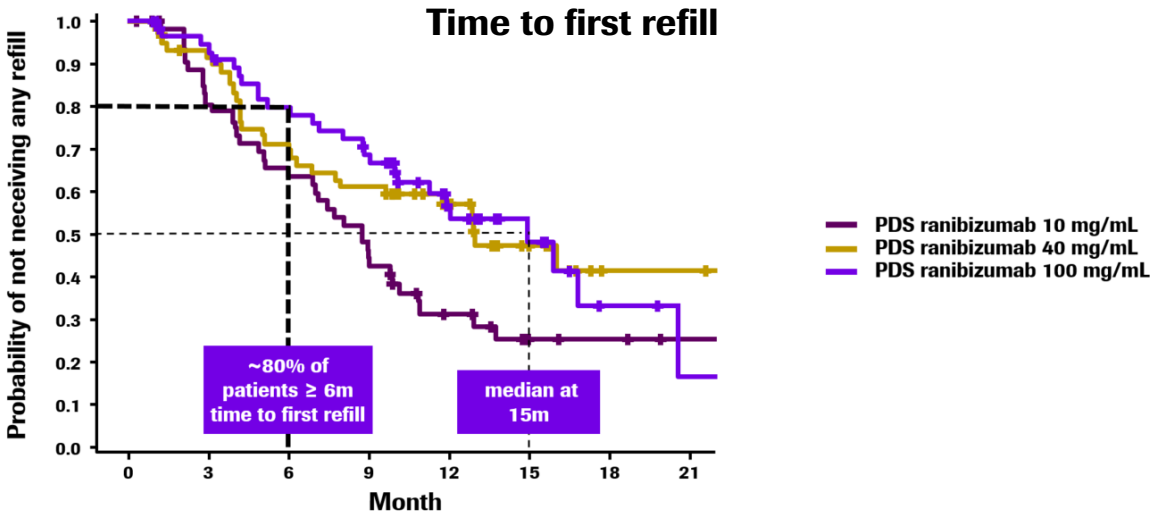
Reduces treatment burden, addresses key unmet need in nAMD

Port Delivery System (PDS)



- Refillable intraocular implant using proprietary needle assembly
- In-office refills
- Customized formulation of ranibizumab

Phase II (LADDER) results in nAMD:



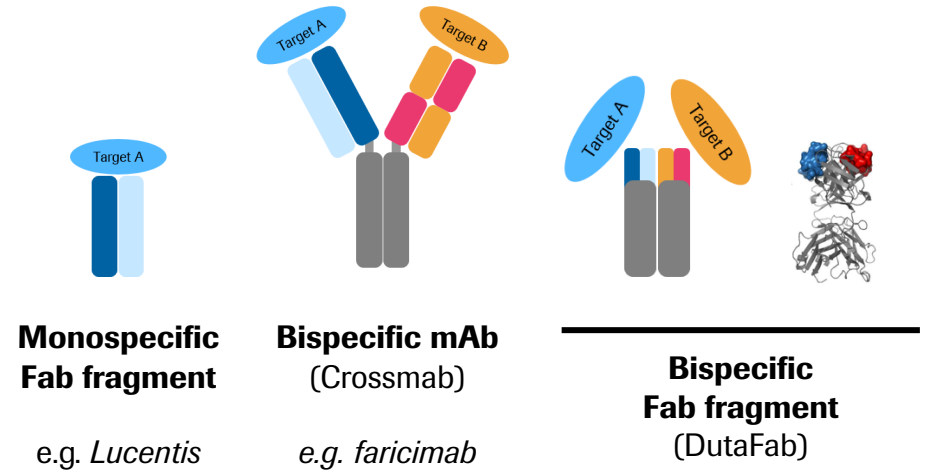
- Median Time to First Refill at 15months, 80% patients ≥ 6m time to first refill
- Ph III (Archway) in nAMD at fixed Q6M dosing presented at ASRS 2020
- Ex-US rights to PDS with ranibizumab acquired from Novartis
- New indications, new MOAs in PDS planned to leverage platform technology
- Phase III (Pagoda) in DME is currently on-going

Campochiaro, Peter A. et al. Ophthalmology, Volume 126, Issue 8, 1141–1154; nAMD=neovascular age-related macular degeneration; Q6M=once every six months dosing; MOA=mechanism of action

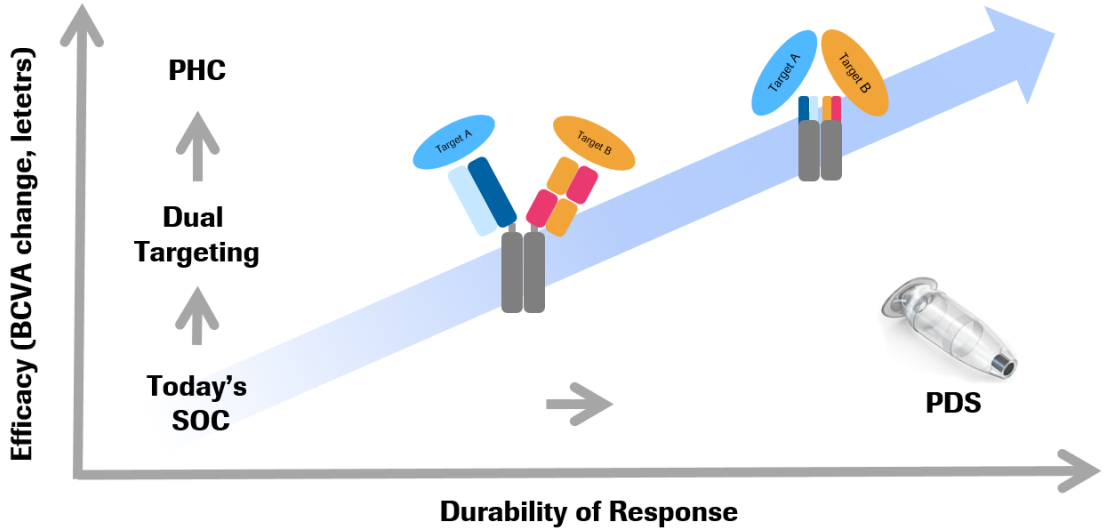
Port Delivery System with DutaFabs

Next generation bispecifics designed for increased efficacy & durability

New bispecific format (DutaFabs)



