

Gene Therapy with RGX-314 for Neovascular AMD: New Results from the Ongoing Phase I/IIa Study

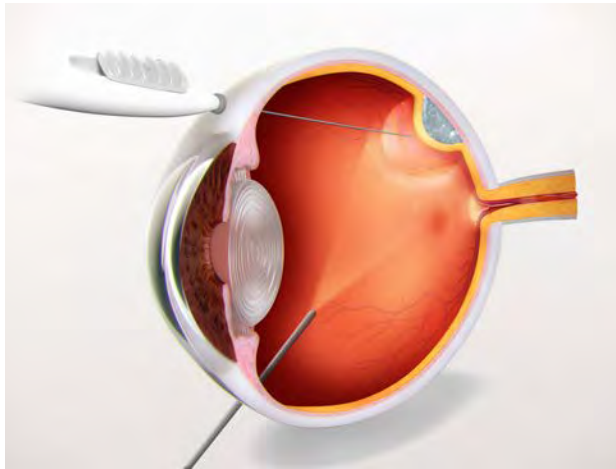
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Financial Disclosures

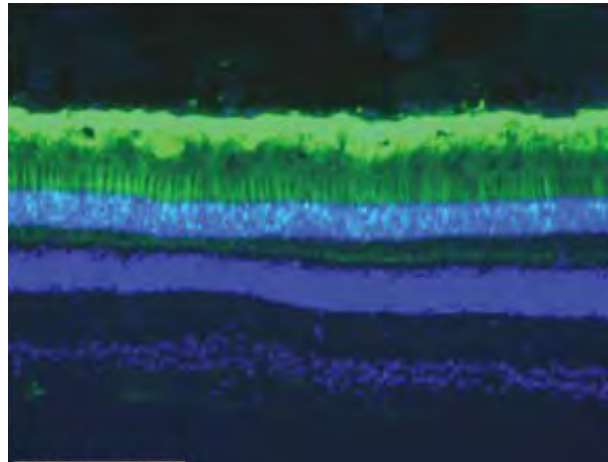
- Acucela (C), Adverum (C, R), Aerie Pharmaceuticals (R), Aldeyra (R), Alimera Sciences (C), Allegro (C), Allergan (C), Apellis (C, R), Arctic Vision (C), Bausch and Lomb (C), Bayer (C), Chengdu Kanghong Biotechnologies (C, R), Clearside Biomedical (R), DORC (C), EyePoint (C), Gemini Therapeutics (R), Genentech (C, R), Graybug Vision (R), Gyroscope (C), IONIS Pharmaceutical (R), IVERIC Bio (C, R), Kodiak Sciences (C, R), LMRI (R), Merck (C), Neurotech Pharmaceuticals (R), NGM Biopharmaceuticals (C, R), Novartis (C, R), ONL Therapeutics (C), Opthea (C, R), Outlook Therapeutics (R), Oxurion (C), Palatin (C), Polyphotonix (C), Recens Medical (C, R), Regeneron (C, R), RegenXBio (C, R), Roche (C, R), Samsung Bioepis (R), Santen (R), Senju (R), Taiwan Liposome Company (R), Takeda (C), Thea Open Innovation (C), Xbrane BioPharma (R)

