Key Takeaways from the RGX-314 Phase I/IIa Clinical Trial for Wet AMD (Cohorts 1-5)

Jeffrey Heier, MD

Peter Campochiaro, MD, Allen Ho, MD, Albert Maguire, MD, David M. Brown, MD,
Robert Avery, MD, Dante Pieramici, MD, Szilard Kiss, MD, Arshad Khanani, MD, Charles Wykoff, MD
Samir Patel, MD, Keunpyo Kim, PhD, Darin Curtiss, PharmD, Stephen Pakola, MD, Sherri Van Everen, PharmD

AAO Retina Subspecialty Days 10/11/2019

Disclosures

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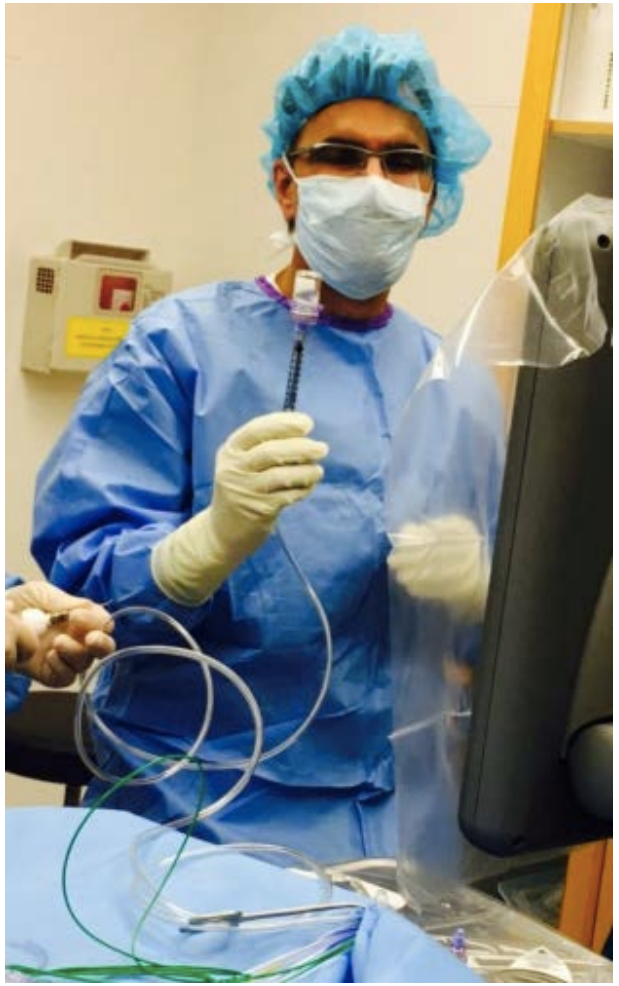
Board of Directors: Ocular Therapeutix

Equity: Adverum, Aldeyra, Allegro, jCyte, and Ocular Therapeutix



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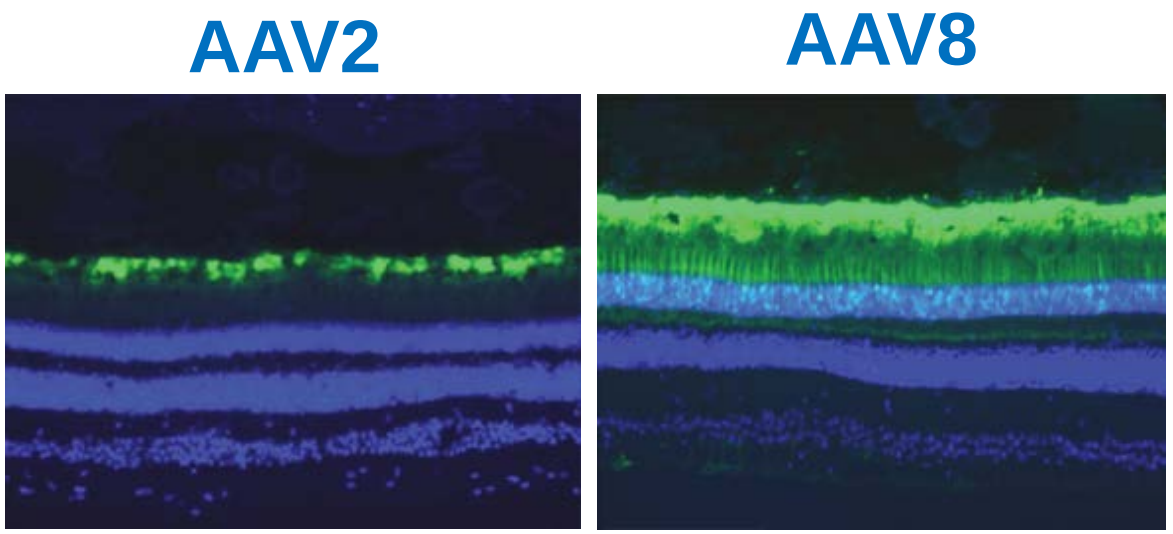
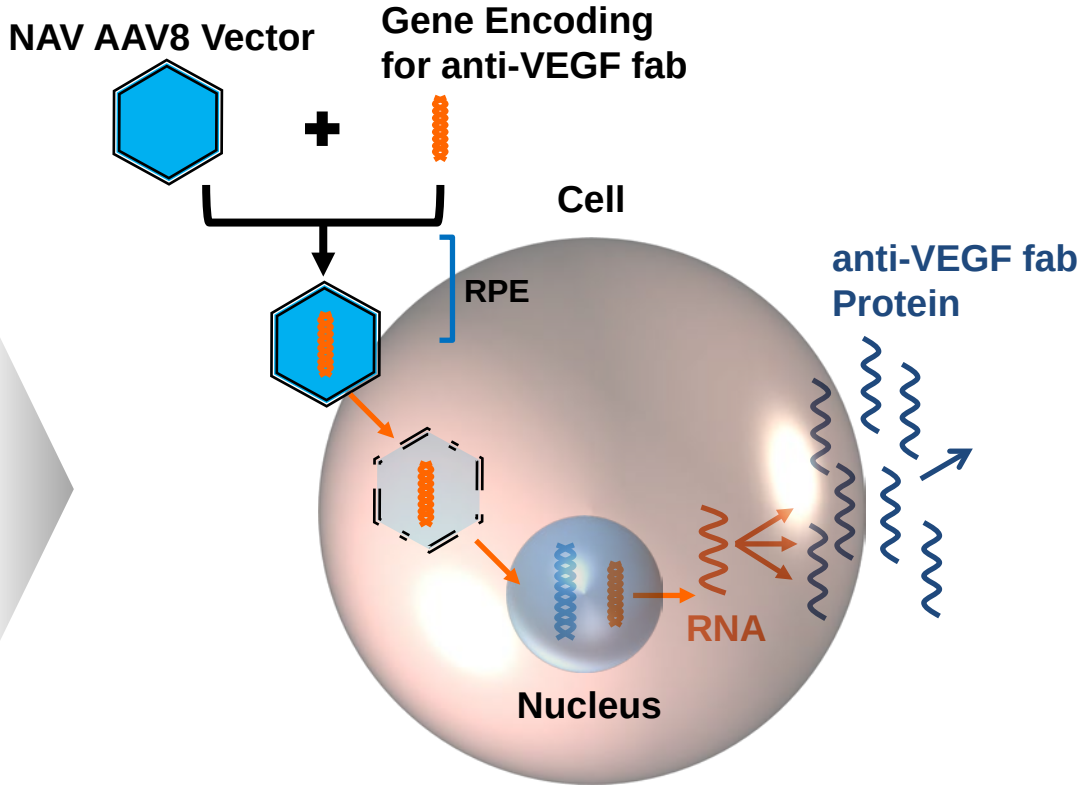
RGX-314 Uses a Novel AAV8 Vector to Deliver an anti-VEGF Fab



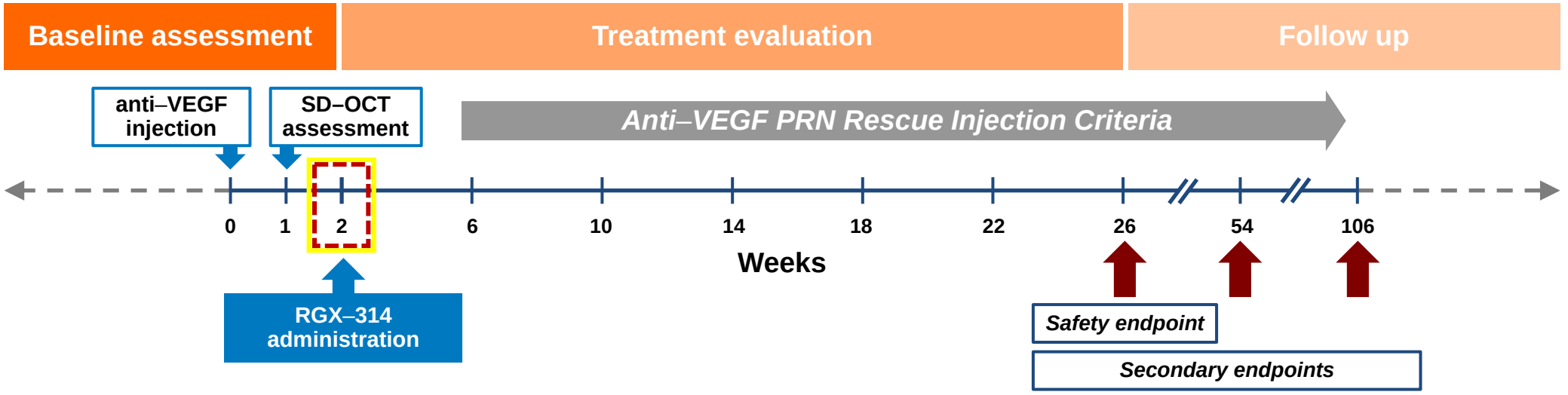
More Efficient Gene Delivery to the RPE[1]



