Additional Positive Long-term and Interim Phase I/IIa Trial Update for RGX-314 for the Treatment of Wet AMD

Conference Call Presentation

April 22, 2020

REGENXBIO®

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Today's Update from RGX-314 Phase I/IIa Trial in Wet AMD

- RGX-314 continues to be well-tolerated at all dose levels
- Cohort 3: Long-term, durable treatment effect demonstrated over 2 years post RGX-314
  - Improved visual acuity and stable retinal thickness
  - Significantly reduced treatment burden
  - Stable intraocular RGX-314 protein expression
- Cohort 5: 73% (8/11) of patients remain anti-VEGF injection-free at 9 months
- Across all Cohorts: Intraocular RGX-314 protein levels at 6 months demonstrate dose-dependent expression

Featured Retina Specialist Key Opinion Leaders / Study Investigators:

- Allen C. Ho, M.D., Director of Retina Research at Wills Eye Hospital and Mid Atlantic Retina
- Robert Avery, M.D., Founder of California Retina Consultants and Research Foundation
- Peter Campochiaro, M.D., Director of the Retinal Cell and Molecular Laboratory at Johns Hopkins Wilmer Eye Institute

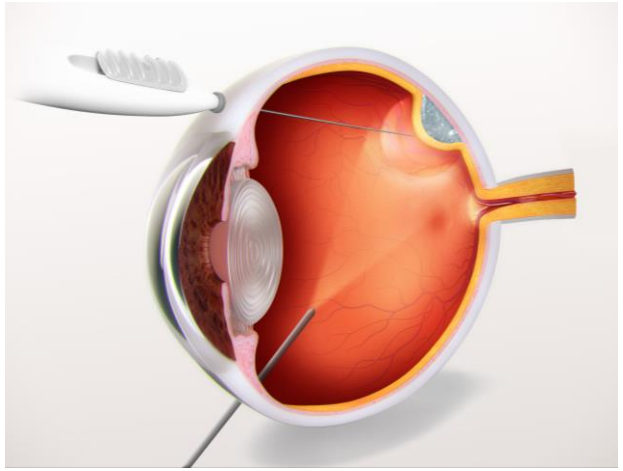
Cohort 3: Long-term, Durable Treatment Effect Over 2 Years

- **50% (3/6) patients anti-VEGF injection free at 2 years**
- **67% (4/6) patients anti-VEGF injection free after 9 months**

	Full Cohort (N=6)	Patients with Zero Injections after 9 months (N=4)
Improved Visual Acuity[1]	+14 letters	+14 letters
Stable Retinal Thickness[1]	+2 µm	+9 µm
Significantly Reduced Treatment Burden[2]	>60% reduction 2.8 inj/year	>90% reduction 0.5 inj/year
Stable Intraocular RGX-314 Protein[3]	217.8 ng/mL at 6 months 227.2 ng/mL at 2 years	273.6 ng/mL at 6 months 291.7 ng/mL at 2 years

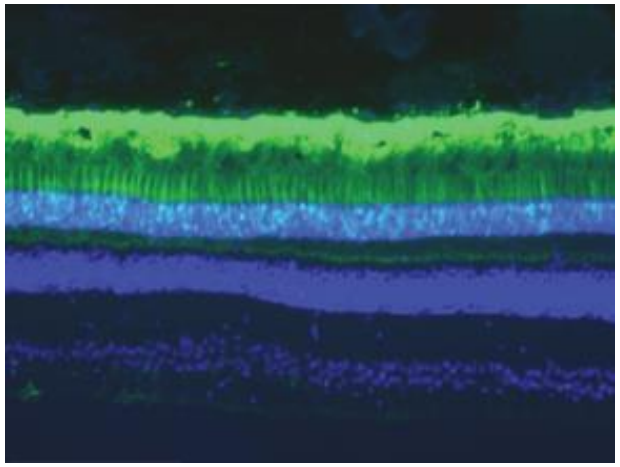
[1]Mean change from baseline at 2 years
[2]Reduction of annualized rate of anti-VEGF injections compared to 12 months prior to RGX-314 administration
[3]Mean RGX-314 protein concentrations

