Subretinal Delivery of Investigational ABBV-RGX-314 as a Gene Therapy for nAMD:

First Time Results of a Fellow Eye Bilateral Dosing Study

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Disclosures

4D Molecular Therapeutics: C, G
AbbVie: C
Adverum Biotechnologies : C, G
Aerie: C
Aldebaran: C
Alexion: G
Allergan: C
Amgen: C
Annexin: C
Annexon: C, G
Apellis: C, G
Arrowhead Pharmaceuticals: C
Ashvattha: C
Aviceda Therapeutics: C, O
Bausch & Lomb: C
Beacon Therapeutics: C
Broadwing Bio: C
Clearside Biomedical: C
Exegenesis: C, G
Eyepoint Pharmaceuticals: C
Frontera Therapeutics: C
Genentech, Inc.: C, G
Gyroscope: C, G
iLumen: C
Iveric Bio: C, G, S
Janssen: C
Kato: C
Kartos: C
Kodiak Sciences: C, G
Kriya: C
NGM Bio: G
Neurotech: G
Nanoscope: C
Notal: C
Novartis: C, G
Ocular Therapeutix: C , G
Oculis: C, G, O
Ocuphire: C
OcuTerra: C, G
Olives Bio: C
Opthea: C, G
Oxular: G
Oxurion: C, G
Perfuse: C
PolyPhotonix: C, O
Protagonist: C
Ray Therapeutics: C
Recens Medical: C, O
Regeneron: C
REGENXBIO: C, G
Roche: C, G
Rezolute: G
RevOpsis: C, O
Sanofi: C
Stealth: C
Thea: C
Unity: C, G
Vanotech: C , G
Vial: C, O

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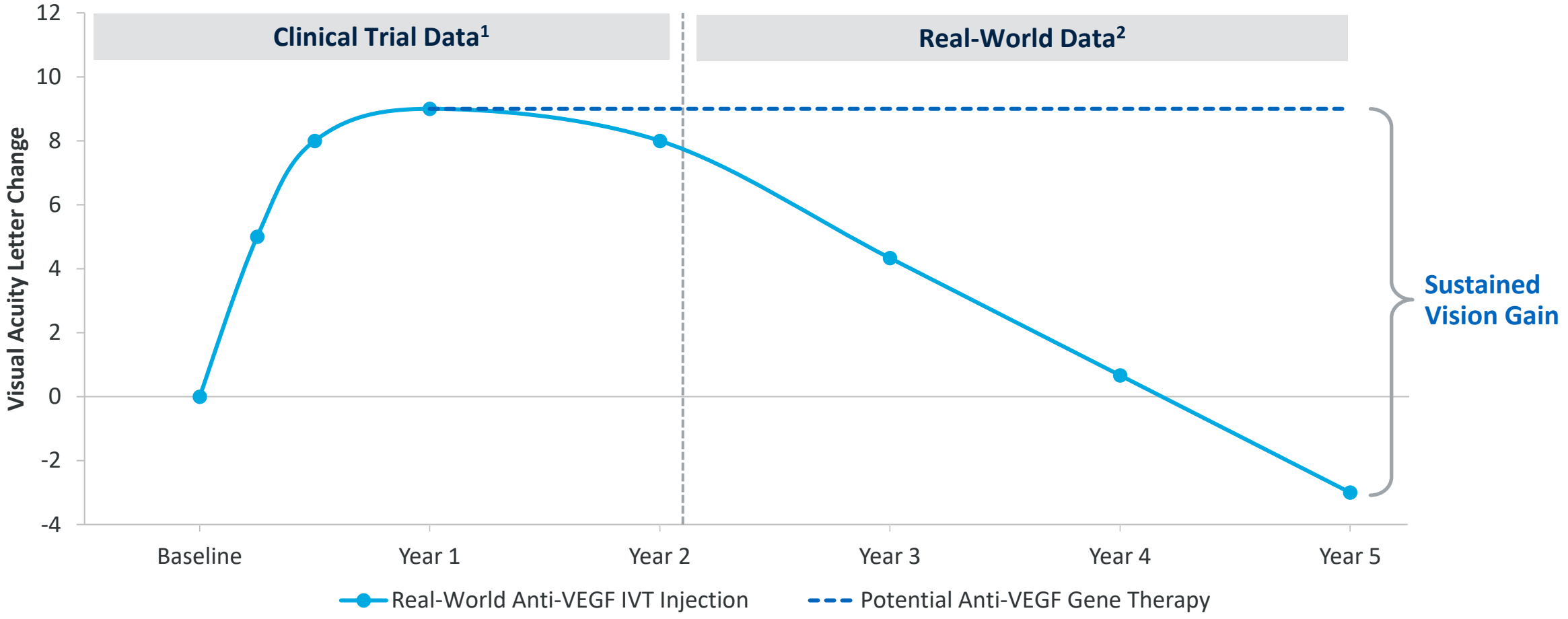
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

Ocular Gene Therapy Has the Potential to Close the Gap Between Randomized Clinical Trials and Real-World Outcomes

Visual Acuity Over Time in nAMD



Adapted from: 1. HARBOR (n = 1098) and CATT data (n = 1208); 2. CATT data; Potential anti-VEGF gene therapy curve hypothesized.
nAMD: Neovascular age-related macular degeneration; VEGF: Vascular endothelial growth factor; IVT: Intravitreal.

