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

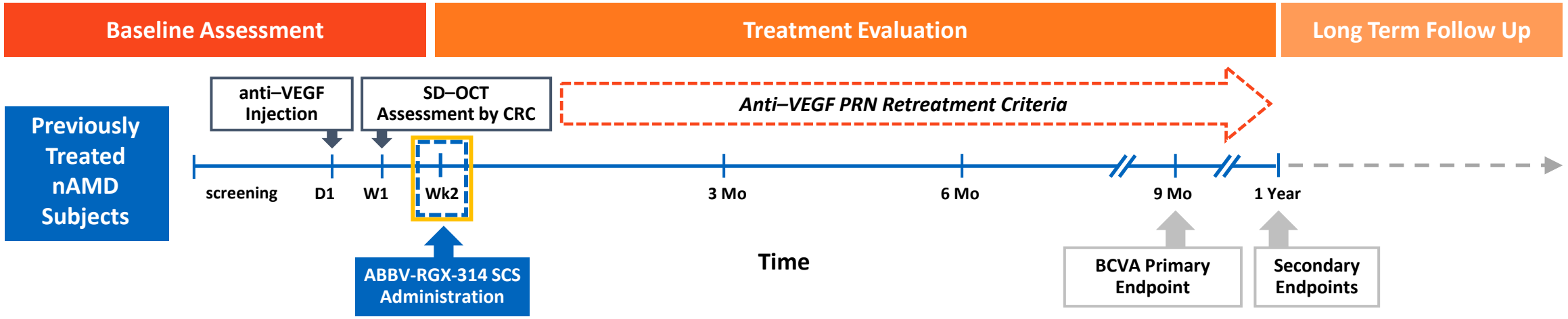
David Boyer, MD
Adjunct Clinical Professor Ophthalmology Keck School of Medicine
Partner Retina Vitreous Associates Medical Group

ASRS
30 July 2023

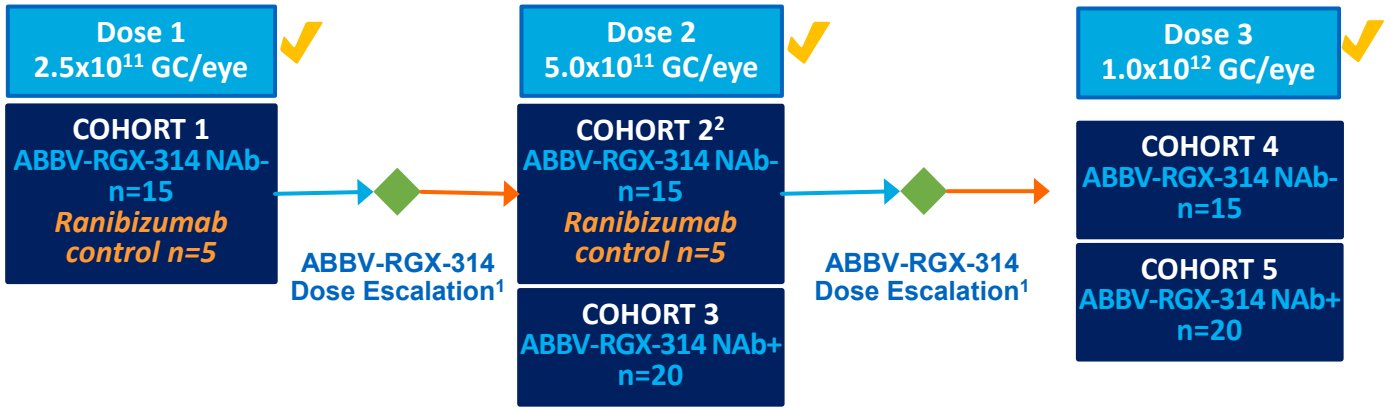
Disclosures

- **Consultant:** 4DMT, Adverum Biotech, AiViva, Alcon, Aldeyra, Alimera, Alkahest, Allegro, Allergan, Allgenesis, Amydis, Annexon, Apellis, AGTC, AsclepiX, Ashvattha, Aviceda, Bausch + Lomb, Bayer, Biovisics, Boehringer Ingelheim, Cell Care, Chengdu Kanghong, Clearside Bio, Curacle, Delsitech, EyePoint, Genentech, Glaukos, jCyte, IvericBio, Kriya, Kyowa Kirin, Lineage Cell, LumiThera, Nanoscope, NGM Bio, Novartis, Ocular Therapeutix, Ocugen, Oculis, Ocuphire, OcuTerra, Ocutrx, Opthea, Optigo, Optos, Oxurion, Palatin, Pfizer, REGENXBIO, Regeneron, RetinAI Medical AG, Ripple, Roche, Sanofi, Santen, Stealth Bio, Surrozen, Syneso, Thea Labs, Unity Bio, Vanotech, Verseon, Vitranu, Vitro Bio, ViviVision,
- **Contracted Research***:* Alcon, Allergan, Genentech, Novartis, Neurotech, Pfizer, Regeneron, Santen
- **Stock***:* Allegro

