ASRS Highlights 2020

Roche Analyst Webcast

South San Francisco, 27 July 2020
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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

**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-03)
- **PI3Ki**
  - HR+ mBC (Ph III: INAVO120)
- **Venclexta + Gazyva**
  - 1L fit CLL (Ph III: CristaLlo)
- **Actemra**
  - severe COVID-19 pneumonia (Ph III: COVACTA, REMDACTA, EMPACTA)

**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

<table>
<thead>
<tr>
<th>Replace/extend existing businesses</th>
<th>Entrering new franchises</th>
<th>Achievements Q2 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>MabThera/Rituxan</td>
<td><strong>Oncology</strong>: Tecentriq (mUC, TNBC, SCLC, HCC, mM), ipatasertib (mCRPC), SERD (HR+ BC)</td>
<td><strong>Entering new franchises</strong></td>
</tr>
<tr>
<td></td>
<td><strong>MS</strong>: Ocrevus</td>
<td><strong>Tecentriq</strong>: US approval in 1L HCC (with Avastin)</td>
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<tr>
<td>Herceptin</td>
<td><strong>Hemophilia A</strong>: Hemlibra</td>
<td><strong>ipatasertib</strong>: Positive Ph III (IPATential150) results in patients with PTEN loss tumors in mCRPC</td>
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<td><strong>Enspryn</strong>: First approvals in Canada, Japan, CH in NMOSD</td>
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<tr>
<td>Avastin</td>
<td></td>
<td><strong>risdiplam</strong>: FIREFISH (SMA) part 2 results in Type 1 patients presented at AAN</td>
</tr>
<tr>
<td>Lucentis</td>
<td></td>
<td><strong>SPARK</strong>: 2 to 3.3 year follow up efficacy/safety data for SPK-8011 hem A gene therapy presented at ISTH</td>
</tr>
<tr>
<td>Tamiflu</td>
<td></td>
<td><strong>Replace/extend existing businesses</strong></td>
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<tr>
<td></td>
<td></td>
<td><strong>Phesgo</strong>: US approval for P+H FDC-SC</td>
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<td></td>
<td><strong>tiragolumab</strong>: Randomized Ph II data presented at ASCO; Ph III trials in 1L NSCLC and 1L SCLC initiated</td>
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<td><strong>SERD</strong>: Clinical data showing excellent efficacy /safety profile presented at ASCO</td>
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<tr>
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<td></td>
<td><strong>glofitamab</strong>: Ph Ib data presented at EHA; Ph III in 2L+ DLBCL initiated</td>
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<td></td>
<td><strong>mosunetuzumab</strong>: BTD designation in 3L+ FL awarded</td>
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<td><strong>PDS</strong>: Positive Ph III (ARCHWAY) results in nAMD</td>
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</tbody>
</table>

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**
- nAMD, DME, RVO
- Glaucoma
- Dry Eye
- Ocular inflammation/infections
- Others

**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

- **nAMD**
  - 2014: 555
  - 2019: 3,081
  - 2024: 3,560
- **DME/DR**
  - 2014: 944
  - 2019: 7,331
  - 2024: 8,471
- **RVO**
  - 2014: 2,000
  - 2019: 2,029
  - 2024: 2,345

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 world¹

Number of VEGF injections correlates with vision improvement¹

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

Opportunity to differentiate on durability of response and efficacy

- Faricimab potential to improve on efficacy
- Anti-VEGF monotherapies
- Faricimab Potential to improve on durability of response
- Port Delivery System with ranibizumab reduces real world Tx burden

For illustrative purposes only
Roche Ophthalmology strategy has four strategic levers

1. Improved Efficacy via novel MOAs
   - anti-VEGF/Ang-2
   - New MOAs utilizing Dutu-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