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

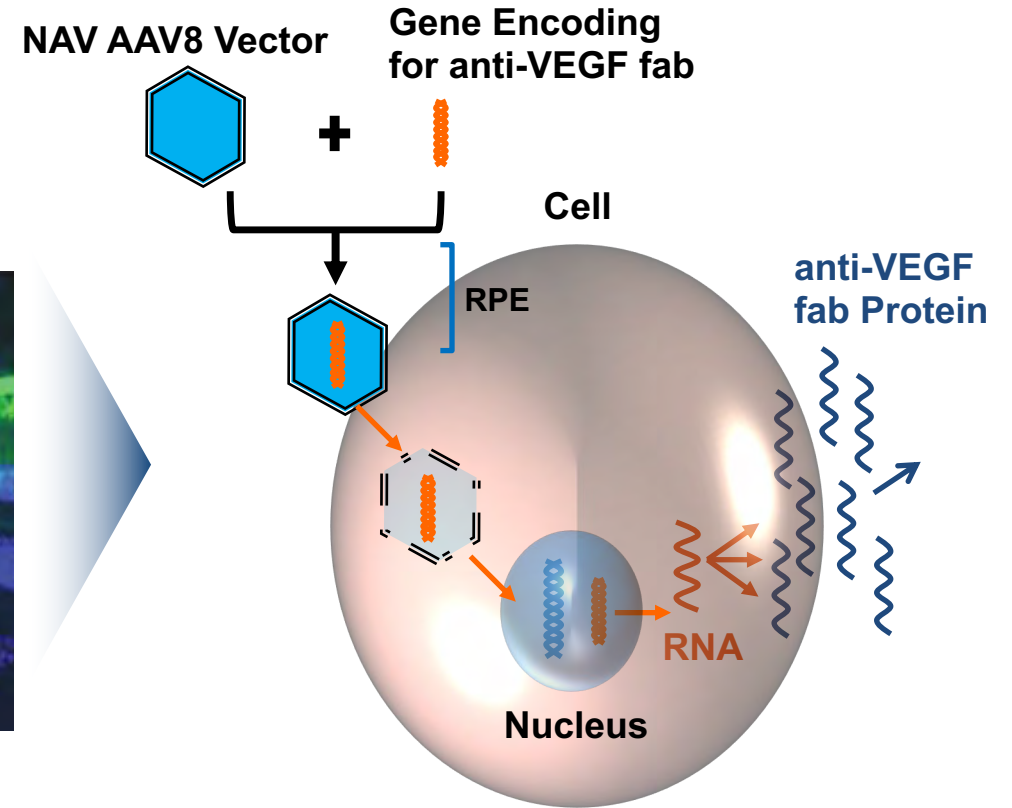


Subretinal Procedure

AAV8



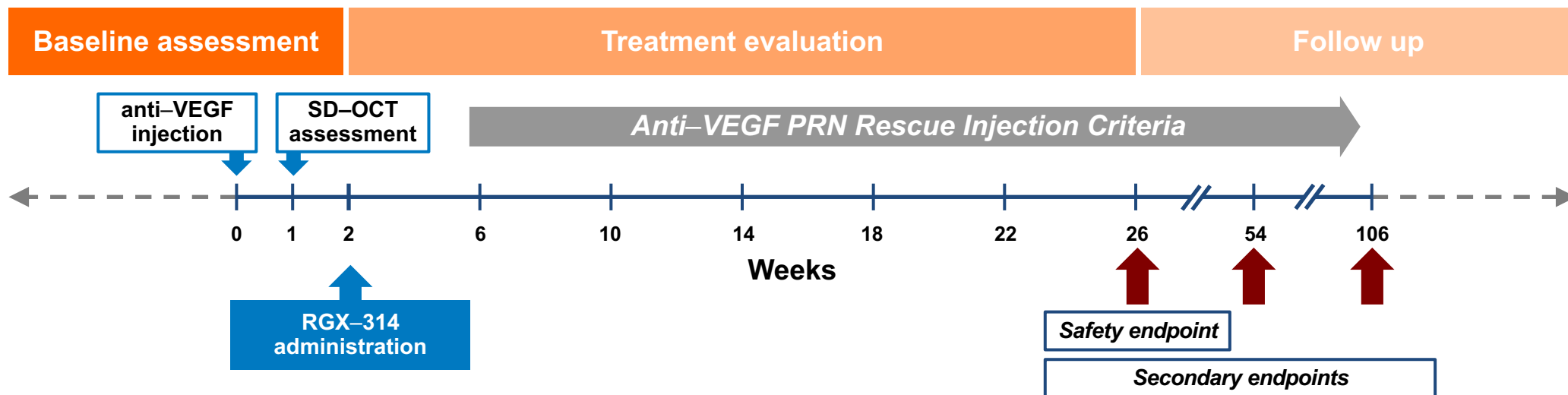
Efficient Gene Delivery to the RPE¹



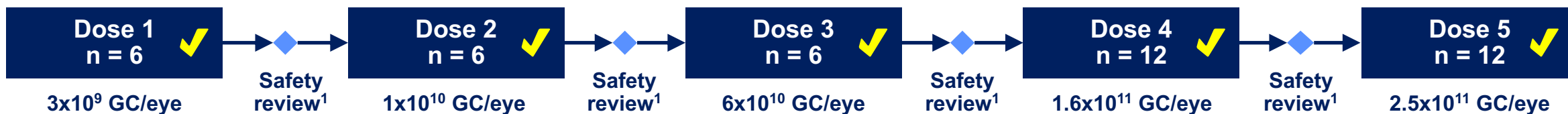
RGX-314 is Designed to Deliver a Gene Encoding for an Anti-VEGF Fab Protein

¹Vandenberghe et al. 2011 *Science Translational Medicine*

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



Previously Treated patients Requiring Frequent Injections



Subretinal Dosing Completed in 42 patients Across Five Dose Cohorts

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

RGX-314 Phase I/IIa Clinical Trial in wAMD



Objectives

Primary

- To determine the safety and tolerability of RGX-314 in previously treated patients with nAMD through 6 months

Secondary

- Expression of RGX-314 protein in the eye
- Effect of RGX-314 on best corrected visual acuity (BCVA) and central retinal thickness (CRT)
- Additional anti-VEGF injections post-RGX-314 (“Rescue”)

Rescue: New or Persistent Fluid/ Loss in Vision

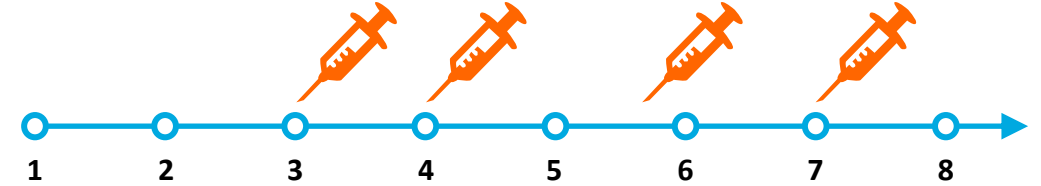
- Per the Investigator's discretion

Subjects: 42 Patients dosed **subretinally**

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

Key Inclusion Criteria

≥ 4 Anti-VEGF in 8 Months



- Male or female ≥ 50 to 89 years of age
- Documented **nAMD with response to anti-VEGF (ranibizumab) at trial entry**
- Vision of 20/63 to 20/400 for the initial patient, then **20/40 to 20/400** for the rest of each cohort
- Pseudophakic (status post cataract surgery)

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	71.7	58.1	45.9	56.1
	# 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 patients¹; one possibly drug-related SAE reported in a patient in Cohort 5²
- Common³ ocular AEs in the study eye included:
 - Post-operative conjunctival hemorrhage (69% of patients) – 100% mild, majority resolved within days to weeks
 - Retinal pigmentary changes⁴ (83% of patients in Cohorts 3-5; 67% of all patients) – 70% mild, one severe²
 - Post-operative inflammation⁵ (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

