Roche

Roche Late Stage Pipeline Event 2021

Late Stage Pipeline Ophthalmology

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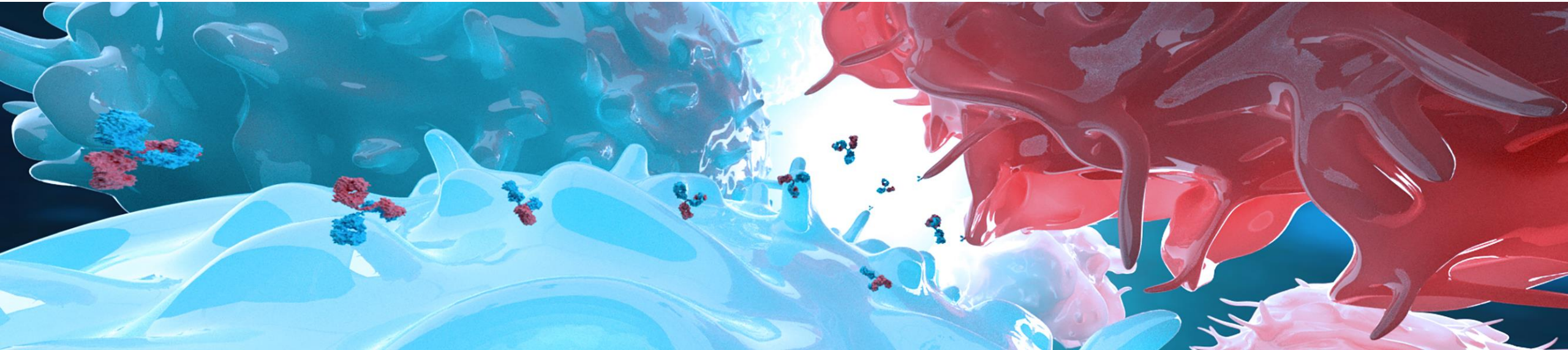
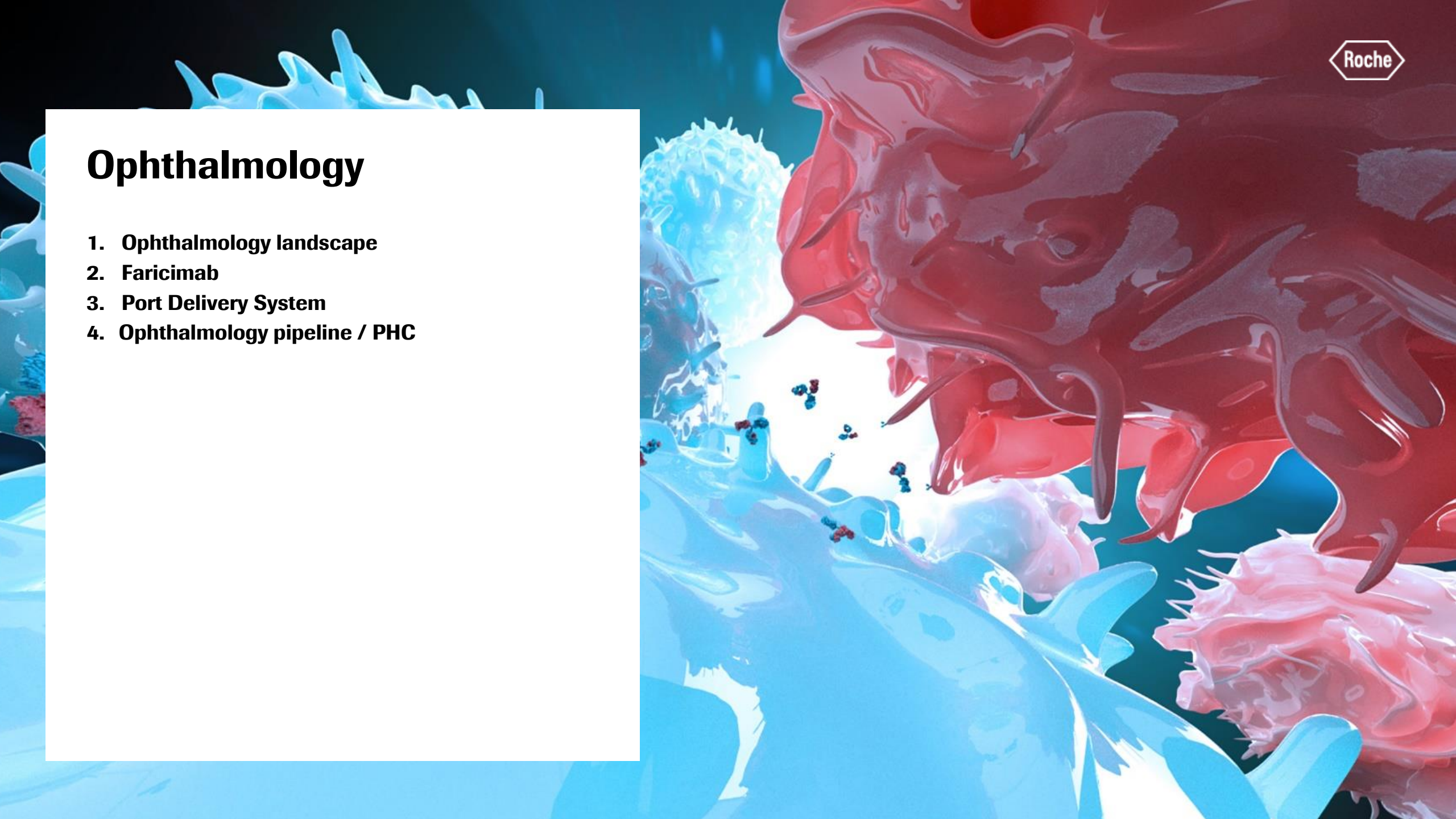
Lifecycle Leader, faricimab