The Potential of Bilateral Dosing of Gene Therapy in nAMD

nAMD is frequently a bilateral disease and the ability to treat both eyes with gene therapy is important

- Two other subretinal AAV gene therapies have treated IRD patients bilaterally[1,2]
- After exposure to AAVs, antibodies are formed, which could impact the potential to dose a 2nd eye[2]
- Outcomes of bilateral dosing may vary, depending on factors such as **route of administration**[1-3]
- For subretinal delivery of ABBV-RGX-314, presence of pre-existing antibodies to AAV8 did not impact safety, protein production or efficacy outcomes in the 1st eye[4]

1. LUXTURNA [package insert]. Philadelphia, PA: Spark Therapeutics, Inc. Revised April 2022. Accessed August 22, 2024. 2. MacLaren RE, et al. *Hum Gene Ther*. 2024;35(15-16):564-575. 3. Yiu G, et al. *Mol Ther Methods Clin Dev*. 2020;16:179-191.
4. Campochiaro, PA *et al.* The Lancet, Volume 403, Issue 10436, 1563 – 1573.
nAMD: Neovascular age-related macular degeneration; AAV: adeno-associated virus: IRD: inherited retinal disease

ABBV-RGX-314 for Treatment of Neovascular Age-related Macular Degeneration (nAMD)

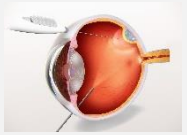
ABBV-RGX-314 PRODUCT CANDIDATE

NAV® VECTOR **AAV8**

GENE **Anti-VEGF fab**

ROUTES OF ADMINISTRATION

Subretinal (nAMD)

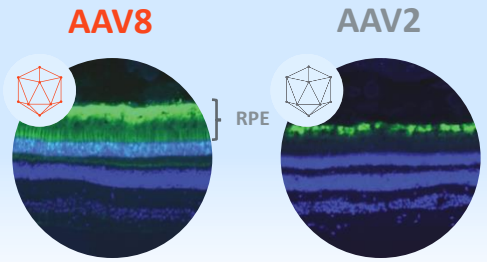


OR Suprachoroidal (nAMD/DR)

MECHANISM OF ACTION

Reducing leaky blood vessel formation by giving ocular cells the ability to produce an anti-VEGF fab

Improved AAV vector technology



More efficient gene delivery to the RPE[1]

+

Leveraging current standard of care in transgene

FDA-approved mAbs and mAb fragments that inhibit VEGF are the current standard of care for treatment of nAMD

ABBV-RGX-314 gene encodes an anti-VEGF mAb fragment (fab)

=

ABBV-RGX-314: AAV8 encoding anti-VEGF fab

Potential for long-term therapeutic anti-VEGF expression

1. Vandenberghe et al. 2011 Science Translational Medicine.

DR: Diabetic Retinopathy; AAV: Adeno-Associated Virus; VEGF: Vascular endothelial growth factor; RPE: Retinal pigment epithelium.