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

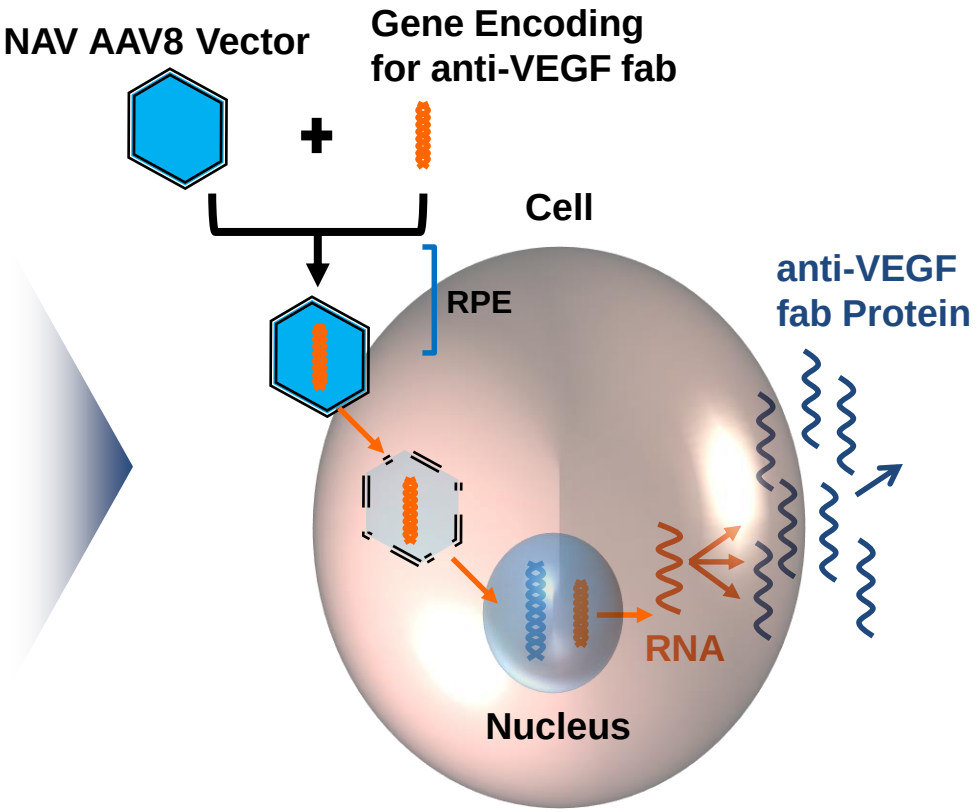


Subretinal Procedure

AAV8



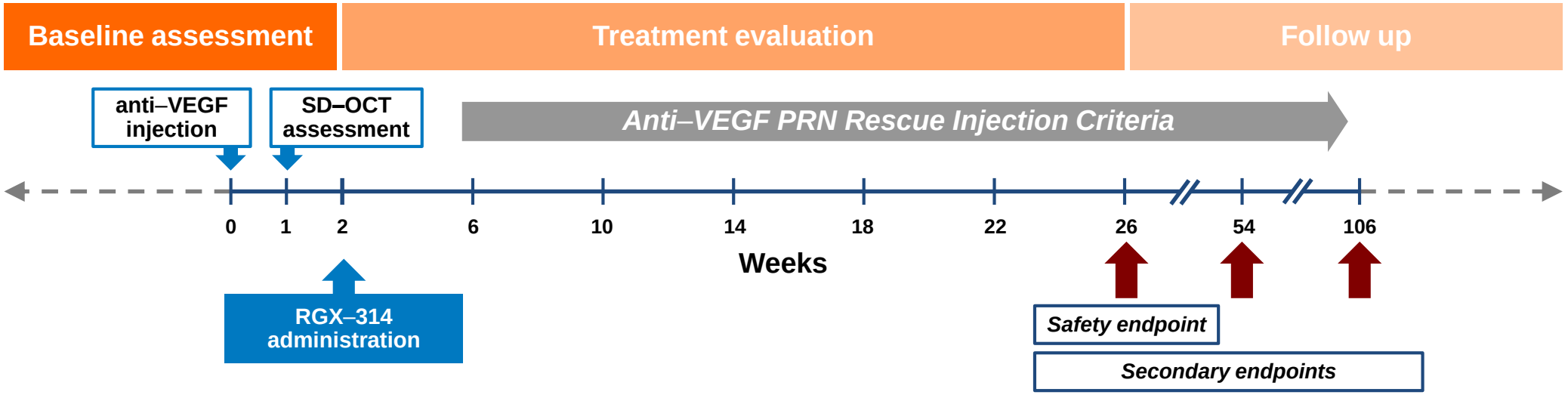
Efficient Gene Delivery to the RPE[1]



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

Subretinal Dosing Completed in 42 patients Across Five Dose Cohorts

[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**	**71.7**	**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 well–tolerated across all doses (n=42)
- No drug-related SAEs reported; 16 SAEs that were not drug-related reported in 10 patients[1]
- Common ocular AEs in the study eye included:
  - Post-operative conjunctival hemorrhage (69% of patients) – 100% mild, majority resolved within days to weeks
  - Mild to moderate retinal pigmentary changes[2] (67% of patients across all cohorts; 83% of patients in Cohorts 3-5) – 71% mild, none severe
    - No evidence of clinical symptoms or changes to visual acuity related to these observations
  - Post-operative inflammation[3] (36% of patients) – resolved within days to weeks, 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) – 90% mild, none severe
  - Retinal hemorrhage (17% of patients) – an anticipated event in the severe wet AMD population, 100% mild
- No reports of clinically-determined immune responses, drug-related ocular inflammation, or post-surgical inflammation beyond what is expected following routine vitrectomy

Data cut April 6, 2020

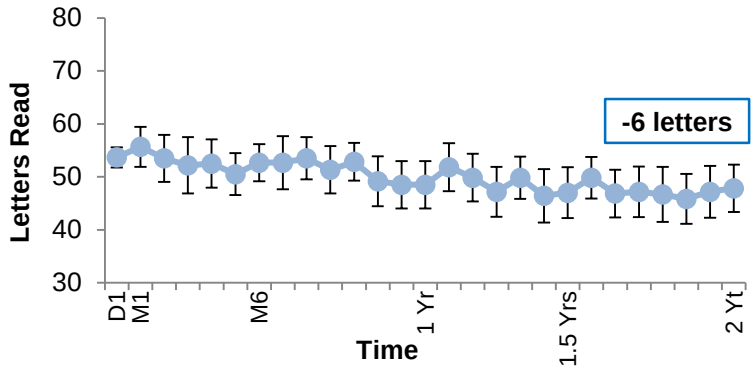
[1]Includes two deaths unrelated to RGX-314; Two ocular procedure-related SAEs: peripheral retinal detachment which was repaired and an endophthalmitis post aqueous sample collection

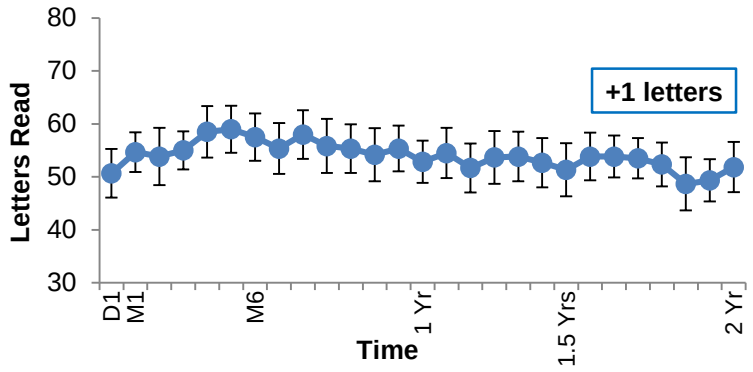
[2]Retinal pigmentary changes observed were hypo and hyper pigmentation on imaging occurring in the bleb area or inferior retina

