Suprachoroidal Delivery of Investigational ABBV-RGX-314 for Neovascular AMD: Results from the Phase II AAVIATE® Study

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Financial Disclosures

Alcon, G
Apellis, G
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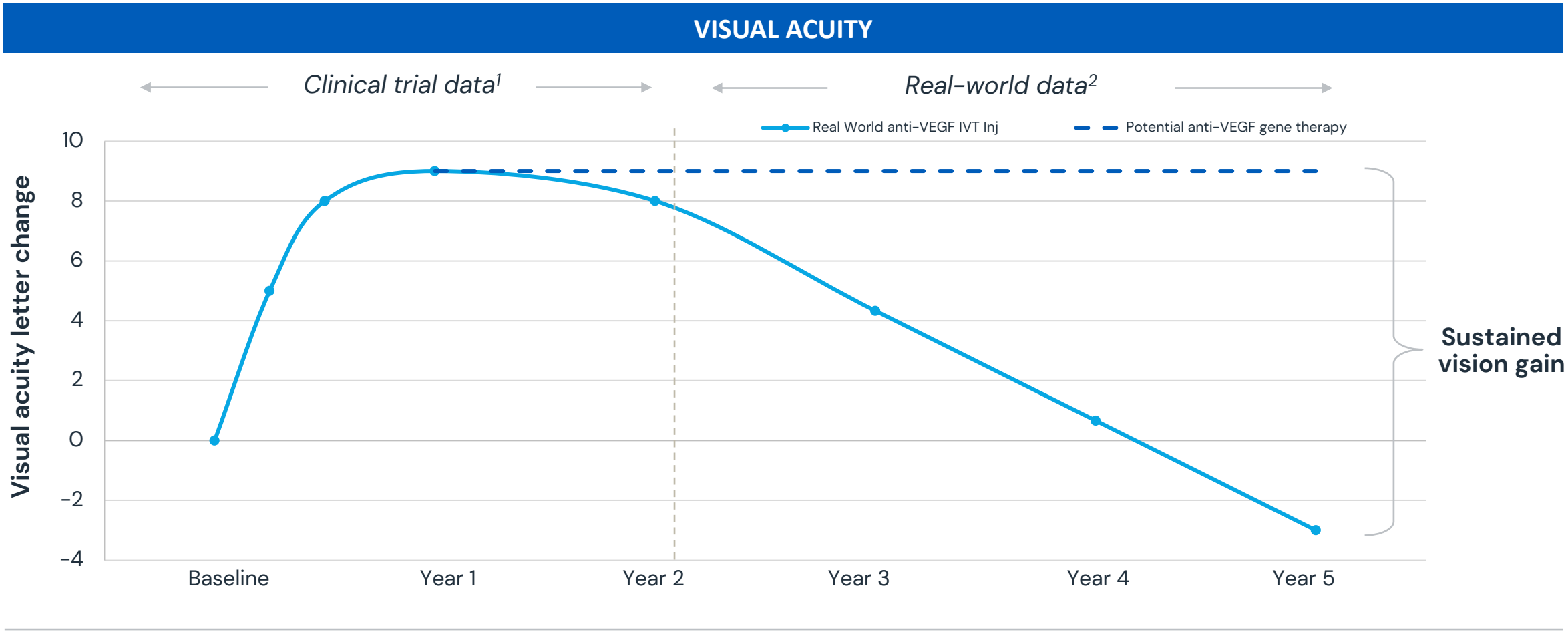
Genentech, C, G, S
Ionis, C, G
Novartis, G, S
Ocuphire, G
Ocuterra, G
Ophtea, G
REGENXBIO, C, G, S
Regeneron, C, G, S
Roche, G
Santen, G
Sydnexis, G

C – Consultant | G – Grants and Research Support | S – Speaker

Unlike Real World experience, a single treatment with ABBV-RGX-314 has the potential to close the gap between randomized clinical trials and real-world outcomes



1. HARBOR (n = 1098) and CATT data (n = 1208); 2. CATT data; Potential anti-VEGF gene therapy curve hypothesized

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

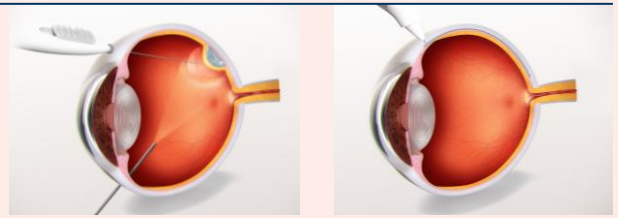
ABBV-RGX–314 PRODUCT CANDIDATE

Vector: AAV8 | **Gene:** anti-VEGF fab

Route of administration:

Subretinal (nAMD) or

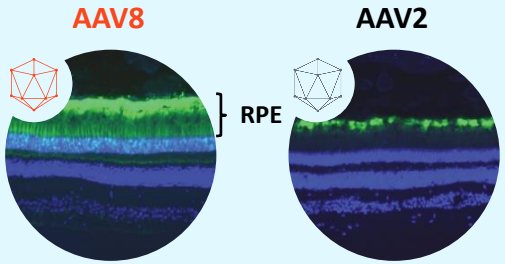
Suprachoroidal (nAMD/DR)



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)**

=

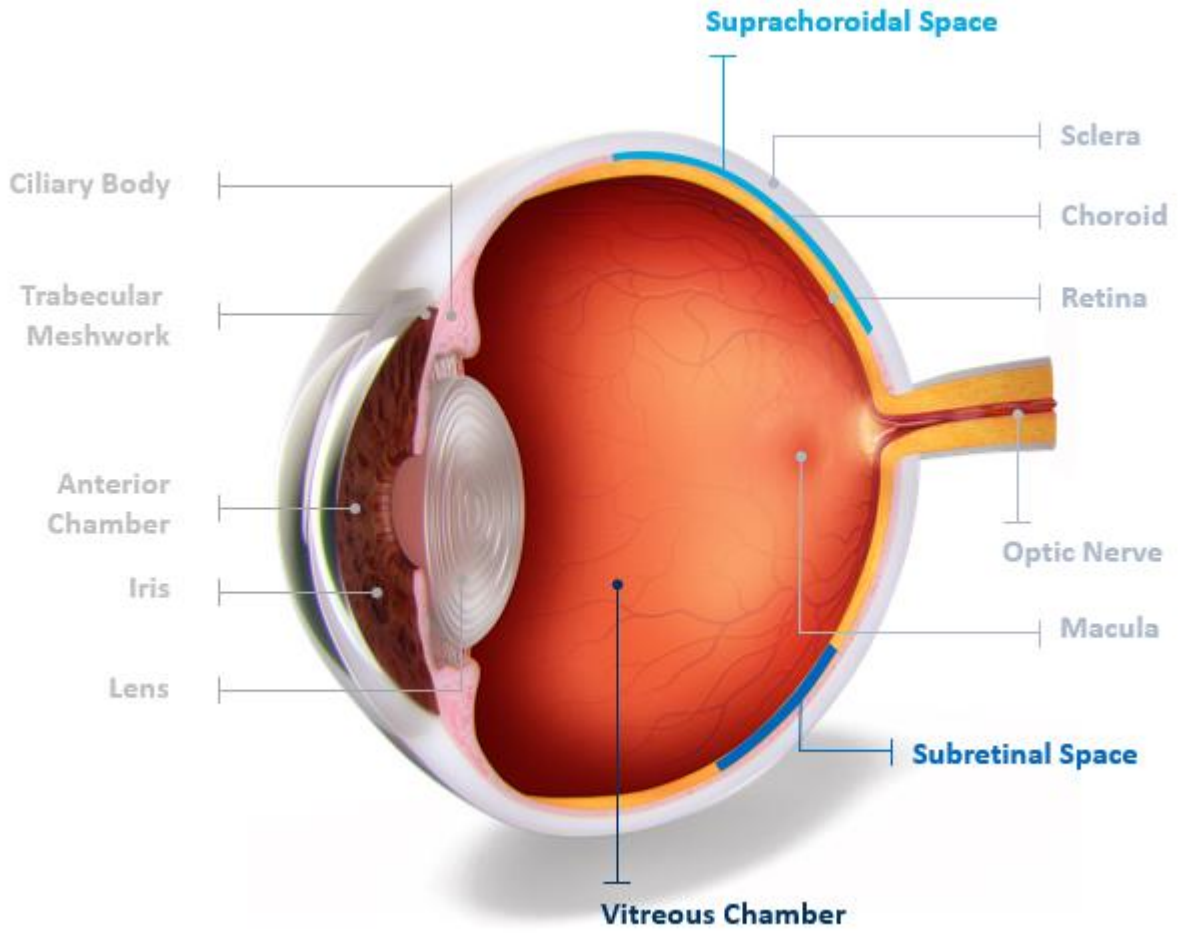
ABBV-RGX–314: AAV8 encoding anti–VEGF fab

Potential for long-term therapeutic anti-VEGF expression

1. Vandenberghe et al. 2011 Science Translational Medicine.

AAV: Adeno-Associated Virus

Ocular gene therapy delivery methods
Comparative profiles



Delivery Space Considerations

Suprachoroidal Space (SCS)[1]

