RGX-314 Program Updates for the Treatment of Wet AMD

Conference Call Presentation

August 4, 2020

REGENXBIO®

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Today's Speakers

- **REGENXBIO Team:**
  - Ken Mills, President and Chief Executive Officer
  - Steve Pakola, M.D., Chief Medical Officer

- **Featured Retina Specialist Key Opinion Leaders:**
  - Robert Avery, M.D., Founder of California Retina Consultants and Research Foundation
  - Dante Pieramici, M.D., Director, California Retina Research Foundation and Partner, California Retina Consultants
  - Peter Kaiser, M.D., Chaney Family Endowed Chair in Ophthalmology Research and Professor of Ophthalmology, Cleveland Clinic Lerner College of Medicine and Cole Eye Institute

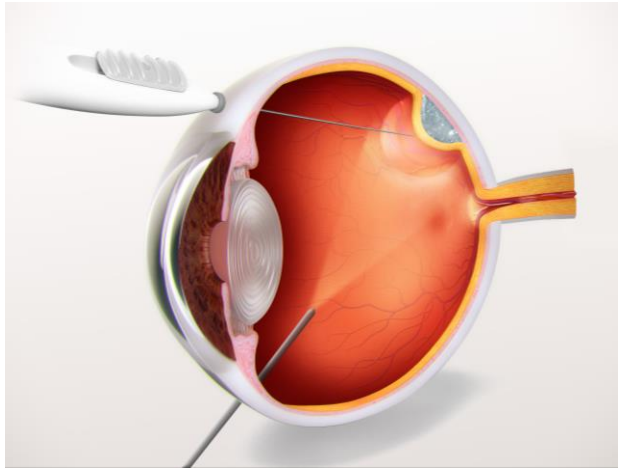
Today's Update from RGX-314 Wet AMD Program

- **On track to initiate RGX-314 subretinal pivotal program for treatment of wet AMD by the end of 2020**

- **1 Year data from Cohorts 4 and 5 in RGX-314 Phase I/IIa subretinal clinical trial**
  - RGX-314 was generally well-tolerated in 42 patients at all dose levels in Phase I/IIa trial
  - Positive interim update from Cohorts 4 and 5 at 1 year to inform pivotal program design
    - Durable treatment effect observed with stable to improved visual acuity and retinal thickness
    - Meaningful reductions in anti-VEGF injection burden over 1 year
      - 61% and 85% reductions in Cohorts 4 and 5, respectively
      - 73% of patients (8/11) in Cohort 5 remain anti-VEGF injection-free over one year
    - Dose-dependent intraocular protein expression levels

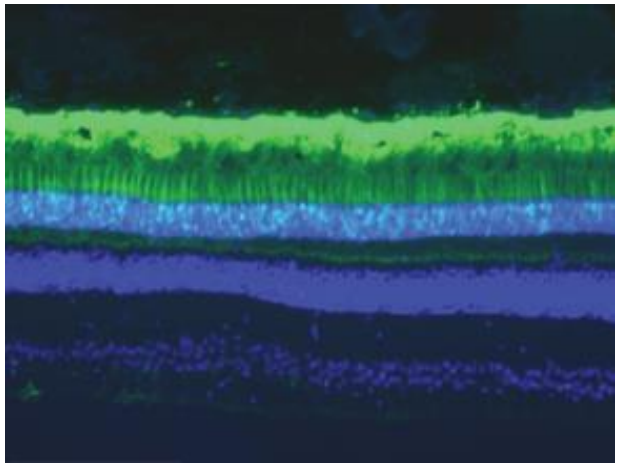
- **Phase II trial for RGX-314 for treatment of wet AMD using suprachoroidal delivery (AAVIATE) is active**
  - Study to evaluate the efficacy, safety and tolerability of RGX-314 delivered to the suprachoroidal space in the eye via SCS Microinjector™
  - Interim data update from Cohort 1 expected by end of 2020