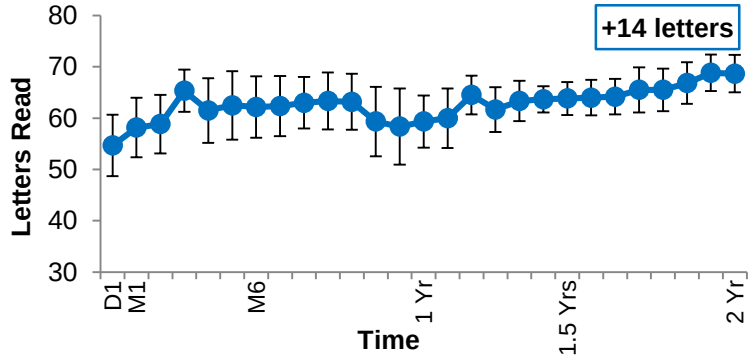
[3]Transient inflammation includes AC cells, flare, or inflammation

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

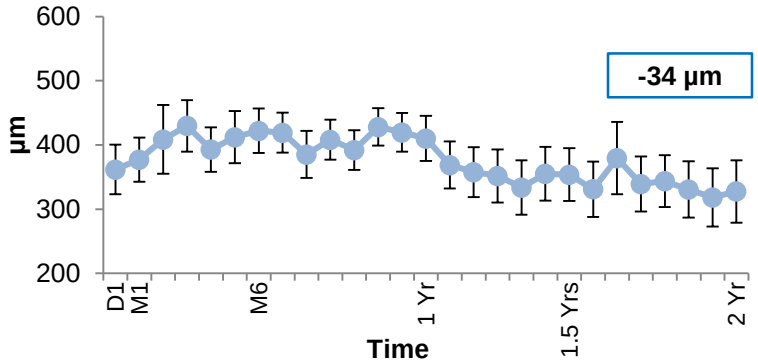
Best Corrected Visual Acuity (BCVA)

