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

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Oct 1, 2021

RGX–314 for Treatment of Neovascular Age-related Macular Degeneration (nAMD)

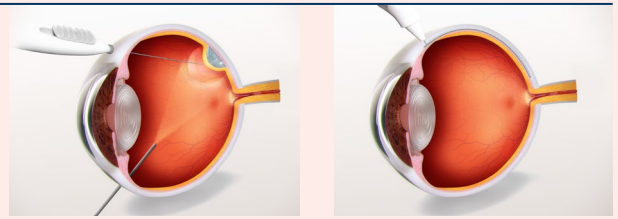
RGX–314 PRODUCT CANDIDATE

Vector: AAV8 | **Gene:** anti-VEGF fab

Route of administration:

Subretinal (nAMD) or

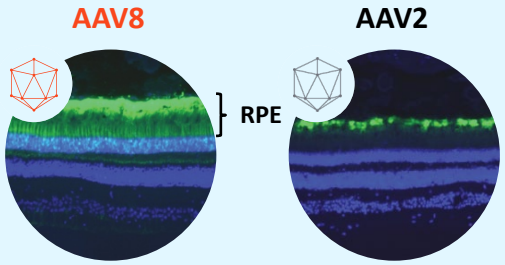
Suprachoroidal (nAMD/DR)



Mechanism of action:

Reducing leaky blood vessel formation by giving ocular cells the ability to produce an anti-VEGF fab

Improved AAV vector technology



More efficient gene delivery to the RPE[1]

+

Leveraging current standard of care in transgene

- FDA-approved mAbs and mAb fragments that inhibit VEGF are the current standard of care for treatment of nAMD
- **RGX–314 gene encodes an anti-VEGF mAb fragment (fab)**

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RGX–314: AAV8 encoding anti–VEGF fab

Potential for long-term therapeutic anti-VEGF expression

1. Vandenberghe et al. 2011 Science Translational Medicine

AAV: Adeno-Associated Virus

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AAVIATE®: RGX-314 Phase II Clinical Trial in nAMD

Primary Objective

- To evaluate the mean change in BCVA for RGX-314 compared with ranibizumab monthly injection at Month 9

Secondary Objectives

- 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 (“Rescue”)

Retreatment Criteria

- Based on worsening vision and/or fluid

Subjects: Up to 95 total

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

Route of Administration

- In-office SCS Microinjector™ delivers 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