RGX-314 Uses a Novel AAV8 Vector to Deliver an anti-VEGF Fab

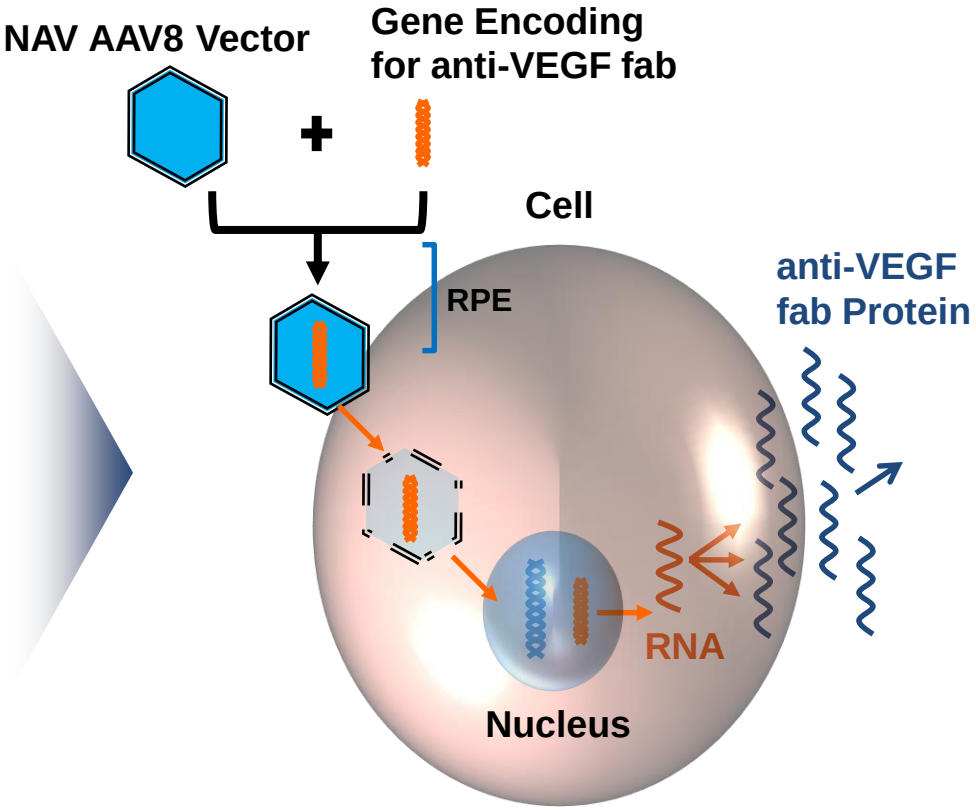


Subretinal Procedure

AAV8



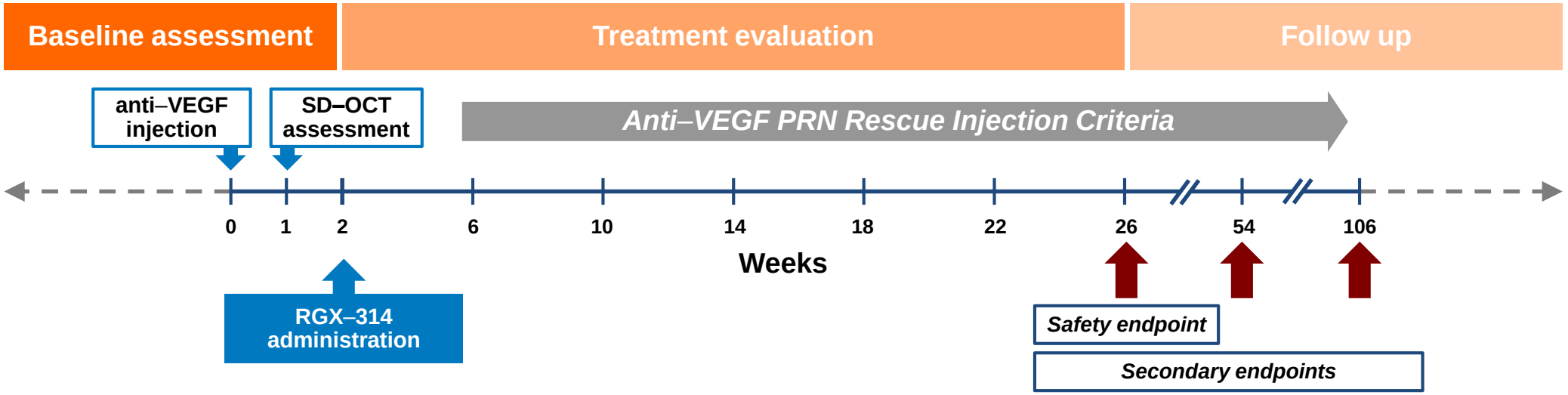
Efficient Gene Delivery to the RPE[1]



RGX-314 is Designed to Deliver a Gene Encoding for an Anti-VEGF Fab Protein

[1]Vandenberghe et al. 2011 *Science Translational Medicine*

RGX-314 Phase I/IIa wAMD Trial Dose Escalation Protocol



Previously treated patients requiring frequent injections

Dose 1 n = 6 ✓	Safety review[1]	Dose 2 n = 6 ✓	Safety review[1]	Dose 3 n = 6 ✓	Safety review[1]	Dose 4 n = 12 ✓	Safety review[1]	Dose 5 n = 12 ✓
$3x10^9$ GC/eye		$1x10^{10}$ GC/eye		$6x10^{10}$ GC/eye		$1.6x10^{11}$ GC/eye		$2.5x10^{11}$ GC/eye

[1]Dose escalation safety review to occur four weeks after final patient in each cohort has been dosed
SD-OCT = spectral domain optical coherence tomography

Anti-VEGF Retreatment Allowed for Any Fluid or Disease Activity

Anti-VEGF may be given beginning 4 weeks post-treatment and **PRN every 4 weeks** thereafter **per investigator's discretion** if one or more of the criteria apply:

CNV-related **increased, new, or persistent fluid**

Vision loss of ≥5 letters associated w/ fluid

New ocular **hemorrhage**

RGX-314 Phase I/IIa wAMD: Demographics

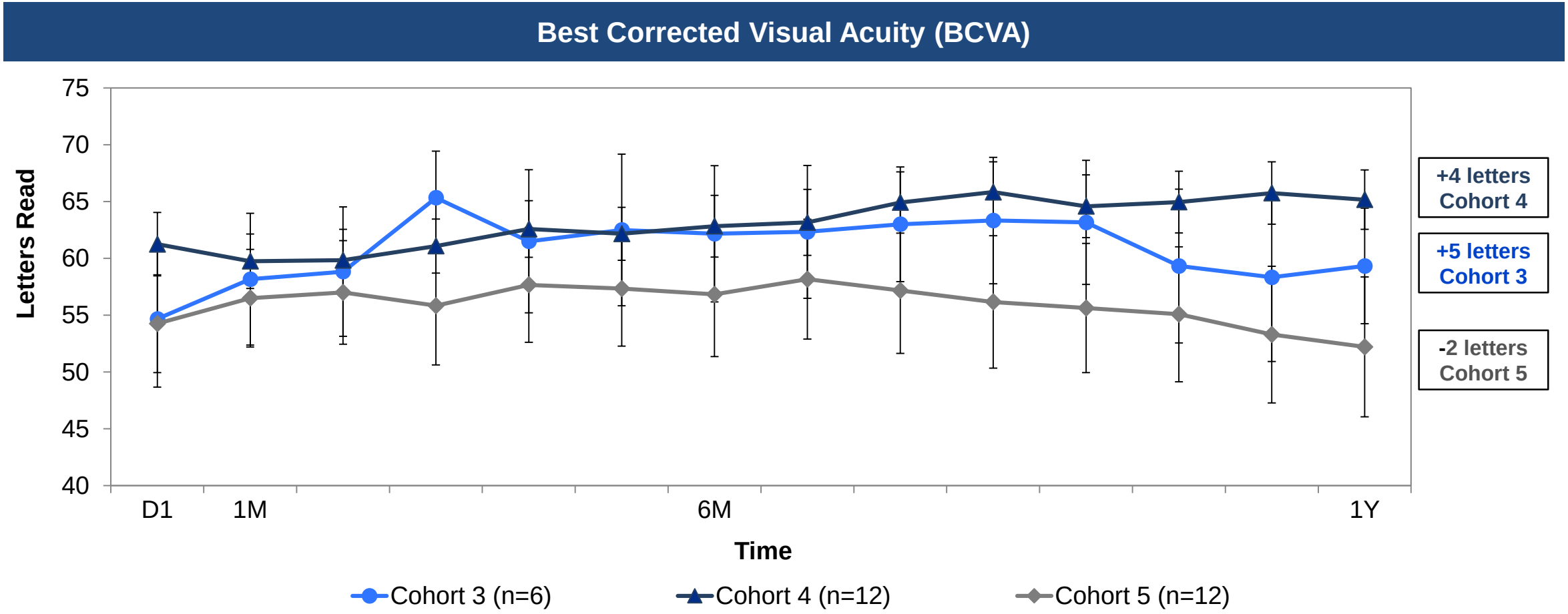
	Variable	Cohort 1 (n=6)	Cohort 2 (n=6)	Cohort 3 (n=6)	Cohort 4 (n=12)	Cohort 5 (n=12)	Total (n=42)
BASELINE	**Mean Age (Years)**	**78.2**	**78.0**	**80.0**	**80.3**	**81.6**	**80.0**
	Baseline BCVA (Snellen equivalents)	53.7 (20/100)	50.7 (20/100)	54.7 (20/80)	61.3 (20/63)	54.3 (20/80)	55.7 (20/80)
	Baseline OCT (reading center)	**361.7** (n=6)	**413.2** (n=6)	**359.8** (n=6)	**411.3** (n=12)	**418.3** (n=12)	**399.1** (n=42)
	Baseline serum AAV8 Nab+ with titer >1:10	**2** (33.3%)	**3** (50.0%)	**4** (66.7%)	**4** (33.3%)	**5** (41.7%)	**18** (42.9%)
PRIOR THERAPY	**Months Since First anti-VEGF Injection**	**53.5**	**59.3**	**71.6**	**58.1**	**45.8**	**56.0**
	# Injections Since Diagnosis (Mean)	**40.7**	**32.5**	**34.2**	**35.7**	**26.7**	**33.1**
	Average Annualized Injections Prior to Entry	**9.6**	**10.5**	**6.8**	**10.2**	**9.9**	**9.6**