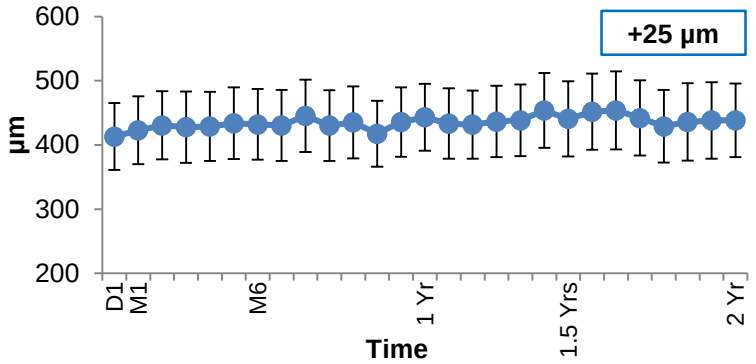


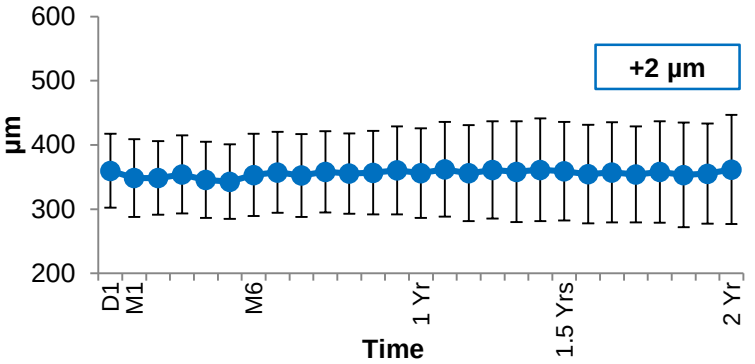




Central Retinal Thickness (CRT) by Central Reading Center





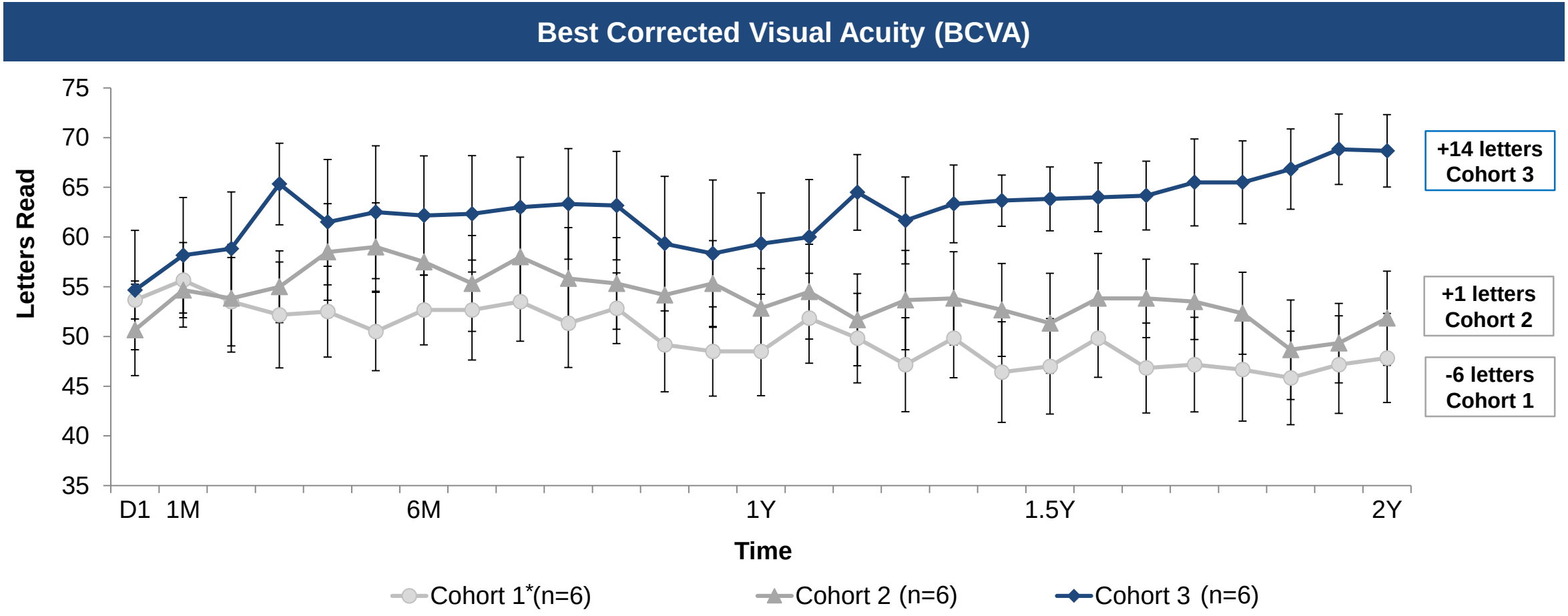


10.3 Injections (annualized)	**9.3 Injections** (annualized)	**2.8 Injections** (annualized)
Cohort 1[1]	**Cohort 2**	**Cohort 3**

[1]One 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 Change in BCVA Over 2 Years

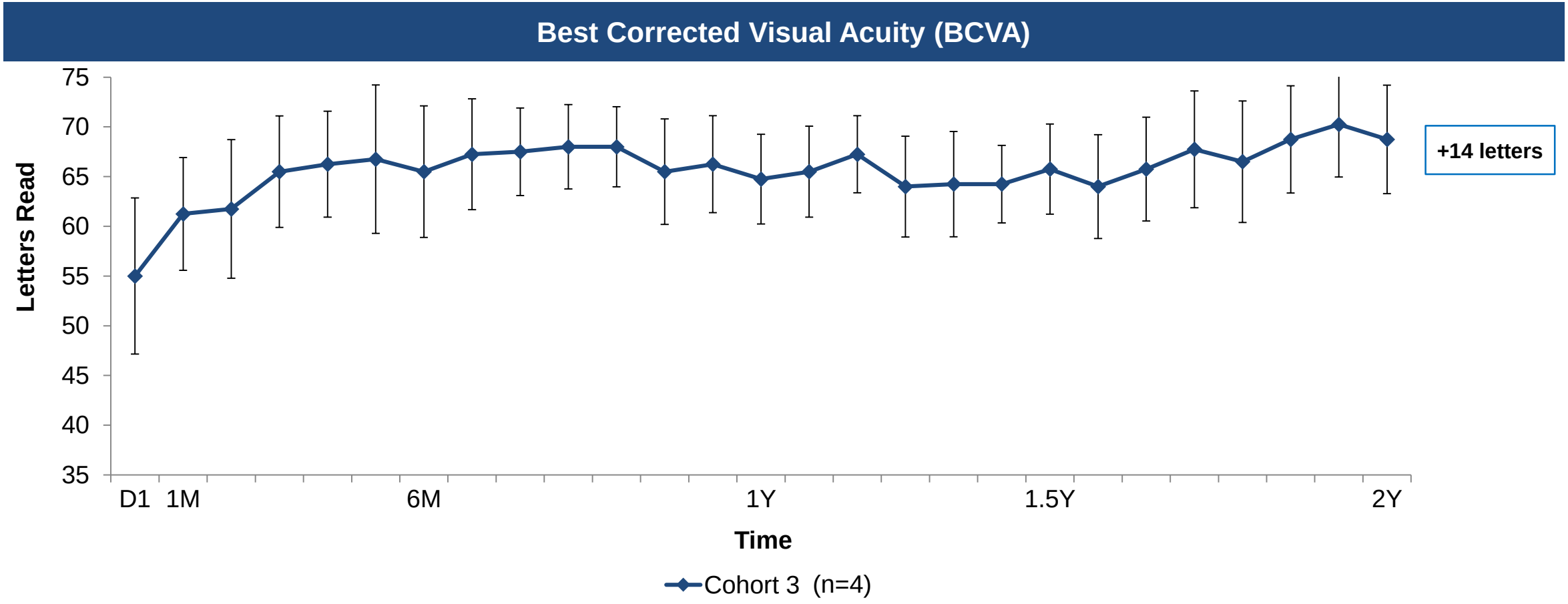
Improved vision over 2 years in Cohort 3