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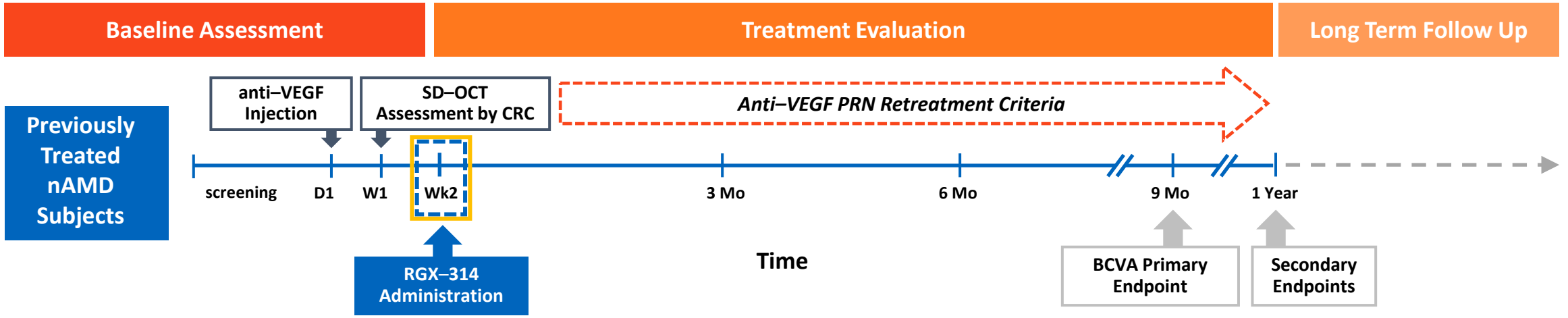
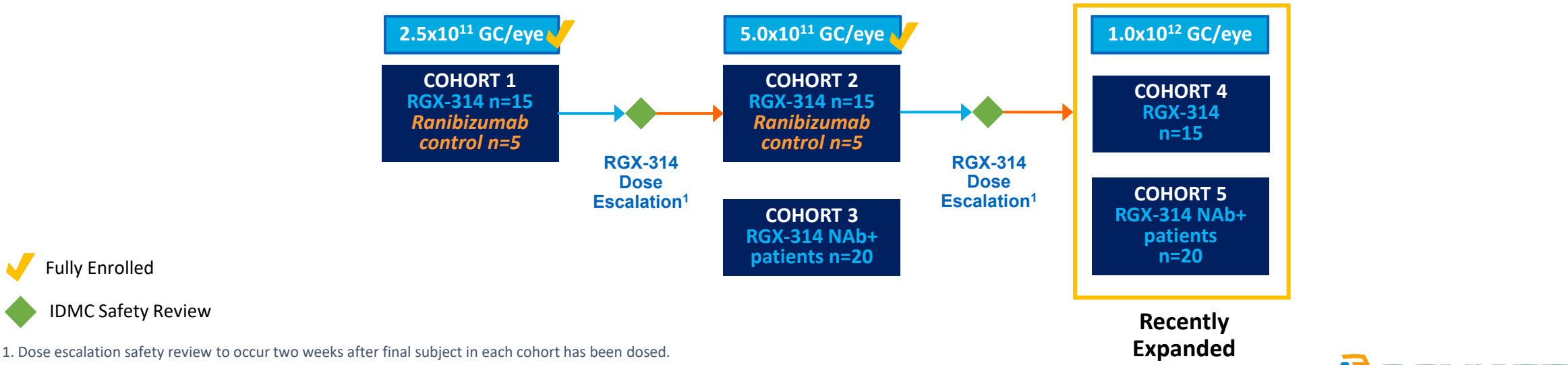
RGX-314 AAVIATE® Study Design



No prophylactic steroids given throughout the study



1. Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed.
NAb+ = AAV8 neutralizing antibody positive

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AAVIATE Baseline Characteristics (Cohort 1 – Cohort 3)

	Variable	Control Ranibizumab (N=10)	Cohort 1 (N=15)	Cohort 2 (N=15)	Cohort 3 (N=20)	Total (N=60)
BASELINE	**Mean Age** (Years)	**75.9**	**74.0**	**77.9**	**72.6**	**74.8**
	Screening BCVA (Letters)	**72.7**	**75.1**	**70.7**	**72.8**	**72.9**
	Screening OCT (Microns)	**240.3**	**269.2**	**275.7**	**265.8**	**264.9**
	Phakic n (%)	**3** (30.0%)	**6** (40.0%)	**7** (46.7%)	**10** (50.0%)	**26** (43.3%)
PRIOR THERAPY	**Months Since nAMD Diagnosis** (Mean)	**26.7**	**30.4**	**19.9**	**18.6**	**23.2**
	# Injections Since nAMD Diagnosis (Mean)	**13.4**	**20.6**	**11.1**	**9.7**	**13.4**
	# Injections in the Past Year (includes Day 1)	**6.8**	**7.2**	**6.0**	**6.2**	**6.5**
	Average Annualized Injections in the Past Year (includes Day 1)	**8.8**	**9.7**	**8.7**	**8.9**	**9.0**

Ocular variables refer to study eye only.
Average annualized injections in the past year is: (Total # of prior injections)/(minimum(366 days, Duration between first injection and Day 1)/365.25).