Ophthalmology

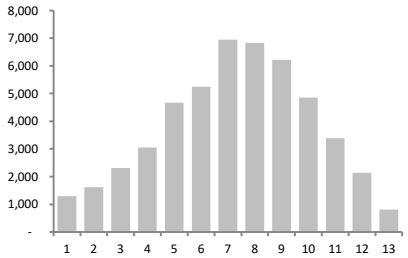
1. Ophthalmology landscape
2. Faricimab
3. Port Delivery System
4. Ophthalmology pipeline / PHC

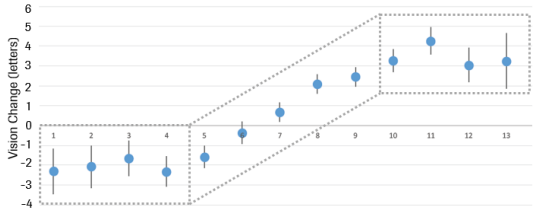


Reduction in treatment burden is a key unmet medical need

Real world vision outcomes are suboptimal

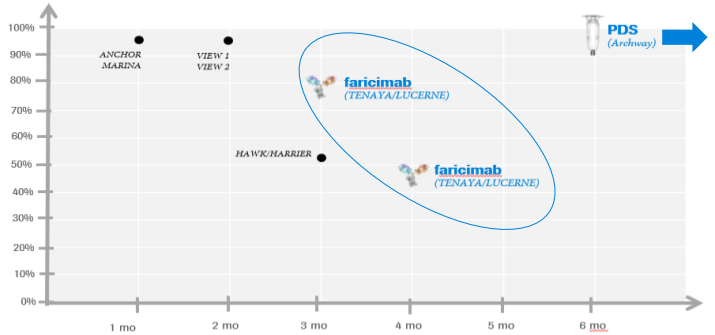
Adherence to IVT therapies is low and infrequent dosing in the real world correlates with vision loss





Only 50% of patients can be extended to Q3M dosing with current IVT therapies

Improved durability will help improve real world outcomes



faricimab and PDS are potential new standards of care

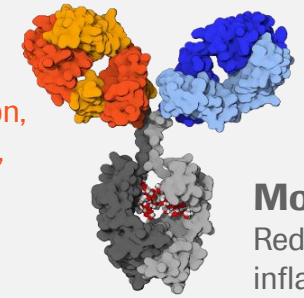
IVT=intravitreal; PDS = Port Delivery System

Faricimab

Filed in US and EU with approvals expected in 2022

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

Anti–Ang-2 Fab
Ang-2 binding leads to pericyte loss, inflammation, cell membrane instability, and increased VEGF sensitivity