Further improving the standard of care

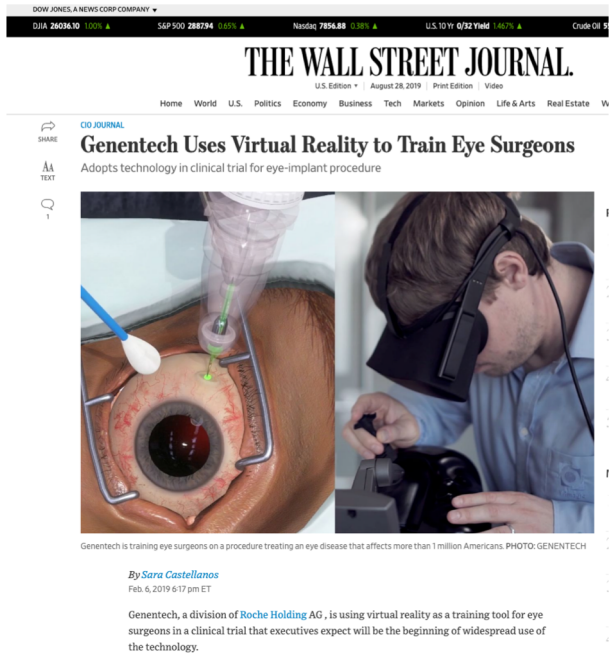


- DutaFabs are a noval bispecific Fab format significantly smaller than bispecific antibodies
- DutaFabs are compatible with the Port Delivery System enabling increased durability beyond Q6M
- 3 DutaFabs are in pre-clinical development targeting different MOAs

SOC=standard of care; PHC=personalized health care; Q6M=every six months dosing; MOA=mechanism of action; PHC=personalized healthcare

Port Delivery System

Virtual reality training of the surgeons



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1

CIO JOURNAL

Genentech Uses Virtual Reality to Train Eye Surgeons

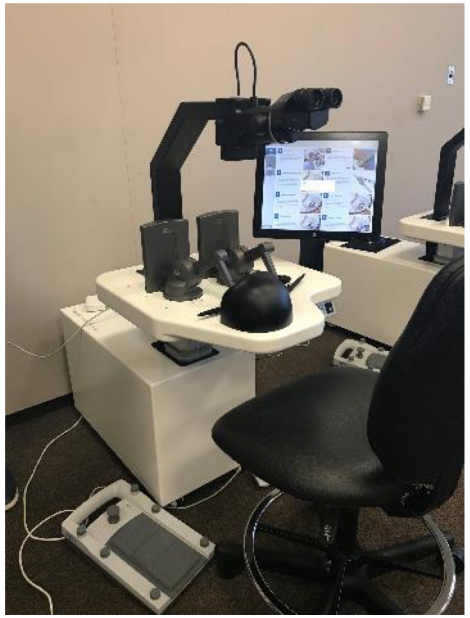
Adopts technology in clinical trial for eye-implant procedure

Genentech is training eye surgeons on a procedure treating an eye disease that affects more than 1 million Americans. PHOTO: GENENTECH

By Sara Castellanos

Feb. 6, 2019 6:17 pm ET

Genentech, a division of Roche Holding AG , is using virtual reality as a training tool for eye surgeons in a clinical trial that executives expect will be the beginning of widespread use of the technology.



- PDS University enables procedural standardization to ensure consistency in outcomes and enhance patient experience
- Virtual reality (VR) technology enables preoperative training of surgeons on PDS procedures (implant insertion and refill)
- Ph III trial (ARCHWAY) represents the first use of VR surgical training in an ophthalmic clinical trial
- Field-based Surgical Device Liaisons (SDLs) support training on site, and facilitate peer to peer discussion and education

PDS=Port Delivery System

Welcome
Karl Mahler, Head of Investor Relations and Group Planning

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

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

PDS: Archway – Phase III topline results
Dante Pieramici, M.D., Retina Specialist and PDS Clinical Investigator

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

Presented by Dante Pieramici, MD

Primary Analysis Results of the Phase 3 Archway Trial of the Port Delivery System With Ranibizumab for Patients With Neovascular AMD

Originally presented at the 38th Annual Scientific Meeting of the American Society of Retina Specialists – July 26, 2020

Peter Campochiaro, MD[1]; Natasha Singh, PharmD[2]; David Kardatzke, PhD[2]; Steven Blotner, PhD[2]; Shienal Patel, BSc[2]; and Giulio Barteselli, MD[2]

[1] The Wilmer Eye Institute, Department of Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, MD;
[2] Genentech, Inc., South San Francisco, CA

Disclosures

Financial Disclosures

- PC: Advisory Board: Advisory Board, Honoraria: Aerpio, Allegro, Applied Genetic Technologies Corporation, Exonate, Genentech, Inc., Merck; Consultant, Honoraria: Alimera, Allergan, Applied Genetic Technologies Corporation, AsclepiX, Astellas, Exonate, Genentech, Inc., Graybug Vision, Merck, Novartis, Perfuse, Wave Life Sciences; Stockholder, Stock: Allegro, Graybug Vision; Investigator, Grants: Aerpio, Alimera, Allegro, Allergan, AsclepiX, Genentech, Inc., Graybug Vision, Oxford Biomedica, Regeneron, Regenxbio, Sanofi Genzyme

- DP: Research Funding: Allegro, Appelis, Gemini, Genentech, , Kodiac, Novartis, Adverum, Regeneron, Regenx Bio, Stealth, Ionis, California Retina Research Foundation, Greybug, Astellas; Consultant: Genentech, Regeneron, Adverum, Gemini, Novartis, Allegro, Kodiac, Regenx, Adverum

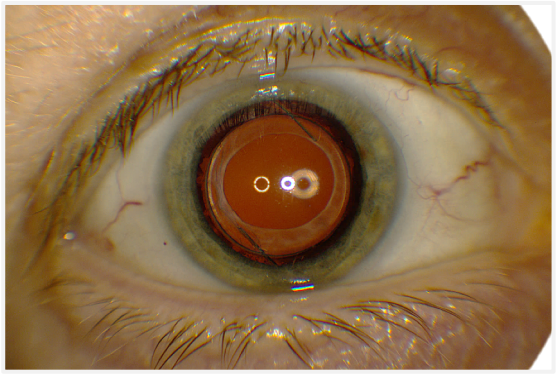
- NS, DK, SB, SP, GB: Employee, Equity: Genentech, Inc.