RGX-314 Phase I/IIa wAMD: Overall Safety

- RGX–314 continues to be generally well–tolerated across all doses (n=42)
- 18 SAEs were reported in 11 patients[1]; one possibly drug-related SAE reported in a patient in Cohort 5[2]
- Common[3] ocular AEs in the study eye included:
  - Post-operative conjunctival hemorrhage (69% of patients) – 100% mild, majority resolved within days to weeks
  - Retinal pigmentary changes[4] (83% of patients in Cohorts 3-5; 67% of all patients) – 70% mild, one severe[2]
  - Post-operative inflammation[5] (36% of patients) – resolved within days to weeks, 100% mild
  - Retinal hemorrhage (24% of patients) – an anticipated event in the severe wet AMD population, 100% mild
  - Post-operative visual acuity reduction (17% of patients) – majority resolved within days to weeks, 100% mild
  - Eye irritation (17% of patients) and eye pain (17% of patients) – 85% mild, none severe
- No reports of clinically-determined immune responses, drug-related ocular inflammation, or post-surgical inflammation beyond what is expected following routine vitrectomy

Data cut July 13th, 2020
[1]Includes two deaths unrelated to RGX-314
[2]Significant decrease in vision
[3]Common ocular AEs defined by ≥ 15% of patients
[4]Retinal pigmentary changes observed were hypo and hyper pigmentation on imaging occurring in the bleb area or inferior retina
[5]Postoperative inflammation includes AC cells, flare, or inflammation

Mean BCVA Over 1 Year

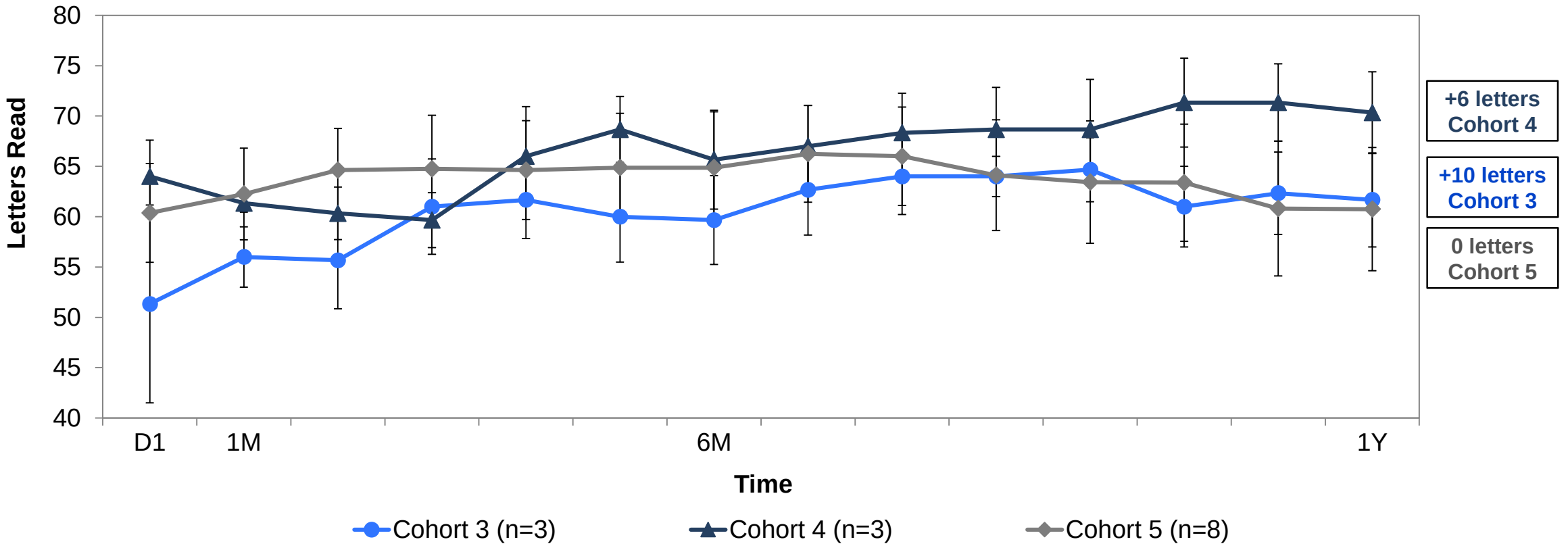


* One patient in Cohort 5 discontinued the study prior to Week 22 visit and another patient has missed the visits since Week 46 visit due to COVID-19. For these patients, subsequent visits were imputed using last observation carried forward (LOCF). Five additional missing BCVA results were interpolated.