Anti–VEGF-A Fab
VEGF-A promotes leakage, abnormal vessel sprouting

Modified Fc
Reduces systemic exposure and inflammatory potential

Positive results over four studies in nAMD/DME

Indication	Ph1	Ph2	Ph3	
DME	*YOSEMITE/RHINE*			✓
nAMD	*TENAYA/LUCERNE*			✓
RVO	*BALATON/COMINO*			

- Joint filing in nAMD/DME in US, EU, and Japan
- Two Ph 3 studies initiated in RVO
- Long-term extension studies initiated in DME and nAMD

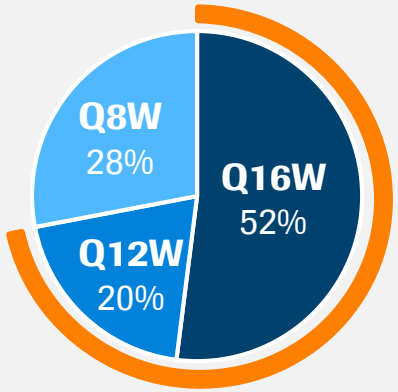
CrossMAb molecule representative of faricimab; Regula JT et al. *EMBO Mol Med*. 2016;8(11):1265-1288, with correction in Regula JT et al. *EMBO Mol Med*. 2019;11(5):e10666; Ang-2=angiopoietin-2; Fab=fragment antigen binding; Fc=fragment crystallizable; VEGF-A=vascular endothelial growth factor-A; DME=diabetic macular edema; DR=diabetic retinopathy; nAMD=neovascular age-related macular degeneration; RVO = retinal vein occlusion

Faricimab: positive data in DME and nAMD

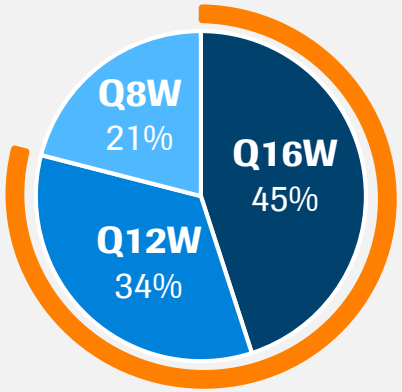
Demonstrating advantages in durability (up to Q16W) and anatomy

75–80% of patients maintained on ≥Q12W dosing, ~50% of patients maintained on ≥Q16W dosing

YOSEMITE/RHINE (DME)



TENAYA/LUCERNE (nAMD)



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

Disease control	• DME: better anatomic outcomes vs. aflibercept:
	  • Change in CST favoring faricimab
	  • More patients showing absence of DME
	  • More patients showing absence of IRF
	• nAMD: Meaningful reductions in CST

Safety	• Faricimab was well tolerated • IOI event rates were low • No cases of vasculitis or occlusive retinitis reported
Long-term data	• Year 2 data and long-term studies (RHONE-X, AVONELLE-X) are ongoing in DME, nAMD

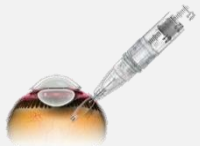
DME=diabetic macular edema; DR=diabetic retinopathy; nAMD=neovascular age-related macular degeneration; CST = central subfield thickness; IRF=intraretinal fluid; IOI=intraocular inflammation

Port Delivery System (PDS)

Filed in US and EU in Q2 2021, with FDA approval expected this year

With PDS, nearly all patients can be maintained on 6m dosing, improving patient compliance and real world outcomes

- **PDS implant:** permanent, refillable intraocular implant. One-time ~30 min outpatient surgical procedure.



- **Refill exchange:** twice yearly in-office refill of the device using proprietary needle assembly. Can only be refilled with proprietary formulation (not other molecules or biosimilars)

Positive Ph 3 results in nAMD with additional trials ongoing in DME, DR

Indication	Ph1	Ph2	Ph3
nAMD	*Archway*		✓
DME	*Pagoda*		
DR	*Pavilion*		

- Ph 3b Velodrome study investigating 9m dosing initiated
- Ph 2/3 long-term extension study (Portal) in nAMD initiated
- Ph 3 Pagoda fully recruited; data expected in 2022