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 Study Has Fully Enrolled 5 Dose Cohorts



Previously Treated Subjects 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 Subjects Across Five Dose Cohorts

1. Dose escalation safety review to occur four weeks after final subject 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**

Subjects Enrolled in the Phase I/IIa Trial Were Chronically Treated

	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	**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	**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	**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**
PRIOR THERAPY	**# Injections Since Diagnosis** (Mean)	**40.7**	**32.5**	**34.2**	**35.7**	**26.7**	**33.1**
PRIOR THERAPY	**Average Annualized Injections Prior to Entry**	**9.6**	**10.5**	**6.8**	**10.2**	**9.9**	**9.6**

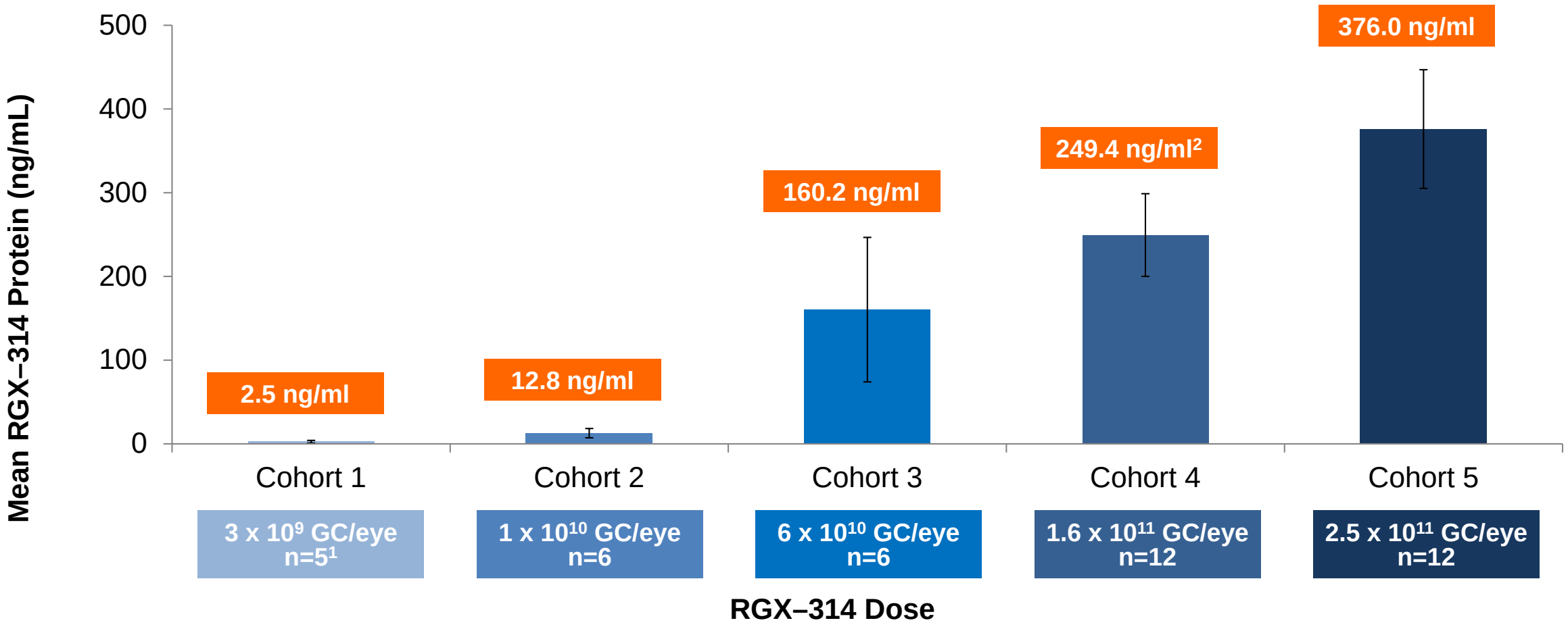
RGX-314 Has Been Well Tolerated in All Cohorts

- RGX–314 was ***well–tolerated*** (n=42)
- ***No drug-related SAEs***
- Most AEs were assessed as mild (Grade 1 – 79%)
- ***No observed clinically determined immune responses***, drug-related ocular inflammation, or any post-surgical inflammation beyond what is expected following routine vitrectomy
- ***Fifteen SAEs*** that were not drug-related were ***reported in nine subjects***
  - ***Two deaths unrelated to RGX-314***
  - ***Two ocular procedure-related SAEs:*** peripheral retinal detachment which was repaired and an endophthalmitis post aqueous sample collection

* Data cut October 9, 2019

Dose Dependent Increase in RGX-314 Protein Observed Across Cohorts

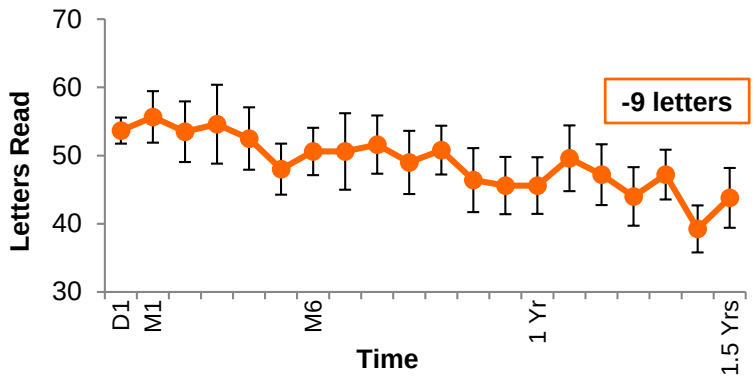
As Measured from Aqueous Samples by ECL 1 Month post-RGX-314

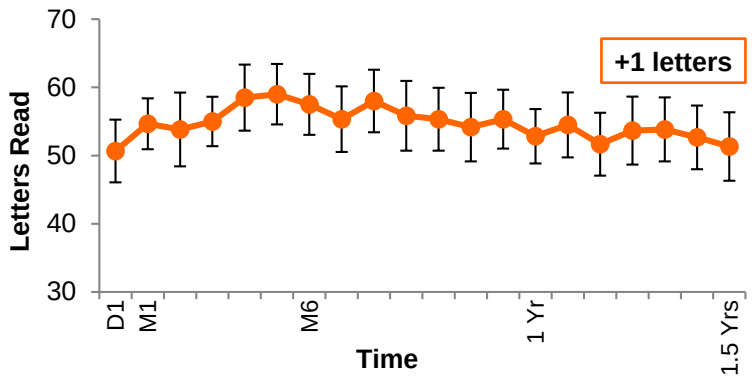


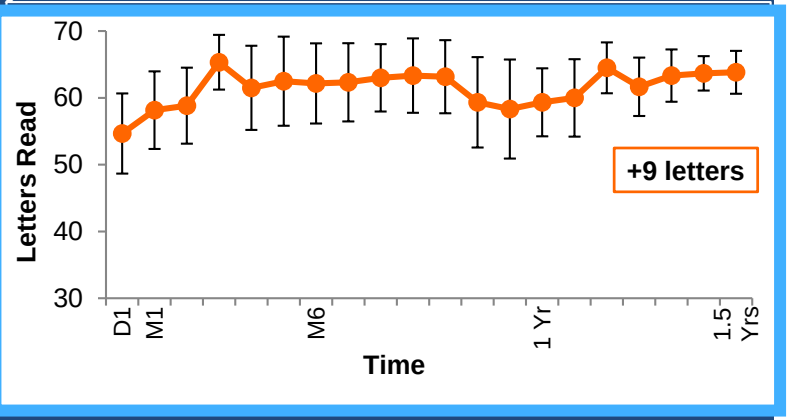
1. N=5; one subject in Cohort 1 did not have aqueous sample taken at Week 6
2. One subject's protein concentration measured at Day 17 post RGX-314 administration (no 4 week sample available)