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AAVIATE Safety Summary

- RGX–314 was **well–tolerated** in Cohorts 1–3 (n=50) with follow-up ranging from 1 month – 12 months
  - **4 SAEs: None** were considered **drug-related**:
    - One death resulting from a complete atrioventricular block (Cohort 1)
    - One hospitalization due to intestinal obstruction (Cohort 1)
    - One CVA (Cohort 2)
    - One gastric ulcer (Cohort 3)
- **RGX-314: Cohort 1** (n=15)
  - **Common ocular TEAEs[1] in the study eye were generally mild with none severe:**
    - Conjunctival Hemorrhage (5/15, 33%)
    - Mild Intraocular Inflammation[2] (4/15, 27%) observed on slit-lamp examination
      - All cases resolved within days to weeks on topical corticosteroids which have been discontinued
    - Worsening of nAMD[3] (3/15, 20%)
    - Conjunctival Hyperemia (2/15, 13%)
    - Dry Eye (2/15, 13%)
  - No cases of chorioretinal vasculitis or occlusion, or hypotony were observed

Data cut Sep 13, 2021
1. Common ocular TEAEs defined as ≥ 10% of RGX-314 treated study eyes
2. 3 patients presented with anterior cell (+0.5, +2, +2) and 1 patient presented with vitreous cell (trace); onset range was 2-6 weeks post-dosing
3. All reported from one investigator at one site
CVA: Cerebrovascular accident; SAE: Serious Adverse Event; TEAE: Treatment Emergent Adverse Event

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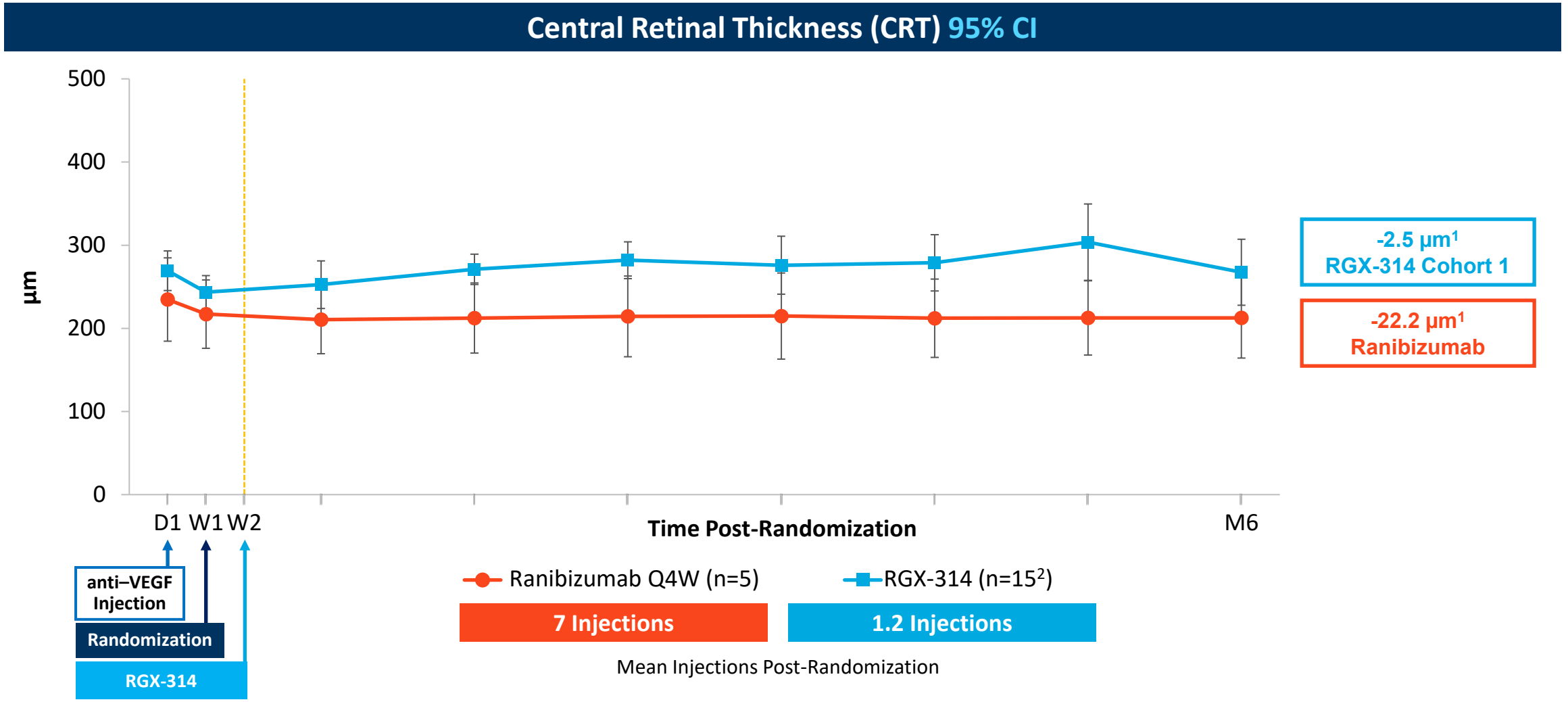
Cohort 1: Mean CRT from Day 1 (Screening) Through Month 6