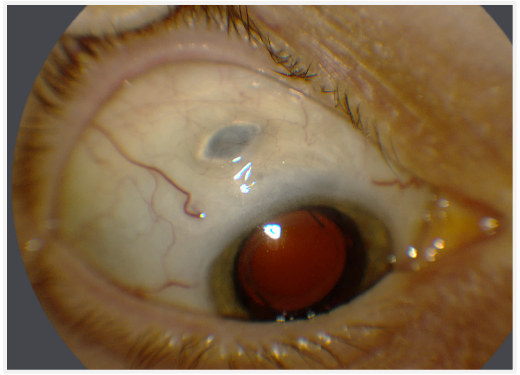
Study Disclosures

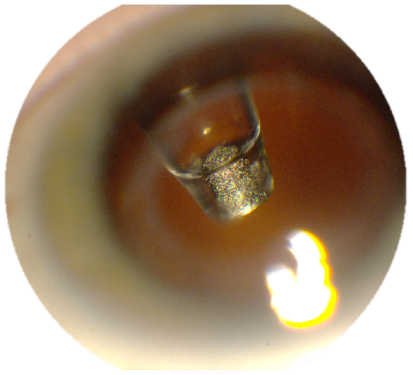
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by Genentech, Inc., a member of the Roche Group, for the study and third-party writing assistance, which was provided by Betsy C. Taylor, PhD, CMPP, of Envision Pharma Group

The Port Delivery System With Ranibizumab (PDS)

Continuous intravitreal delivery of a customized formulation of ranibizumab







Innovative, investigational drug delivery system

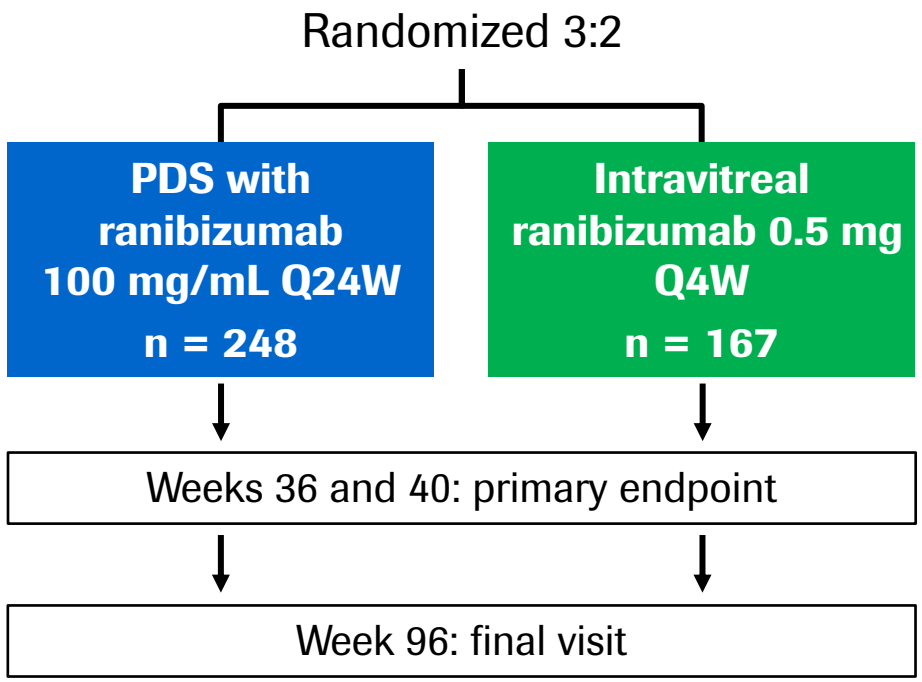
- Permanent, refillable intraocular implant
- A novel, customized formulation of ranibizumab
- Implant surgically placed at the pars plana
- In-office refill-exchange procedures

Ladder phase 2 trial of the PDS for nAMD

- PDS 100 mg/mL vision and anatomic outcomes comparable with monthly ranibizumab 0.5 mg
- PDS was generally well tolerated
- Supported evaluation in Archway phase 3 trial

Ladder, NCT02510794.
nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab.

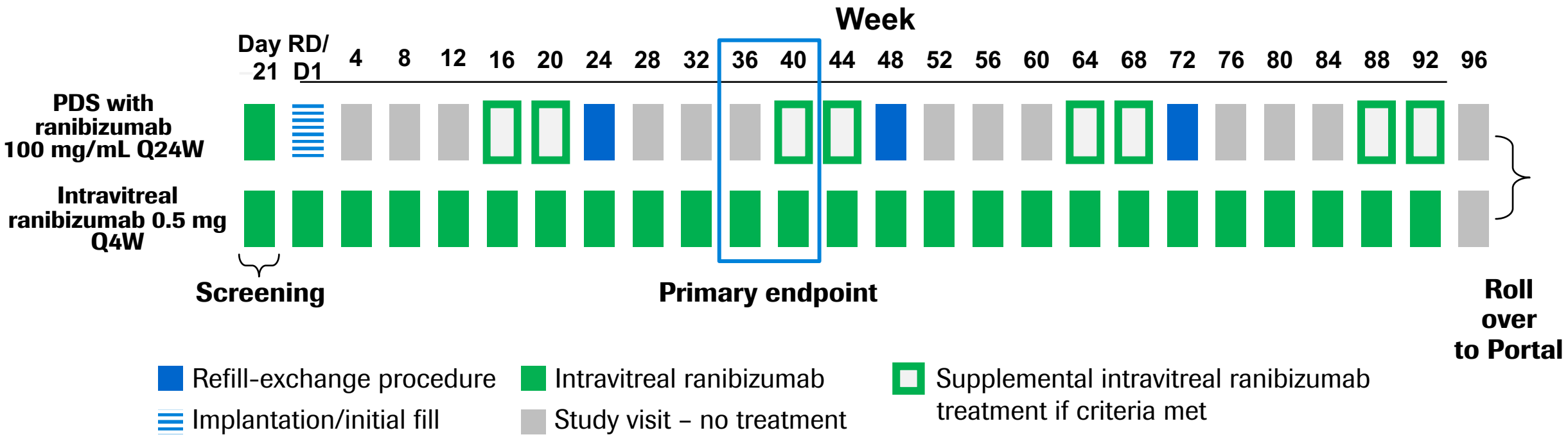
Archway: Designed to Evaluate the Efficacy and Safety of the PDS for the Treatment of nAMD



Primary objective	Evaluate noninferiority and equivalence of PDS 100 mg/mL Q24W versus intravitreal ranibizumab 0.5 mg Q4W
Primary endpoint	Change in BCVA score from baseline averaged over weeks 36 and 40
Secondary endpoints	• Change in BCVA score from baseline over time • Change in CPT from baseline over time and at week 36 • Percentage of PDS-treated patients who received supplemental treatment during first refill-exchange interval • Incidence and severity of ocular and systemic AEs, SAEs, and ocular AEs of special interest

[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. AE, adverse event; BCVA, best-corrected visual acuity; CPT, center point thickness; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; SAE, serious adverse event; VEGF, vascular endothelial growth factor.