Cohort 3: Sustained Visual and Anatomic Outcomes over 1.5 years

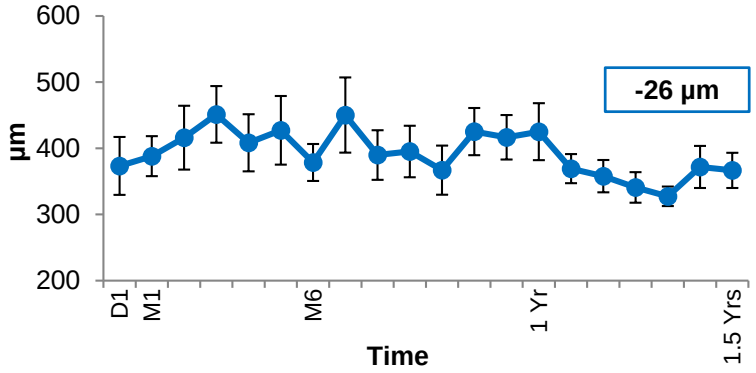
Best Corrected Visual Acuity (BCVA)

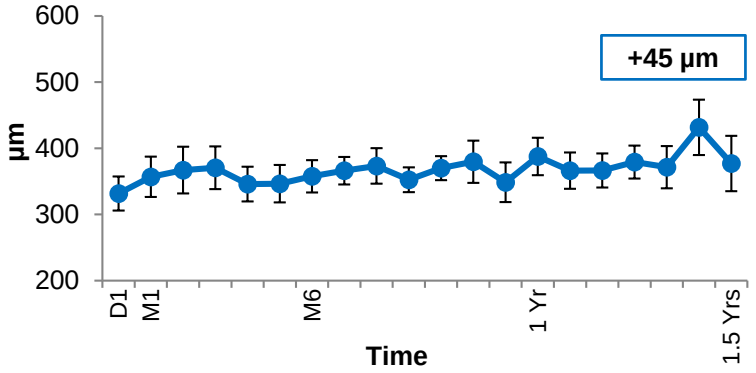


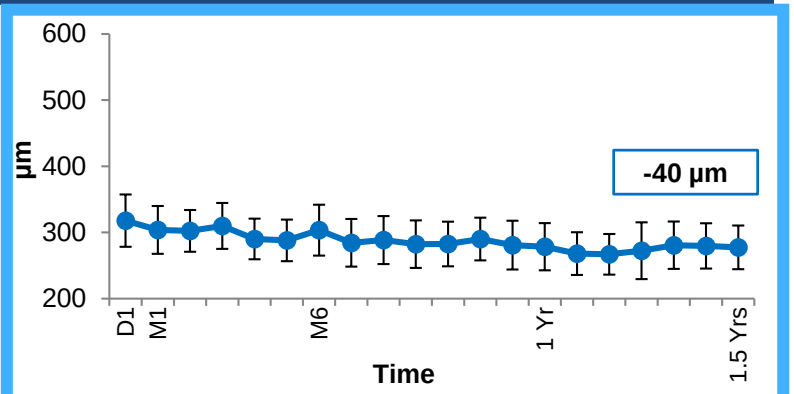




Central Retinal Thickness (CRT) on Heidelberg SD-OCT







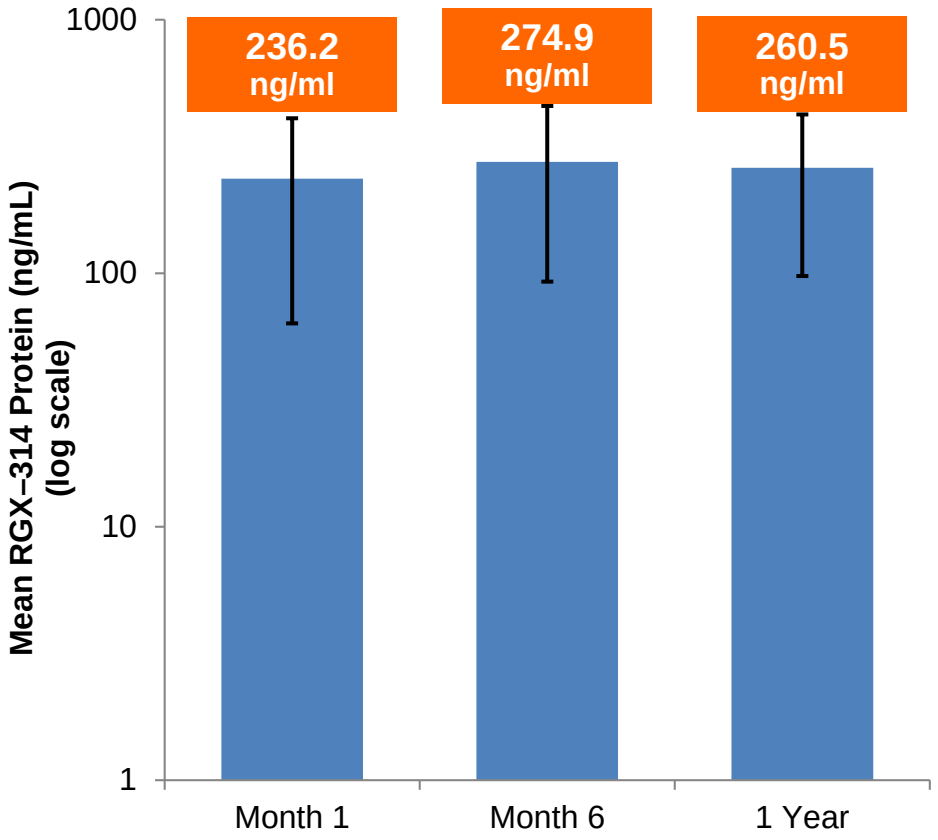
10.5 Injections (annualized)	**9.0 Injections** (annualized)	**2.6 Injections** (annualized)
Cohort 1[1]	**Cohort 2**	**Cohort 3**

1. One subject in Cohort 1 discontinued from the study at four months with four injections and was imputed as requiring one injection per every 4 weeks visit.

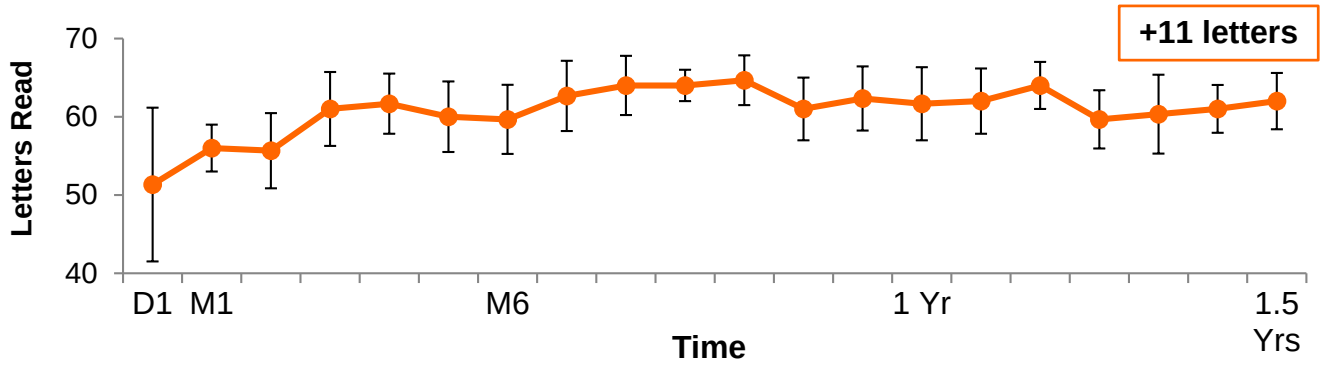
Cohort 3: Injection-free Subjects Continue to Do Well Over 1.5 Years

Anti-VEGF Injection-free Subjects (n= 3 of 6)

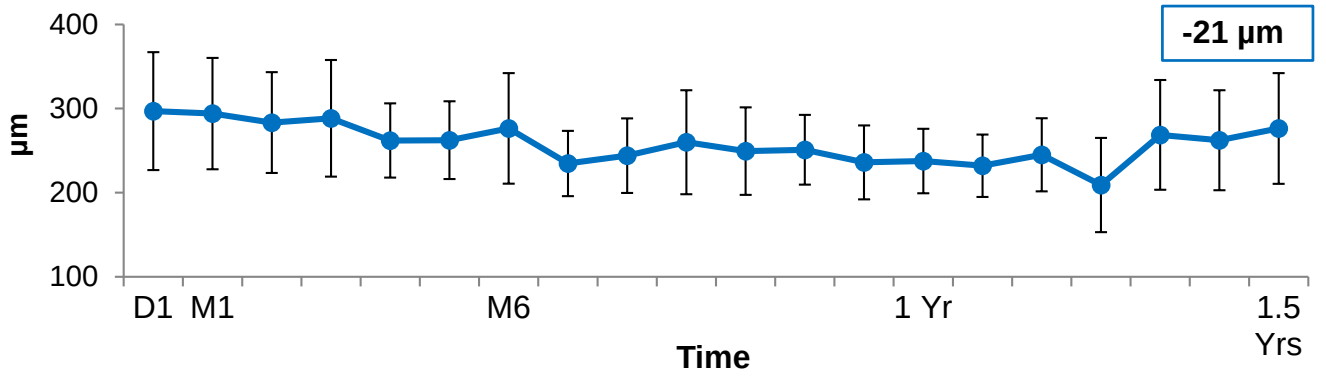
Sustained RGX-314 Protein Levels Over 1 Year



Best Corrected Visual Acuity (BCVA)