¹Includes two deaths unrelated to RGX-314

²Significant decrease in vision

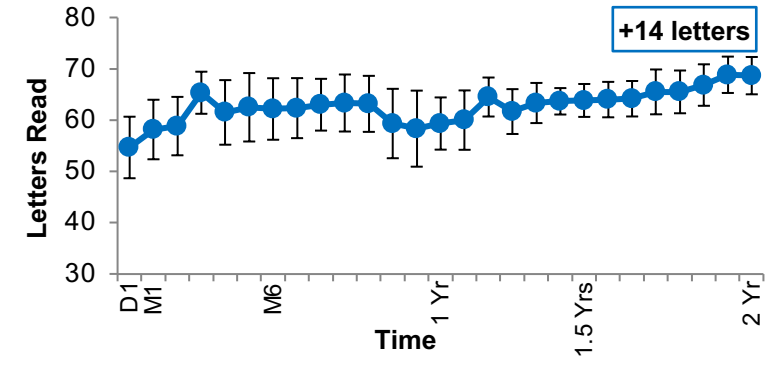
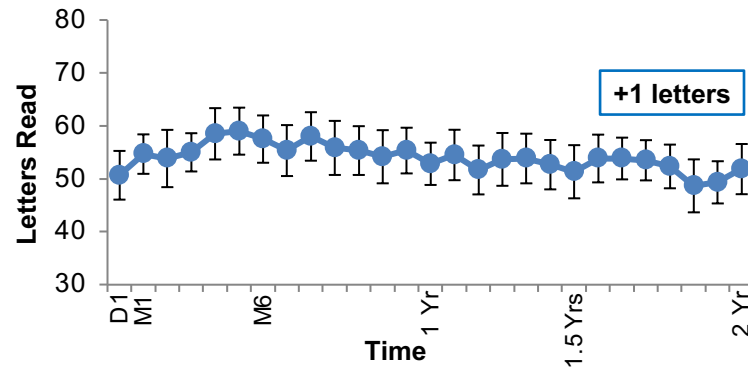
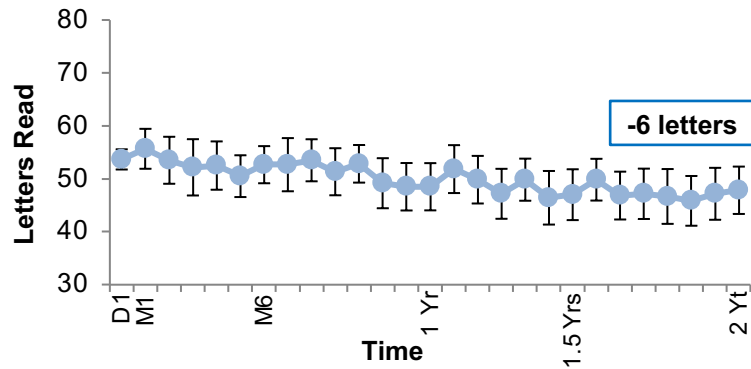
³Common ocular AEs defined by ≥ 15% of patients

⁴Retinal pigmentary changes observed were hypo and hyper pigmentation on imaging occurring in the bleb area or inferior retina

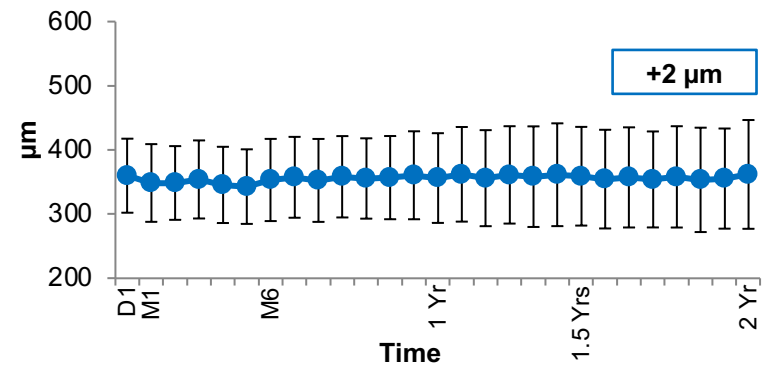
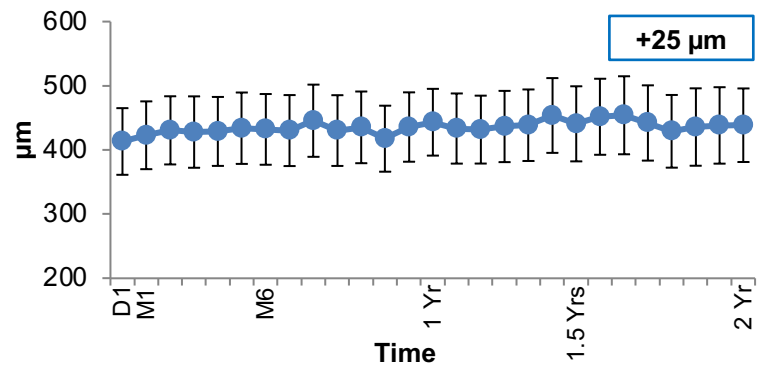
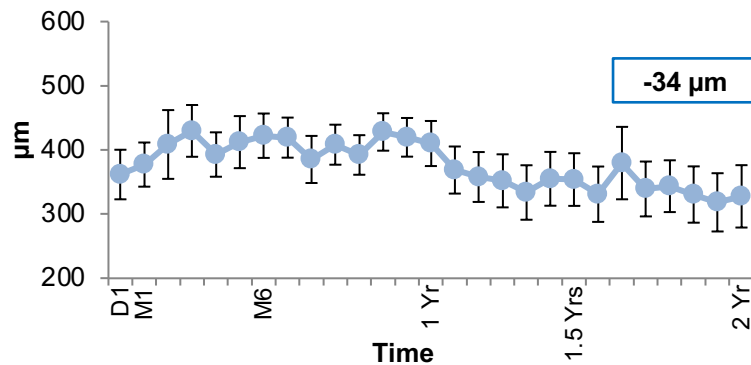
⁵Postoperative inflammation includes AC cells, flare, or inflammation

Mean Change in BCVA and CRT and Average Injections Over 2 Years in Cohorts 1-3

Best Corrected Visual Acuity (BCVA)