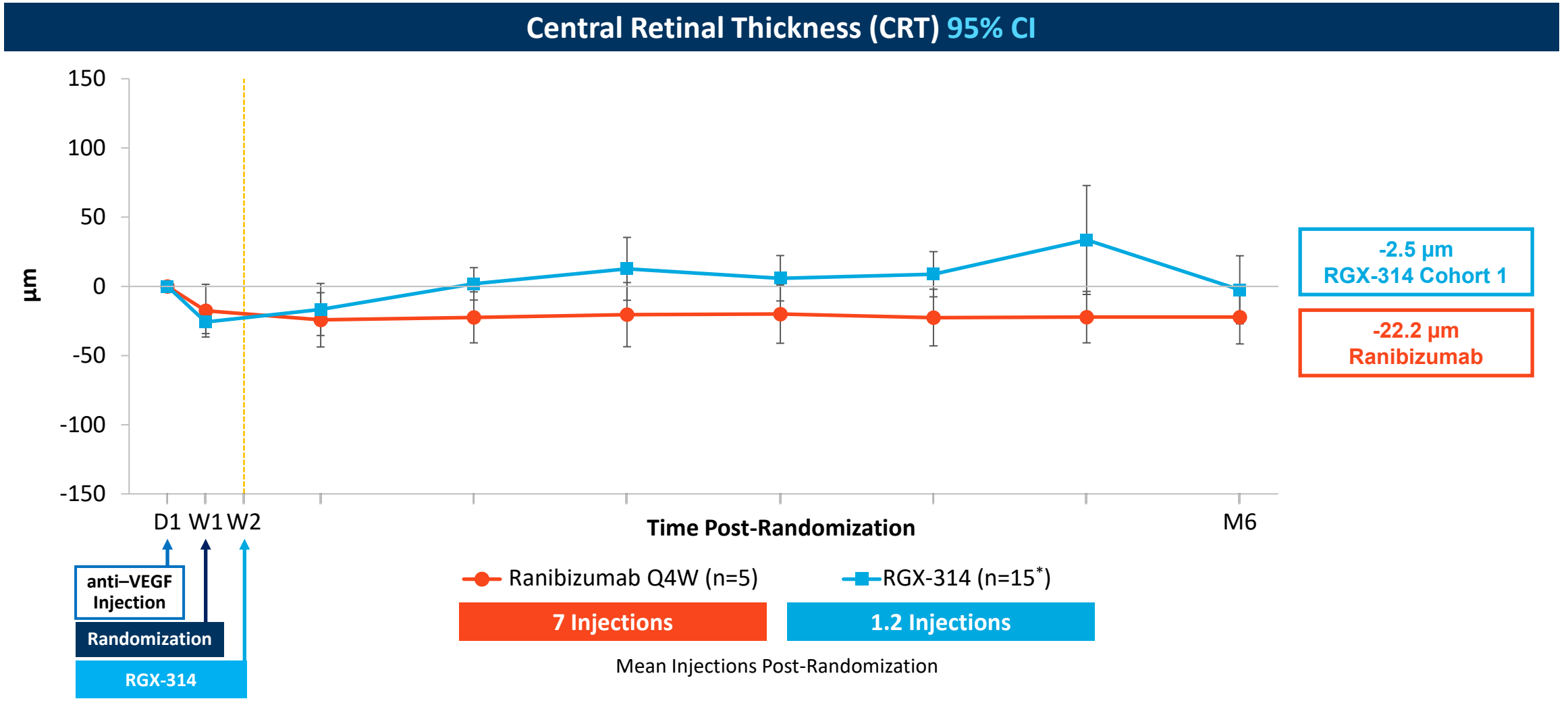


Data cut Sep 13, 2021

1. Values are mean change from Day 1.

2. One patient discontinued the study after Week 12, and only data up to week 12 is included for the subject. For one patient who has missing Weeks 8 and 28 visits, the missing data has been interpolated using the average of before and after the missing visit.