Mean BCVA Over 1 Year

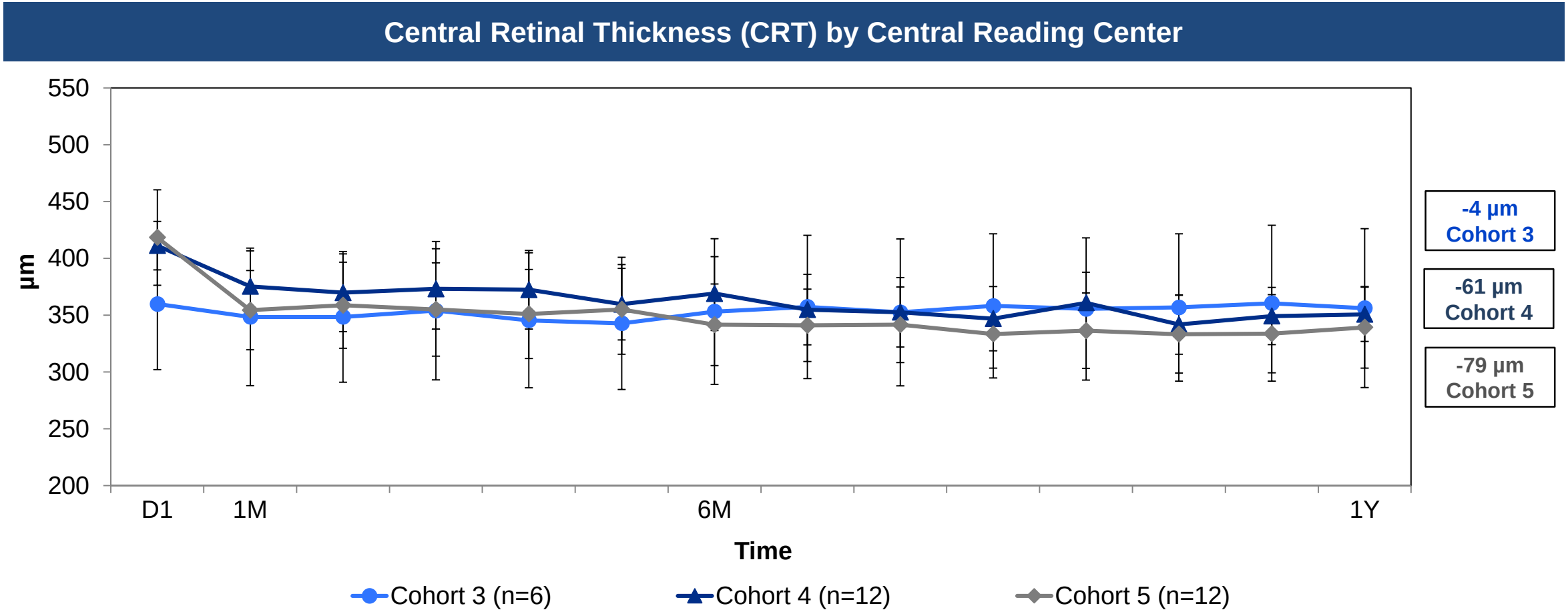
Anti-VEGF Injection Free Subjects

Best Corrected Visual Acuity (BCVA)



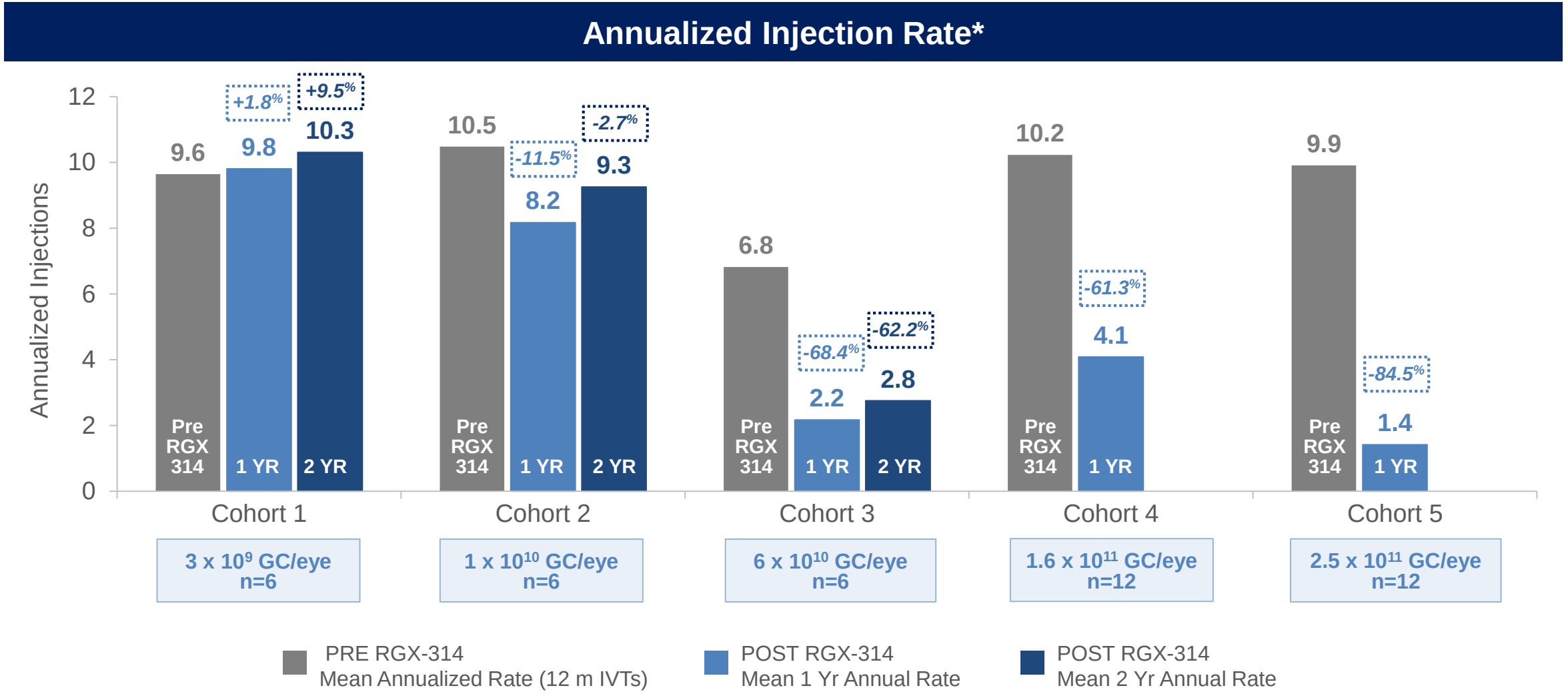
* One patient in Cohort 5 discontinued the study prior to Week 22 visit (subject injection-free at time of discontinuation) and was not included. Another patient in Cohort 5 has missed the visits since Week 46 due to COVID-19 and these visits were imputed using last observation carried forward (LOCF). Three additional missing BCVA results were interpolated.