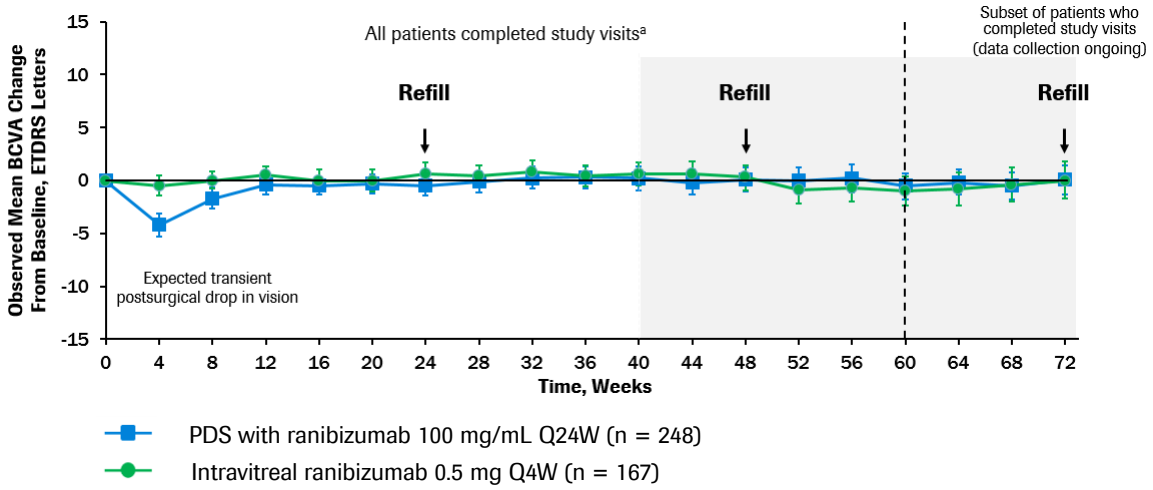
PDS=Port Delivery System with ranibizumab; IVT=intravitreal; DME=diabetic macular edema; DR=diabetic retinopathy; nAMD=neovascular age-related macular degeneration; RVO=retinal vein occlusion

PDS: nearly all patients able to be maintained on 6m dosing

Strong patient preference for PDS

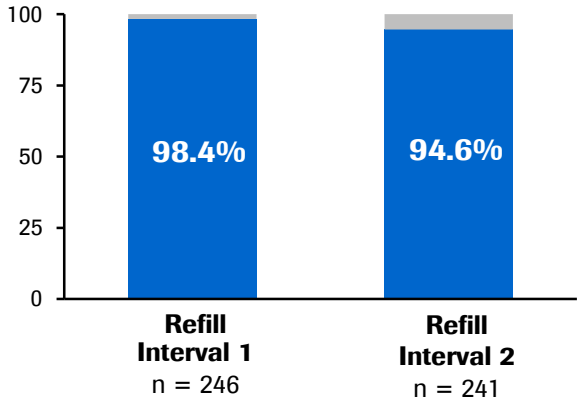
Equivalent Vision

PDS maintained vision through week 72



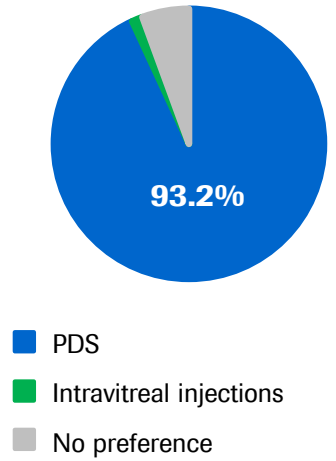
Treatment Durability

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



Patient preference

93% of patients preferred PDS over intravitreal injections



BCVA=best-corrected visual acuity; PDS=Port Delivery System with ranibizumab

Preparing for a global launch in nAMD

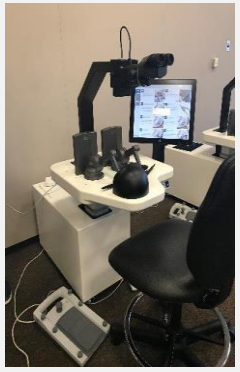
US launch planned for 2021, ex-US for 2022

Virtual reality training


THE WALL STREET JOURNAL.