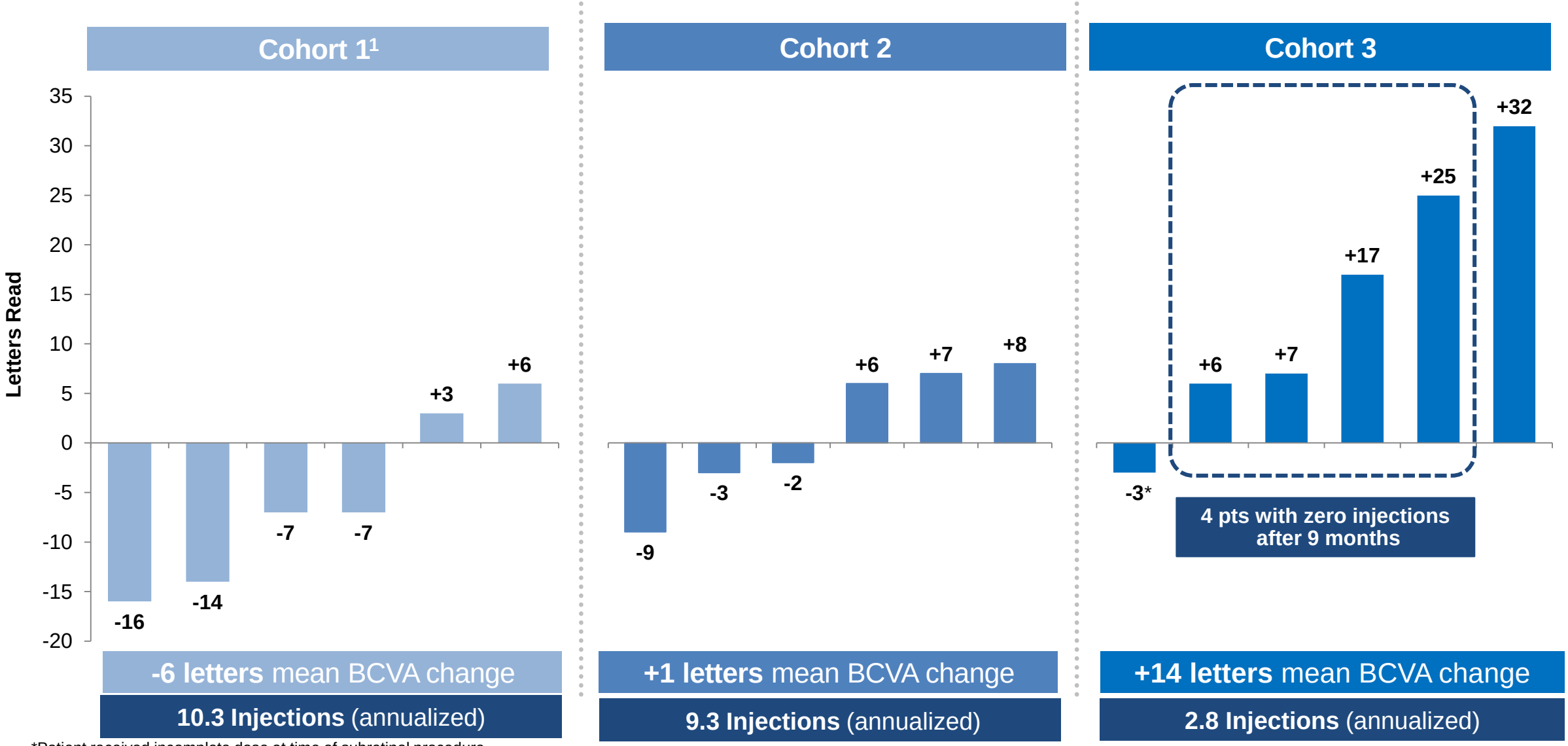
*One patient in Cohort 1 discontinued the study prior to Week 22 visit. For this patient, subsequent visits (Week 22 and after) were imputed using last observation carried forward (LOCF). Two other missing BCVA results at Week 14 and Week 74 in Cohort 1 were interpolated.

Mean Change in BCVA Over 2 Years

Improved vision over 2 years in Cohort 3 patients with zero anti-VEGF injections after 9 months



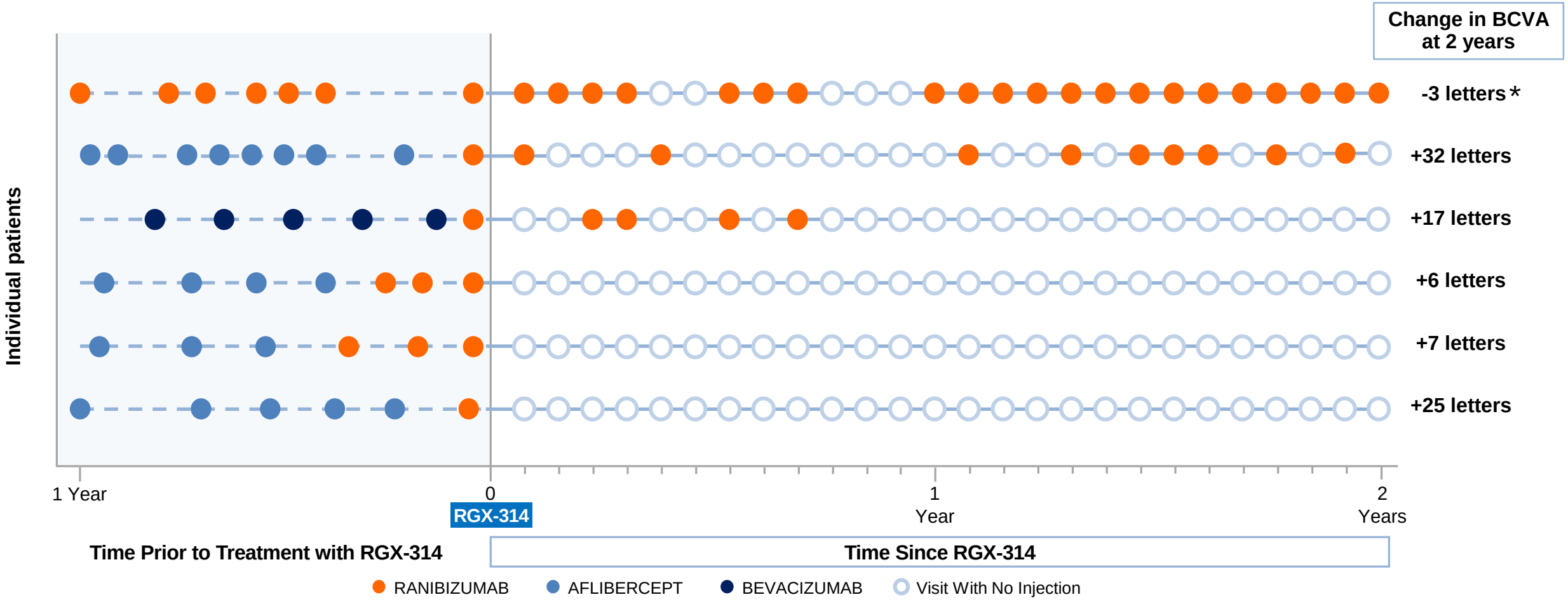
Individual Patient Visual Acuity Change from Baseline at 2 Years in Cohorts 1-3



*Patient received incomplete dose at time of subretinal procedure

[1]One 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.