Archway Treatment Regimen: PDS With Fixed 24-Week Refill-Exchanges



Criteria for Supplemental Intravitreal Ranibizumab: Disease Activity Due to nAMD[a]				
CST + BCVA		BCVA		CST
Increase of ≥ 100 µm on SD-OCT from lowest measurement and decrease of ≥ 10 letters from best recorded score	or	Decrease of ≥ 15 letters from best recorded score	or	Increase of ≥ 150 µm on SD-OCT from lowest measurement

[a] Eligible for supplemental intravitreal ranibizumab treatment with open-label intravitreal ranibizumab at weeks 16 and 20 (after implant insertion) and at weeks 40, 44, 64, 68, 88, and 92 if any of the 3 criteria were met.
BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; RD, randomization; SD-OCT, spectral domain optical coherence tomography.

Baseline Demographics and Ocular Characteristics Were Well Balanced Across Treatment Arms

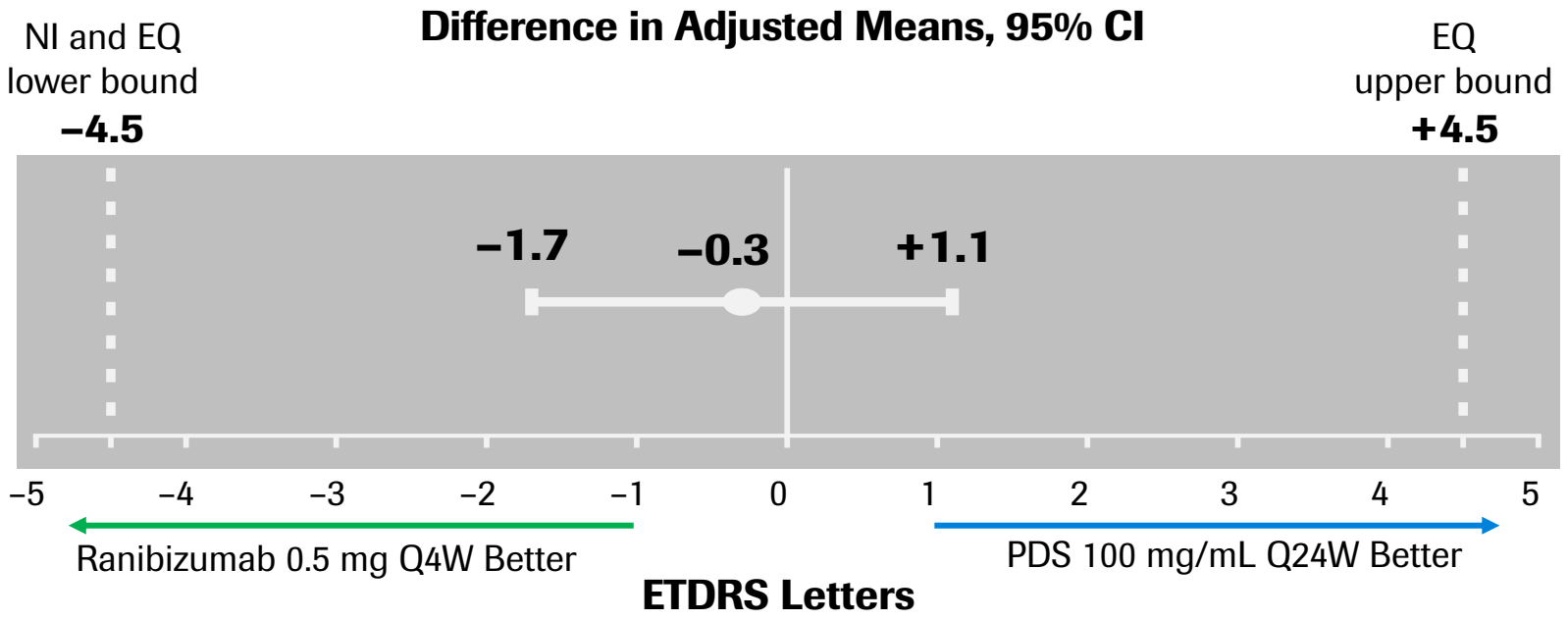
Characteristic	PDS With Ranibizumab 100 mg/mL Q24W (n = 248)	Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)
Age, years		
Mean (SD)	75.2 (8.1)	74.8 (7.6)
Range	51–96	54–89
Sex, n (%)		
Male	41.5	40.1
Baseline BCVA, ETDRS letter score		
Mean (SD)	74.4 (10.5)	75.5 (10.3)
Snellen equivalent	20/32	20/32
Baseline CPT, µm		
Mean (SD)	176.9 (54.8)	177.2 (49.1)
Time since nAMD diagnosis, months		
Mean (SD)	5.9 (9.5)	5.3 (2.0)
Number of prior anti-VEGF injections		
Mean (SD)	5.0 (2.1)	5.0 (1.5)

- Baseline BCVA in Archway was assessed after a mean of 5 anti-VEGF injections
- 98% study retention through week 40; no impact due to COVID-19

*; CPT measured from inner limiting membrane to the inner third of the retinal pigment epithelium.
BCVA, best-corrected visual acuity; CPT, center point thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; 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.

Primary Endpoint: PDS Q24W Was Noninferior and Equivalent to Monthly Ranibizumab

Change in BCVA From Baseline Averaged Over Weeks 36 and 40, ETDRS Letters	PDS With Ranibizumab 100 mg/mL Q24W (n = 248)	Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)	Difference in Adjusted Means
Adjusted mean (95% CI)	+0.2 (–0.7, +1.1)	+0.5 (–0.6, +1.6)	–0.3 (–1.7, +1.1)