Mean CRT Over 1 Year



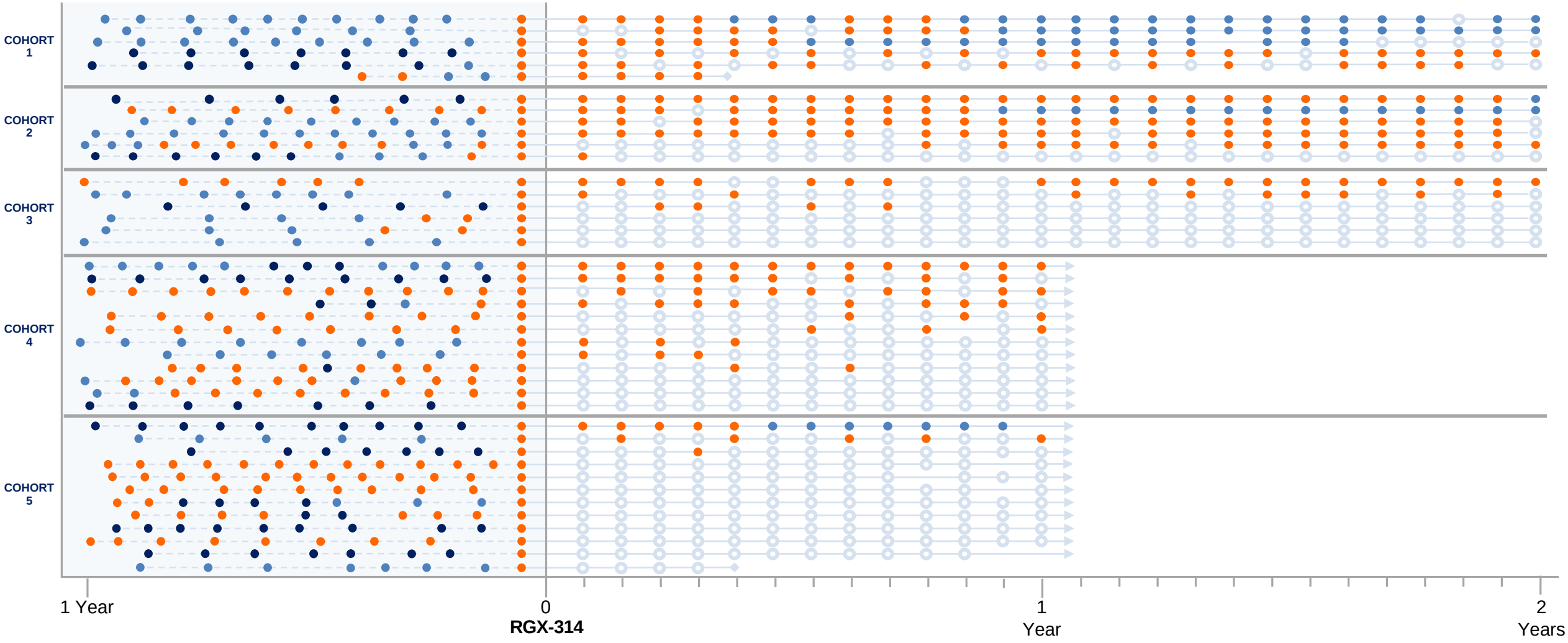
*One patient in Cohort 5 discontinued the study prior to Week 22 visit and another patient has missed the visits since Week 46 visit due to COVID-19. For these patients, subsequent visits were imputed using last observation carried forward (LOCF). Seven additional missing CRT results were interpolated.

Mean Change in Annualized Injection Rate PRE and POST RGX-314 in Cohorts 1-5

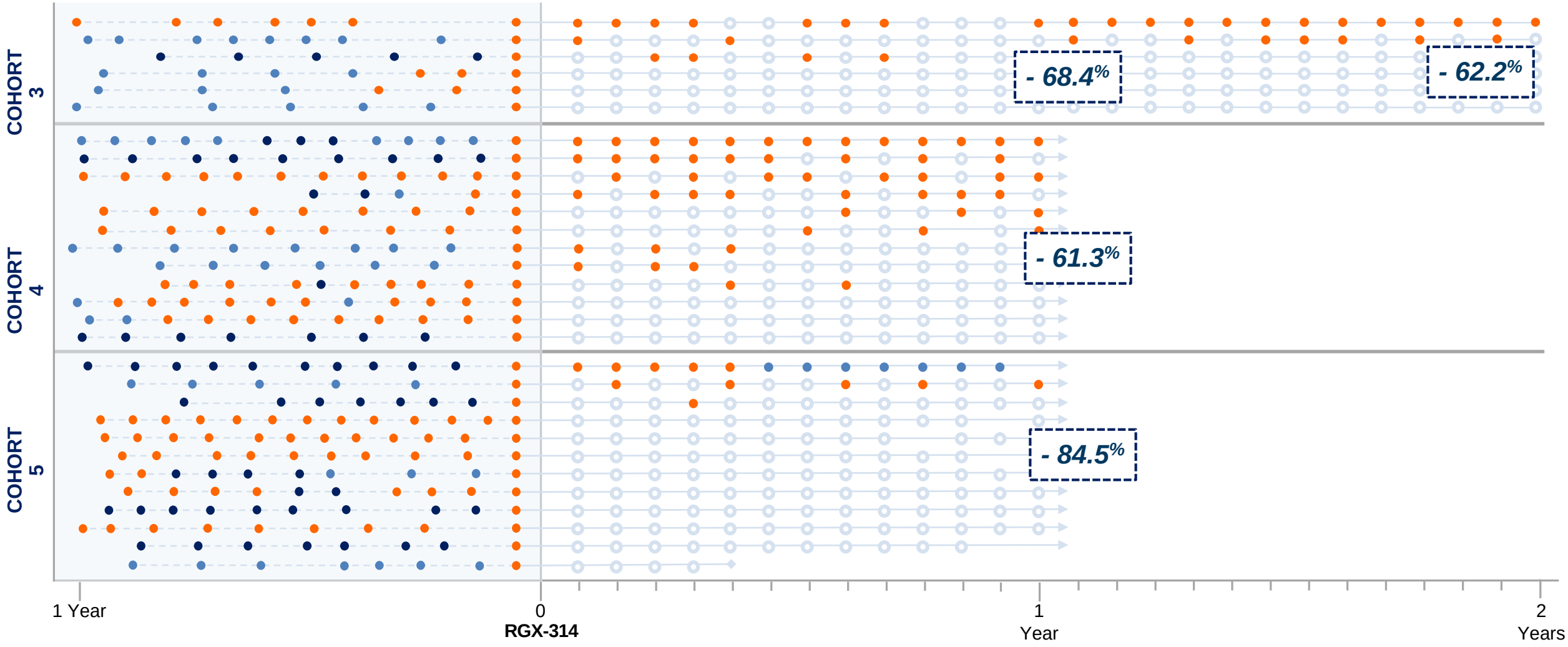


*Prior annual rate is (Total # of prior IVTs)/(minimum(366 days, Duration between first ever IVT and Day 1)/365.25). Post RGX-314 annual rate is (Total # of IVTs on Study)/(Duration on Study/365.25) where on study is defined from RGX-314 administration to a specified cut-off date.