AAVIATE®: ABBV-RGX-314 Suprachoroidal (SCS) Phase II Clinical Trial in nAMD



No prophylactic steroids given throughout the study



✓ Fully Enrolled

◆ IDMC Safety Review

1. Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed.
2. Subjects in Cohort 2 received two doses of 100µL, all other cohorts received one dose of 100µL.

SCS: Suprachoroidal Space; 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 (“Rescue”)

Retreatment Criteria

- Based on worsening vision and/or fluid

Subjects: 95 patients enrolled in Cohorts 1-5

- **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 (Cohort 1 to 5)

	Variable	Control Ranibizumab (N=10)	Cohort 1 Dose 1 NAb- (N=15)	Cohort 2 Dose 2 NAb- (N=15)	Cohort 3 Dose 2 NAb+ (N=20)	Cohort 4 Dose 3 NAb- (N=15)	Cohort 5 Dose 3 NAb+ (N=20)	Total (N=95)
BASELINE	**Mean Age** (Years)	75.9	74.0	77.9	72.6	79.7	75.0	75.6
	Screening BCVA (Letters)	72.7	75.1	70.7	72.8	73.1	73.4	73.0
	Screening OCT (Microns)	240.3	269.2	275.7	265.8	256.9	271.0	264.9
	Phakic n (%)	3(30.0%)	6 (40.0%)	7 (46.7%)	10 (50.0%)	4 (26.7%)	10 (50.0%)	40 (42.1%)
PRIOR THERAPY	**Months Since nAMD Diagnosis** (Mean)	26.7	30.4	19.9	18.6	23.5	22.4	23.1
	# Injections Since nAMD Diagnosis (Mean)	13.4	20.6	11.1	9.7	16.4	13.4	13.8
	# Injections in the Past Year (includes Day 1)	6.8	7.2	6.0	6.2	7.1	6.5	6.6
	Average Annualized Injections in the Past Year (includes Day 1)	8.8	9.7	8.7	8.9	9.3	9.5	9.2

Average annualized injections in the past year is: (Total # of prior injections)/(minimum(366 days, Duration between first injection and Day 1)/365.25). NAb+ = AAV8 neutralizing antibody positive; NAb- = AAV8 neutralizing antibody negative/low

AAVIATE® Interim Safety Summary

- ABBV-RGX–314 was well–tolerated in Cohorts 1–5 (n=85) with follow-up ranging from 1–12 months post dosing
  - 15 SAEs: None considered drug-related
  - No cases of chorioretinal vasculitis or occlusion, or hypotony were observed