Genentech Uses Virtual Reality to Train Eye Surgeons

Adopts technology in clinical trial for eye-implant procedure

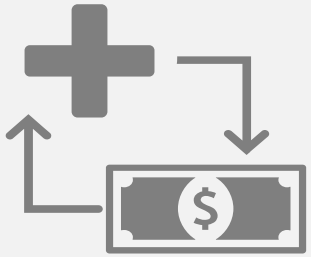


- Virtual reality (VR) technology enables preoperative training of surgeons on PDS procedures (implant insertion and refill)
- >200 US surgeons trained in Ph III across ~100 sites; ex-US VELODROME trial ongoing in 15+ countries

Field-based support

- Surgical Device Specialists (SDS) support training on site, and facilitate peer to peer discussion and education
- Focus on ensuring consistency in outcomes and enhancing the patient experience

Payer discussions ongoing

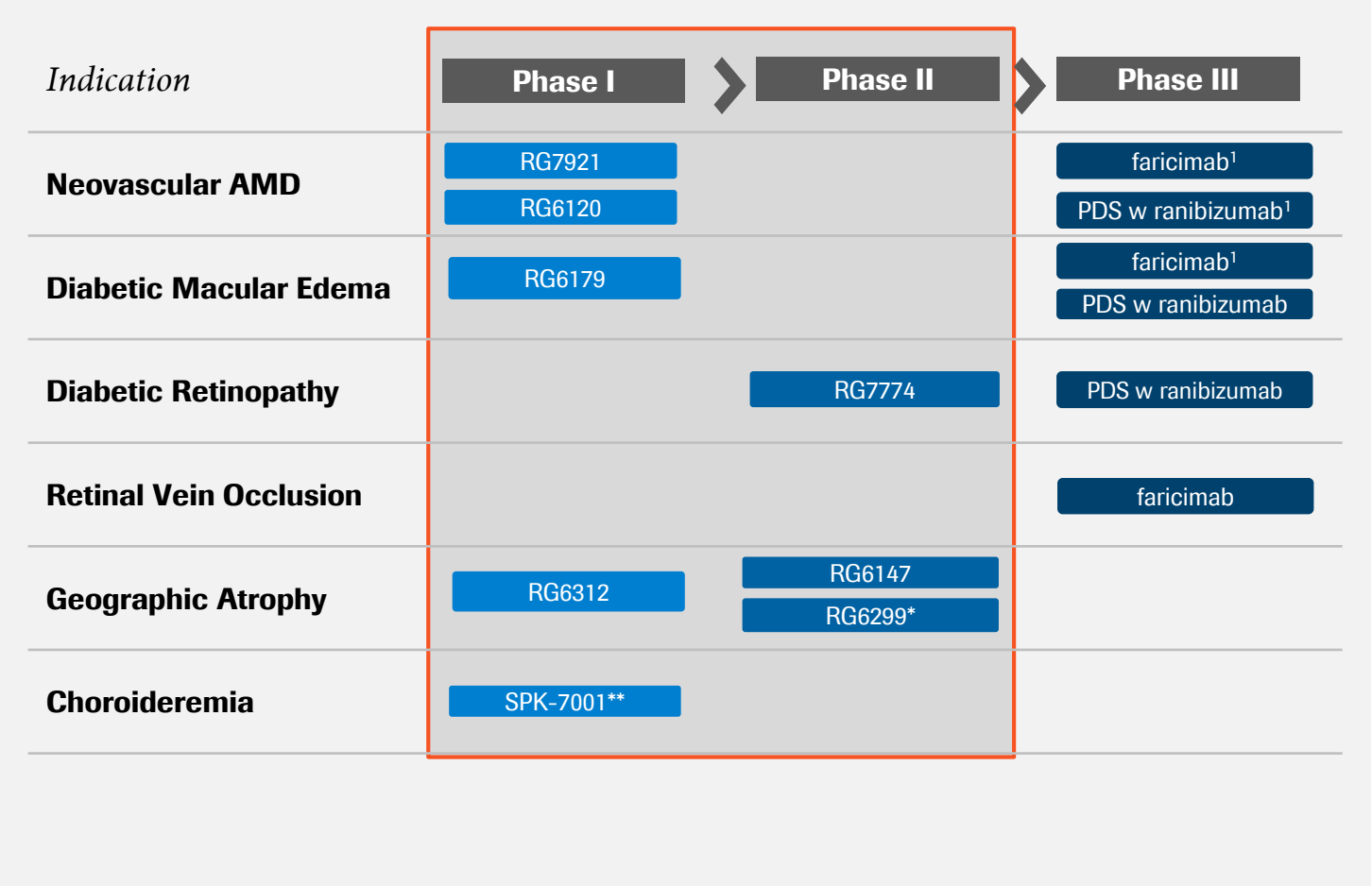


- Currently engaging with payers
- Considerations for reimbursement: PDS device, implant procedure, drug, refill procedure