Cohort 1-5 Injections PRE and POST RGX-314 Over 2 Years



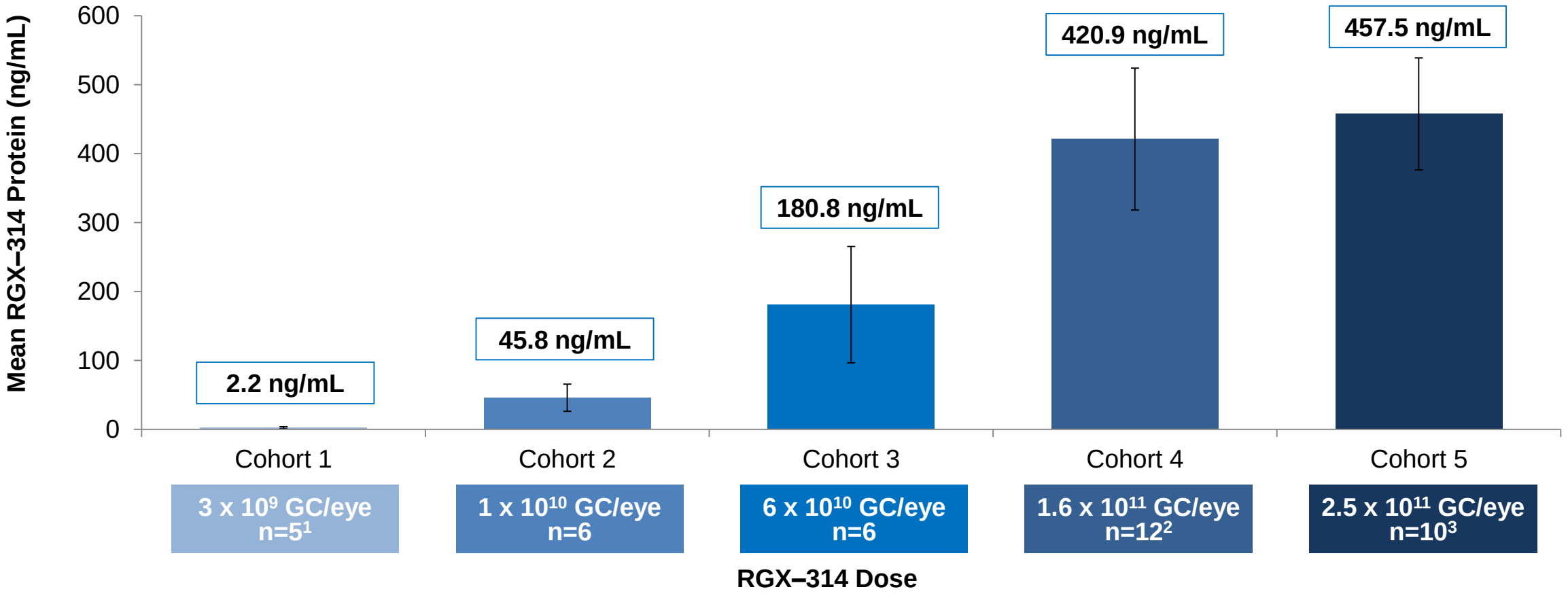
Cohort 3-5 Injections PRE and POST RGX-314



RGX-314 Protein Levels at Year 1 in All Cohorts

Dose-dependent intraocular RGX-314 protein levels across all 5 cohorts

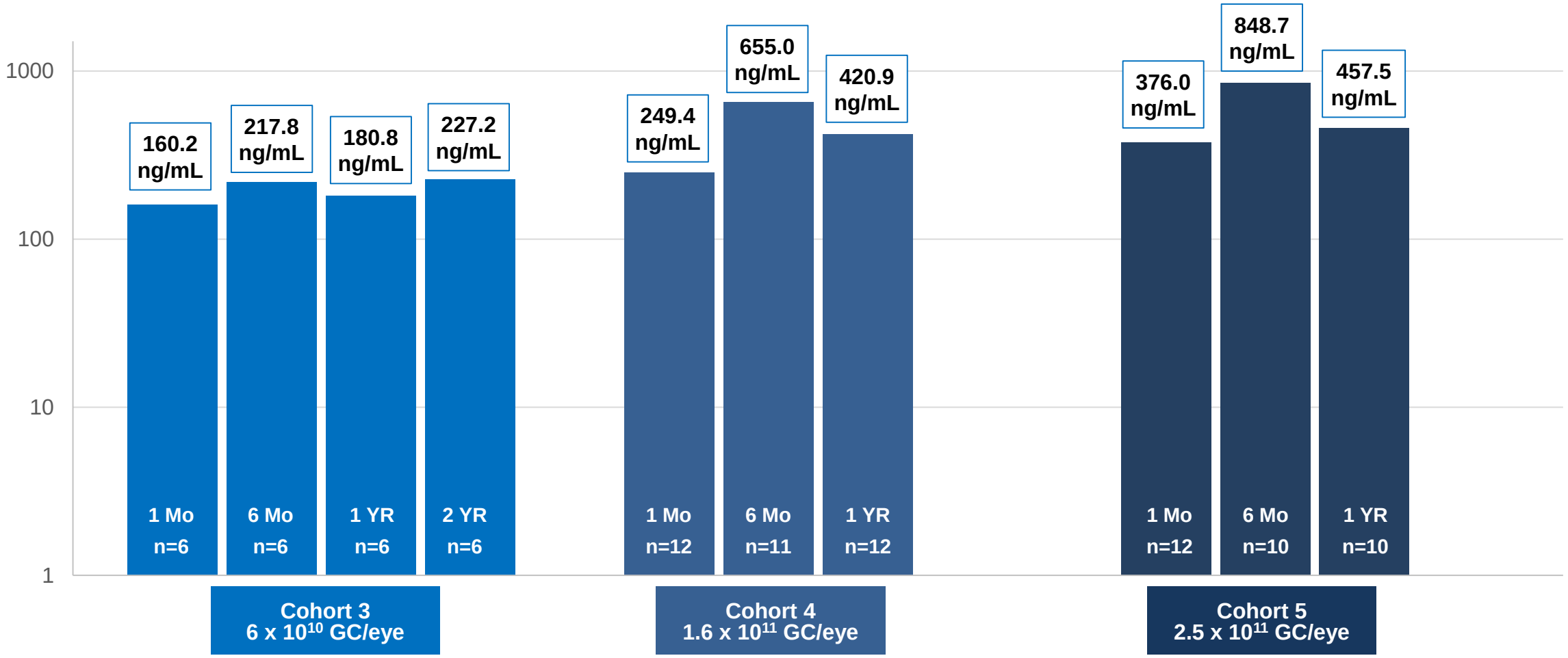
As Measured from Aqueous Samples by ECL



[1]One patient in Cohort 1 discontinued the study prior to Week 22 visit.
[2]One unscheduled visit has been assigned to Week 54.
[3]One patient in Cohort 5 discontinued the study prior to Week 26; one patient did not have a 1 year sample taken, and 2 other samples included were taken out of the visit window.