Central Retinal Thickness (CRT) by Central Reading Center



10.3 Injections (annualized)

Cohort 1¹

9.3 Injections (annualized)

Cohort 2

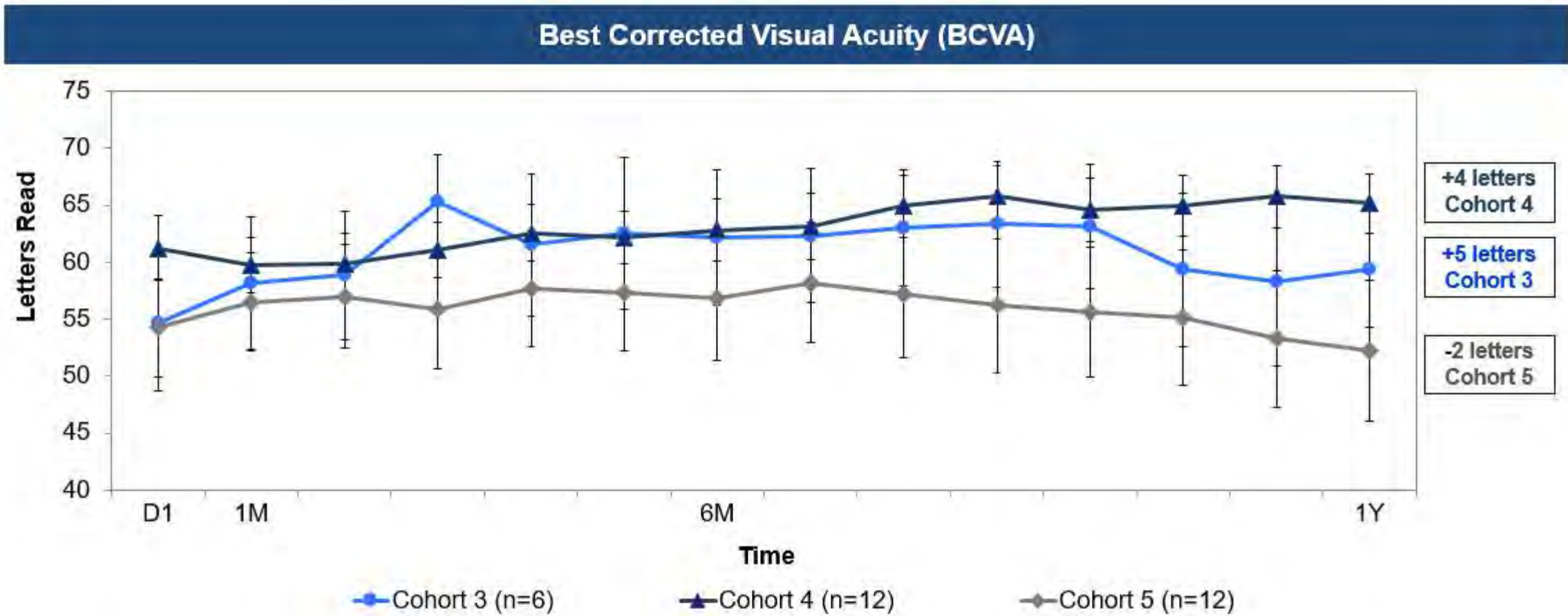
2.8 Injections (annualized)

Cohort 3

¹One patient in Cohort 1 discontinued the study prior to Week 22 visit. For this patient, subsequent visits (Week 22 and after) were imputed using last observation carried forward (LOCF). Two other missing BCVA results at Week 14 and Week 74 in Cohort 1 were interpolated.

Note: two missing BCVA values in Cohort 1, three missing CRT values in Cohort 1, and one missing CRT value in Cohort 3 have been interpolated.

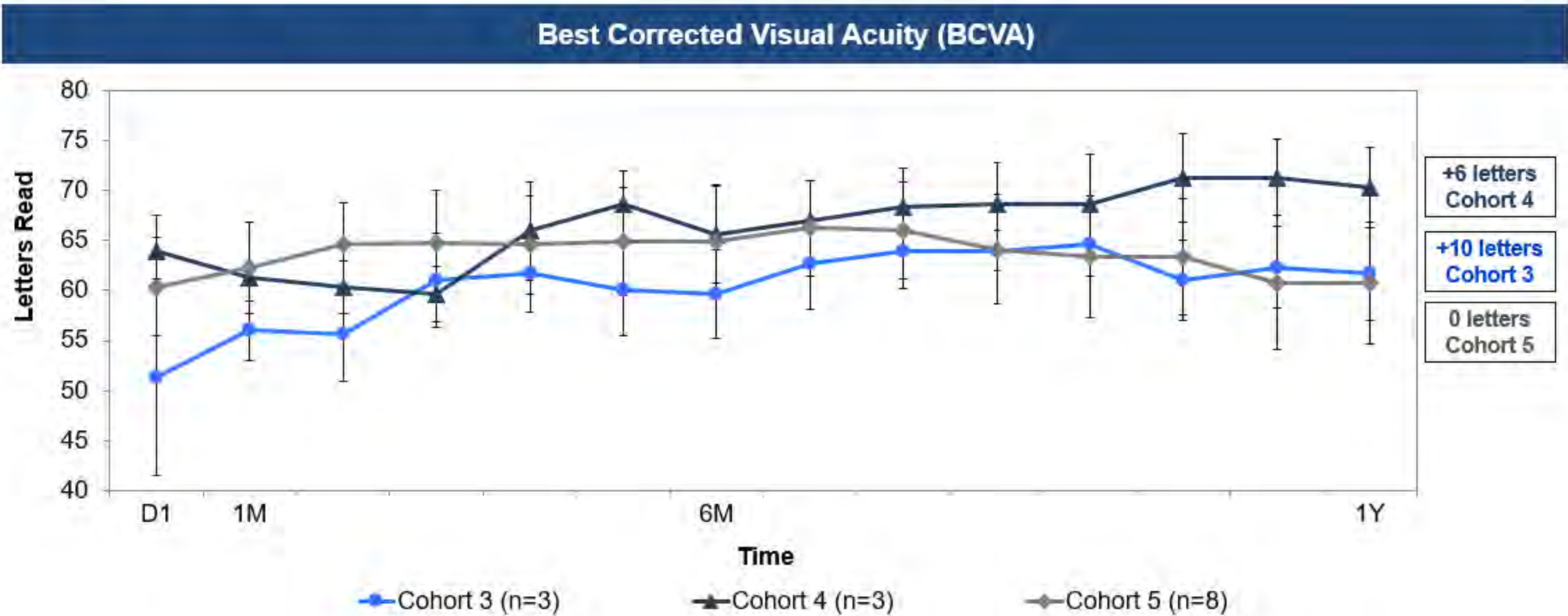
Mean BCVA Over 1 Year in Cohorts 3-5



* 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.