Current Program Status for ABBV-RGX-314

Subretinal

Phase 1/2a trial is complete

Phase 2 pharmacodynamic trial is ongoing

Phase 2b/3 pivotal trials are ongoing

ATMOSPHERE ASCENT

LONG-TERM FOLLOW-UP STUDY

Subretinal ABBV-RGX-314 for **nAMD** in patients from parent trials

FELLOW EYE SUB-STUDY

Investigating bilateral nAMD treatment

Suprachoroidal

Phase 2 trial is ongoing

AAVIATE

LONG-TERM FOLLOW-UP STUDY

Suprachoroidal ABBV-RGX-314 for **nAMD**

Phase 2 trial is ongoing

ALTITUDE

LONG-TERM FOLLOW-UP STUDY

Suprachoroidal ABBV-RGX-314 for **DR**

SUBRETINAL PROGRAM: Interim Results of Previous Studies

ABBV-RGX-314 for nAMD

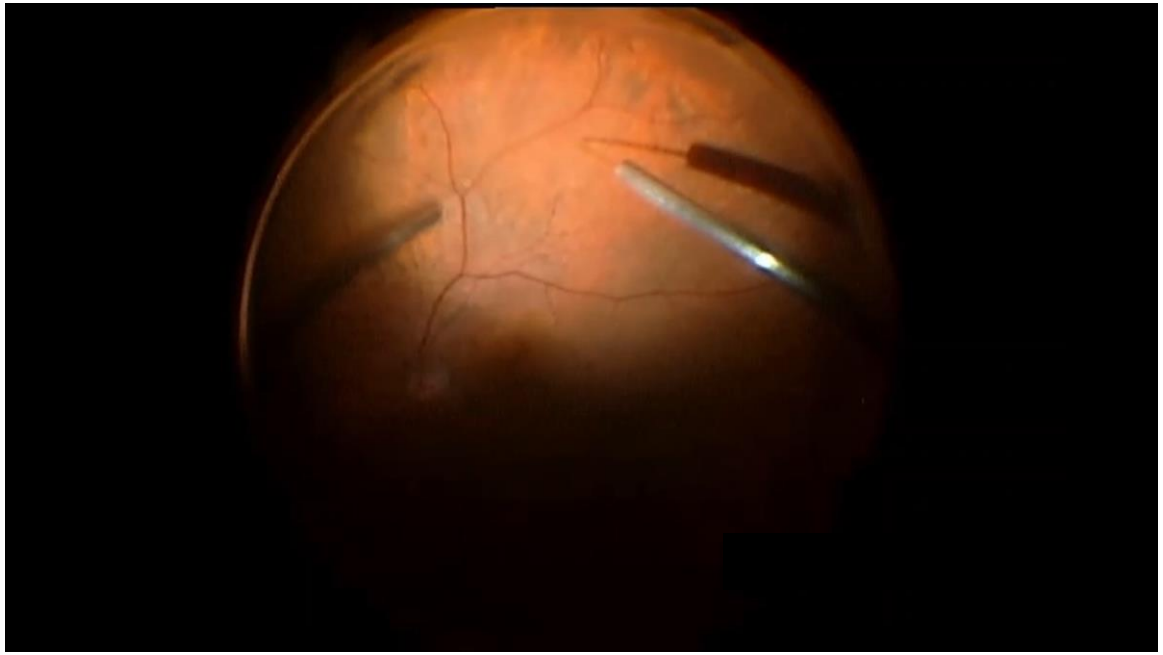
OVERALL SAFETY

ABBV-RGX-314 has been well tolerated across Phase I/IIa (up to 4 years)[1] and Phase II Pharmacodynamic studies (at 6 months)[2] at doses similar to pivotal study

EFFICACY ENDPOINTS

With a single injection of ABBV-RGX-314 at dose levels similar to the pivotal trial, patients demonstrate a long-term, durable treatment effect up to 4 years[1]

Stable to improved visual acuity	Meaningful reductions in anti-VEGF injection burden



Video: A. Khanani

Two Pivotal Trials Currently Enrolling: ATMOSPHERE® and ASCENT™

A fellow eye substudy is being conducted to evaluate the potential of **bilateral dosing in nAMD with subretinal ABBV-RGX-314**

1. Campochiaro PA. Presented at: AAO Annual Meeting; 2022, data cut August 29, 2022 (n=6). 2. Eichenbaum D. Presented at: Angiogenesis; 2024, data cut: November 20, 2023 (n=60).
nAMD: Neovascular age-related macular degeneration; VEGF: Vascular endothelial growth factor.
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

First Ever Bilateral Gene Therapy Clinical Trial for Treatment of nAMD

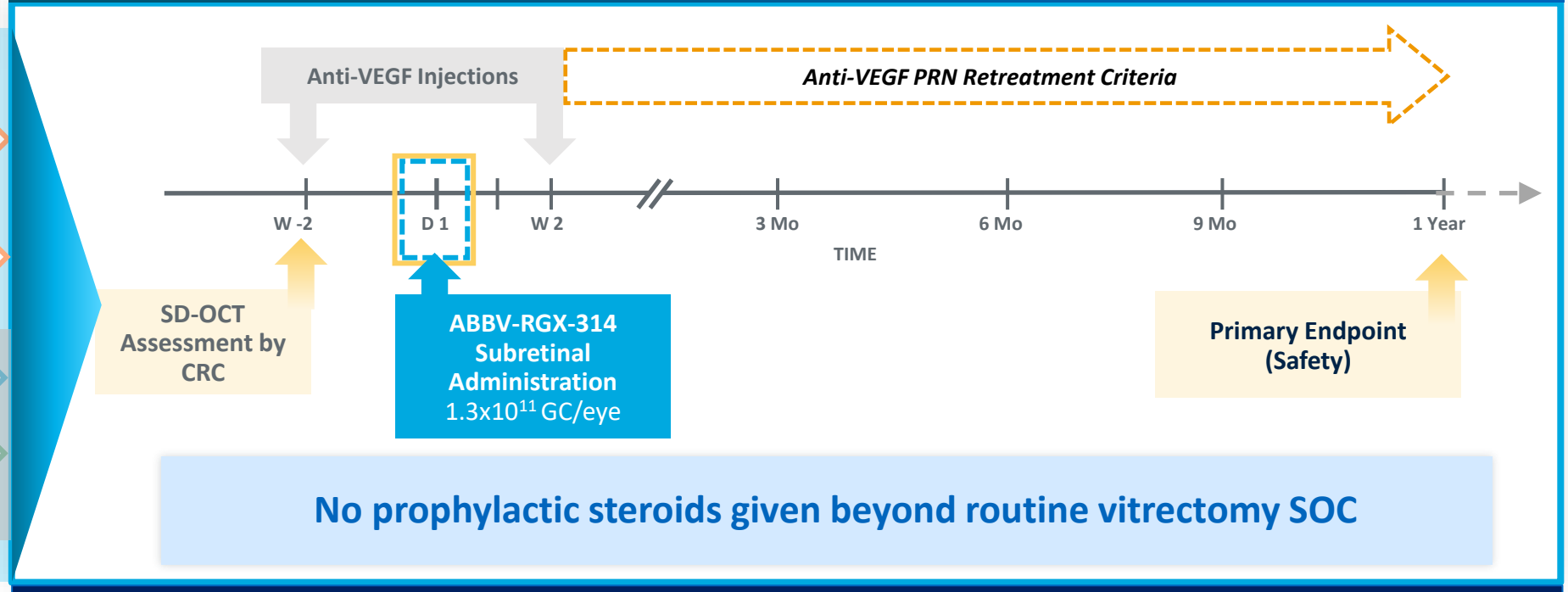
Fellow Eye Sub-Study of Subretinal ABBV-RGX-314