- Targeted access and broad transduction of the retinal cells observed in preclinical studies
- Compartmentalized AAV delivery
- Minimal exposure to the vitreous and anterior segment

Subretinal Space[2,3]

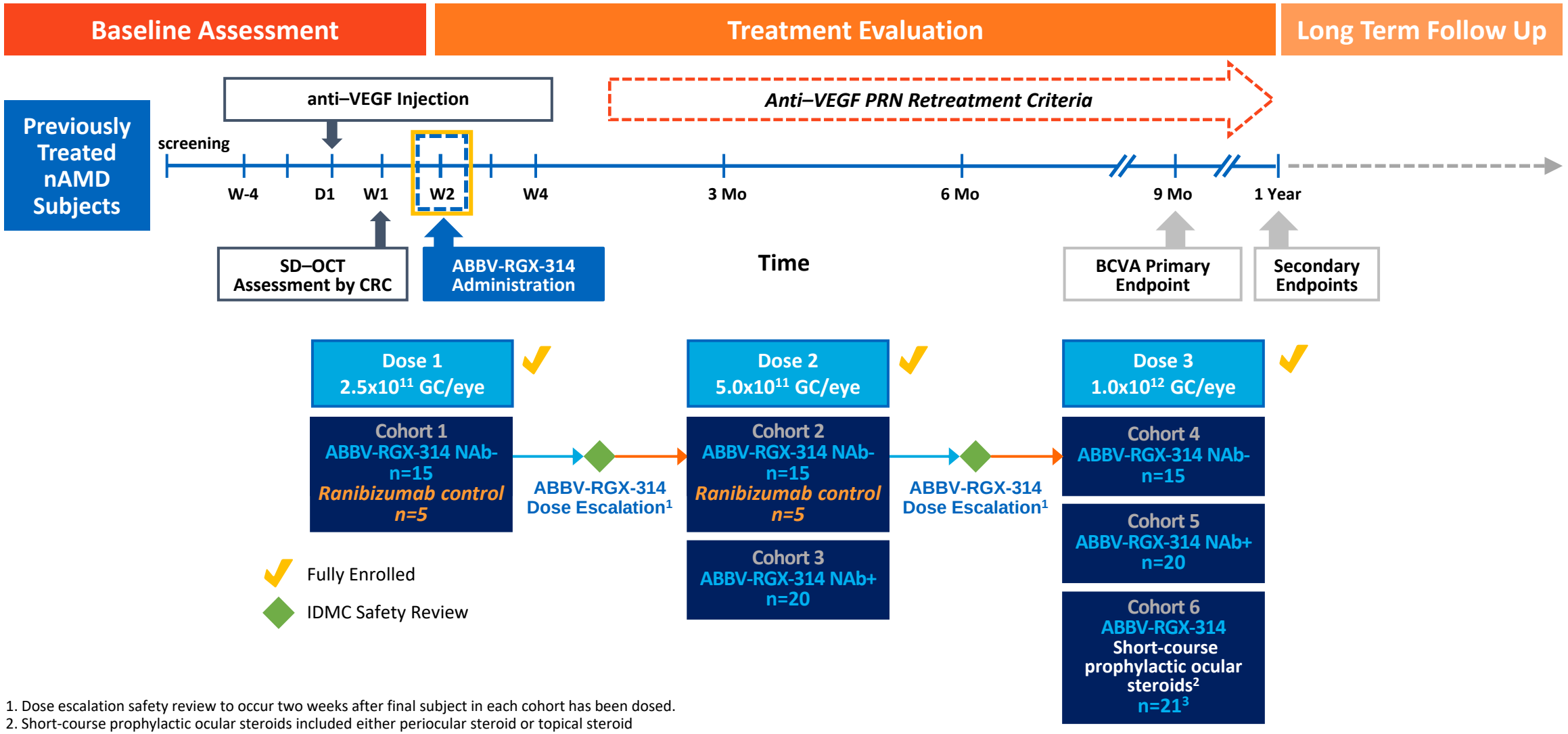
- Targeted access and broad transduction of the retinal cells observed in preclinical studies
- Compartmentalized AAV delivery
- Minimal exposure to the vitreous and anterior segment
  - Low risk of immune response
  - Low risk of inflammation

Vitreous Chamber

- Inner limiting membrane (ILM) presents physical barrier, potentially limiting direct transduction of the retina[3]
  - Limited transduction of the retina observed in preclinical studies[4]
- Broad exposure to the vitreous and anterior segment
  - High risk of immune response[5,6]
  - High risk of inflammation[7]

[1] Ding, K., et al. 2019 *Journal of Clinical Investigation*, [2] Vandenberghe et al. 2011 *Science Translational Medicine*, [3] Maclaren et al. 2016 *Lancet*, [4] Yin L, et al. 2011 *IOVS*, [5] Bennett, J., et al., 2017 *Human Gene Therapy*, [6] Heier JS, et al. 2016 *Lancet*, [7] Bouquet C, et al. 2019 *JAMA Ophthalmology*

AAVIATE®: Study Design



1. Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed.
2. Short-course prophylactic ocular steroids included either periocular steroid or topical steroid
3. Additional anti–VEGF Run-in Injections given at W-4 and W4

NAb+ = AAV8 neutralizing antibody positive; NAb- = AAV8 neutralizing antibody negative/low.