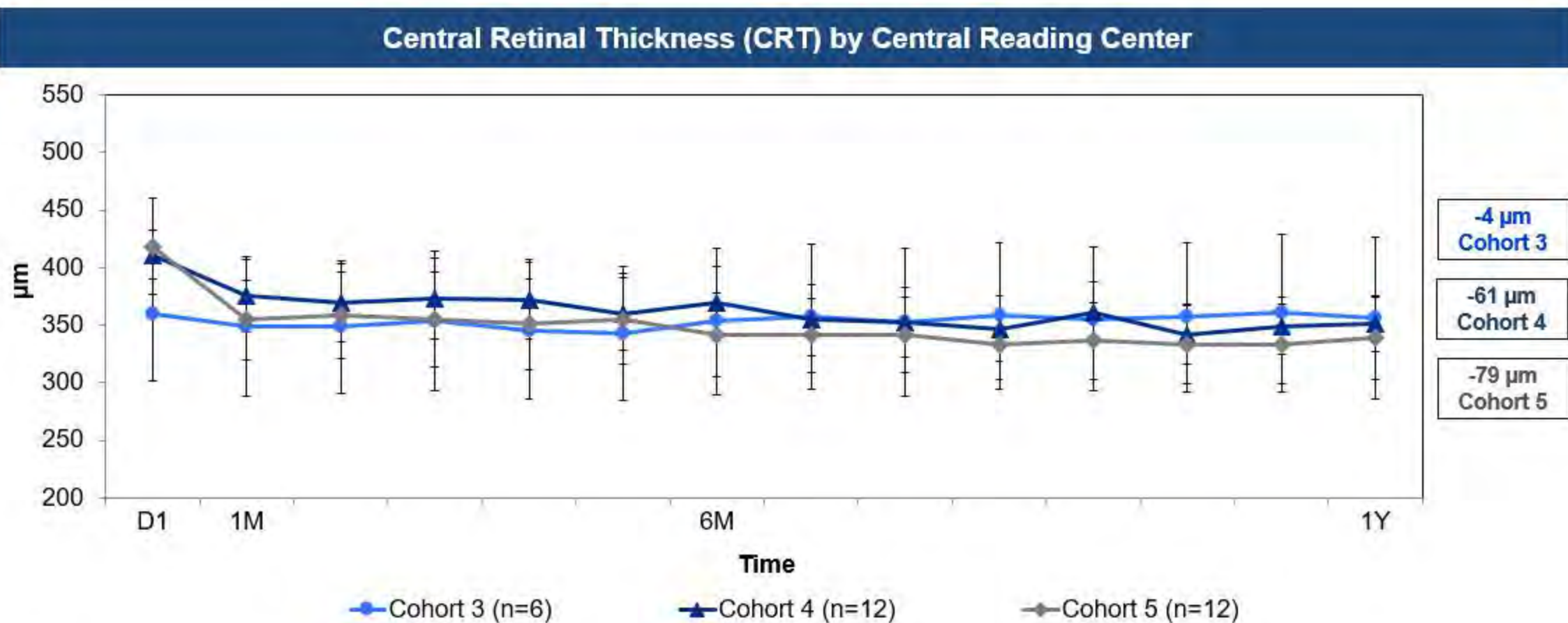
Mean BCVA Over 1 Year in Cohorts 3-5

Anti-VEGF Injection Free Subjects



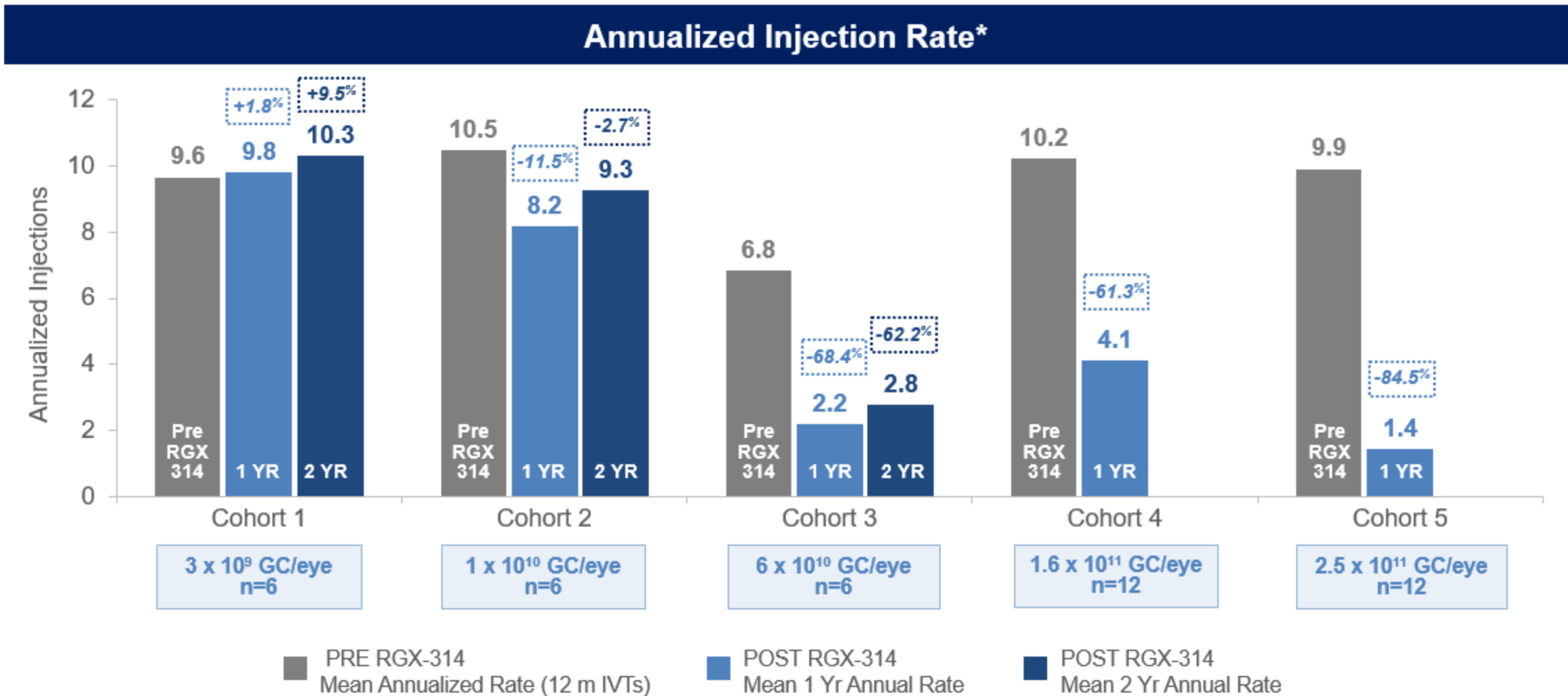
* One patient in Cohort 5 discontinued the study prior to Week 22 visit (subject injection-free at time of discontinuation) and was not included. Another patient in Cohort 5 has missed the visits since Week 46 due to COVID-19 and these visits were imputed using last observation carried forward (LOCF).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