1st Eye treated:

- PHASE 1/2a STUDY n=3
- PHASE 2 PHARMACODYNAMIC STUDY n=7
- ATMOSPHERE
- ASCENT

Masked n=10

2nd Eye Treatment Evaluation (n=20)



No prophylactic steroids given beyond routine vitrectomy SOC

Study is designed to monitor safety, immune responses, and efficacy of ABBV-RGX-314 treatment in the fellow eye

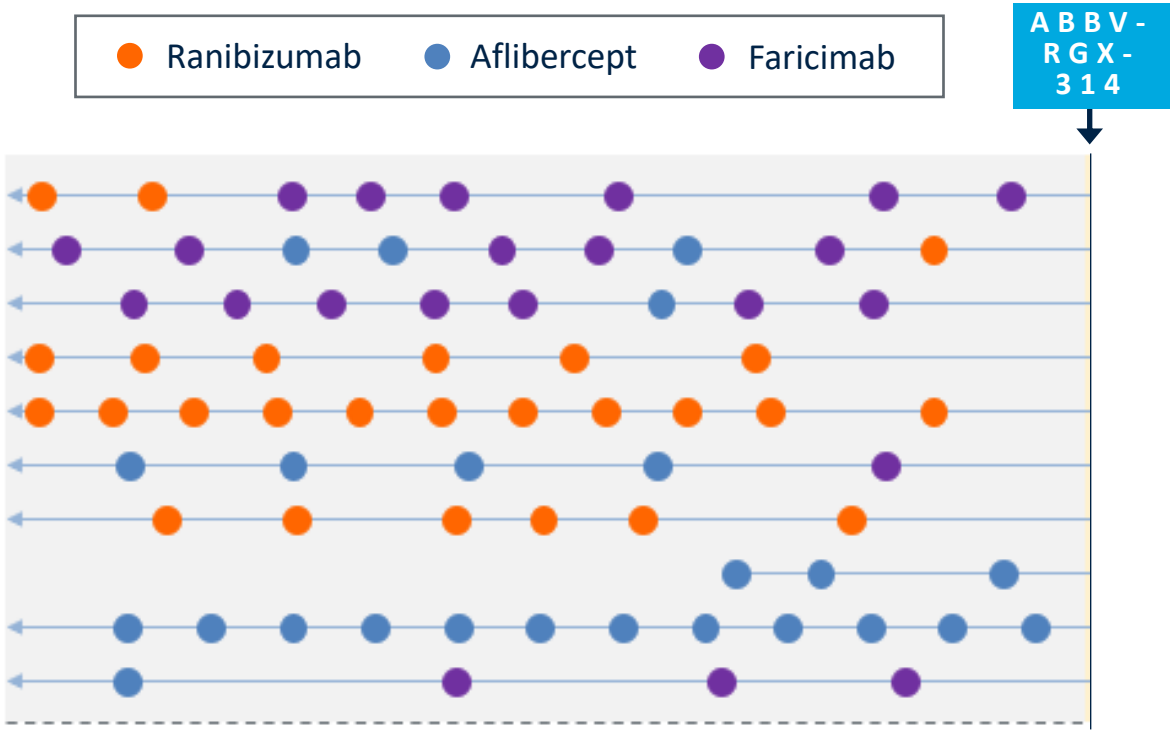
nAMD: Neovascular age-related macular degeneration; VEGF: Vascular endothelial growth factor; SOC: Standard of care; CRC: Central reading center; PRN: pro re nata; GC: genome copies.
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

Fellow Eye Sub-Study (FESS): Open Label Patient Population

FESS BASELINE DEMOGRAPHICS
(Open Label Patients Only)

	2nd Study Eye (n=10)
Mean age (years)	77.6
BCVA (letters)	72.1 (~20/40)
OCT (µm)	254.4
Injections in the past year (#)*	**8.2**
Average annualized injections in the past year (#)*	9.0