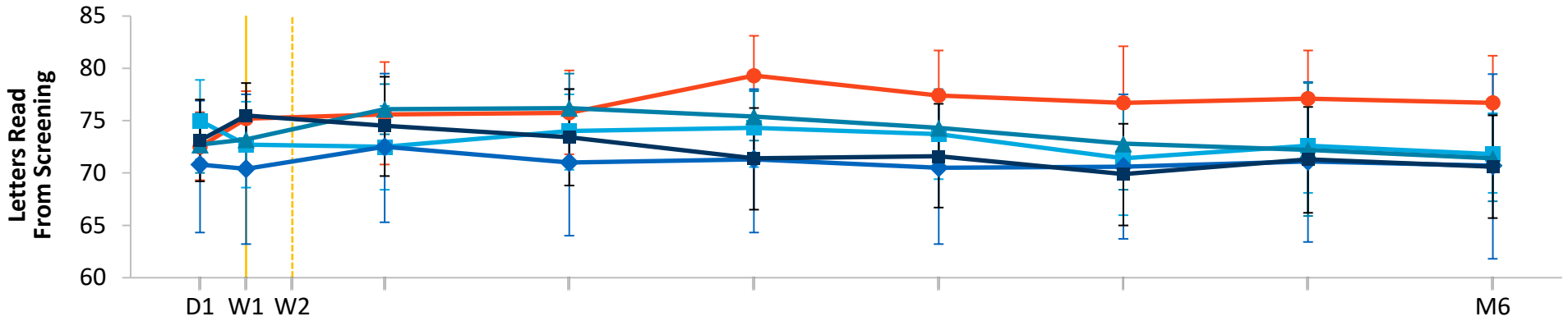
Cohort 1 to 4: Common Ocular TEAEs[1] in the Study Eye through 6 Months	Cohort 1 Dose 1 NAb- (N=15)	Cohort 2 Dose 2 NAb- (N=15)	Cohort 3 Dose 2 NAb+ (N=20)	Cohort 4 Dose 3 NAb - (N=15)	Total (N=65)
Intraocular Inflammation[2]	4 (26.7%)	3 (20.0%)	2 (10.0%)	6 (40.0%)	15 (23.1.%)
Conjunctival Hemorrhage	5 (33.3%)	2 (13.3%)	3 (15.0%)	1 (6.7%)	11 (16.9%)
Intraocular Pressure Increased[3]	1 (6.7%)	2 (13.3%)	3 (15.0%)	3 (15.0%)	9 (13.8%)
Conjunctival Hyperemia	2 (13.3%)	1 (6.7%)	1 (5.0%)	3 (20.0%)	7 (10.8%)
Episcleritis[4]	0	3 (20.0%)	2 (10.0%)	2 (13.3%)	7 (10.8%)

No meaningful differences based on **baseline AAV8 NAbs**

Data cut: August 01, 2022.
1. Includes AEs for total group ≥10% with onset up to 6m visit.
2. 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.
3. Intraocular pressure increased and ocular hypertension have been combined into one group. All mild to moderate and all controlled.
4. All mild (grade 1), presented 2-6 weeks post injection and resolved on topical corticosteroid or NSAID treatment.

Cohorts 1–4: Mean BCVA and CRT from Day 1 (Screening) Through Month 6

Best Corrected Visual Acuity (BCVA) 95% CI



+4.0 Letters (n=10) Ranibizumab

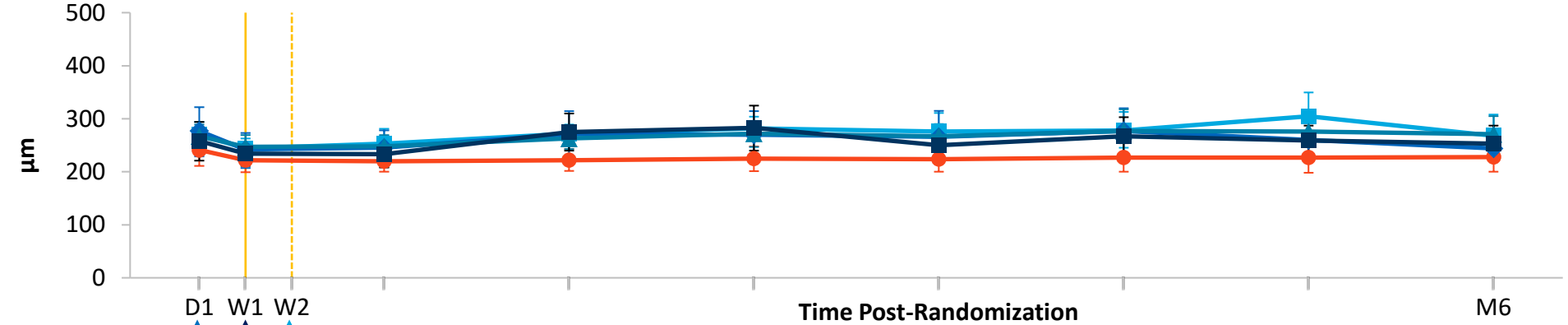
-2.8 Letters (n=14) ABBV-RGX-314 Cohort 1