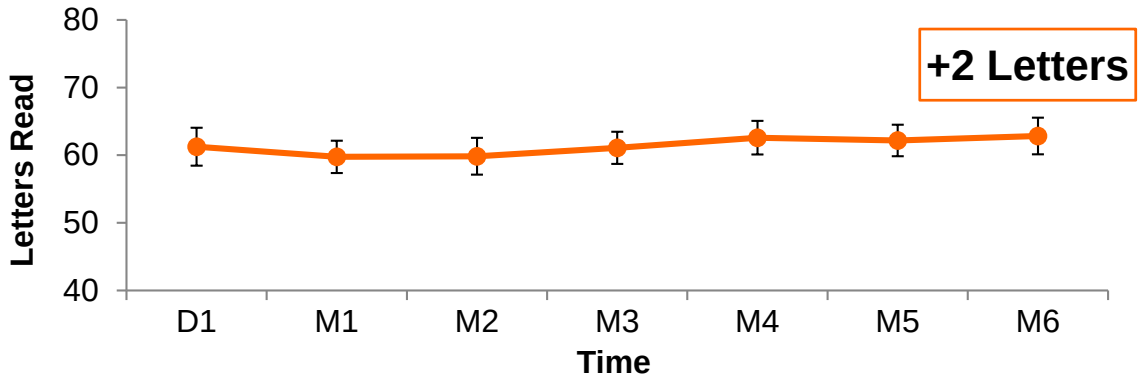


Central Retinal Thickness (CRT) on Heidelberg SD-OCT

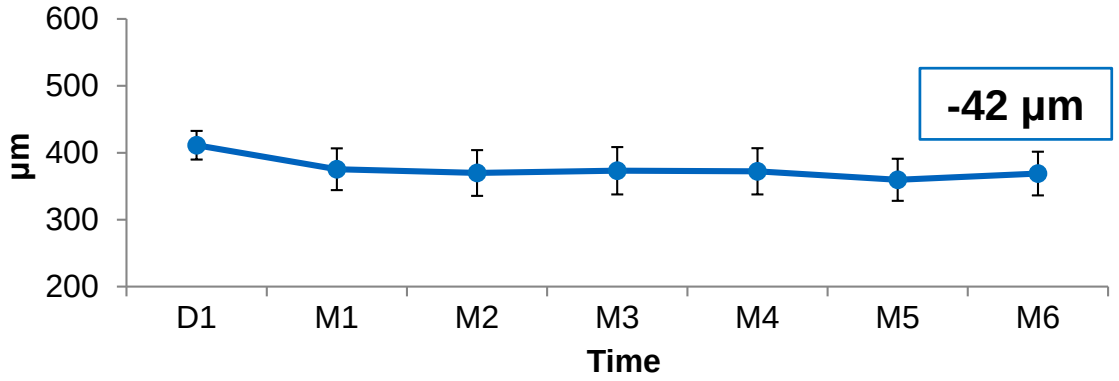


Cohort 4: Visual and Anatomic Outcomes

Best Corrected Visual Acuity (BCVA)



Central Retinal Thickness (CRT) on Heidelberg SD-OCT*



2.2 inj / 6 mo

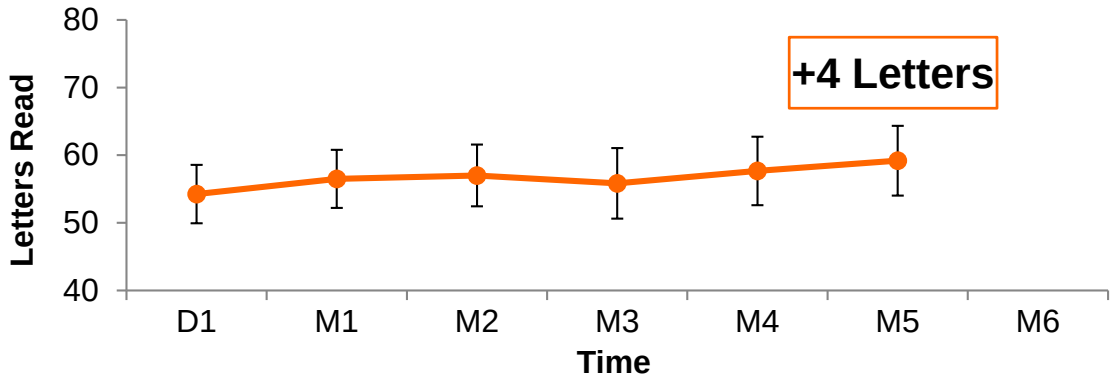
Cohort 4 (n=12)

- **Stable to improved vision and OCT** on average
- **42% (5 of 12) injection-free** at 6 months
- 2 patients with incomplete response to anti-VEGF receiving monthly injections

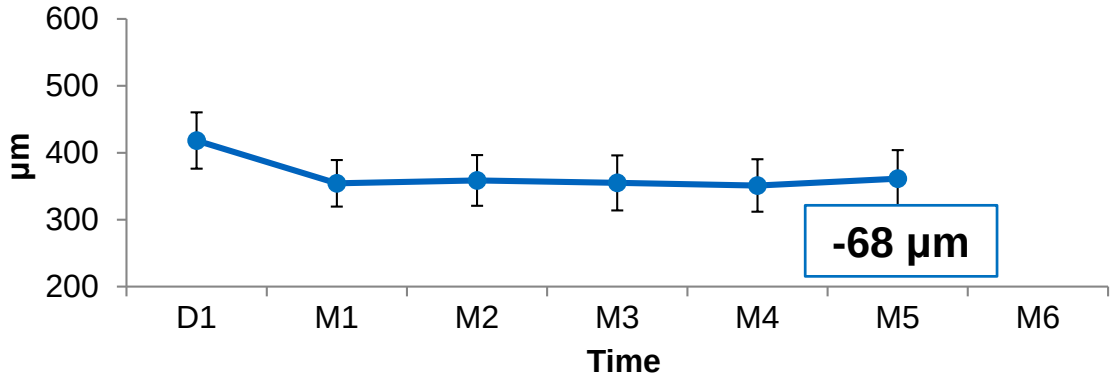
- SD-OCT data read by a central reading center (Duke Reading Center).

Cohort 5: Visual and Anatomic Outcomes

Best Corrected Visual Acuity (BCVA)



Central Retinal Thickness (CRT) on Heidelberg SD-OCT*



0.8 inj / 5 - 6 mo

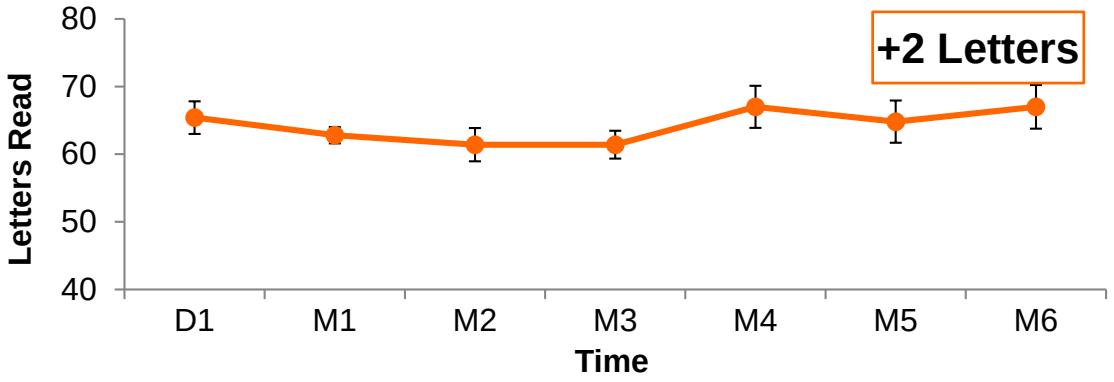
Cohort 5

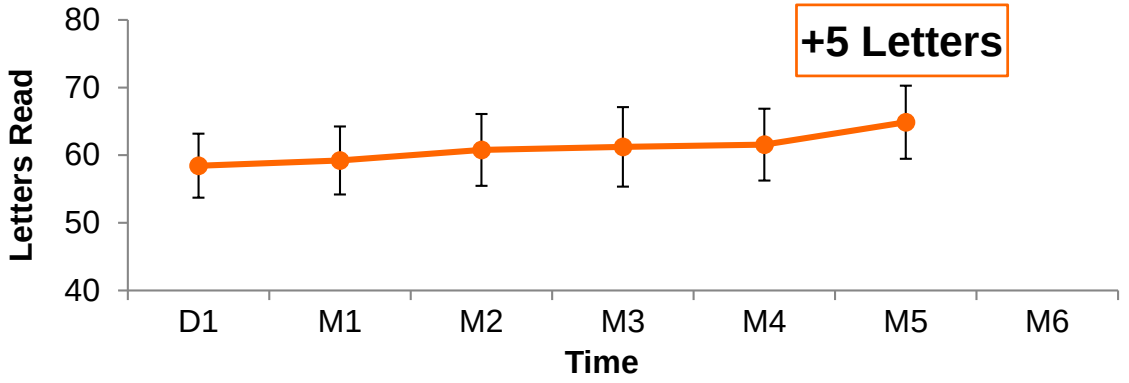
- **Stable to improved vision and OCT** on average
- **75% (9 of 12) injection free** at 5-6 months
- Highest clinical response observed