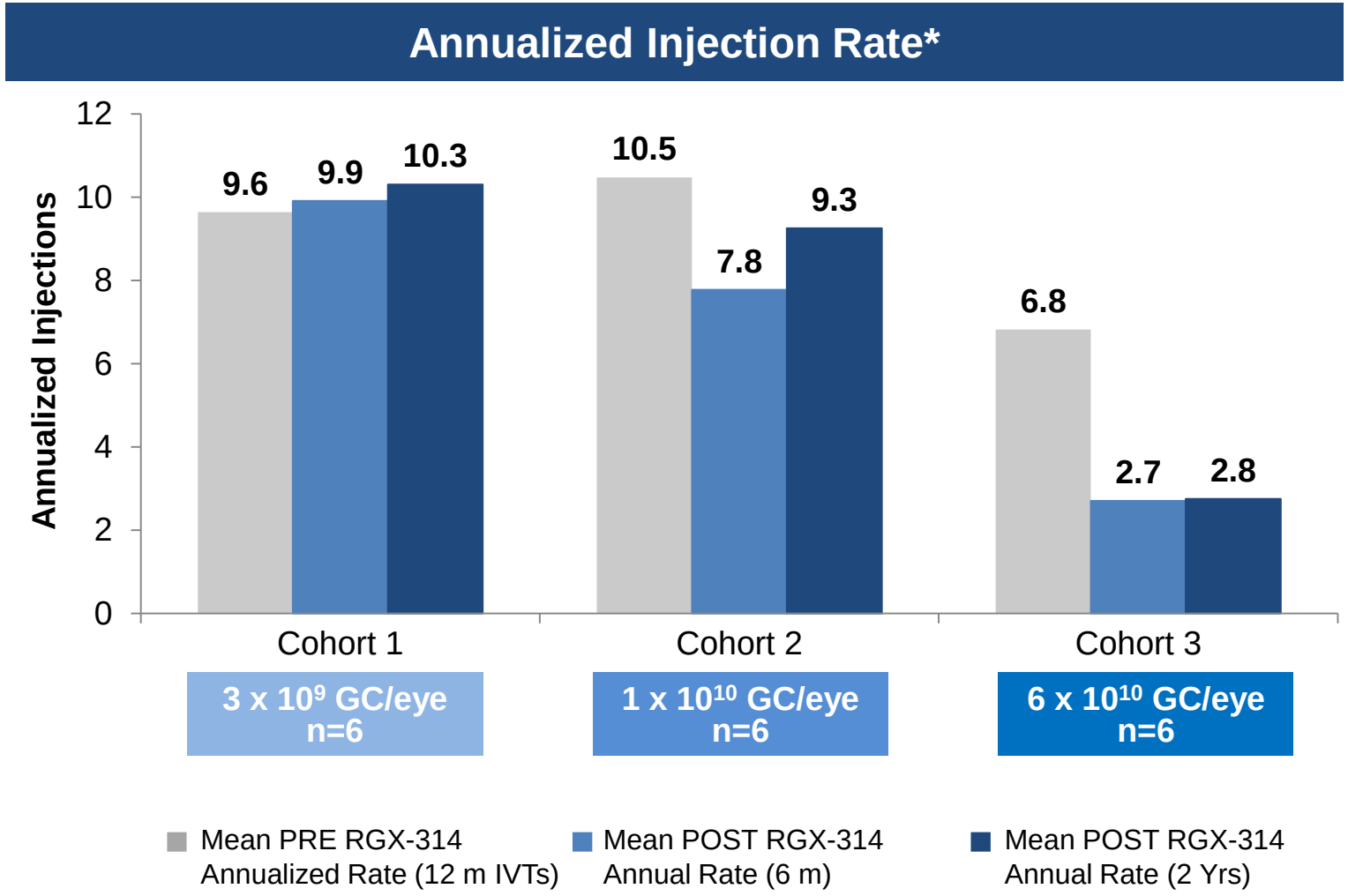
Cohort 3 Injections PRE and POST RGX-314 Over 2 Years



*Patient received incomplete dose at time of subretinal procedure

Mean Change in Annualized Injection Rate PRE and POST RGX-314 in Cohorts 1-3

Significantly reduced treatment burden in Cohort 3



In Cohort 3:

50% (3/6) patients anti-VEGF injection free over 2 years post RGX-314

67% (4/6) patients anti-VEGF injection free after 9 months post RGX-314

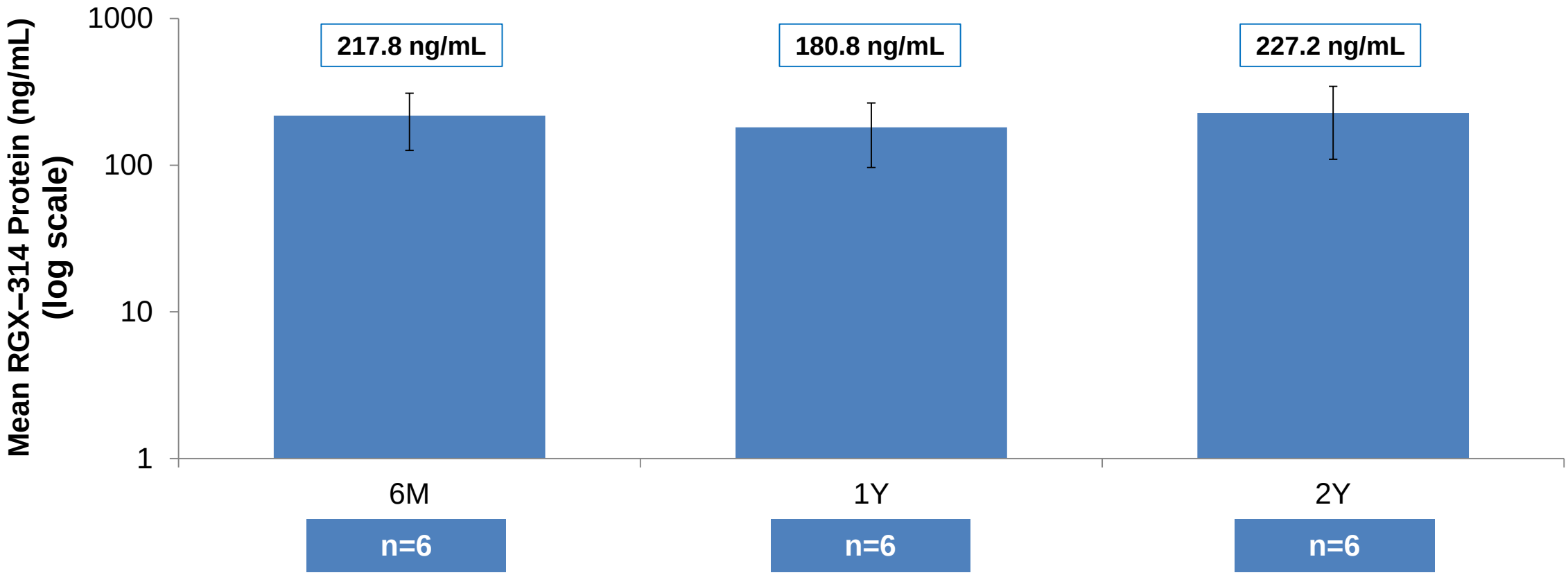
>60% reduction compared to 12 months prior to RGX-314 administration