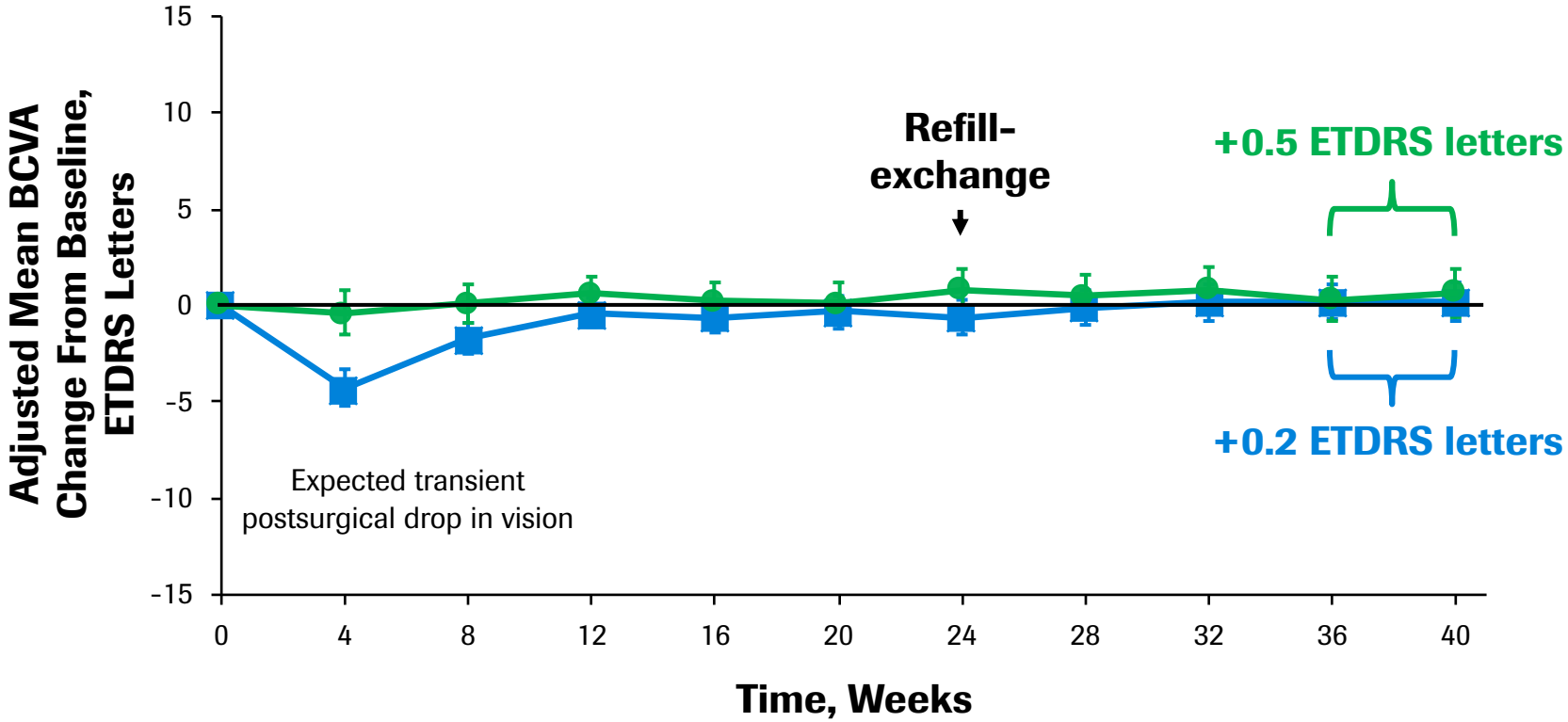


Patients received a mean of 5.0 anti–vascular endothelial growth factor injections before baseline. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. Adjusted means estimated using a mixed-effect model for repeated measures with adjustment for change from baseline in BCVA as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline BCVA (< 74 ETDRS letters vs ≥ 74 ETDRS letters). The protocol-specified noninferiority lower bound margin was 4.5 letters and the equivalence margin was ± 4.5 letters.
BCVA, best-corrected visual acuity; EQ, equivalence; ETDRS, Early Treatment Diabetic Retinopathy Study; NI, noninferiority; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

PDS Q24W Maintained Vision Over 40 Weeks

Adjusted Mean BCVA Change From Baseline

Mean of 5 Previous Anti-VEGF Injections at baseline



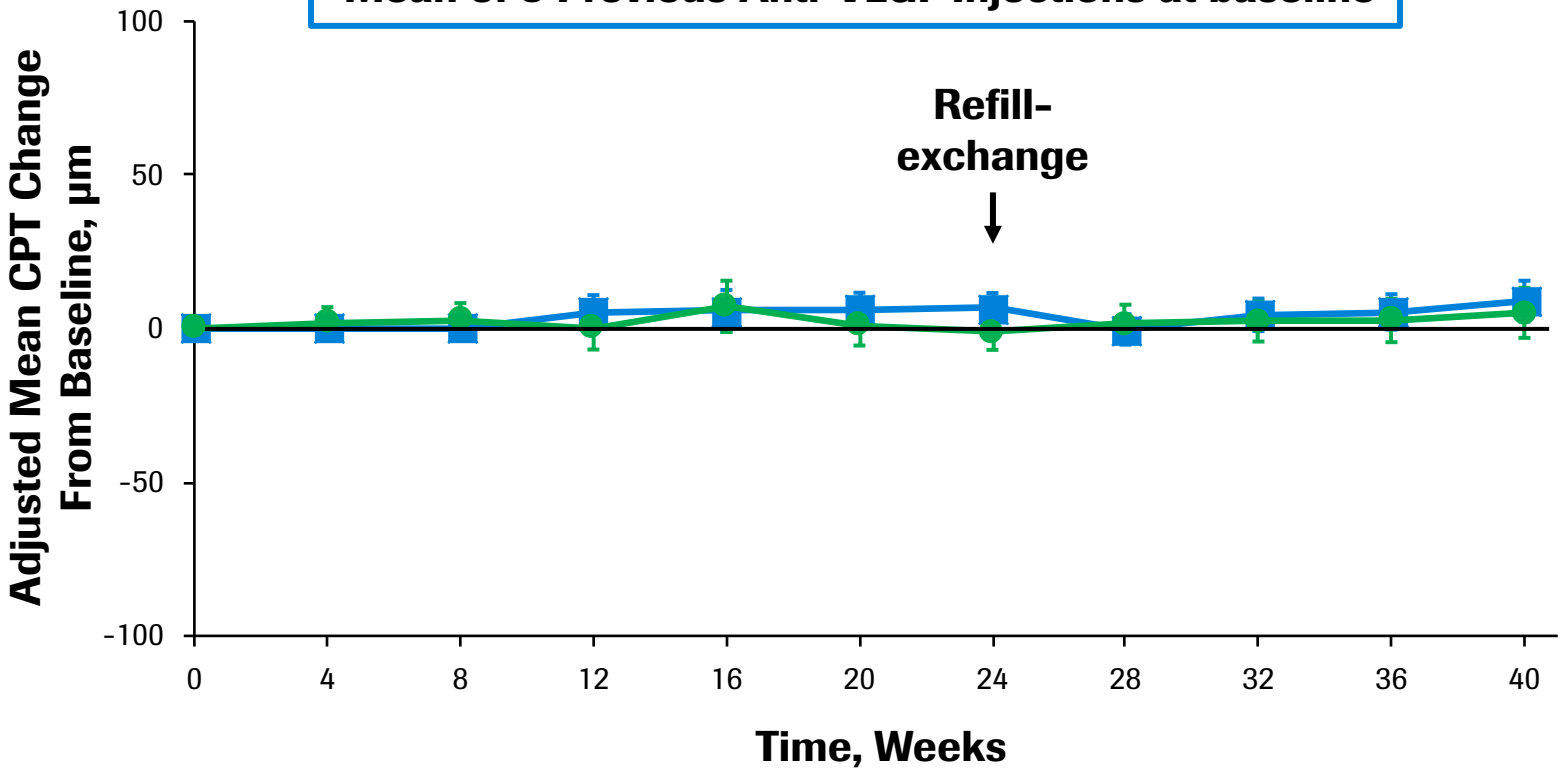
Baseline		Weeks 36/40	
ETDRS	Snellen	ETDRS	Snellen
74.4	20/32	74.6	20/32
75.5	20/32	76.0	20/32