INJECTIONS IN YEAR PRIOR TO TREATMENT



2nd eyes had a high treatment burden, despite use of more durable agents

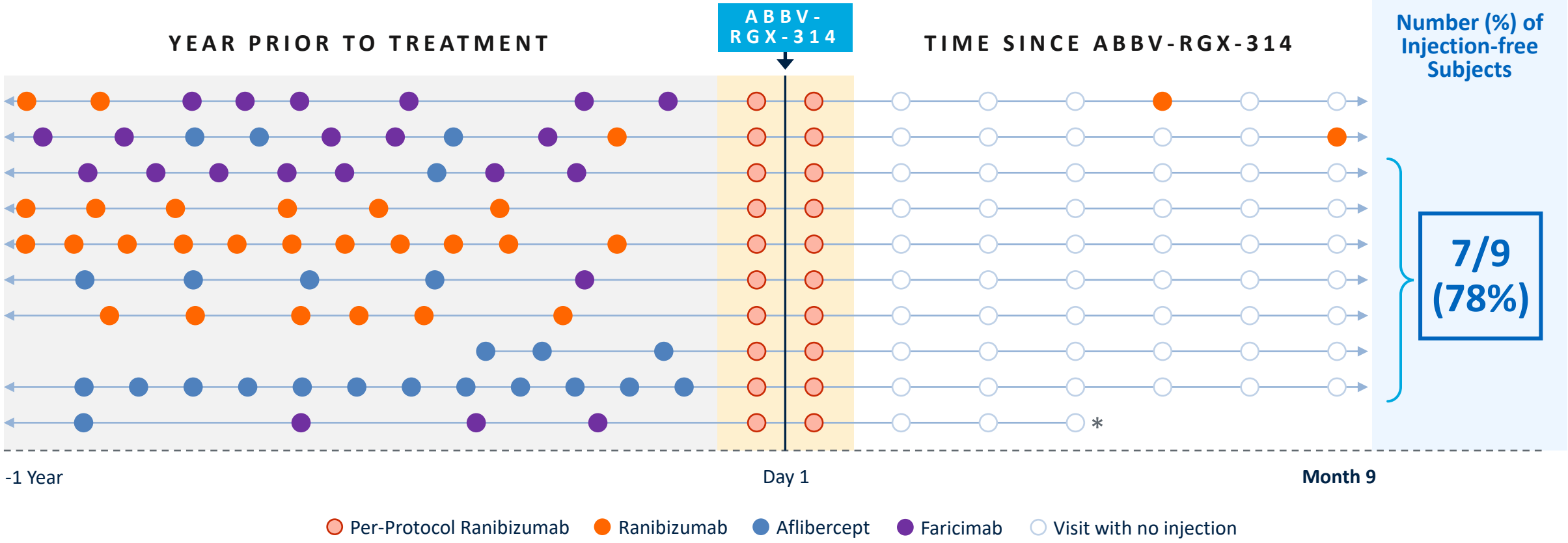
Data cut: September 11, 2024.
2nd eyes dosed approximately 1 year or more post-administration in 1st eye. Ocular variables refer to study eye only. Average annualized injections in the past year is: (Total # of prior injections)/(minimum (366 days, Duration between first injection and Week -2)/365.25). *Includes anti-VEGF injection at baseline visit.
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

Safety Summary for 2nd Eyes through Month 9

- **ABBV-RGX-314 was well-tolerated by all open-label subjects (n=10)**
- **No drug-related SAEs**
- No cases of intraocular inflammation, chorioretinitis, vasculitis, occlusion, or hypotony were observed
- Common AEs[1] in the treated fellow eye included:
  - Retinal pigmentary changes all occurring in periphery (20%) – all mild
  - Post-operative conjunctival hemorrhage (20%) – all resolved within days to weeks

Data cut: September 11, 2024.
2nd eyes dosed approximately 1 year or more post-administration in 1st eye.
1. Includes AEs for total open-label group ≥15% with onset up to 9m visit. Subjects are counted once for each Preferred Term regardless of the number of events.
SAE: Serious Adverse Event; AE: Adverse event.
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