RGX-314 Protein Levels in Cohorts 3-5

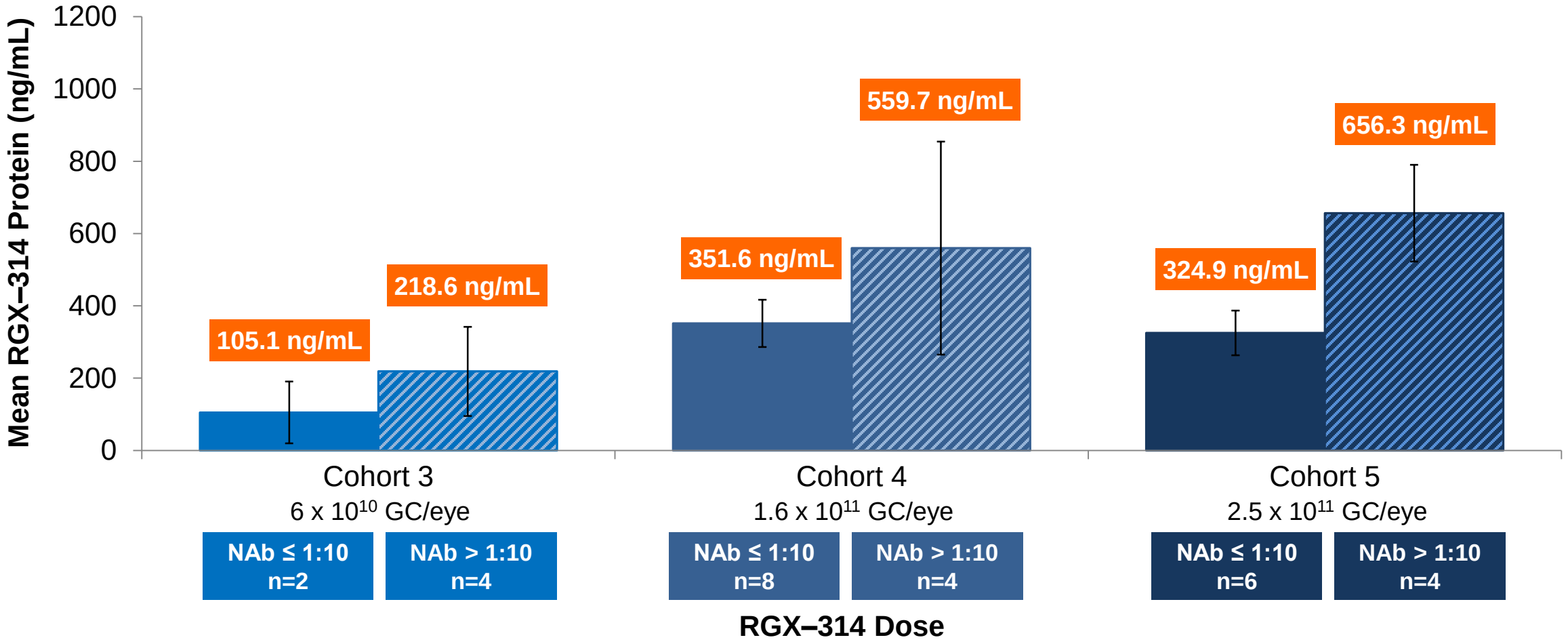
As Measured from Aqueous Samples by ECL



Note: Five samples were taken outside of the visit window and were assigned to the closest visit.

RGX-314 Protein Levels Based on AAV8 NAb Status[1]

As Measured from Aqueous Samples by ECL 1 Year post-RGX-314



[1] Baseline serum NAb positive is defined as Day 8 titer value >1:10 and baseline serum NAb negative is defined as Day 8 titer value of <1:5, 1:5, or 1:10.

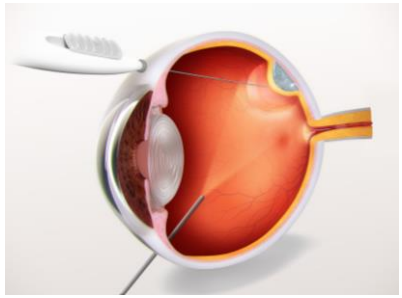
Summary of Data Across Cohorts 3 through 5 at 1 Year

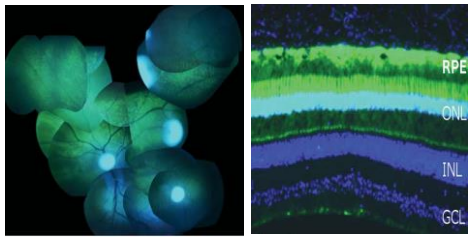
	Cohort 3 6x10^{10} GC/eye		Cohort 4 1.6x10^{11} GC/eye		Cohort 5 2.5x10^{11} GC/eye	
	Full Cohort (N=6)	Patients with 0 Injections (N=3)	Full Cohort (N=12)	Patients with 0 Injections (N=3)	Full Cohort (N=12)	Patients with 0 Injections (N=8)
Stable to Improved Visual Acuity[1]	+5 letters	+10 letters	+4 letters	+6 letters	-2 letters	0 letters
Stable to Improved Retinal Thickness[1]	-4 µm	+3 µm	-61 µm	-62 µm	-79 µm	-95µm
Significantly Reduced Treatment Burden[2]	68% reduction 2.2 inj/year	100%	61% reduction 4.1 inj/year	100%	85% reduction 1.4 inj/year	100%
Durable Intraocular RGX-314 Protein[3]	217.8 ng/mL at 6 months (n=6) 180.8 ng/mL at 1 year (n=6)	274.9 ng/mL at 6 months (n=3) 260.5 ng/mL at 1 year (n=3)	655.0 ng/mL at 6 months (n=11) 420.9 ng/mL at 1 year (n=12)	693.6 ng/mL at 6 months (n=3) 472.5 ng/mL at 1 year (n=3)	848.7 ng/mL at 6 months (n=10) 457.5 ng/mL at 1 year (n=10)	694.4 ng/mL at 6 months (n=7) 427.8 ng/mL at 1 year (n=7)

[1]Mean change from baseline at 1 year
[2]Reduction of annualized rate of anti-VEGF injections compared to 12 months prior to RGX-314 administration
[3]Mean RGX-314 protein concentrations

RGX-314 Routes of Administration

Subretinal Delivery[1]





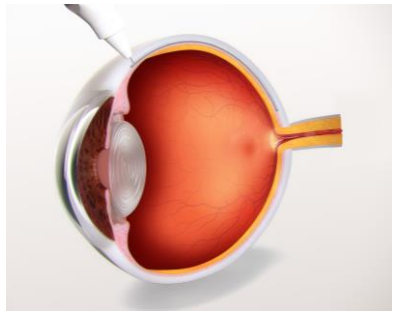
Retinal transduction achieved via subretinal delivery of AAV8 in non-human primates AAV8.GFP 1.0 x 10^{11} GC