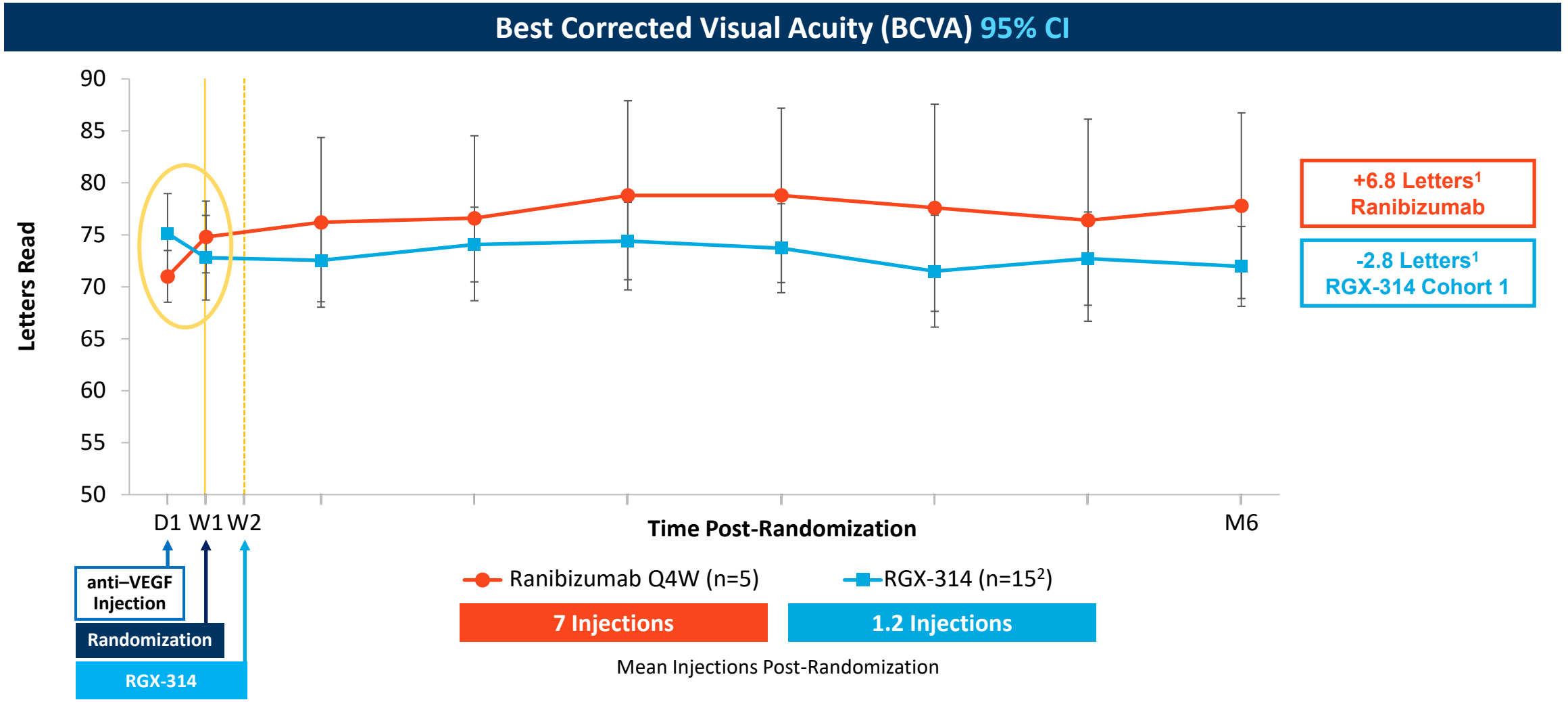
Cohort 1: Mean Change in CRT from Day 1 (Screening) Through Month 6



Data cut Sep 13, 2021

*One patient discontinued the study after Week 12, and only data up to week 12 is included for the subject. For one patient who has missing Weeks 8 and 28 visits, the missing data has been interpolated using the average of before and after the missing visit.