78% of Treated 2nd Eyes Were Injection-free through 9 Months

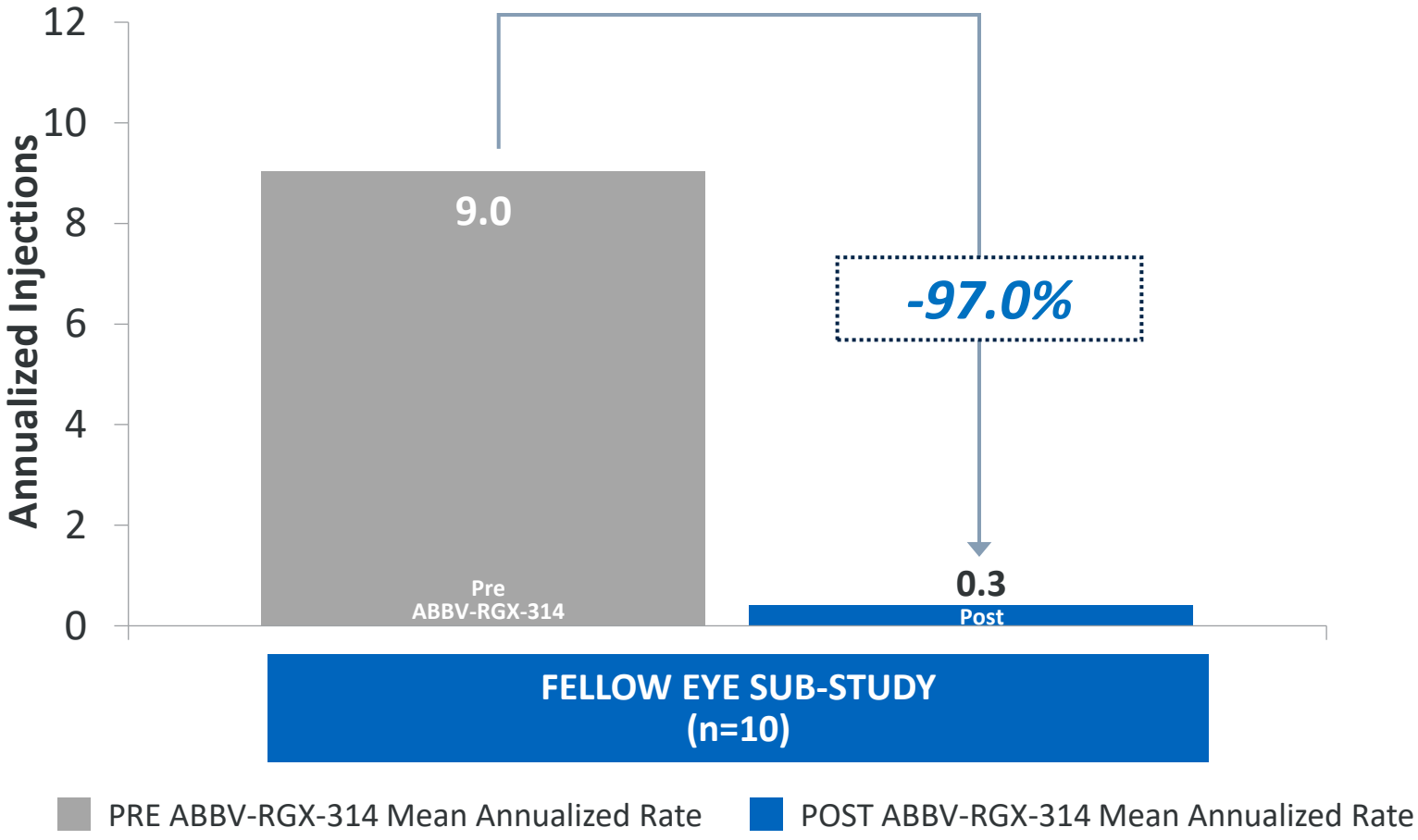


100% of Treated 2nd Eyes Required Either Zero or One Supplemental injection post-ABBV-RGX-314 administration

Data cut: September 11, 2024.
*One subject withdrew after their Month 2 visit.
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

Subjects Had Meaningful Reduction in Anti-VEGF Injection Burden in 2nd Eyes Treated

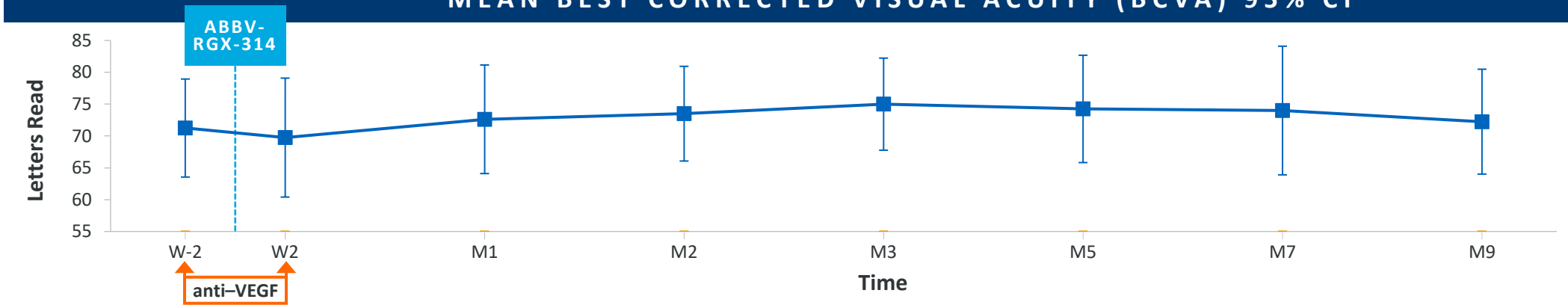
Annualized Injection Rate Based on Month 9 Data



Data cut: September 11, 2024.
Average annualized injections in the past year is: (Total # of prior injections)/(minimum(366 days, Duration between first injection and Week -2)/365.25) and includes anti-VEGF injection at baseline visit 1 (Week -2). Prior Year injections were capped at 13. Post-dosing annualized rate is calculated based on supplemental injections through Month 9. This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

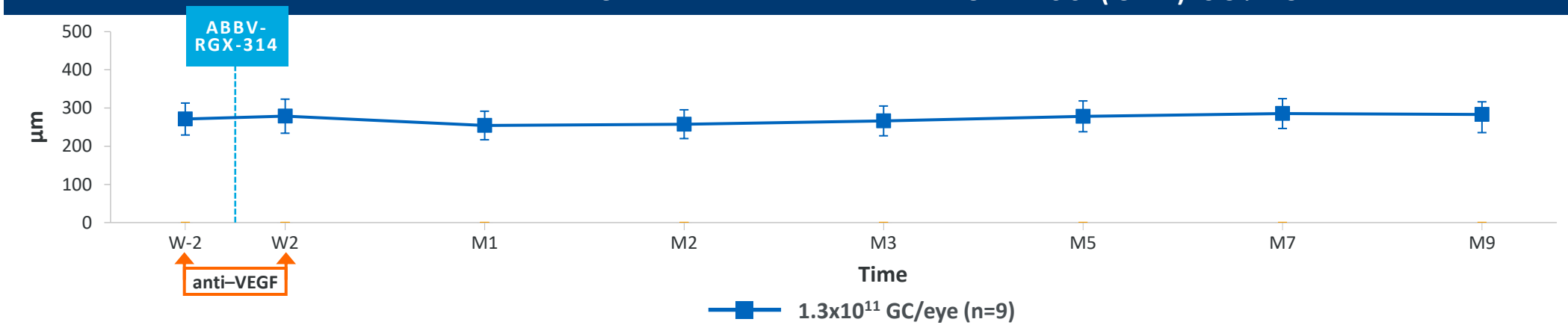
Treated 2nd Eyes Demonstrated Sustained BCVA and CRT through Month 9