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**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approved</th>
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<tbody>
<tr>
<td>Neovascular AMD</td>
<td>RG7921</td>
<td>RG6179</td>
<td>faricimab</td>
<td>Lucentis 0.5 mg PFS</td>
</tr>
<tr>
<td></td>
<td>RG6120*</td>
<td>RG7774</td>
<td>PDS w ranibizumab</td>
<td></td>
</tr>
<tr>
<td>Diabetic Macular Edema</td>
<td>RG6179</td>
<td>RG7774</td>
<td>faricimab</td>
<td>Lucentis 0.3 mg PFS</td>
</tr>
<tr>
<td>Diabetic Retinopathy</td>
<td>RG7774</td>
<td>RG7774</td>
<td>PDS w ranibizum#</td>
<td>Lucentis 0.3 mg PFS</td>
</tr>
<tr>
<td>Retinal Vein Occlusion</td>
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<td></td>
<td></td>
<td>Lucentis 0.5 mg PFS</td>
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<tr>
<td>Myopic CNV</td>
<td></td>
<td></td>
<td></td>
<td>Lucentis 0.5 mg PFS</td>
</tr>
<tr>
<td>Geographic Atrophy</td>
<td>RG6312*</td>
<td>RG6147</td>
<td></td>
<td>Actemra/ RoActemra</td>
</tr>
<tr>
<td>Giant Cell Arteritis</td>
<td>RG6312*</td>
<td>RG7929</td>
<td></td>
<td>satralizumab</td>
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<tr>
<td>Neuromyelitis Optica</td>
<td></td>
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<tr>
<td>Choroideremia</td>
<td>RG6247+</td>
<td>RG6299*</td>
<td>faricimab</td>
<td>Lucentis 0.5 mg PFS</td>
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<tr>
<td>X-linked RP</td>
<td>RG6318+</td>
<td></td>
<td>PDS w ranibizum#</td>
<td></td>
</tr>
<tr>
<td>Inherited retinal Dx**</td>
<td></td>
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<td></td>
<td>Luxturna**</td>
</tr>
</tbody>
</table>

**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
Imaging
Real World Data
Home Vision Monitoring

Lucentis
Faricimab
PDS

Treat intermediate disease early…
…to avoid irreversible vision loss

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

- 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=nevovascular 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. +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. PTI: nAMD-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.


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

- 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

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

- 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)
Patients will be randomized 1:1:1 into 3 arms.

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

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

- 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

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

Factor B and downstream product levels

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

- 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](http://webvision.med.utah.edu)
Next generation Retinal Gene Therapy

Safe procedure for transducing across the entire retina

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

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

- 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
- 3 DutaFabs are in pre-clinical development targeting different MOAs

Further improving the standard of care

Efficacy (BCVA change, letters)

Durability of Response

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

- 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
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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; Natasha Singh, PharmD; David Kardatzke, PhD; Steven Blotner, PhD; Shienal Patel, BSc; and Giulio Barteselli, MD

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


- 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

Patients with nAMD responsive to any anti-VEGF treatment\textsuperscript{a}

\textbf{N = 415}\textsuperscript{b}

Randomized 3:2

- **PDS with ranibizumab 100 mg/mL Q24W**
  - \textit{n = 248}

- **Intravitreal ranibizumab 0.5 mg Q4W**
  - \textit{n = 167}

Weeks 36 and 40: primary endpoint

Week 96: final visit

**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

\textsuperscript{a} nAMD in study eye diagnosed within 9 months of screening; ≥ 3 intravitreal injections of any anti-VEGF agent within previous 6 months. \textsuperscript{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.
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.

**Criteria for Supplemental Intravitreal Ranibizumab: Disease Activity Due to nAMD**

<table>
<thead>
<tr>
<th>CST + BCVA</th>
<th>BCVA</th>
<th>CST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase of ≥ 100 μm on SD-OCT from lowest measurement and decrease of ≥ 10 letters from best recorded score</td>
<td>Decrease of ≥ 15 letters from best recorded score</td>
<td>Increase of ≥ 150 μm on SD-OCT from lowest measurement</td>
</tr>
</tbody>
</table>

*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

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

- 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

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

**Table:**

<table>
<thead>
<tr>
<th>Difference in Adjusted Means, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranibizumab 0.5 mg Q4W Better</td>
</tr>
<tr>
<td>PDS 100 mg/mL Q24W Better</td>
</tr>
</tbody>
</table>

**Graph:**

![Graph showing the comparison of BCVA change with different treatment groups](image)

\[ \text{ETDRS Letters} \]

**Difference in Adjusted Means, 95% CI**

- **NI and EQ lower bound**
  -4.5

- **EQ upper bound**
  +4.5

**Ranibizumab 0.5 mg Q4W Better**

**PDS 100 mg/mL Q24W Better**

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.
Adjusted means from a mixed-effect model for repeated measures (MMRM) analysis and vertical bars represent 95% 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.