Cohort 1: Mean BCVA from Day 1 (Screening) Through Month 6

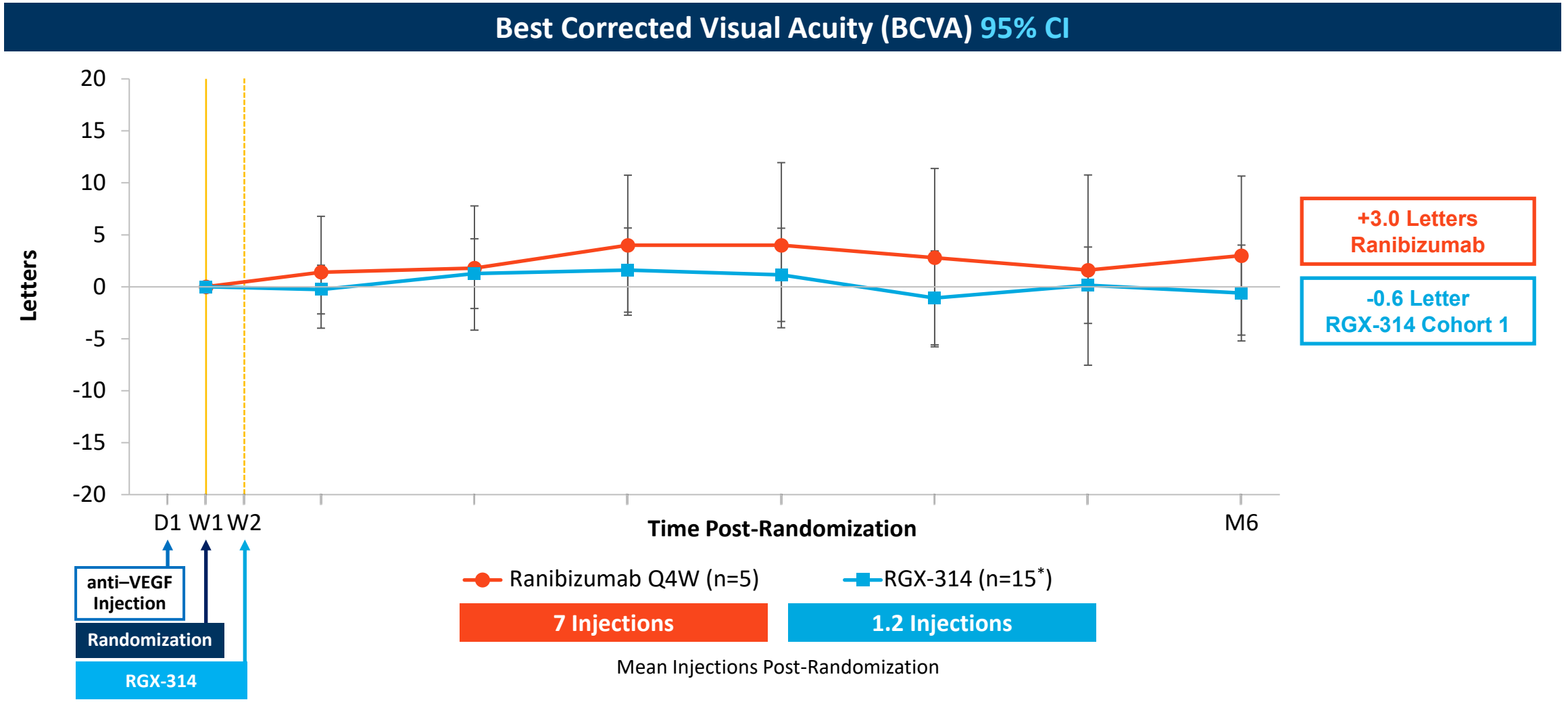


Data cut Sep 13, 2021

1. Values are mean change from Day 1.

2. One patient discontinued the study after Week 12, and only data up to week 12 is included for the subject. For one patient who has missing Weeks 8 and 28 visits, the missing data has been interpolated using the average of before and after the missing visit.