Mean CRT Over 1 Year in Cohorts 3-5



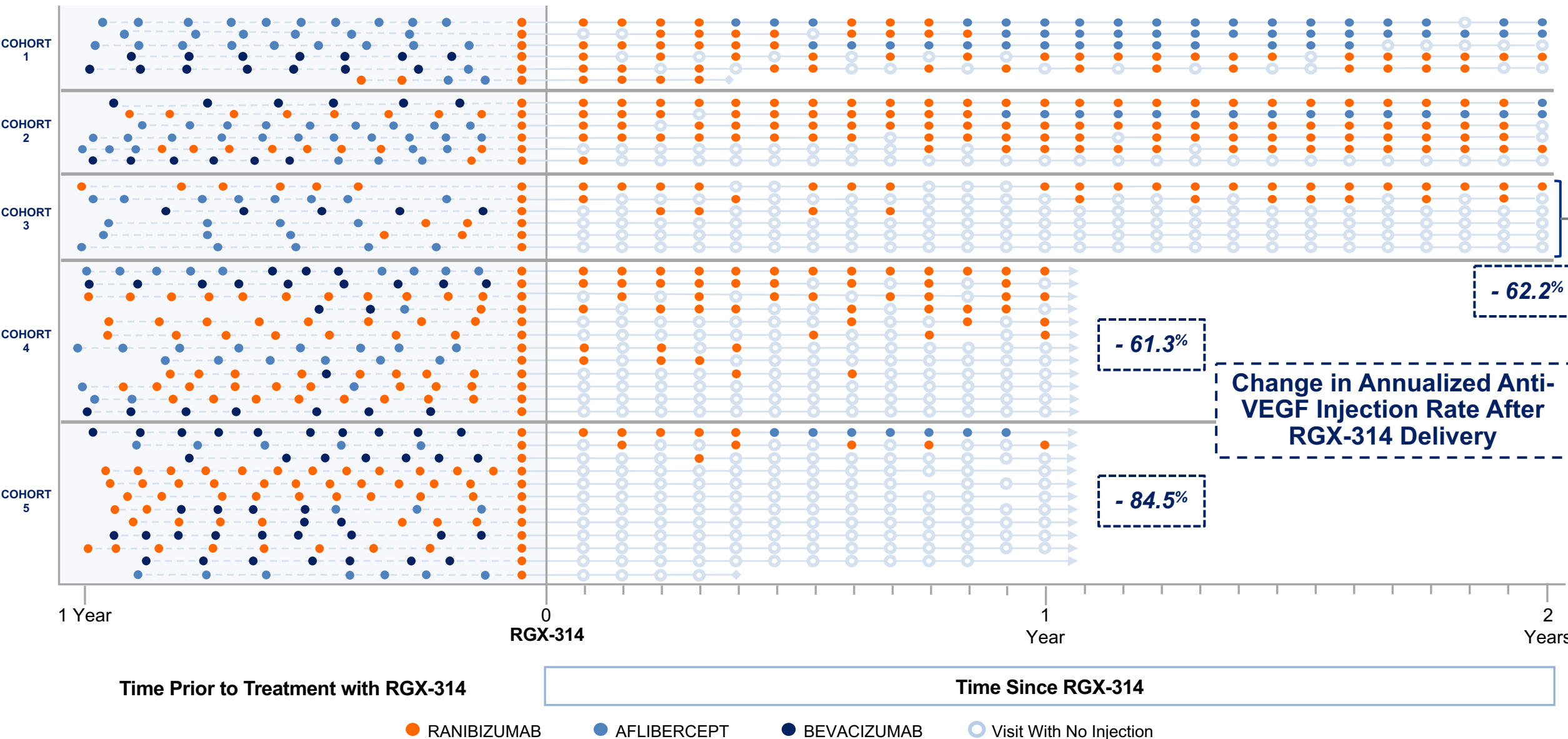
*One patient in Cohort 5 discontinued the study prior to Week 22 visit and another patient has missed the visits since Week 46 visit due to COVID-19. For these patients, subsequent visits were imputed using last observation carried forward (LOCF). Seven additional missing CRT results were interpolated.

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.