AAVIATE®: ABBV-RGX-314 Phase II Clinical Trial in nAMD

Primary Objective

- To evaluate the mean change in BCVA for ABBV-RGX-314 compared with ranibizumab monthly injection at Month 9

Secondary Objectives

- Safety and tolerability of ABBV-RGX-314
- Change in central retinal thickness (CRT) as measured by Spectral Domain Optical Coherence Tomography (SD-OCT)
- Additional anti-VEGF injections post-ABBV-RGX-314

Retreatment Criteria

- Based on worsening vision and/or fluid

Subjects: 116 patients enrolled in Dose Levels 1-3

- **15 study sites** across the United States

Route of Administration

- In-office SCS Microinjector™ delivers ABBV-RGX-314 to the **suprachoroidal space**

Key Inclusion Criteria

- Male or female ≥ 50 to 89 years of age
- Previously treated nAMD subjects with fluid on OCT at trial entry
- Documented response to anti–VEGF at trial entry (assessed by Reading Center)
- BCVA between ≤ 20/25 and ≥ 20/125 (≤ 83 and ≥ 44 Early Treatment Diabetic Retinopathy Study [ETDRS] letters) in the study eye
- Phakic or Pseudophakic

AAVIATE® Baseline Characteristics – All Patients (Dose Levels 1–3)

	Variable	Control Ranibizumab (N=10)	Dose Level 1 2.5×10^{11} (N=15)	Dose Level 2 5.0×10^{11} (N=35)	Dose Level 3 1.0×10^{12} (N=56)	Total (N=116)
BASELINE	**Mean Age** (Years)	75.9	74.0	74.9	77.3	76.0
	Screening BCVA (Letters)	72.7	75.1	71.9	72.8	72.8
	Screening OCT (Microns)	240.3	269.2	270.0	247.9	256.7
	Phakic n (%)	3 (30.0%)	6 (40.0%)	17 (48.6%)	29 (51.8%)	55 (47.4%)
PRIOR THERAPY	**Months Since nAMD Diagnosis** (Mean)	27.1	30.2	19.0	20.9	22.1
	# Injections Since nAMD Diagnosis (Mean)	13.4	20.6	10.3	12.4	12.9
	# Injections in the Past Year (includes 1 protocol mandated)	6.8	7.2	6.1	6.3	6.4
	Average Annualized Injections in the Past Year ((includes 1 protocol mandated)	8.8	9.7	8.8	8.9	9.0

Average annualized injections in the past year is: (Total # of prior injections)/(minimum(366 days, Duration between first injection and Day 1)/365.25). One patient in DL3 is missing number of historical injections.

AAVIATE® Dose Level 1–3 Interim Safety Summary through 6 Months

ABBV-RGX–314 has been well–tolerated in Dose Level 1–3 for AAVIATE (n=106)

- No study drug-related SAEs
- No cases of chorioretinitis, vasculitis, occlusion, or hypotony

Common Ocular TEAEs[1] in the Study Eye through Month 6	Dose Level 1 **No** PPX (N=15)	Dose Level 2 **No** PPX (N=35)	Dose Level 3 (N=56)		
			No PPX (N=35)	**With** PPX One-time Subtenon Steroid (N=11)	**With** PPX Topical Steroid (N=10)
Episcleritis[2]	0	5 (14.3%)	13 (37.1%)	2 (18.2%)	3 (30.0%)
Conjunctival Hyperemia	2 (13.3%)	2 (5.7%)	14 (40%)	2 (18.2%)	1(10.0%)
Intraocular Inflammation (IOI)[3]	4 (26.7%)	6 (17.1%)	7 (20.0%)	2 (18.2%)	0
Conjunctival Hemorrhage	5 (33.3%)	5 (14.3%)	3 (8.6%)	2 (18.2%)	0
Intraocular Pressure Increased[4]	1 (6.7%)	5 (14.3%)	5 (14.3%)	3 (27.3%)	0

Zero cases of IOI with short-course prophylactic topical steroids

Data cut: November 06, 2023.
1. Includes AEs ≥10% of the total groups.
2. All mild to moderate (grade 1 and 2), presented within 1 week to 26 weeks post injection and resolved or are tapering off topical corticosteroids.
3. All cases were mild to moderate (range +0.5 to 2+), most presented 2-6 weeks post injection, predominantly as anterior cells on slit lamp examination. Resolved on topical corticosteroids
4. Intraocular pressure increased and ocular hypertension have been combined into one group. All mild to moderate and all controlled.