nAMD=neovascular age related macular degeneration; PDS = Port Delivery System

Industry leading ophthalmology pipeline

Eight NMEs in early stage development (Ph 1/2)



Approved:

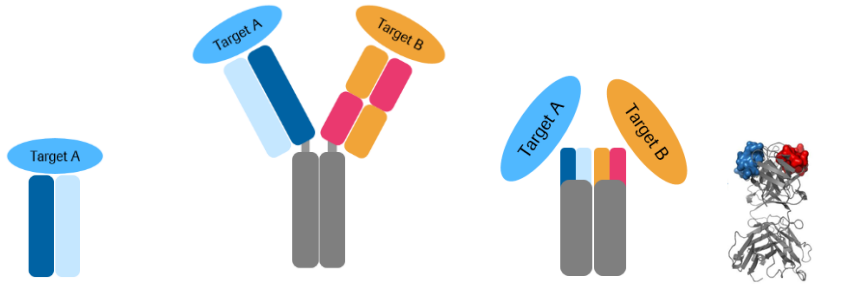
LUCENTIS® RANIBIZUMAB INJECTION

LUXTURNA™ voretigene neparvovec-rzyl for subretinal injection

PDS=Port Delivery System; NME=new molecular entity; Lucentis PFS is marketed by Novartis outside the U.S.; * Study conducted by Ionis, Roche option to in-license; Roche option to in-license; **with Spark Therapeutics, approved for patients with biallelic *RPE65* mutation-associated retinal dystrophy; [1] regulatory submissions initiated

Port Delivery System is a platform technology

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



Monospecific Fab fragment

e.g. *Lucentis*

Bispecific mAb (Crossmab)

e.g. faricimab

Bispecific Fab fragment (DutaFab)

Positive PDS Ph3 has enabled acceleration of DutaFabs in PDS platform

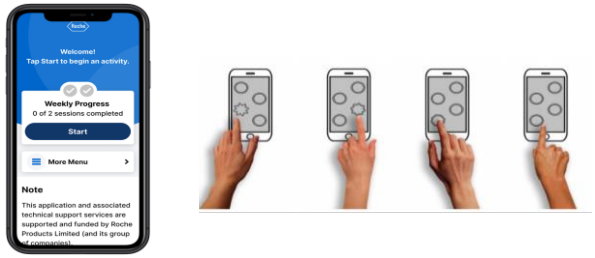
- DutaFabs are a novel bispecific Fab format significantly smaller than bispecific antibodies
- DutaFabs are compatible with the Port Delivery System enabling increased durability beyond Q6M
- Two DutaFabs are in clinical development with distinct targets, including Ang2/VEGF

* Nature Communications, volume 12, Article number: 708 (2021); PDS = Port Delivery System

Ophthalmology Personalized Healthcare

Remote monitoring & advanced analytics to help treat vision loss early

Remote vision monitoring

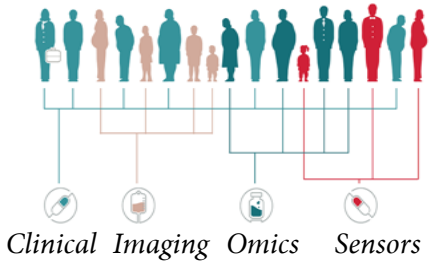


- App-based designed test to detect changes in vision in-between office visits
- Vision alerts sent to doctor
- Ongoing Home Vision Monitoring pilot to support patients during COVID-19

Retinal imaging and algorithms

- Demonstrated PoC utilizing internal algorithms in disease detection, prediction of progression and response to treatment

Data portfolio



- RWD and data sharing partnerships:

INSIGHT Health Data Research Hub · Verana Health · CATT · inoveon

nAMD=neovascular age related macular degeneration; PoC=proof of concept

Doing now what patients need next