-1.7 letters (n=19) ABBV-RGX-314 Cohort 3

-0.07 Letters (n=15) ABBV-RGX-314 Cohort 2

-2.5 Letters (n=15) ABBV-RGX-314 Cohort 4

Central Retinal Thickness (CRT) 95%CI



4.6 µm (n=19) ABBV-RGX-314 Cohort 3

-2.5 µm (n=14) ABBV-RGX-314 Cohort 1

-2.9 µm (n=15) ABBV-RGX-314 Cohort 4

-33 µm (n=15) ABBV-RGX-314 Cohort 2

-12.3 µm (n=10) Ranibizumab

anti–VEGF Injection

Randomization

ABBV-RGX-314 Admin

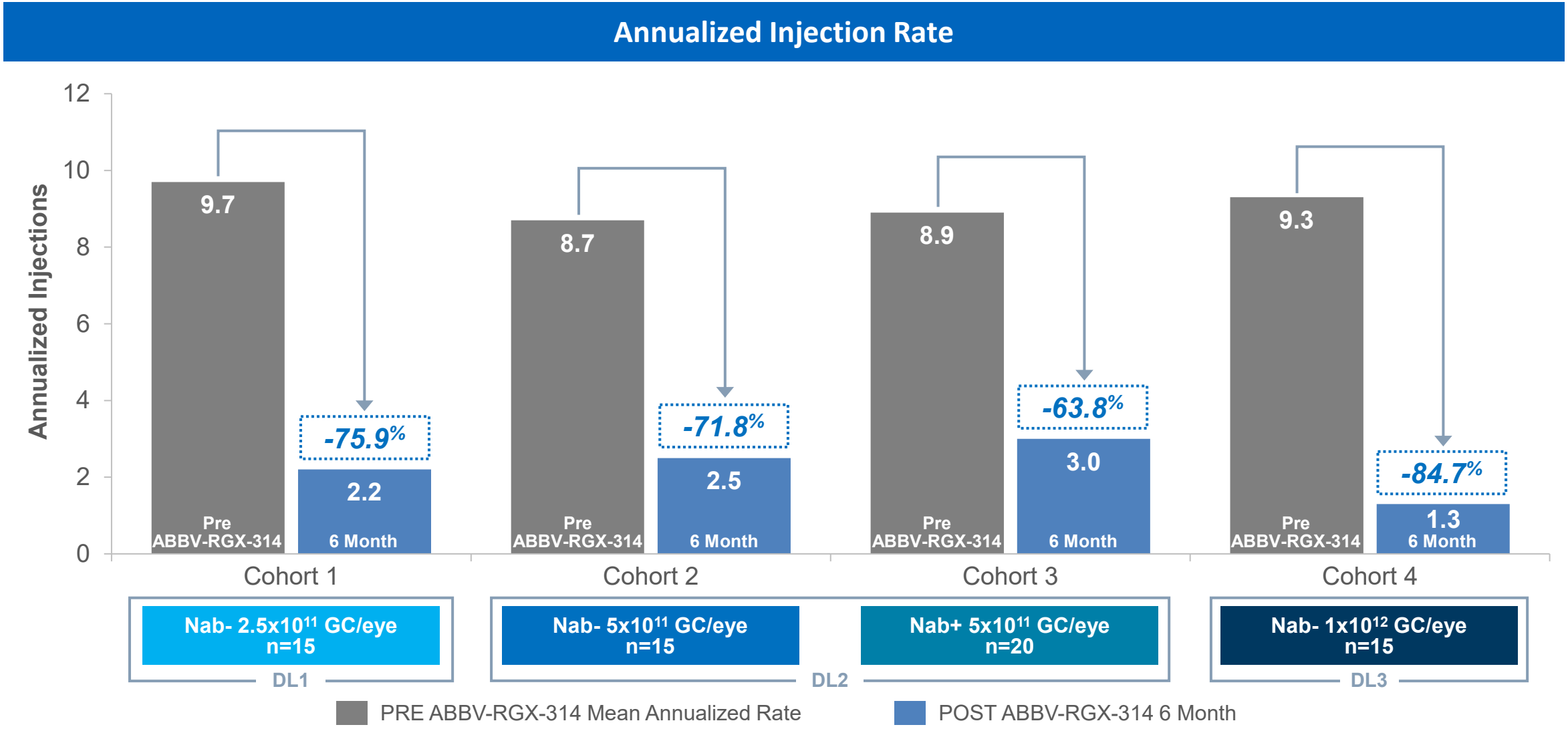
Ranibizumab | ABBV-RGX-314 Cohort 1 | ABBV-RGX-314 Cohort 2 | ABBV-RGX-314 Cohort 3 | ABBV-RGX-314 Cohort 4