- SD-OCT data read by a central reading center (Duke Reading Center).
  - 1 subject discontinued after 4 months

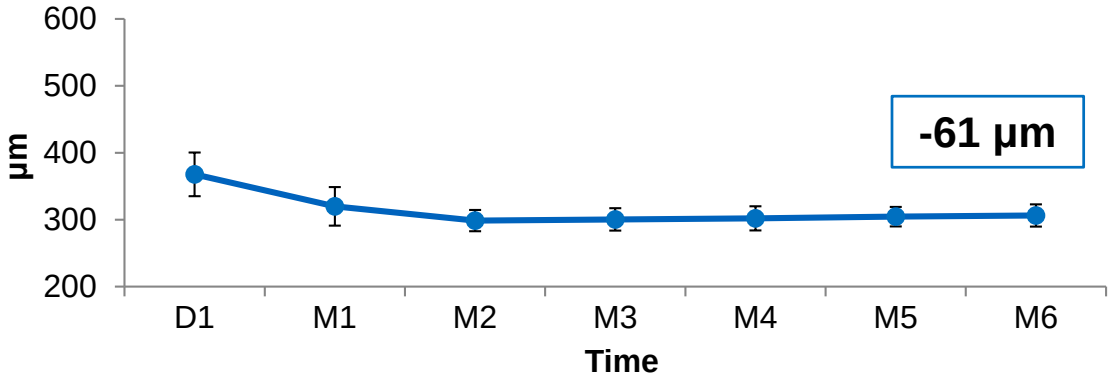
Cohort 4 and Cohort 5: Anti-VEGF Injection-free Subjects

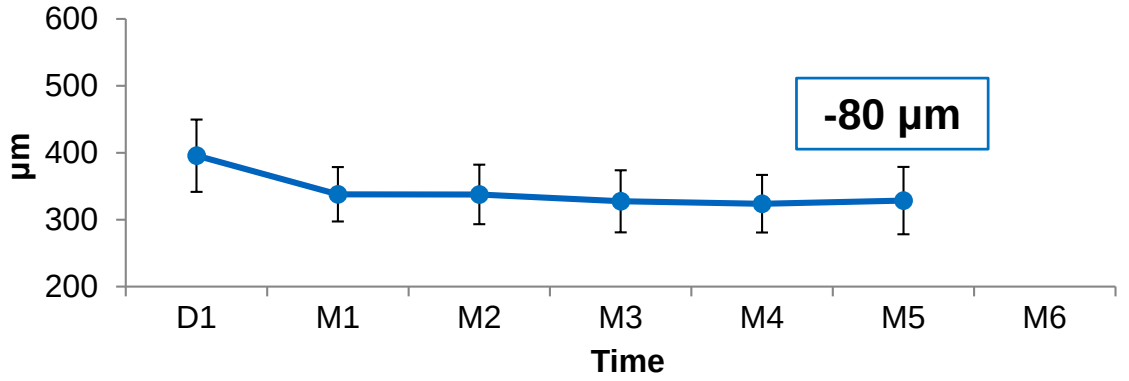
Best Corrected Visual Acuity (BCVA)





Central Retinal Thickness (CRT) on Heidelberg SD-OCT*





0 Injections

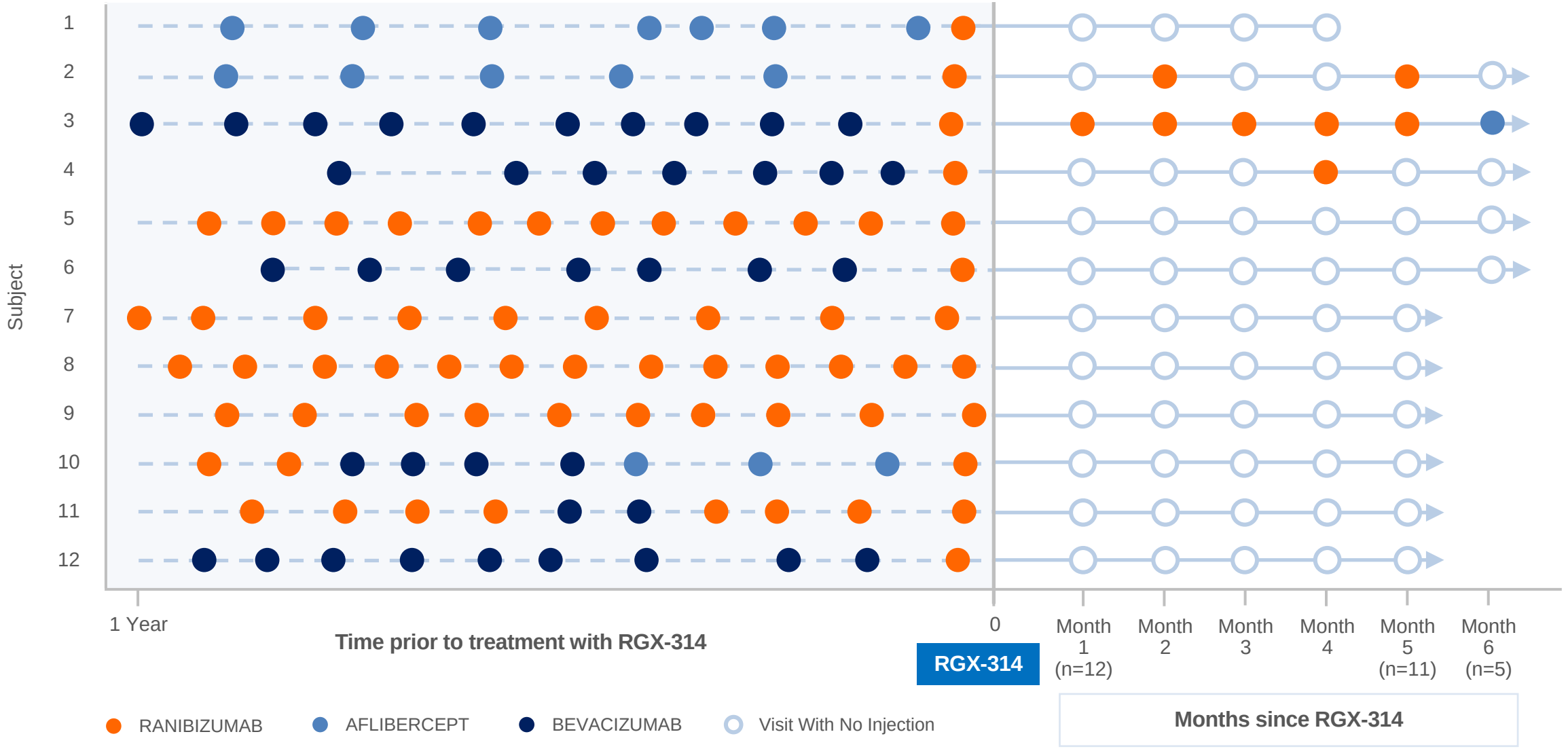
Cohort 4 (n=5) 42%

0 Injections

Cohort 5 (n=9) 75%

- SD-OCT data read by a central reading center (Duke Reading Center).

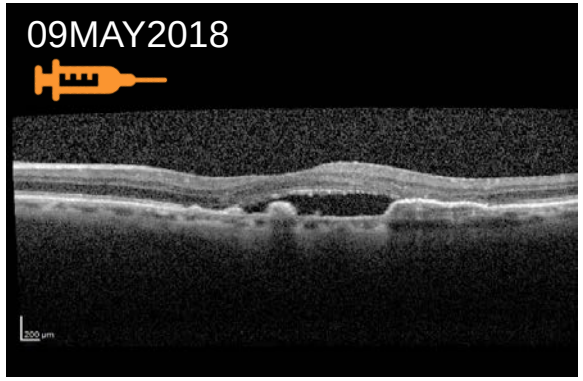
Cohort 5: Injections Pre and Post RGX-314 (n=12)

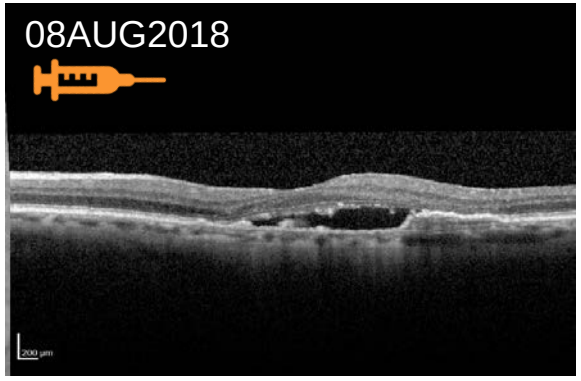


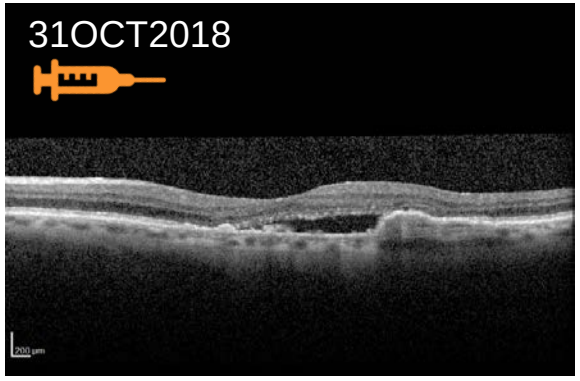
- Subject #1 discontinued after 4 months * Data cut October 9, 2019