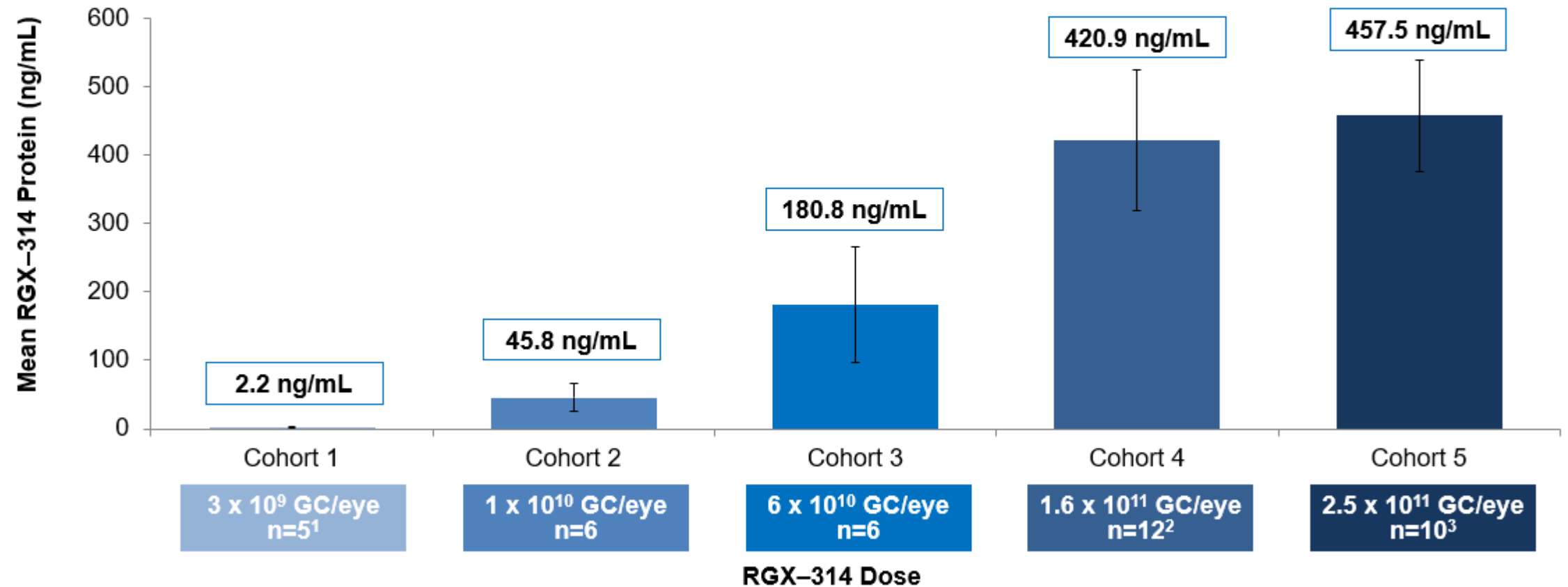
Cohort 1-5 Injections PRE and POST RGX-314 Over 2 Years



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



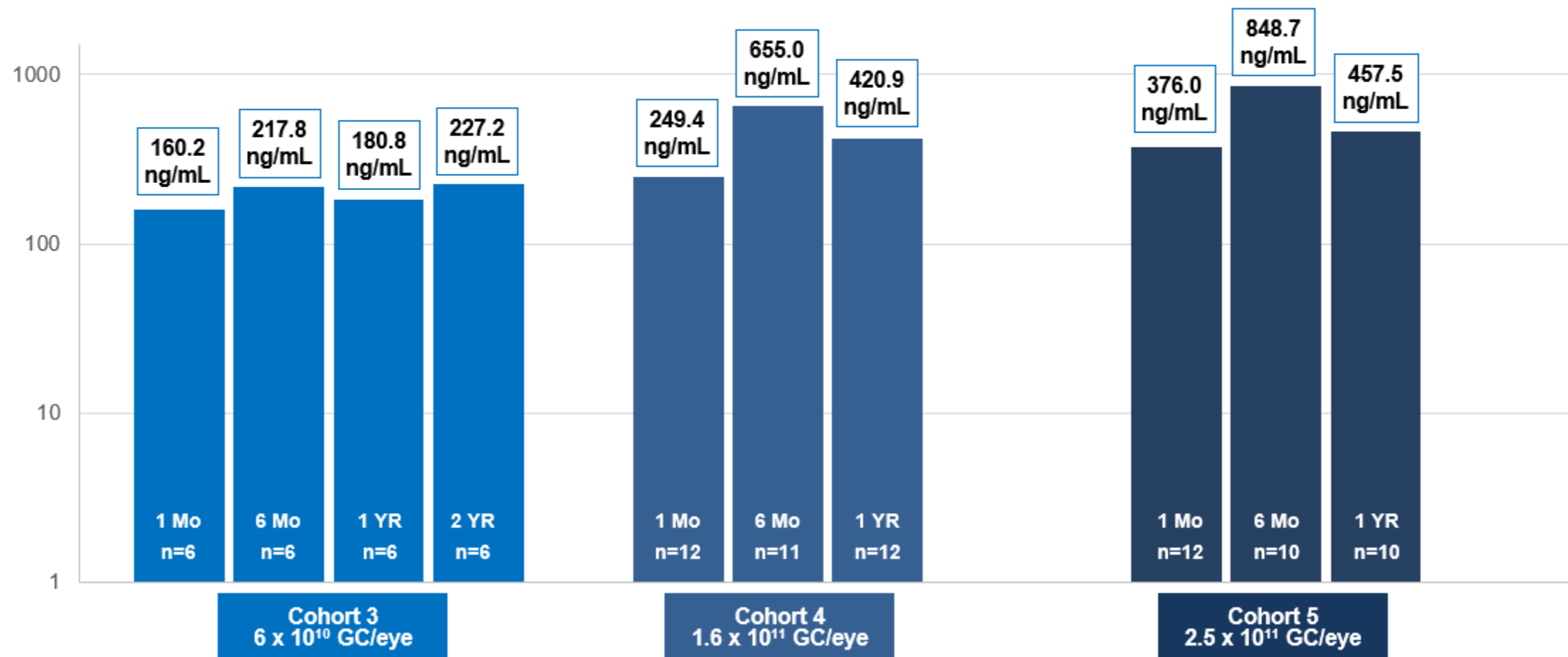
¹One patient in Cohort 1 discontinued the study prior to Week 22 visit.