Cohort 1: Mean Change in BCVA from Week 1 (Randomization) Through Month 6



Data cut Sep 13, 2021

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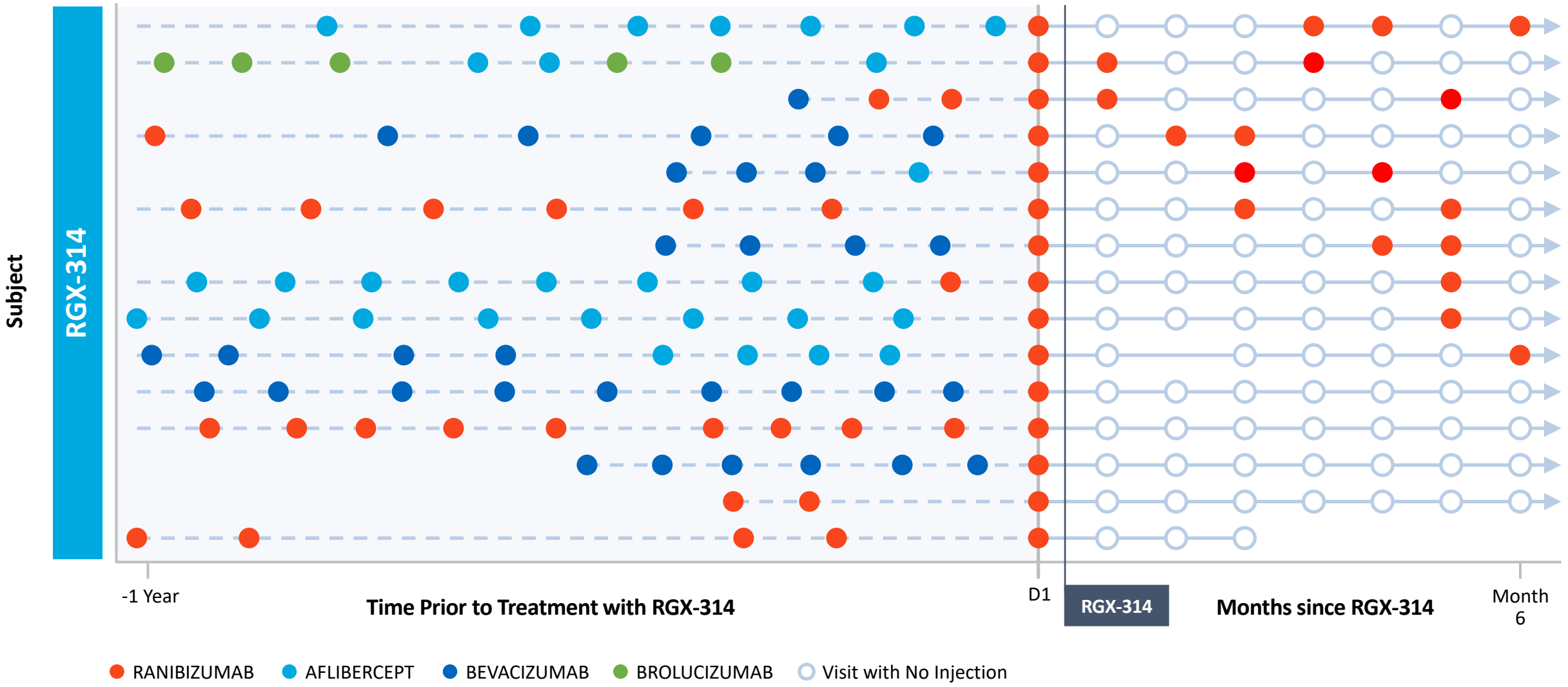
Cohort 1 Injections: Pre and Post RGX-314 (n=15)

Change in annualized injection rate -75.9%



Change in annualized injection rate is the difference between historical annualized injection rate and on-study annualized injection rate up to 6 months post-RGX-314.
Historical annualized injection rate is (Total # of prior injections)/(minimum(366 days, Duration between first injection and Day 1)/365.25).
On-study annualized injection rate is (Total # of injections on Study)/(Duration on Study/365.25) where on-study is defined from post-D1 to a specified cut-off date.