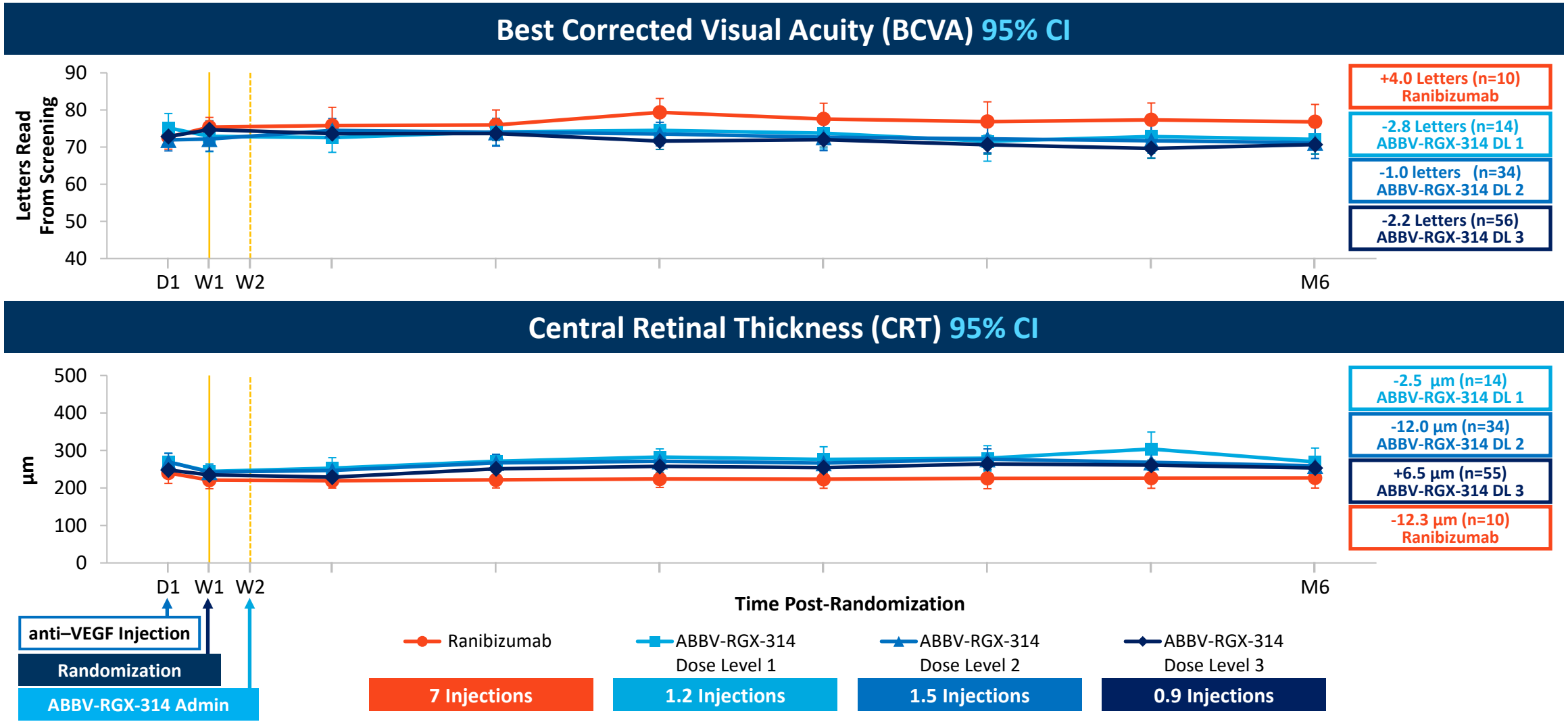
AAVIATE® Cohort 6 with Short-course Prophylactic Ocular Steroids:
Zero cases of IOI with Topical Steroids