7 Injections | 1.2 Injections | 1.3 Injections | 1.6 Injections | 0.7 Injections

Mean Injections Post-Randomization

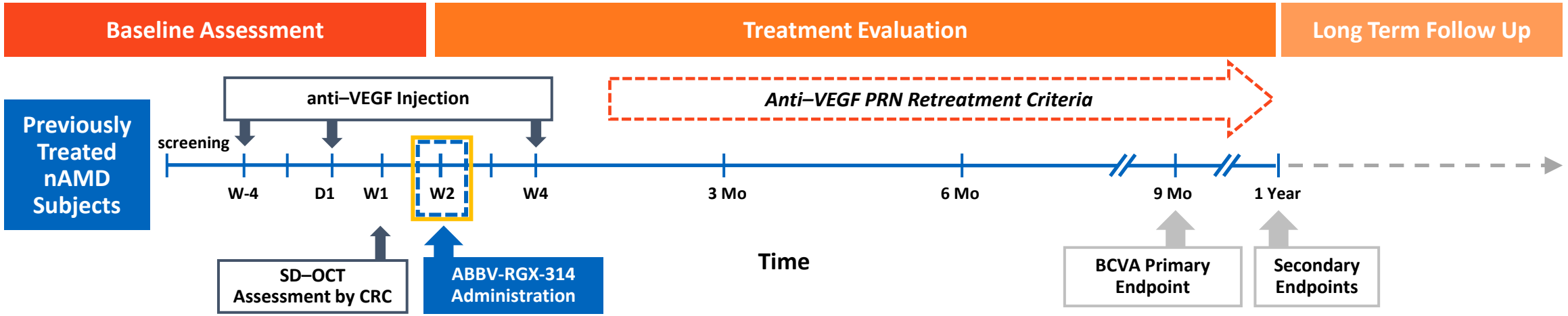
Data cut: August 1, 2022.

Mean Change in Annualized Injection Rate PRE and POST ABBV-RGX-314 in Cohorts 1–4

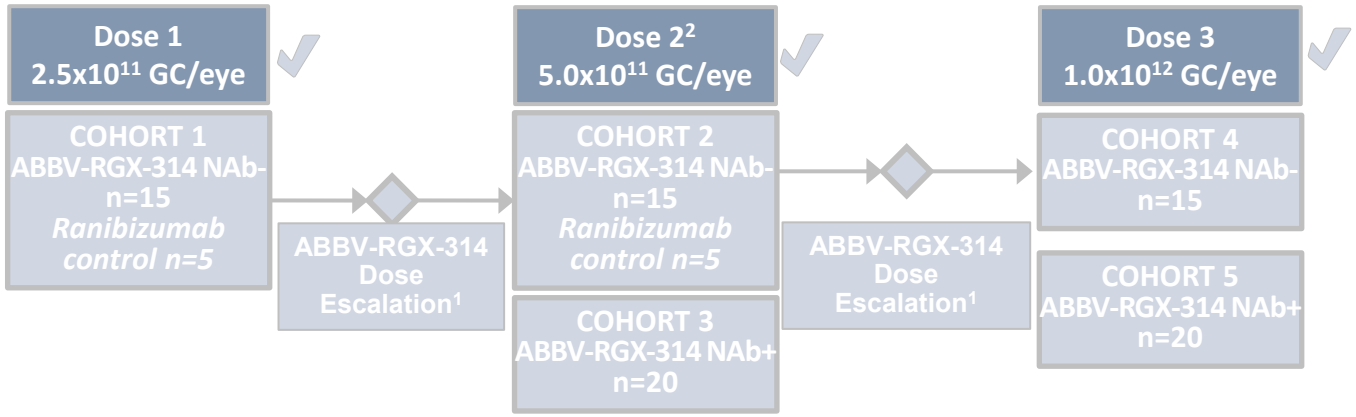


Data cut: August 1, 2022.

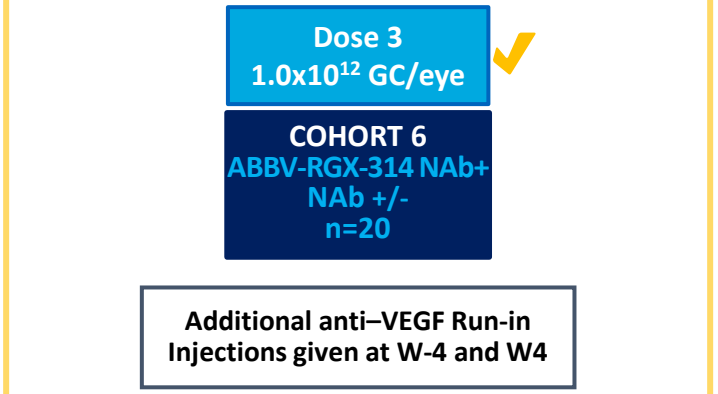
AAVIATE®: Study Design with Addition of Cohort 6



No prophylactic steroids given for Cohorts 1–5



Prophylactic ocular steroids added for Cohort 6



1. Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed.
2. Subjects in Cohort 2 received two doses of 100µL, all other cohorts received one dose of 100µL.