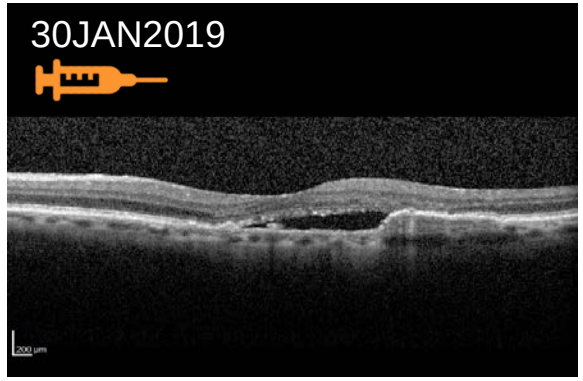
Cohort 5
2.5x10^{11} GC/eye

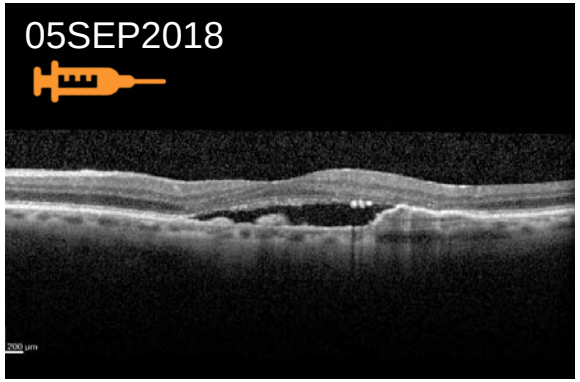
Case A: Subject History Prior to RGX-314