ABBV-RGX-314

	SUBJECT	Dosing	D2	W1	W2	W4	W6	W8	W10	W12	W14	W16	W18	W20	W22	W24	W26
Periocular Steroid	COHORT 6		Periocular Steroid														
	Patient 1			0	0	0	0		0		–		0		0		0
	Patient 2			0	0	0	0		0		0		0		0		0
	Patient 3			0	0	0	0		0		0		0		0		0
	Patient 4			0	–	0	0		0		0.5* AC		0		0		0
	Patient 5			0	0	0	0		0		0		0		0		0
	Patient 6			0	0	0	0		0		0		0		0		0
	Patient 7			0	0	0	0		0		0		0		0		0
	Patient 8			0	1* AC	0	0		0		0		0		0		0
	Patient 9			0	0	0	0		0		0		0		0		0
	Patient 10			0	0	0	0		0		0		0		0		0
	Patient 11[1]			0	0	0	0		0		0		0		0		0
Topical Steroid			Topical Steroid Drops (7 weeks)														
	Patient 1			0	0	0	0		0		0		0		0		0
	Patient 2			0	0	0	0		0		0		0		0		0
	Patient 3			0	0	0	0		0		0		0		0		0
	Patient 4			0	0	–	0		0		0		0		0		0
	Patient 5			0	0	0	0		0		0		0		0		0
	Patient 6			–	0	0	0		0		0		0		0		0
	Patient 7			0	0	0	0		0		0		0		0		0
	Patient 8			0	0	0	0		0		0		0		0		0
	Patient 9			0	0	0	0		0		0		0		0		0
	Patient 10			0	0	0	0		0		0		0		0		0

Data cut: November 06, 2023.
*Topical steroids PRN.
1. Subject received an incomplete dose of ABBV-RGX-314
IOI: Intraocular Inflammation: anterior chamber cells and flare, vitreous chamber cells and haze. Timepoints are post-dosing.

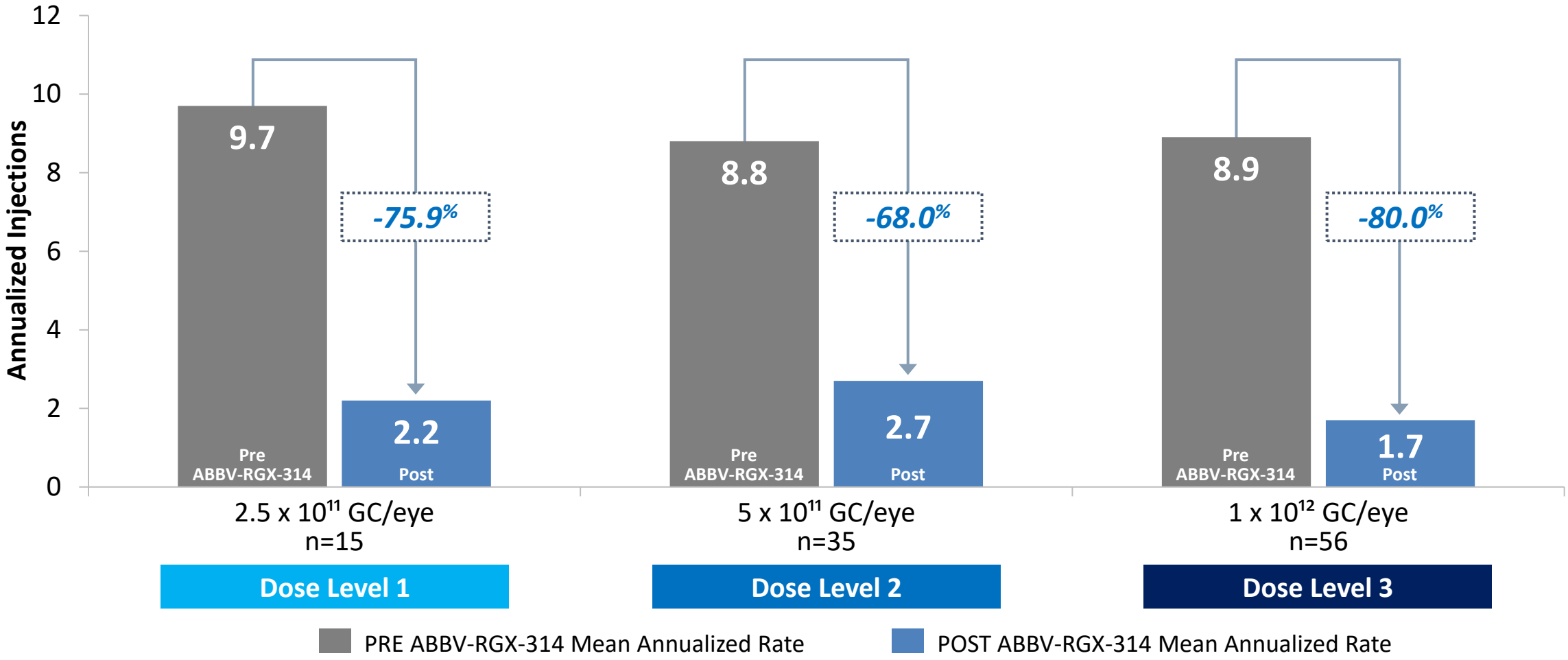
Dose Levels 1–3: Mean BCVA and CRT from Day 1 Through Month 6



Data cut: November 06, 2023.
Cohort 6 (DL3) patients were randomized at D1 and received additional anti–VEGF run-in injections at W-4 and W4.