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

AAVIATE® Dose Level 3 with Short-course Prophylactic Ocular Steroids: Interim Safety

ABBV-RGX–314 has been well–tolerated in Dose Level 3 for AAVIATE (n=55)

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

	No PPX Steroid 26 Weeks Follow-up	w/PPX 6–26 Weeks Follow-up		
Common Ocular TEAEs[1] in the Study Eye	**AAVIATE: C4/C5 Dose Level 3** (N=35)	**AAVIATE: C6 Dose Level 3** (N=20)	**One-time Subtenon Steroid** (N=10)	**Topical Steroid** (N=10)
Conjunctival Hyperemia	14 (40%)	1 (5.0%)	1 (10.0%)	0
Episcleritis[2]	13 (37.1%)	5 (25.0%)	2 (20.0%)	3 (30.0%)
Intraocular Inflammation	7 (20.0%)	2 (10.0%)[3]	2 (20.0%)[3]	0
Intraocular Pressure Increased[4]	5 (14.3%)	1 (5.0%)	1 (10.0%)	0
Conjunctival Hemorrhage	3 (8.6%)	1 (5.0%)	1 (10.0%)	0

Data cut: June 12, 2023.
1. Includes AEs ≥10% of the total groups. Total group is defined from combined DL3 group for AAVIATE and ALTITUDE (N=84).
2. All mild to moderate (grade 1 and 2), presented within 1 week to 26 weeks post injection and have resolved or are tapering off topical corticosteroids.
3. Two cases were mild (0.5+ and 1+), presented 2–14 weeks post injection as anterior cells on slit lamp examination, and have 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:
IOI (AC Cells, AC Flare, Vit Cells, Vit Haze)

ABBV-RGX-314

	SUBJECT	Dosing	D2	W1	W2	W4	W6	W8	W10	W12	W14	W16	W18	W20	W22	W24	W26
Periocular Steroid	COHORT 5		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		
	Patient 5			0	0	0	0		0		0		0				
	Patient 6			0	0	0	0		0		0						
	Patient 7			0	0	0	0		0		0						
	Patient 8			0	1* AC	0	0		0		0						
	Patient 9			0	0	0	0		0								
	Patient 10			0	0	0	0										
Topical Steroid	COHORT 6		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		
	Patient 5			0	0	0	0		0		0		0		0		
	Patient 6			–	0	0	0		0		0		0				
	Patient 7			0	0	0	0		0		0						
	Patient 8			0	0	0	0		0		0						
	Patient 9			0	0	0	0		0		0						
	Patient 10			0	0	0	0										

* Topical steroids PRN
Timepoints are post-dosing.
IOI: Intraocular Inflammation; AC: anterior chamber; Vit: vitreous chamber
Data cut: June 12, 2023.

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

ABBV-RGX-314 Cohorts 1-5 (n=85): Safety

- Suprachoroidal ABBV-RGX-314 has been well-tolerated

ABBV-RGX-314 Cohorts 1-4 (n=65): 6 Month Results

- ABBV-RGX-314 treated patients had **stable vision and retinal thickness,** with a **meaningful reduction in treatment burden** across all dose levels; **highest reduction in treatment burden seen in Cohort 4 (Dose 3):**
  - 85% reduction in annualized injection rate
  - 67% injection-free
- No meaningful differences in patient outcomes with and without **baseline AAV8 NAbs**
- Intraocular inflammation (IOI) resolved with topical corticosteroids
  - **Cohorts 1–3 (Dose 1 and 2)** - all mild and similar incidence observed across doses
  - **Cohort 4 (Dose 3)** - mild to moderate with increased incidence compared to prior doses

Cohort 6 (Dose 3) initial safety results: zero cases of IOI with short-course prophylactic topical steroids (n=10)[1]

Data cut: August 01, 2022.
1. Data cut: June 12, 2023.

Thank You