### Adjusted Mean BCVA Change From Baseline

<table>
<thead>
<tr>
<th>Time, Weeks</th>
<th>Baseline</th>
<th>Weeks 36/40</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ETDRS Snellen</td>
<td>ETDRS Snellen</td>
</tr>
<tr>
<td>0</td>
<td>74.4</td>
<td>74.6</td>
</tr>
<tr>
<td>4</td>
<td>74.6</td>
<td>76.0</td>
</tr>
<tr>
<td>8</td>
<td>74.4</td>
<td>76.0</td>
</tr>
<tr>
<td>12</td>
<td>74.6</td>
<td>76.0</td>
</tr>
<tr>
<td>16</td>
<td>74.6</td>
<td>76.0</td>
</tr>
<tr>
<td>20</td>
<td>74.4</td>
<td>76.0</td>
</tr>
<tr>
<td>24</td>
<td>74.4</td>
<td>76.0</td>
</tr>
<tr>
<td>28</td>
<td>74.6</td>
<td>76.0</td>
</tr>
<tr>
<td>32</td>
<td>74.6</td>
<td>76.0</td>
</tr>
<tr>
<td>36/40</td>
<td>74.6</td>
<td>76.0</td>
</tr>
<tr>
<td>40</td>
<td>74.6</td>
<td>76.0</td>
</tr>
</tbody>
</table>

**PDS Q24W Maintained Vision Over 40 Weeks**
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)**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 36</th>
<th>Week 36 Change From BL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDS with ranibizumab 100 mg/mL Q24W (n = 248)</td>
<td>176.9 µm</td>
<td>182.3 µm</td>
<td>+5.4 µm</td>
</tr>
<tr>
<td>Intravitreal ranibizumab 0.5 mg Q4W (n = 167)</td>
<td>177.4 µm</td>
<td>180.0 µm</td>
<td>+2.6 µm</td>
</tr>
</tbody>
</table>

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

- 98.4% received 0 supplemental treatments
- 1.6% received 1-2 supplemental treatments

Total Number of Ranibizumab Treatments Through Week 40\(^a,b\)

- PDS With Ranibizumab 100 mg/mL Q24W: 2.0 treatments
- Intravitreal Ranibizumab 0.5 mg Q4W: 10.7 treatments

\(^a\) 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

PDS insertion and refill-exchange procedures were generally well tolerated.

<table>
<thead>
<tr>
<th>MedDRA Preferred Term, n (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>PDS With Ranibizumab 100 mg/mL Q24W (n = 248)</th>
<th>Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time From Surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤ 1 Month &gt; 1 Month</td>
<td>Total&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Conjunctival bleb/conjunctival filtering bleb leak</td>
<td>11 (4.4%) 6 (2.4%) 16 (6.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Vitreous hemorrhage</td>
<td>12 (4.8%) 1 (0.4%) 13 (5.2%)</td>
<td>4 (2.4%)</td>
</tr>
<tr>
<td>Cataract&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1 (0.4%) 9 (3.6%) 10 (4.0%)</td>
<td></td>
</tr>
<tr>
<td>Conjunctival erosion</td>
<td>1 (0.4%) 5 (2.0%) 6 (2.4%)</td>
<td>0</td>
</tr>
<tr>
<td>Conjunctival retraction</td>
<td>1 (0.4%) 4 (1.6%) 5 (2.0%)</td>
<td>0</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0 4 (1.6%) 4 (1.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Rhegmatogenous retinal detachment</td>
<td>1 (0.4%) 1 (0.4%) 2 (0.8%)</td>
<td>0</td>
</tr>
<tr>
<td>Hyphema</td>
<td>1 (0.4%) 0 1 (0.4%)</td>
<td>0</td>
</tr>
</tbody>
</table>