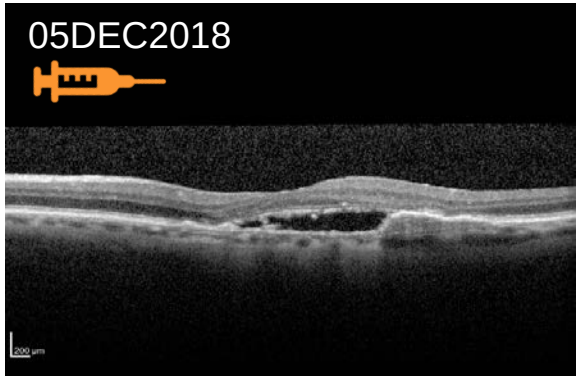


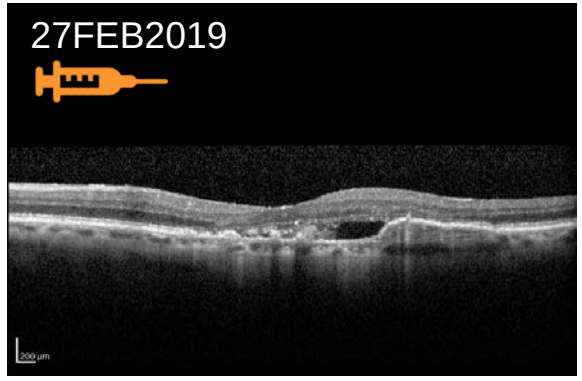


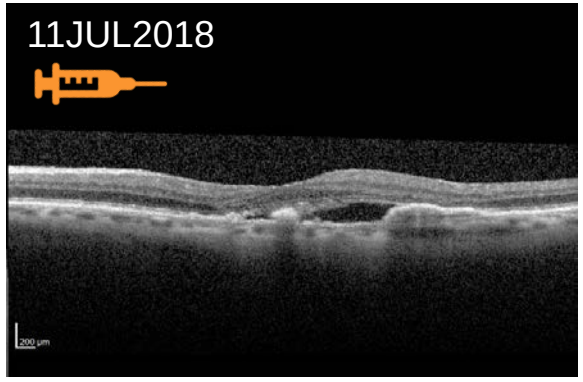


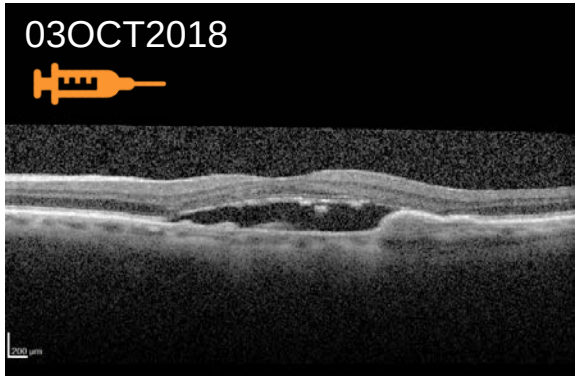


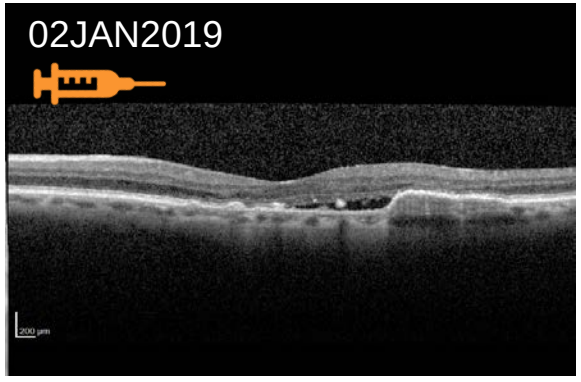


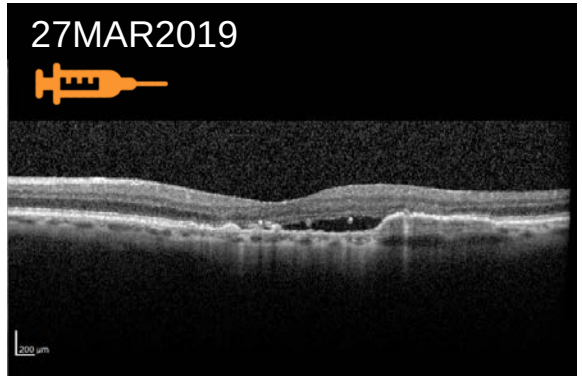








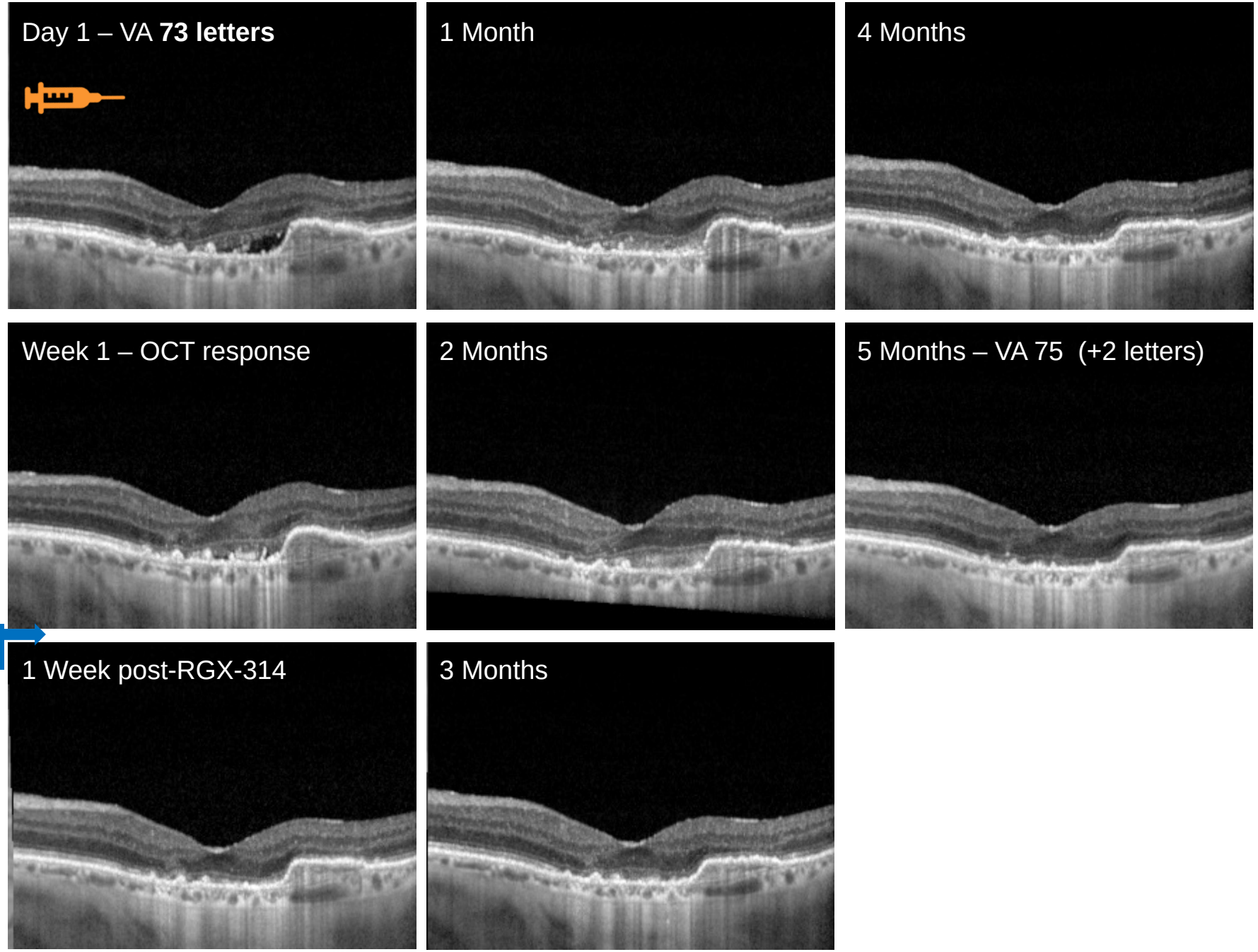




Cohort 5
2.5x10^{11} GC/eye

Case A: 13 Injections in Year Prior with 0 Rescue Injections after RGX-314

Age: 87
Total prior anti-VEGF hx: 40
Last year anti-VEGF: 13
Rescue Inj in Study: 0



Cohort 5
2.5x10^{11} GC/eye

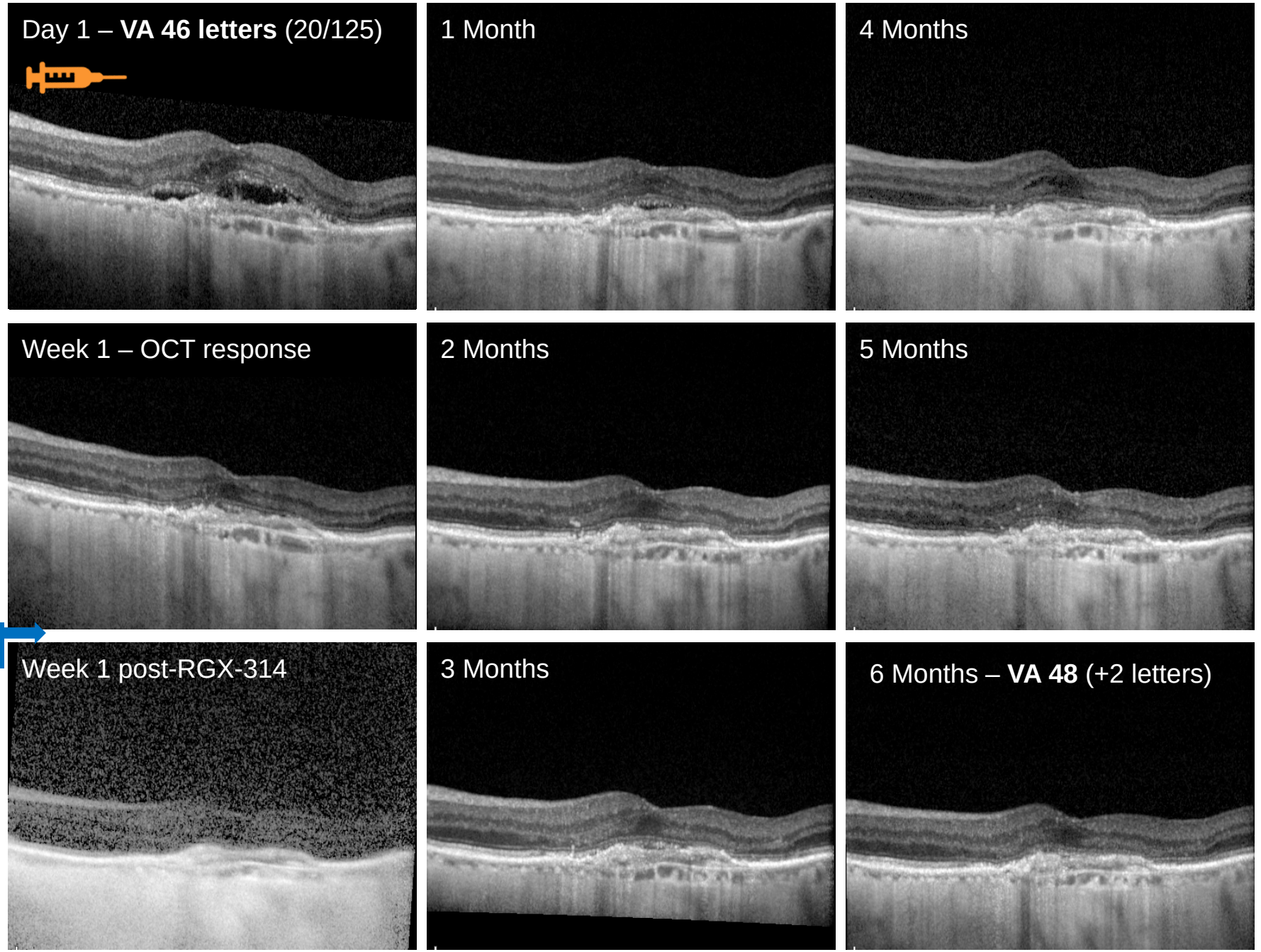
Case B: 8 Injections in Year Prior with 0 Rescue Injections after RGX-314

Age: 86

Total prior anti-VEGF hx: 20

Last year anti-VEGF: 8

Rescue Inj in Study: 0



RGX-314 Program Next Steps

RGX-314 Gene Therapy

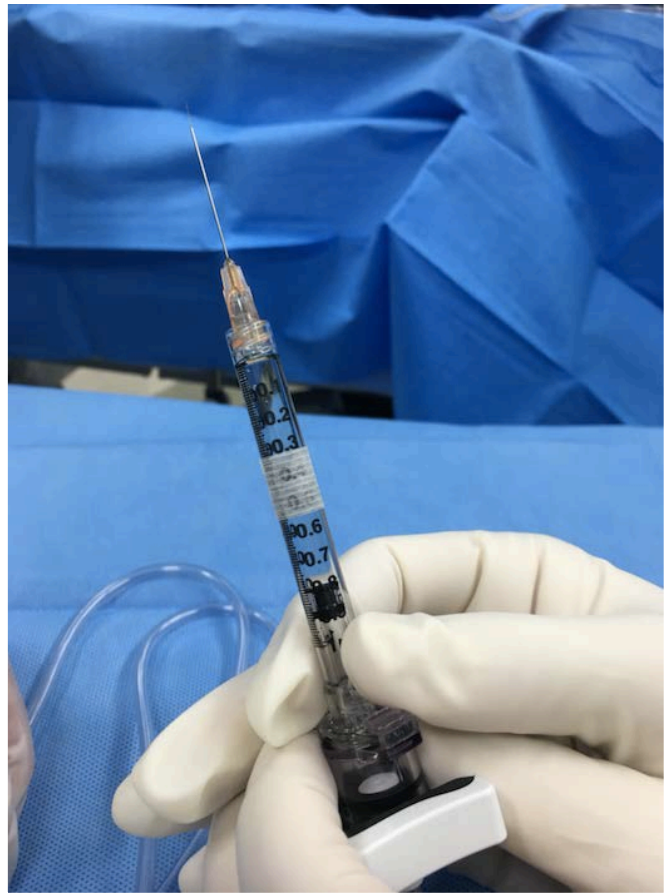
wAMD moving to Phase IIb Study by the end of the year

Diabetic Retinopathy IND by end of the year

Expanding to evaluate SCS delivery using Clearside's proprietary, in-office SCS Microinjector™

Key takeaways from the RGX-314 Phase I/IIa wAMD Clinical Trial

- RGX-314 Phase I/IIa wAMD study has fully enrolled 42 patients in 5 dose cohorts
- Patients enrolled were severe wAMD requiring frequent anti-VEGF injections
- Subretinal RGX-314 was well tolerated in 5 dose Cohorts
- Dose dependent increase in ocular protein observed across cohorts
- Cohort 3: subjects continue to demonstrate good vision and anatomic outcomes over 1.5 years
- Cohort 4: reduction in injection burden with stable to improved anatomic and visual outcomes
- Cohort 5: highest clinical response observed with 75% of subjects injection-free with stable to improved anatomic and visual outcomes*
- RGX-314 moving into Phase IIb trial for wet AMD, Phase II diabetic retinopathy trial, and in-office suprachoroidal delivery via SCS Microinjector™