*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 from RGX-314 administration through 24 months for C1-C3

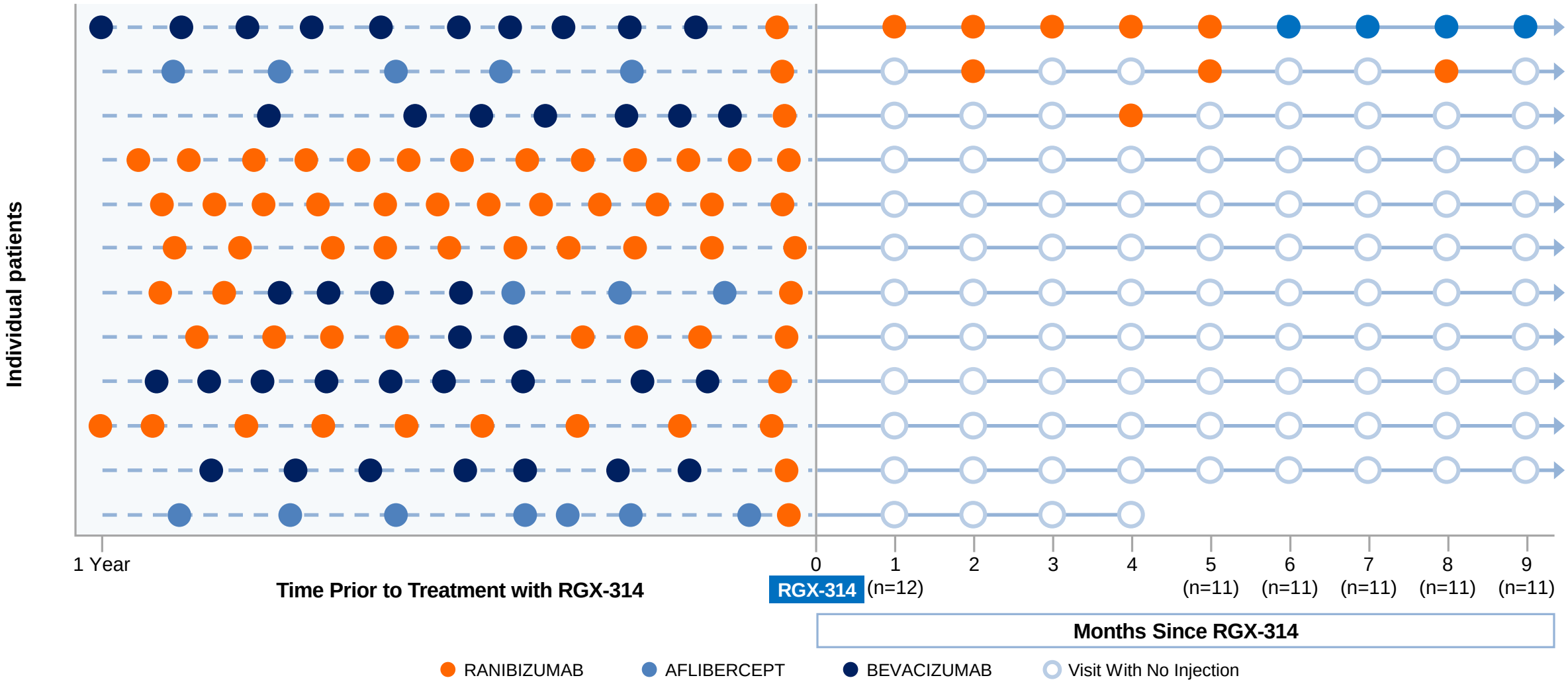
RGX-314 Protein Levels Over 2 Years in Cohort 3