MEAN BEST CORRECTED VISUAL ACUITY (BCVA) 95% CI



+1.1 Letters

MEAN CENTRAL RETINAL THICKNESS (CRT) 95% CI

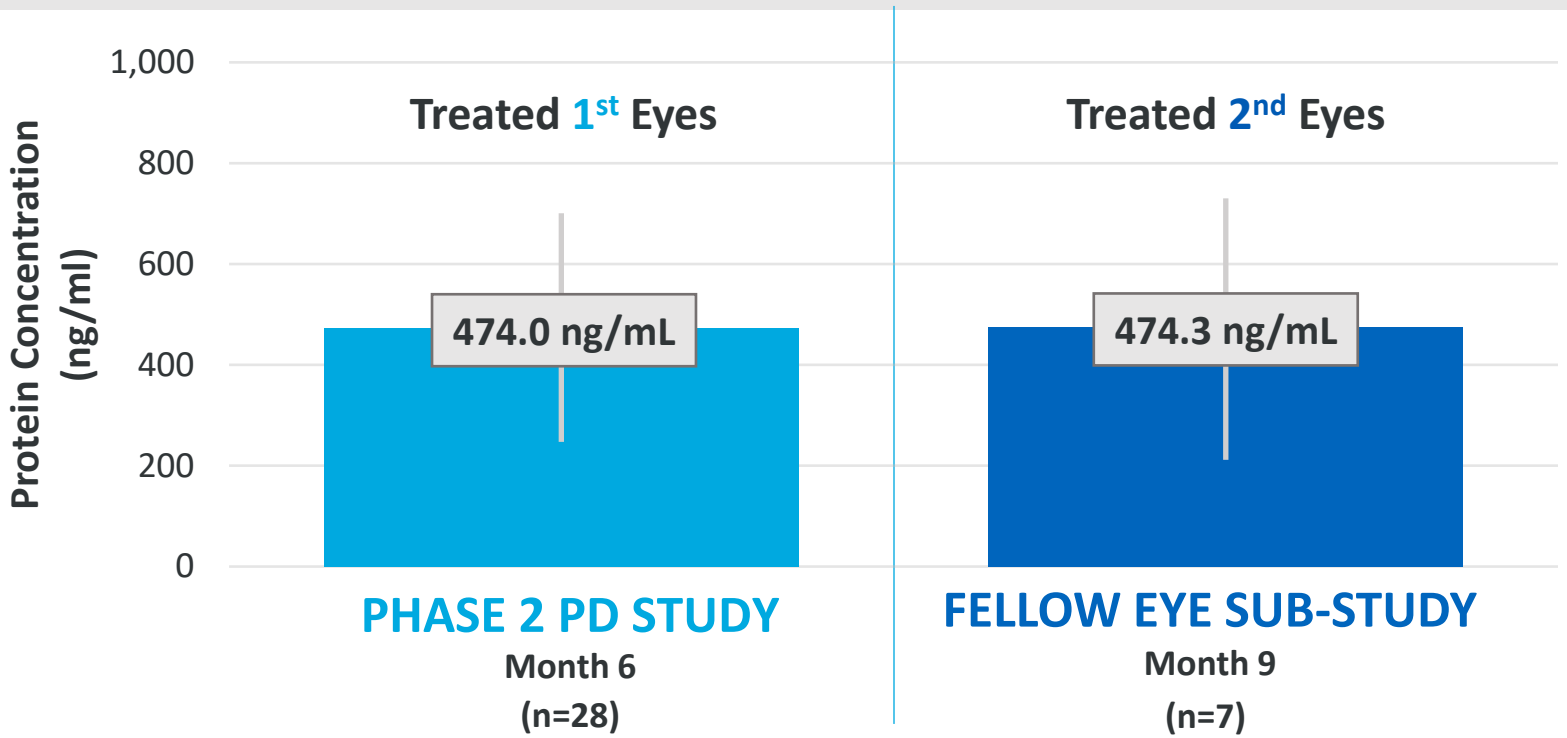


+11.7 µm

0.2 Injections — **Mean on-study Supplemental Injections through Month 9**

Data cut: September 11, 2024.
One subject withdrew after their Month 2 visit and is not included.
GC: genome copies.
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

Treated 2nd Eyes Produce Similar Levels of Aqueous Protein as 1st Eyes after Bilateral Treatment with ABBV-RGX-314