Adjusted means from a mixed-effect model for repeated measures (MMRM) analysis and vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. Adjusted means estimated using a MMRM with adjustment for change from baseline in BCVA as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline BCVA (< 74 ETDRS letters vs ≥ 74 ETDRS letters).
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; VEGF, vascular endothelial growth factor.

PDS Controlled Retinal Thickness Through Week 40 Similar to Monthly Ranibizumab

Adjusted Mean CPT Change From Baseline

Mean of 5 Previous Anti-VEGF Injections at baseline



Prespecified Secondary Endpoint (Week 36)		
Baseline	Week 36	Week 36 Change From BL
176.9 µm	182.3 µm	+5.4 µm
177.4 µm	180.0 µm	+2.6 µm

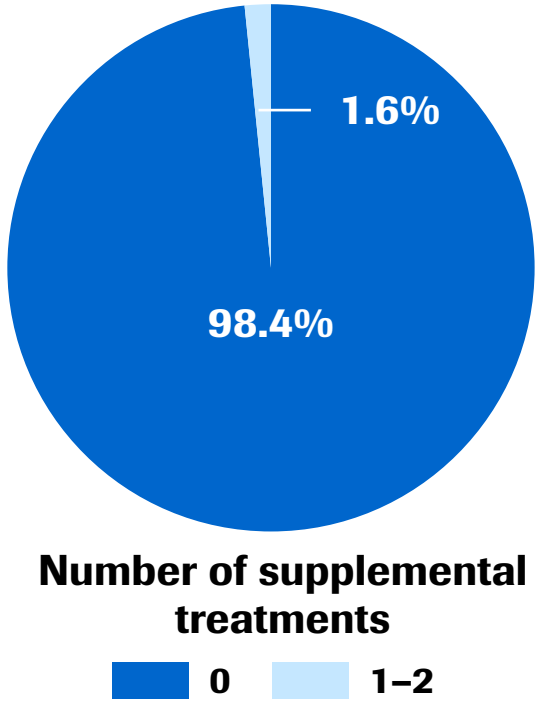
PDS with ranibizumab 100 mg/mL Q24W (n = 248)

Intravitreal ranibizumab 0.5 mg Q4W (n = 167)

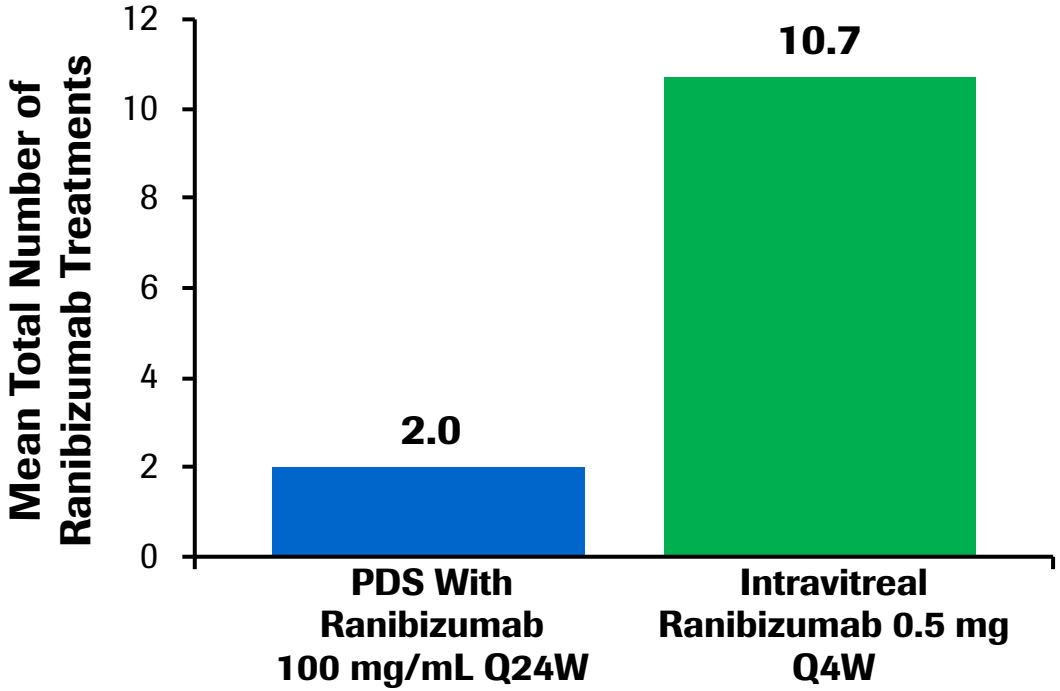
CPT defined as retinal thickness in the center of the fovea measured between the inner limiting membrane and the inner third of the retinal pigment epithelium layer. Adjusted means were estimated using a mixed-effect model for repeated measures with adjustment for change from baseline in CPT score as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline best-corrected visual acuity (< 74 Early Treatment Diabetic Retinopathy Study [ETDRS] letters vs ≥ 74 ETDRS letters).
BL, baseline; CPT, center point thickness; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

~98% of PDS-Treated Patients Did Not Receive Supplemental Treatment During First Refill-Exchange Interval

Percentage of PDS Patients Who Received Supplemental Treatment Before First Refill-Exchange at Week 24



Total Number of Ranibizumab Treatments Through Week 40[a,b]



Includes initial fill and refill-exchange

[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 at weeks 16 and 20 (first refill-exchange interval) and week 40 (second refill-exchange interval). Patients could also receive supplemental treatment at week 44 for the second refill-exchange interval; week 44 data not included in this analysis.
PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

Ocular Adverse Events of Special Interest[a]