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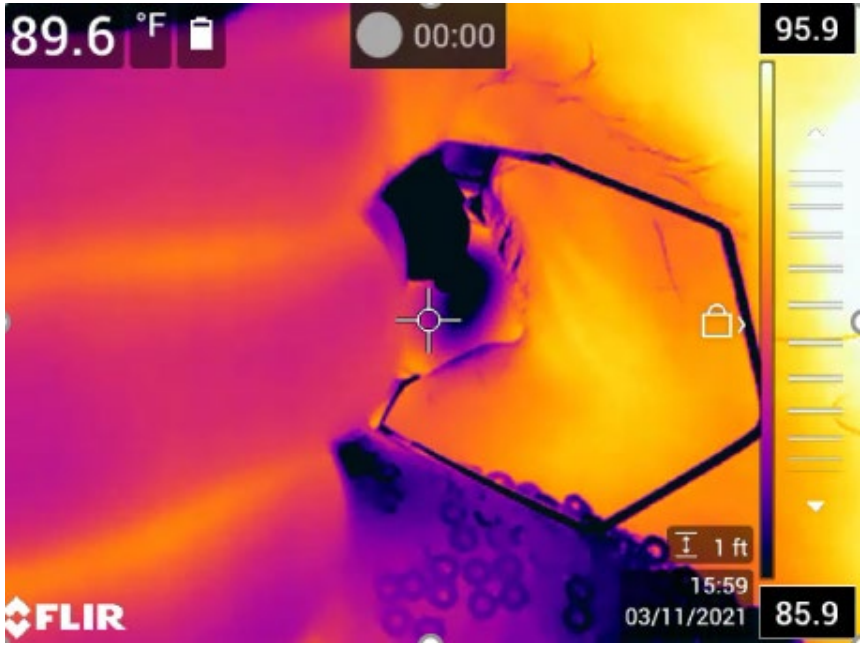
Summary of Initial Results from the Phase II AAVIATE® Study

RGX-314 Cohorts 1-3 (n=50): Safety

- Suprachoroidal RGX-314 has been well-tolerated

RGX-314 Cohort 1 (n=15): 6 Month Results

- Stable visual acuity and central retinal thickness
- Meaningful reduction in injection burden in RGX-314 treated subjects (75.9%)
- 4 patients with mild intraocular inflammation resolved within days to weeks with topical corticosteroids



Video: N. London

AAVIATE study has been expanded to Cohorts 4 and 5 (Dose level 3: $1x10^{12}$ GC/eye, NAb- and NAb+ patients)

Data cut September 13, 2021

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Acknowledgments

- **Allen Ho, MD** (Philadelphia, PA)
- **Arshad Khanani, MD** (Reno, NV)
- **Brandon Busbee, MD** (Nashville, TN)
- **Charles Wykoff, MD PhD** (Houston, TX)
- **Daniel Su, MD** (Beverly Hills, CA)
- **Dante Pieramici, MD** (Santa Barbara, CA)
- **David Boyer, MD** (Beverly Hills, CA)
- **David Liao, MD** (Beverly Hills, CA)
- **Dennis Marcus, MD** (Augusta, GA)
- **Dilsher Dhoot, MD** (Bakersfield, CA)
- **Jeff Heier, MD** (Boston, MA)
- **John Pitcher, MD** (Albuquerque, NM)
- **Mark Barakat, MD** (Phoenix, AZ)
- **Nikolas London, MD** (San Diego, CA)
- **Peter Campochiaro, MD** (Baltimore, MD)
- **Robert Avery, MD** (Santa Barbara, CA)
- **Stephen Huddleston, MD** (Memphis. TN)