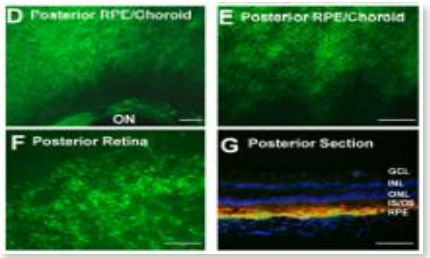
- Established route of delivery for gene therapy
- Direct and broad transduction of the retina observed
- Minimal exposure to the vitreous and anterior segment
  - Low risk of immune response
  - Low risk of inflammation
- No corticosteroid prophylaxis for RGX-314[3]

AAV Neutralizing Antibody (NAb) Status

- All patients eligible, regardless of NAb status

Suprachoroidal Delivery[2]





Retinal transduction achieved via suprachoroidal delivery of AAV8 in non-human primates AAV8.GFP 4.75 x 10^{11} GC

- In-office, non-surgical approach using SCS Microinjector™
- Direct and broad transduction of the retina
- Minimal exposure to the vitreous and anterior segment
  - Low risk of immune response
  - Low risk of inflammation
- No corticosteroid prophylaxis

AAV NAb Status

- ~70% patients without NAbs to AAV8[4]

[1] Vandenberghe et al. 2011 Science Translational Medicine
[2] Ding, K., et al. 2019 Journal of Clinical Investigation
[3] Patients receive routine vitrectomy-related ocular steroids as per standard of care
[4] Calcedo R, et al. 2009 Journal of Infectious Disease

AAVIATE Phase II Trial: RGX–314 for wet AMD

Objectives

Primary

- To evaluate the mean change in BCVA for RGX-314 compared with ranibizumab monthly injection at Week 40.

Secondary

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

Subjects: Up to 40 total (randomized 3:1)

Route of administration: Suprachoroidal using SCS Microinjector™

Sites: **Fifteen** leading retinal centers across the United States

Key inclusion criteria

- Male or female ≥ 50 to 89 years of age
- Previously treated wet AMD subjects requiring no more than 10 anti–VEGF injections in the 12 months prior to trial entry
- Documented response to anti–VEGF at trial entry (assessed by SD–OCT)
- BCVA between ≤ 20/25 and ≥ 20/125 (≤ 83 and ≥ 44 Early Treatment Diabetic Retinopathy Study [ETDRS] letters) in the study eye.

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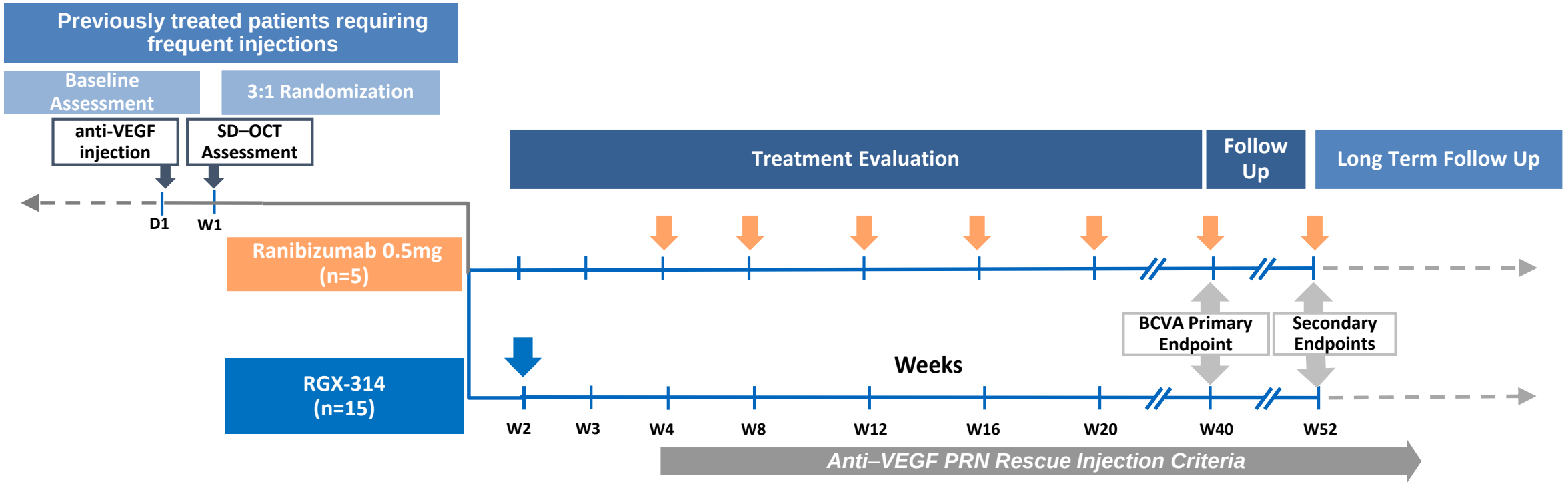
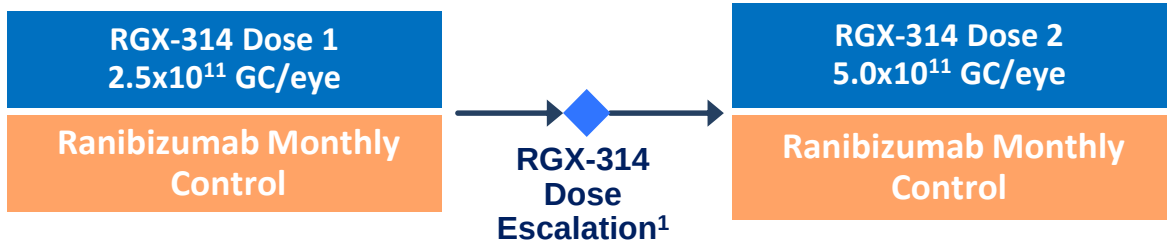
AAVIATE Phase II Dose-escalation Trial: RGX-314 for wet AMD





[1] Dose escalation safety review to occur two weeks after final subject in Cohort 1 has been dosed

SD-OCT = spectral domain optical coherence tomography

Anticipated Upcoming Milestones for RGX-314 in 2020

On-track to provide updates for subretinal and suprachoroidal programs

Initiate pivotal trial for RGX-314 subretinal delivery in 2H 2020

Dose patients in Phase II trial for RGX-314 suprachoroidal delivery in wet AMD in Q3 2020

Initiate Phase II trial for RGX-314 suprachoroidal delivery in diabetic retinopathy in 2H 2020

Q&A

Featured Retina Specialist Key Opinion Leaders / Study Investigators:

Robert Avery, M.D., Founder of California Retina Consultants and Research Foundation

Dante Pieramici, M.D., Director, California Retina Research Foundation and Partner, California Retina Consultants

Peter Kaiser, M.D., Chaney Family Endowed Chair in Ophthalmology Research and Professor of Ophthalmology, Cleveland Clinic Lerner College of Medicine and Cole Eye Institute

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