PDS insertion and refill-exchange procedures were 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)
	Time From Surgery			
	≤ 1 Month	> 1 Month	Total[c]	Total[c]
Conjunctival bleb/ conjunctival filtering bleb leak	11 (4.4%)	6 (2.4%)	16 (6.5%)	0
Vitreous hemorrhage	12 (4.8%)	1 (0.4%)	13 (5.2%)	4 (2.4%)
Cataract[d]	1 (0.4%)	9 (3.6%)	10 (4.0%)	6 (3.6%)
Conjunctival erosion	1 (0.4%)	5 (2.0%)	6 (2.4%)	0
Conjunctival retraction	1 (0.4%)	4 (1.6%)	5 (2.0%)	0
Endophthalmitis	0	4 (1.6%)	4 (1.6%)	0
Rhegmatogenous retinal detachment	1 (0.4%)	1 (0.4%)	2 (0.8%)	0
Hyphema	1 (0.4%)	0	1 (0.4%)	0

- All cases of vitreous hemorrhage resolved spontaneously; no cases required vitrectomy
- 1 of 248 PDS-treated patients had irreversible vision loss due to an adverse event (*E. faecalis* endophthalmitis)
- 1 PDS patient experienced device dislocation into the eye during a refill-exchange procedure; following removal, the patient's vision returned to baseline
- 3/4 endophthalmitis patients had vision return to baseline; 2/4 remained on PDS treatment
- 2/2 patients had rhegmatogenous retinal detachment repaired with vitrectomy
- Conjunctival bleb was predominantly conjunctival thickening; all cases classified as non-serious
- 9 cases of conjunctival erosion/retraction were addressed with flap revisions or coverage of implant flange with partial thickness cornea
- Cataract rates comparable across arms; no cases of traumatic cataract

[a] Protocol-defined ocular adverse events of special interest potentially related to the PDS implant or implant procedure. [b] Frequency counts by preferred term. Multiple occurrences of the same adverse event in in an individual are counted only once for each column. [c] All data through week 40. [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).
MedDRA, Medical Dictionary for Regulatory Activities; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

Serious Nonocular AEs Through Week 40

Systemic safety of PDS Q24W was generally comparable with monthly ranibizumab

MedDRA Preferred Term, n (%)	PDS With Ranibizumab 100 mg/mL Q24W (n = 248)	Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)
Total number of patients with ≥ 1 AE	28 (11.3%)	16 (9.6%)
Overall total number of AEs	36	24
Pneumonia[a]	3 (1.2%)	0
Urinary tract infection	2 (0.8%)	1 (0.6%)
Cerebrovascular accident	3 (1.2%)	1 (0.6%)
Syncope	0	2 (1.2%)
Pancreatitis	2 (0.8%)	0
Chest pain	0	2 (1.2%)
Acute respiratory failure	2 (0.8%)	0

None of the serious nonocular AEs were suspected to be related to study treatment

[a] No cases were related to COVID-19.
Observed data, safety-evaluable population who received ≥ 1 dose of study drug according to the actual treatment. Events chosen with ≥ 2 events in either arm.
AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

The PDS Patient Preference Questionnaire (PPPQ)

- The PPPQ was administered to all patients in the PDS arm at week 40
- The PPPQ is a 3-item questionnaire that captures a **patient's preference** for treatment, the **strength of their preference**, and the **reasons for their preference**

PPPQ

1) Which method of administration did you prefer?

☐ Intravitreal injections. ☐ Port Delivery System ☐ No preference

2) If you have a preference for one of the administration routes, how strong is this preference?

☐ Very strong ☐ Fairly strong ☐ Not very strong

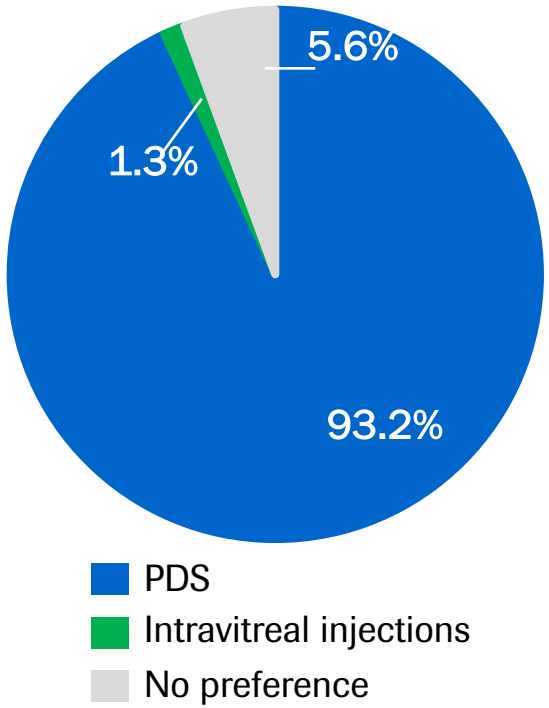
3) If you have a preference for one of the administration routes, what are the main reasons for your preference? Please choose all that apply:

☐ Less worry or nervousness
☐ Requires less time for treatment
☐ Less discomfort
☐ Fewer treatments
☐ Other reason

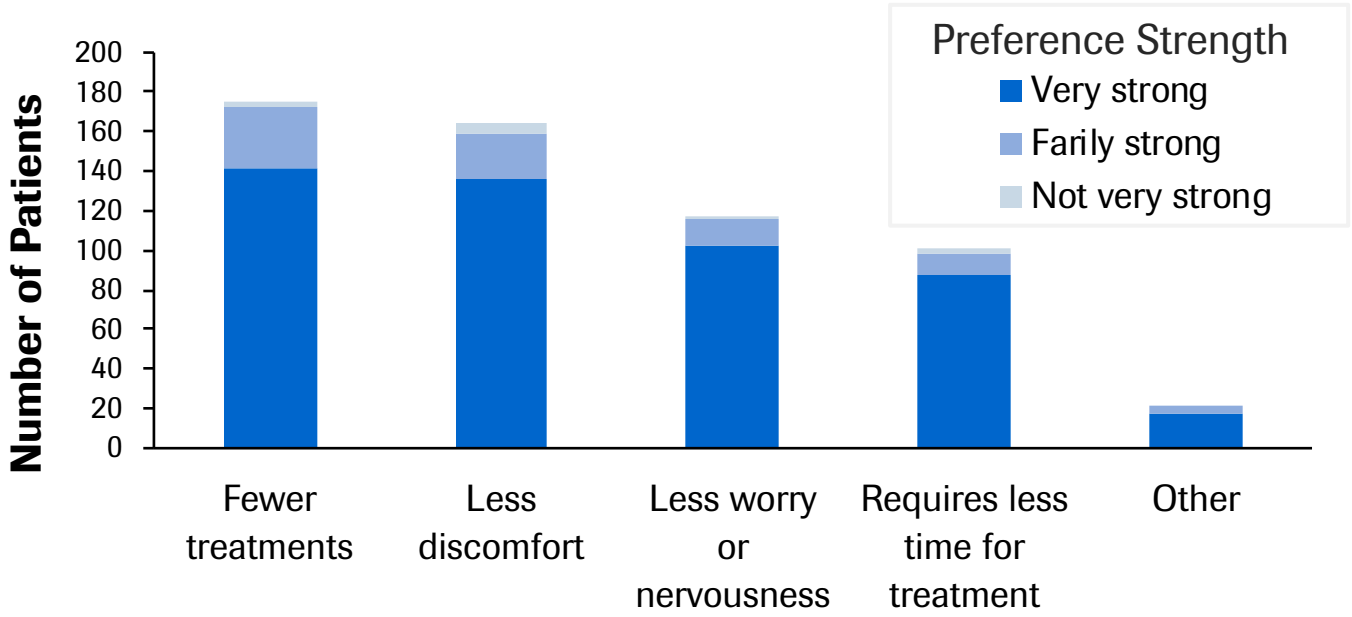
93% of PDS Patients Preferred PDS over Intravitreal Injections