* Data cut October 9, 2019

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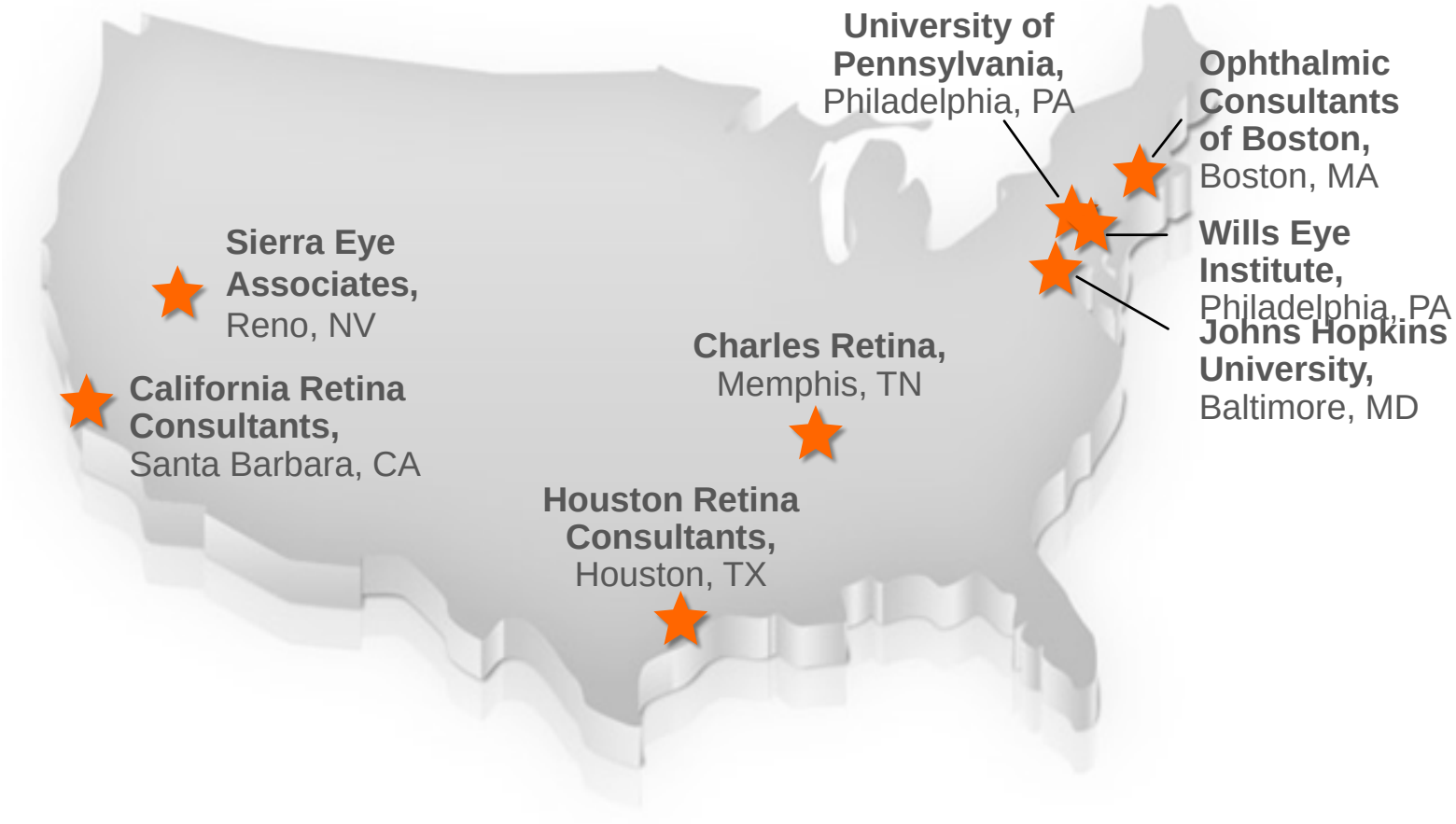
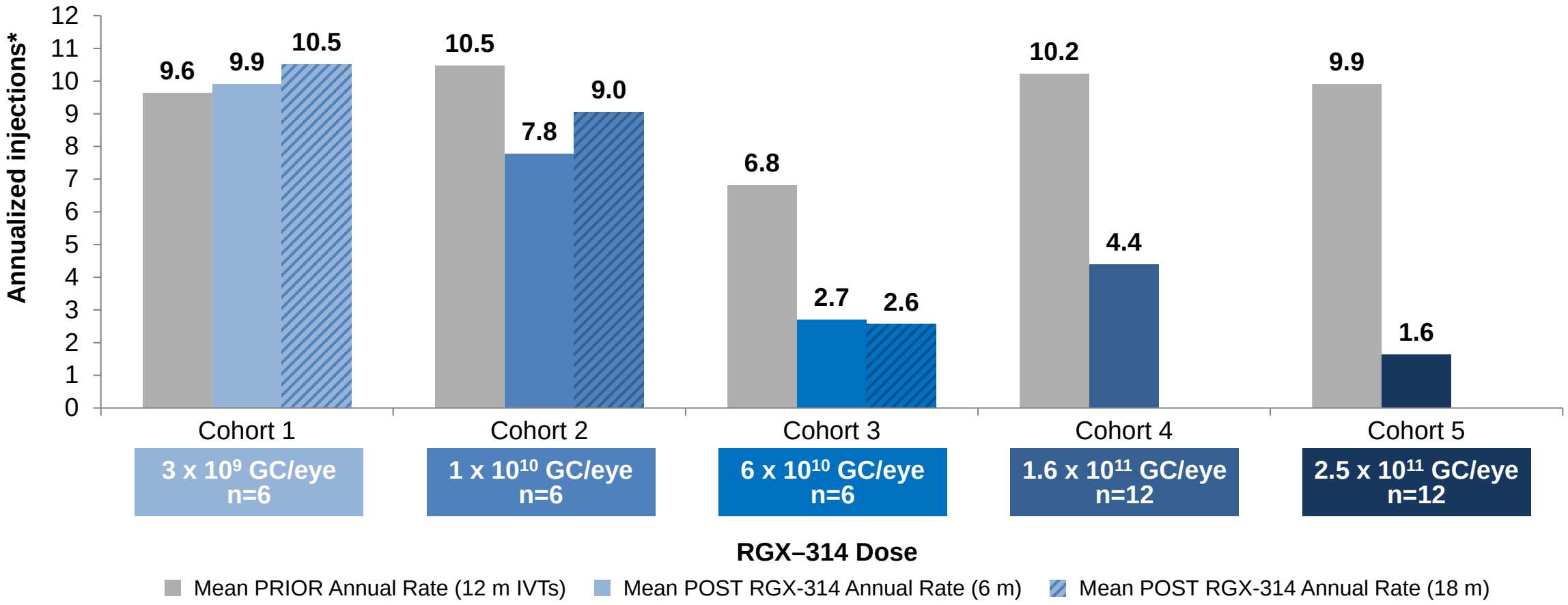


Supplemental Information

Mean Change in Annualized Injection Rate Pre and Post RGX-314: >80% Reduction in Cohort 5

Comparison of injection rate PRIOR and POST RGX-314



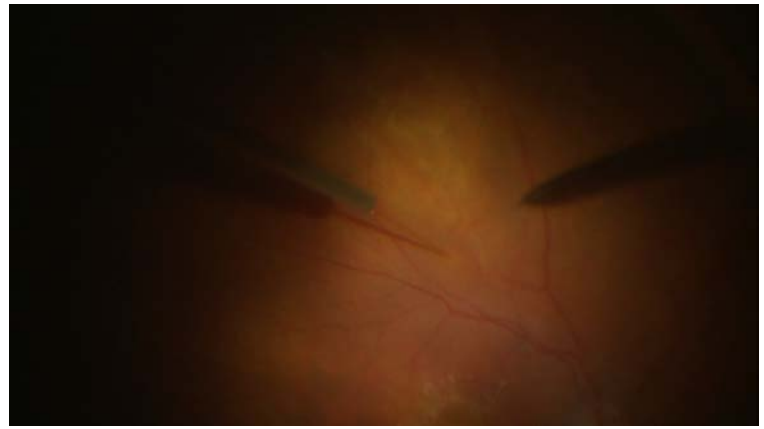
*Prior annual rate is (Total # of prior IVTs)/(minimum(366 days, Duration between first ever IVT and Day 1)/365.25). Post RGX-314 annual rate is (Total # of IVTs on Study)/(Duration on Study/365.25) where on Study is from RGX-314 administration through 18 months for C1-C3 and up to 6 months for C4 –C5.

RGX-314: Standardized Automated Subretinal Delivery Procedure

Step 1 – Vitrectomy

Step 2 – Subretinal Injection

MedOne MicroDose Syringe



Performed Under Local Anaesthesia in the OR

- Standard **small gauge** vitrectomy to perform a core vitrectomy
- Automated delivery with a **MedOne subretinal cannula** attached to the vitrectomy machine
- **Inject 250µl** to create subretinal bleb in a healthy area of retina
- Target superior to the superotemporal arcade vessel or outside the arcades
- Can create another **bleb** area if needed
- Keep margin of the bleb at least 2DA **away from the fovea**

Air fluid exchange and then **Sub-conj steroid injection** at the end of procedure
(No systemic steroids used in protocol)
No positioning mandated and patient is discharged home with follow-up the next day

Cohort 5
2.5x10^{11} GC/eye

Case C: 12 Injections in Year Prior with 0 Rescue Injections after RGX-314

Age: 80

Total prior anti-VEGF hx: 20

Last year anti-VEGF: 12

Rescue Inj in Study: 0