- 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

<sup>a</sup> Protocol-defined ocular adverse events of special interest potentially related to the PDS implant or implant procedure. <sup>b</sup> Frequency counts by preferred term. Multiple occurrences of the same adverse event in an individual are counted only once for each column. <sup>c</sup> All data through week 40. <sup>d</sup> 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).
Serious Nonocular AEs Through Week 40

Systemic safety of PDS Q24W was generally comparable with monthly ranibizumab

<table>
<thead>
<tr>
<th>MedDRA Preferred Term, n (%)</th>
<th>PDS With Ranibizumab 100 mg/mL Q24W (n = 248)</th>
<th>Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients with ≥ 1 AE</td>
<td>28 (11.3%)</td>
<td>16 (9.6%)</td>
</tr>
<tr>
<td>Overall total number of AEs</td>
<td>36</td>
<td>24</td>
</tr>
<tr>
<td>Pneumonia&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3 (1.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>2 (0.8%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>3 (1.2%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>0</td>
<td>2 (1.2%)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>2 (0.8%)</td>
<td>0</td>
</tr>
<tr>
<td>Chest pain</td>
<td>0</td>
<td>2 (1.2%)</td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td>2 (0.8%)</td>
<td>0</td>
</tr>
</tbody>
</table>

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

<sup>a</sup> 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

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

Preference Among Patients (PDS Arm, n = 234)

- 93.2% preferred PDS
- 5.6% preferred Intravitreal injections
- 1.3% no preference

Preference Reasons Among Patients Who Preferred PDS

- Fewer treatments: 180
- Less discomfort: 160
- Less worry or nervousness: 120
- Requires less time for treatment: 100
- Other: 20

Preference Strength
- Very strong
- Fairly strong
- Not very strong

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)

For patients with missing Week 40 values the last post-baseline observation was imputed. Percentages are based on total number of patients who completed the measure. Patients could select multiple reasons for their preference.

PDS, Port Delivery System with ranibizumab; PPPQ, PDS patient preference questionnaire.
Thank You to All Participating Archway Investigators, Study Sites, and Patients

Aaberg Jr., Thomas
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Barakat, Mark
Battle, Ivan
Bhisitkul, Robert
Blinder, Kevin
Boyer, David
Brooks, H. Logan
Brown, David M.
Brown, Jamin
Burgess, Stuart

Callanan, David
Campbell, Peter
Campochiaro, Peter
Carlson, John
Chang, Margaret
Chaudhry, Nauman
Chen, Sanford
Clark, William
Crews, Kent
Dhoot, Dilsher
Dreyer, Richard
Eichenbaum, David
Engstrom, Robert
Falk, Naomi
Feiner, Leonard
Ferrone, Philip
Freeman, William
Goff, Mitchell
Goldberg, Roger
Gonzalez, Victor
Graff, Jordan
Gupta, Sunil
Haug, Sara
Heier, Jeffrey
Hershberger, Vrinda
Higgins, Patrick
Holekamp, Nancy
Hong, Bryan
Howard, James
Huddleston, Stephen
Jhaveri, Chirag
Johnson, Robert
Khanani, Arshad
Kitchens, John
Klancnik, James
Kwong, Henry
Lai, Michael
Lim, Jennifer
London, Nikolas
Marcus, Dennis
McCannel, Colin
Michels, Mark
Miller, Daniel
Mitra, Robert
Moore, Jeffrey
Nielsen, Jared
Ohr, Matthew
Phelps, Brian
Pieramici, Dante
Pollack, John
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Regillo, Carl
Schadlu, Ramin
Schneiderman, Todd
Sheth, Veeral
Sigler, Eric
Singer, Michael
Stoltz, Robert
Suan, Eric
Suner, Ivan

Tabassian, Ali
Thompson, John
Tosi, Joaquin
Wagner, Alan
Waheed, Nadia
Walker, Joseph
Wells, Joseph
Wieland, Mark
Williams, Patrick
Wirthlin, Robert
Wolfe, Jeremy
Wong, Robert
Wykoff, Charles
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