Mean Change in Annualized Injection Rate PRE and POST ABBV-RGX-314 by Dose Level

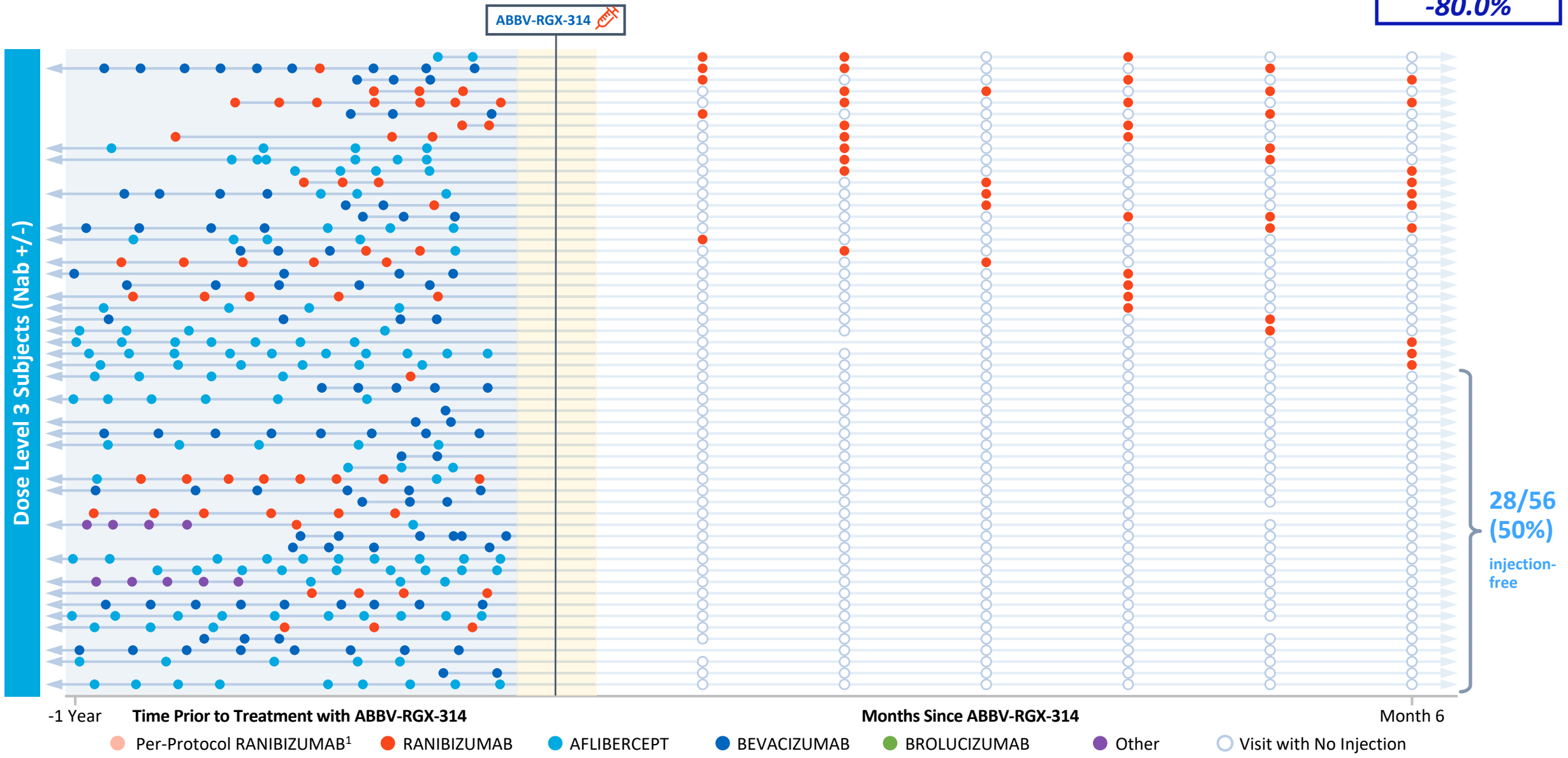
Annualized Injection Rate based on Month 6 Data



Data cut: November 06, 2023.
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 screening visit 1 (Week -2). Post-dosing annualized rate is calculated based on supplemental injections at Month 6.