Stable intraocular RGX-314 protein expression

As Measured from Aqueous Samples by ECL



Cohort 5: Injections PRE and POST RGX-314 over 9 Months

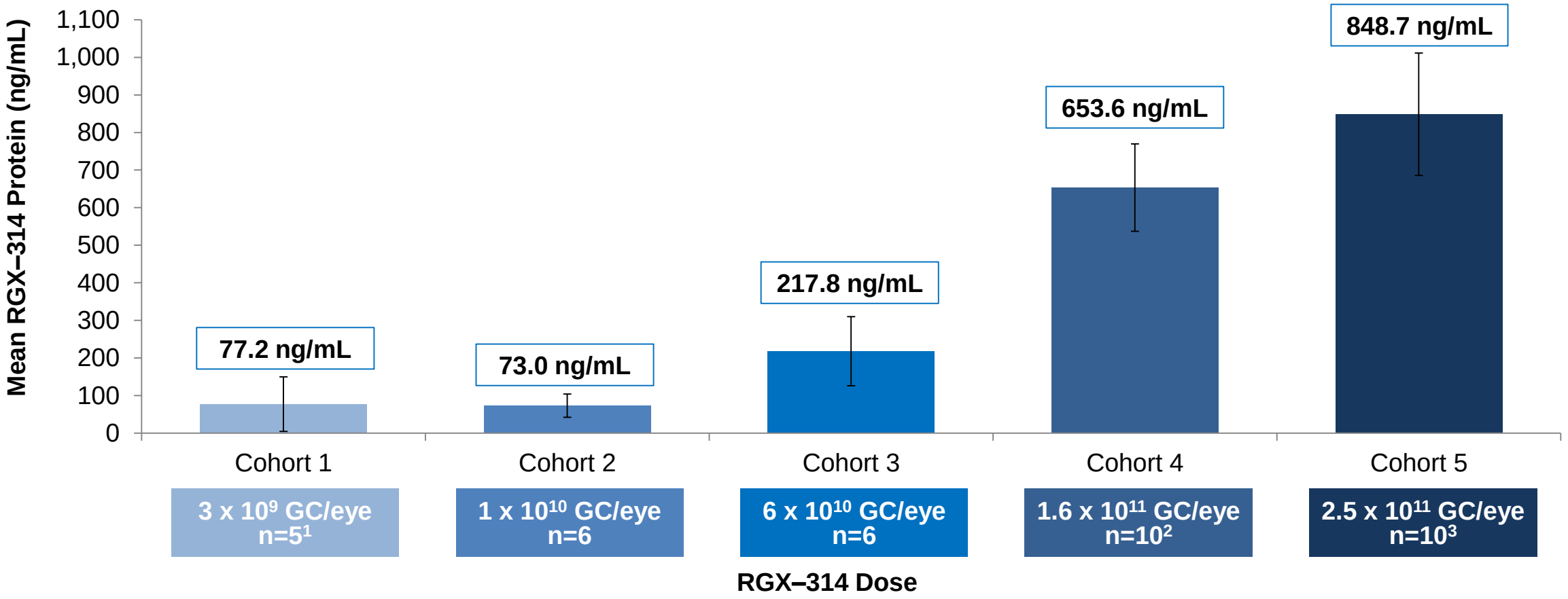


Note: One patient discontinued the study after 4 months.

RGX-314 Protein Levels at Month 6

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]Two patients in Cohort 4 did not have aqueous samples taken at Week 26
[3]One patient in Cohort 5 discontinued the study prior to Week 26 and another patient did not have aqueous sample taken at Week 26

Summary of Data Update from RGX-314 Phase I/IIa Trial in Wet AMD

- RGX-314 continues to be well-tolerated at all dose levels
- Cohort 3: Long-term, durable treatment effect demonstrated over 2 years
  - Improved visual acuity and stable retinal thickness
  - Significantly reduced treatment burden
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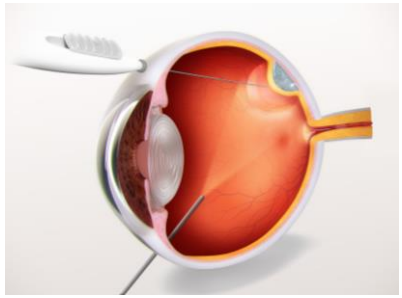
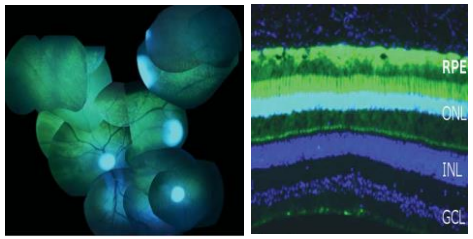
- Cohort 5: 73% (8/11) of patients remain anti-VEGF injection-free at 9 months
- Across all Cohorts: Intraocular RGX-314 protein levels at 6 months demonstrate dose-dependent expression

RGX-314 Routes of Administration

Subretinal Delivery[1]





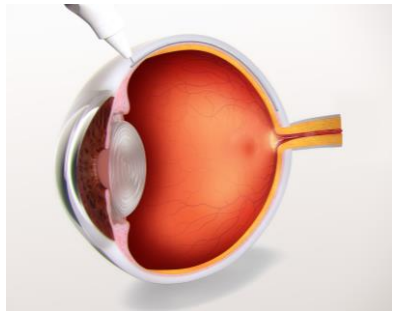
Retinal transduction achieved via subretinal delivery of AAV8 in non-human primates AAV8.GFP 1.0 x 10^{11} GC

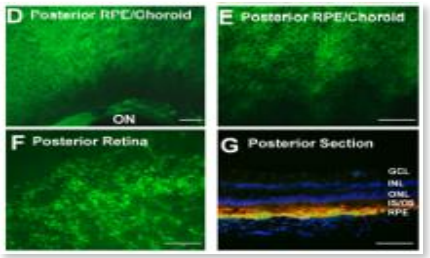
- Established route of delivery for gene therapy
- Direct and broad transduction of the retina observed
- Minimal exposure to the vitreous and anterior segment
  - Low risk of immune response
  - Low risk of inflammation
- No oral corticosteroid prophylaxis

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 oral corticosteroid prophylaxis

AAV NAb Status

- ~70% patients without NAbs to AAV8[3]

[1] Vandenberghe et al. 2011 Science Translational Medicine, 2 Ding, K., et al. 2019 Journal of Clinical Investigation, 3 Calcedo R, et al. 2009 Journal of Infectious Disease

Anticipated Upcoming Milestones for RGX-314 in Wet AMD in 2020

On-track to provide updates for subretinal and suprachoroidal programs

One-year data from Phase I/IIa trial Cohorts 4 & 5 expected in mid-2020

Begin dosing patients in a pivotal trial for RGX-314 subretinal delivery in 2H 2020

Initiate Phase II trial for RGX-314 suprachoroidal delivery in 1H 2020

Q&A

Featured Retina Specialist Key Opinion Leaders / Study Investigators:

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