Responses to the PPPQ at Week 40[a]

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



Preference Reasons Among Patients Who Preferred PDS[c]



3 patients preferred intravitreal injections

- Fairly strongly: Requires less time for treatment (n = 1)
- Fairly strongly: Other reason (n = 1)
- Not very strongly: Other reason (n = 1)

[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. [c] Patients could select multiple reasons for their preference.
PDS, Port Delivery System with ranibizumab; PPPQ, PDS patient preference questionnaire.

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Archway Met Primary Endpoint: PDS Q24W Equivalent to Monthly Ranibizumab

Equivalent Vision, Controlled Retinal Thickness

- PDS noninferior and equivalent for BCVA change at weeks 36/40
- PDS controlled retinal thickness as well as monthly ranibizumab through week 40

Treatment Durability, Reduced Treatment Burden

- 98% of PDS patients did not receive supplemental treatment before first refill-exchange
- ~5x fewer treatments through week 40 for PDS patients
- 93% of PDS patients preferred PDS over intravitreal injections

Favorable Benefit-Risk Profile

- PDS surgery-device-drug combination was generally well tolerated

PDS maintained vision while reducing treatment burden through continuous delivery of ranibizumab

BCVA, best-corrected visual acuity; PDS, Port Delivery System with ranibizumab; Q24W, every 24 weeks.

Welcome
Karl Mahler, Head of Investor Relations and Group Planning

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

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

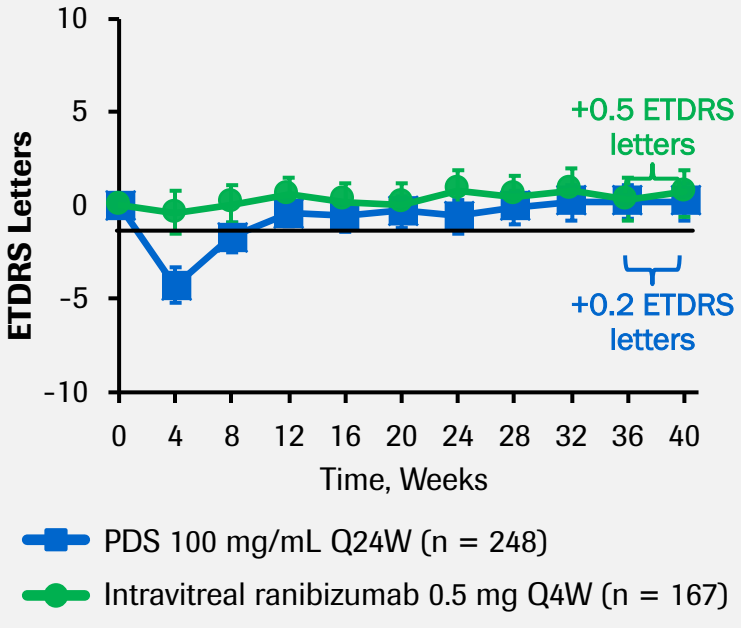
PDS: Archway – Phase III topline results
Dante Pieramici, M.D., Retina Specialist and PDS Clinical Investigator

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

PDS demonstrated Equivalent BCVA, >98% 6-month Durability, and >93% Patient Preference

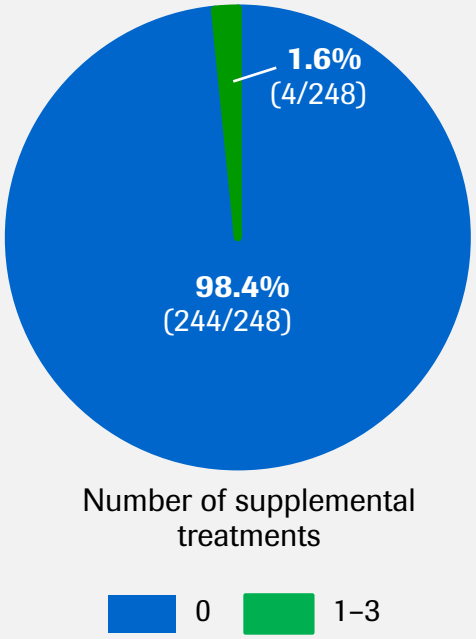
Equivalent Vision

Adjusted Mean BCVA Change From Baseline



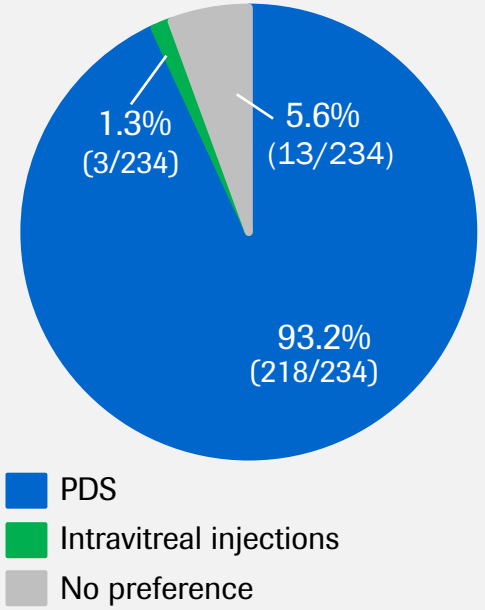
Treatment Durability

Percentage of PDS Patients Who Received Supplemental Treatment Before First Refill-Exchange at Week 24



Patient Preference

Preference Among Patients in the PDS Arm at Week 40



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.

Doing now what patients need next