²One unscheduled visit has been assigned to Week 54.

³One 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

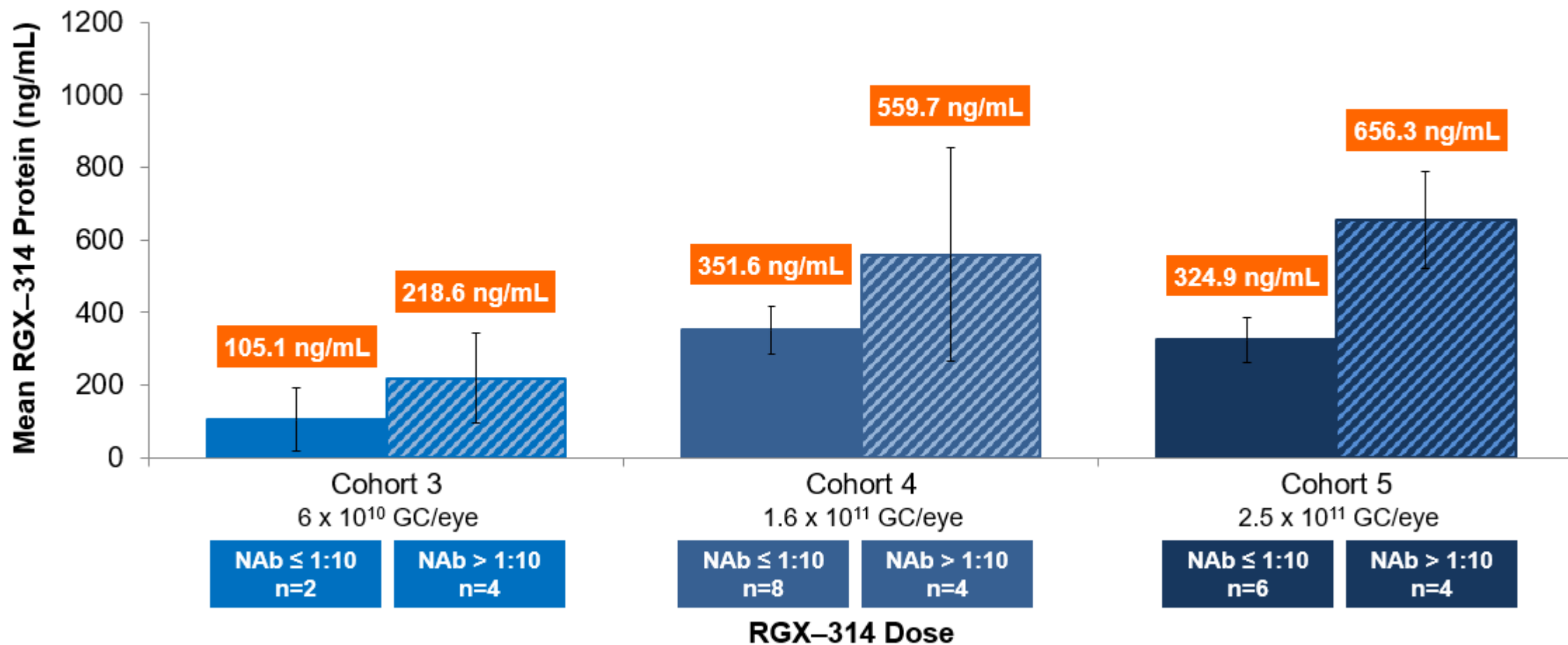
As Measured from Aqueous Samples by ECL



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 Status¹

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.

Interim Conclusions from RGX-314 Phase I/IIa Trial in Wet AMD

- RGX-314 Phase I/IIa wAMD study has fully enrolled 42 patients in 5 dose cohorts
- RGX-314 continues to be generally well-tolerated across all dose levels
- Intraocular RGX-314 protein levels demonstrate dose-dependent expression across all cohorts at one year with stable intraocular RGX-314 protein expression in C3 over 2 years.
- Long-term, durable treatment effect demonstrated over 1 year (C4 & 5) and 2 years post RGX-314 (C3)
 - Stable to improved visual acuity and retinal thickness
 - Meaningful reductions in anti-VEGF injection burden
- Baseline serum NAbs to AAV8 did not impact protein production for RGX-314 given subretinally

RGX-314 Routes of Administration

Subretinal Delivery¹



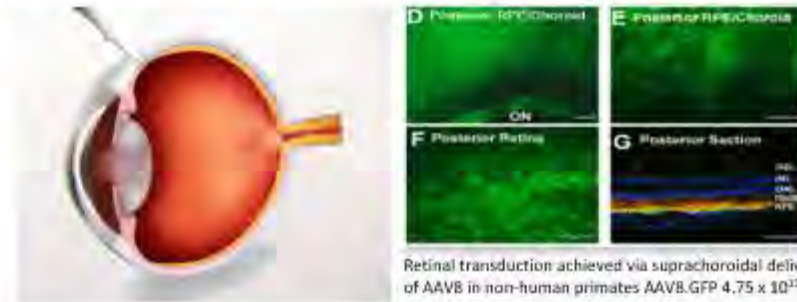
Retinal transduction achieved via subretinal delivery of AAV8 in non-human primates AAV8.GFP 1.0×10^{13} GC

- 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-314³

AAV Neutralizing Antibody (NAb) Status

- All patients eligible, regardless of NAb status

Suprachoroidal Delivery²



Retinal transduction achieved via suprachoroidal delivery of AAV8 in non-human primates AAV8.GFP 4.75×10^{13} 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 NAb to AAV8⁴

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

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**

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**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**

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