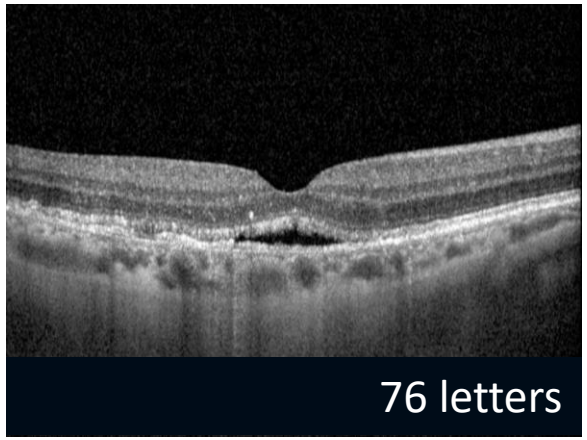
As Measured from Aqueous Samples by ECL at Month 6 (Ph2 Parent Study Eye) and Month 9 (Treated Fellow Eye) post-ABBV-RGX-314 ($1.3x10^{11}$ GC/eye)

Data cut: September 30, 2024.
Samples in the Phase 2 PD Study were not collected at Month 9, and samples were not collected in the FESS at Month 6.
One subject withdrew after their Month 2 visit. Two subjects' protein data were not available by the time of data cut.
PD: pharmacodynamic; ECL: electrochemiluminescence; GC: genome copies.
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

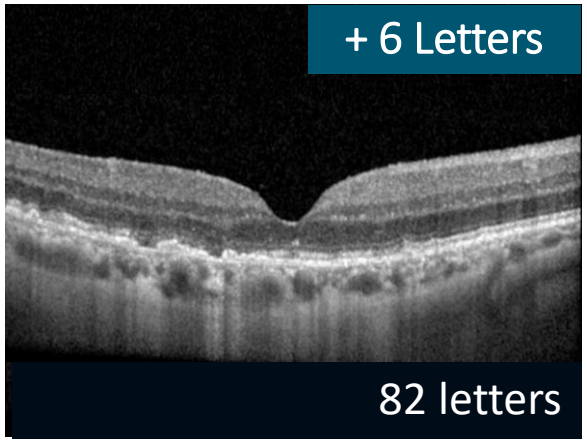
Patient Case: Pivotal Doses Administered in Both Eyes

Injection-free in Both Eyes

1st Eye: OD
Low Dose
$6.4x10^{10}$ GC/eye



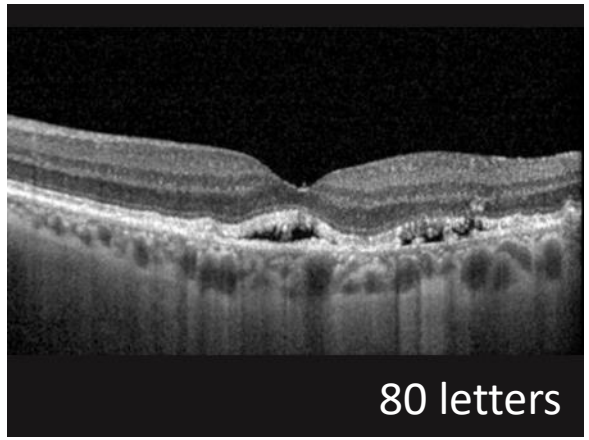
Baseline



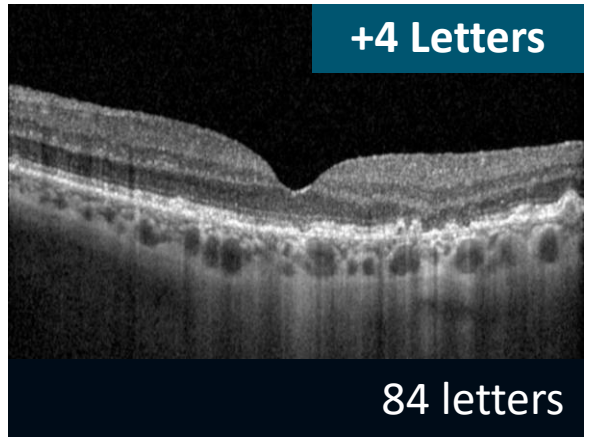
1 Year

Received 9 injections in the prior year

2nd Eye: OS
High Dose
$1.3x10^{11}$ GC/eye



Baseline



Month 9

Received 7 injections in the prior year

Data cut: September 11, 2024.
This slide presents results from an individual patient and is not indicative of outcomes experienced by all patients in this trial. Case courtesy of Stephen Huddleston MD.
GC: genome copies.
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

2nd Eyes Treated Achieved Similar Safety and Efficacy Outcomes to 1st Eyes Treated with ABBV-RGX-314

9 Month Results of ABBV-RGX-314 Subretinal 2nd Eye Treatment

Well-tolerated

Sustained vision and anatomy

Similar protein expression

Meaningful reduction in anti-VEGF injections in patients with high treatment burden

- 78% Injection-free
- 100% Required 0 or 1 Supplemental injection
- 97% Reduction in anti-VEGF treatment burden

Results from Open label participants only.
Data cut: September 11, 2024; Mean protein data cut: September 30, 2024.
Average annualized injections in the year prior to treatment with ABBV-RGX-314: 9.0 injections.
This is a preliminary analysis performed by REGENXBIO for an ongoing trial.

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