Dose Level 3: Injections Pre and Post ABBV-RGX-314 (n=56) – 6 Month Data

Change in Annualized Injection Rate -80.0%



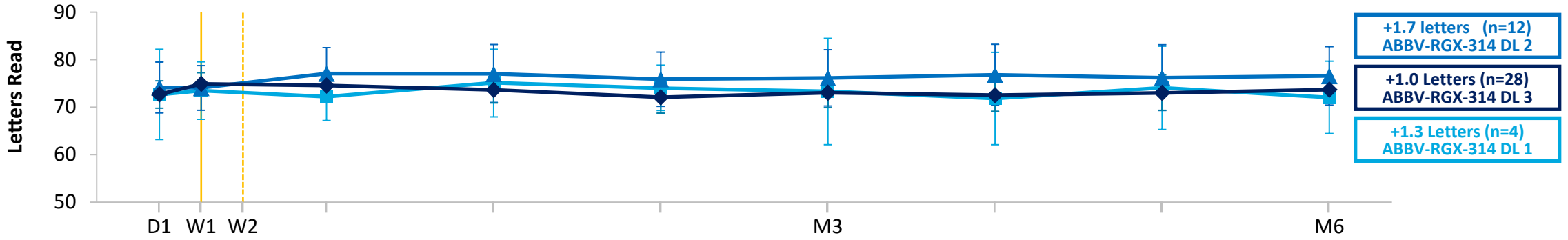
Data cut: November 06, 2023.

1. Protocol specified Ranibizumab injections included either 1 run-in injection or 2 run-in injections and 1 post ABBV-RGX-314 injection.

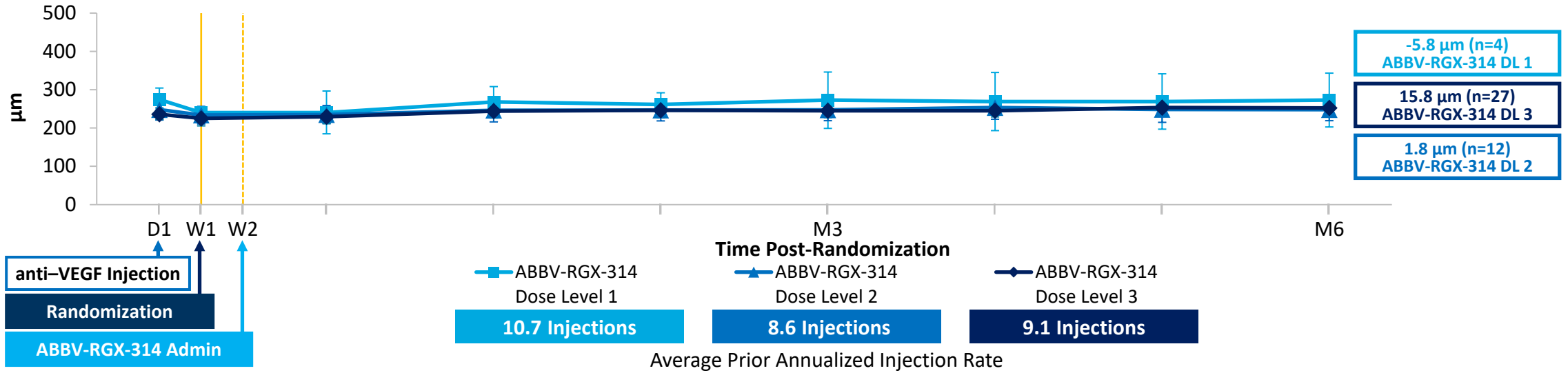
Dose Levels 1–3: No Anti-VEGF Injections over 6 Months

Mean BCVA and CRT from Day 1

Best Corrected Visual Acuity (BCVA) 95% CI



Central Retinal Thickness (CRT) 95% CI



Data cut: November 06, 2023. Cohort 6 (DL3) patients were randomized at D1 and received additional anti–VEGF run-in injections at W-4 and W4.

Summary of Interim Results from the Phase II AAVIATE® nAMD Study

ABBV-RGX-314 Dose Levels 1-3 (n=106): 6 Month Results

- Suprachoroidal ABBV-RGX-314 has been well-tolerated
- **Zero cases of IOI** in subset of Dose Level 3 with short-course prophylactic topical steroids
- **ABBV-RGX-314 continues to demonstrate stable vision and retinal thickness, with a meaningful reduction in treatment burden with the highest reduction seen in Dose Level 3:**
  - 80% reduction in annualized injection rate
  - 50% injection-free

Dose Level 3 continues to show encouraging interim results with a well-tolerated profile, including zero cases of IOI with short-course prophylactic topical steroids

Data cut: November 06, 2023.