Gene Therapy for Neovascular AMD:

Subretinal RGX-314: Phase I/IIa Long-Term Follow-Up Results up to 4 Years

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Financial Disclosure

I have the following financial interests or relationships to disclose:

Allegro: Stock Options – Public or Private Corp

AsclipiX: Consultant/Advisor, Grant Support

Ashvattha Therapeutics: Consultant/Advisor, Grant Support

Bausch + Lomb: Consultant/Advisor

Catawba Research: Consultant/Advisor

Celanese: Consultant/Advisor

Clearside: Consultant/Advisor

Cove Therapeutics: Equity/Stock Holder – Private Corp

ExgenesisBio: Consultant/Advisor, Grant Support

Exonate: Consultant/Advisor

GENENTECH: Consultant/Advisor, Grant Support

Genzyme: Grant Support

Graybug Vision: Stock Options – Public or Private Corp

Gyroscope: Consultant/Advisor

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Mallinckrodt Pharmaceuticals: Grant Support

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Oxford BioMedica: Grant Support

Perfuse: Consultant/Advisor

Regeneron: Consultant/Advisor, Grant Support

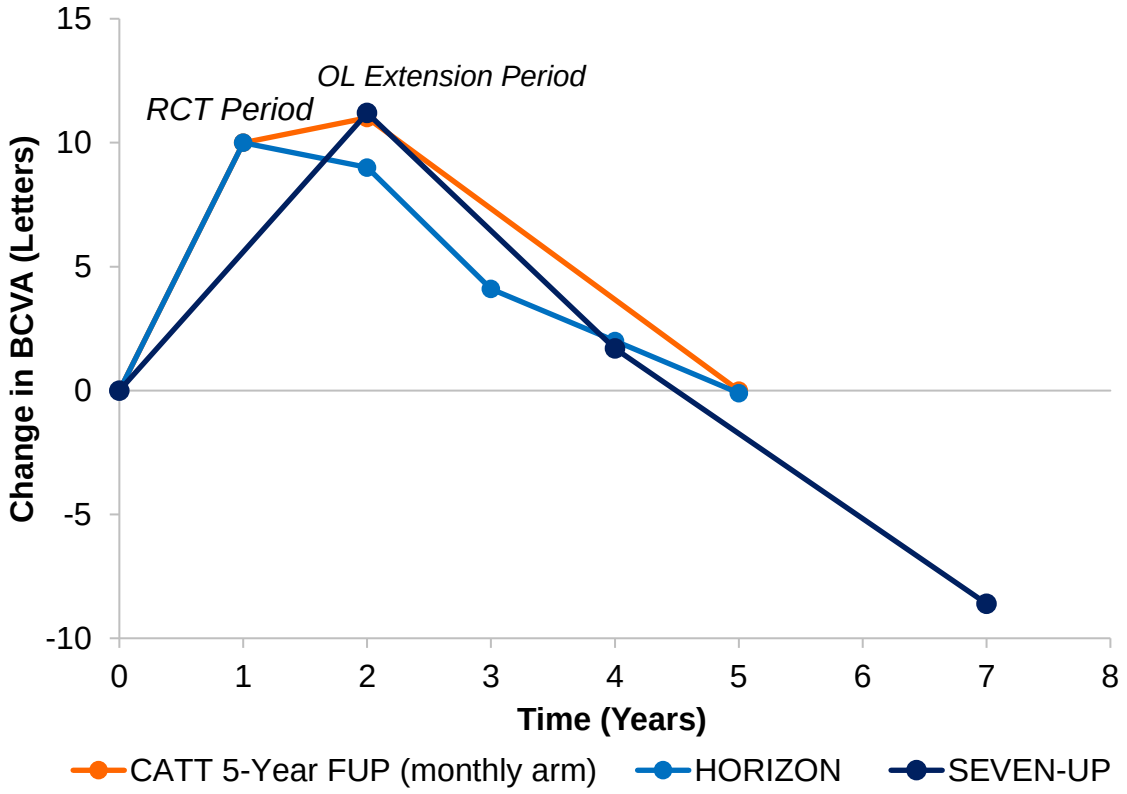
REGENXBIO: Grant Support

Roche: Consultant/Advisor, Grant Support

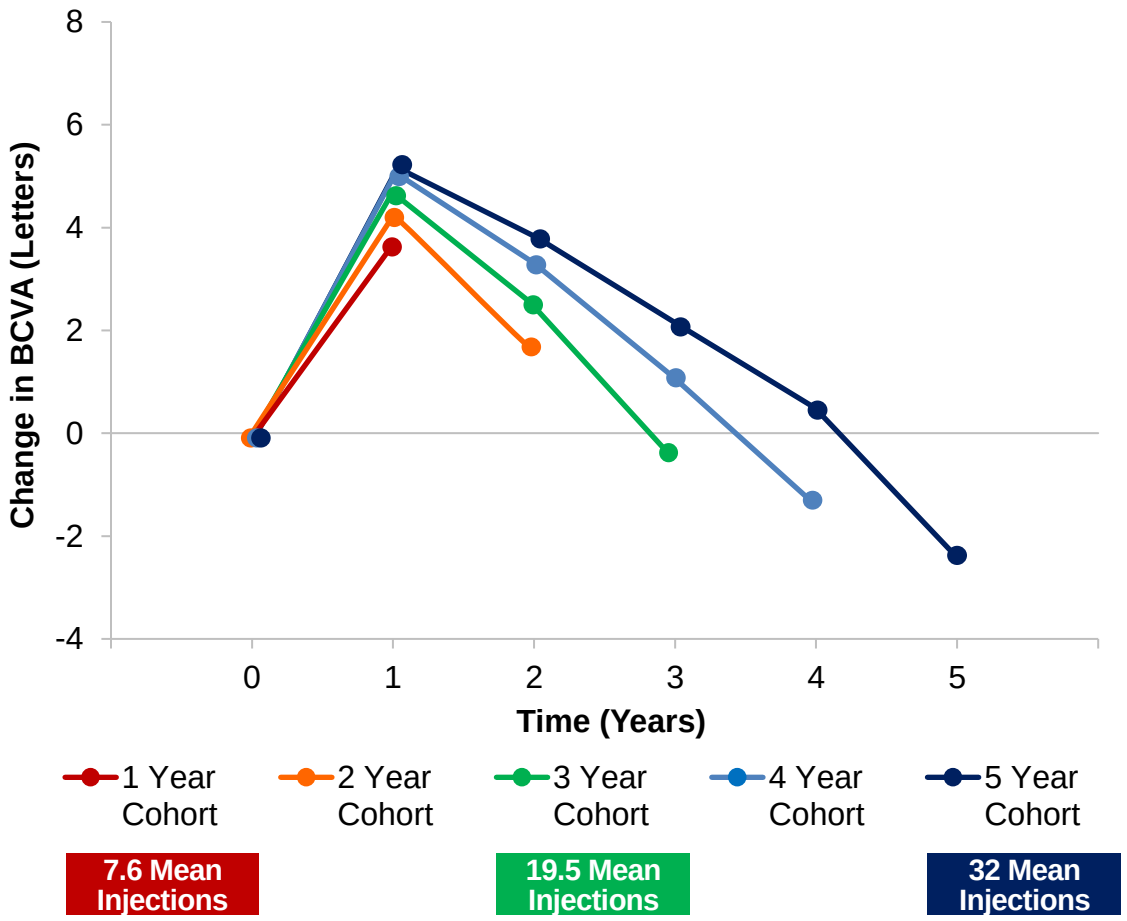
Wave Life Sciences: Consultant/Advisor

Vision outcomes in nAMD decrease over time despite anti-VEGF therapy

Mean VA Change after RCTs[1]



Mean VA Change in Real World Practice[2]



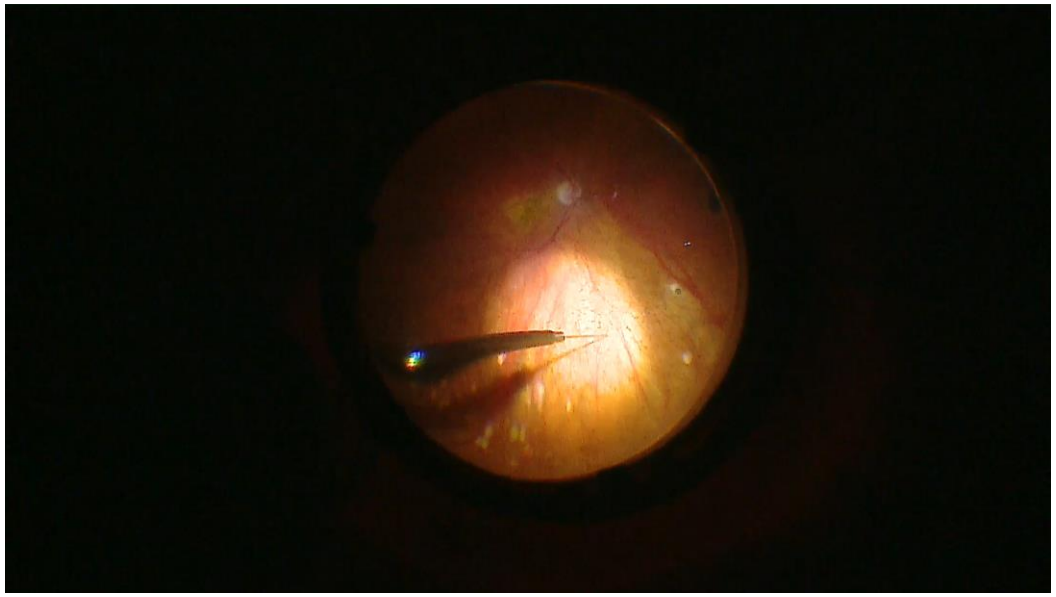
RCT: Randomized Controlled Trial; OL: Open-label

[1]Singer, 2012 (HORIZON). Rofagha, 2013 (SEVEN-UP). Maguire, 2016 (CATT).

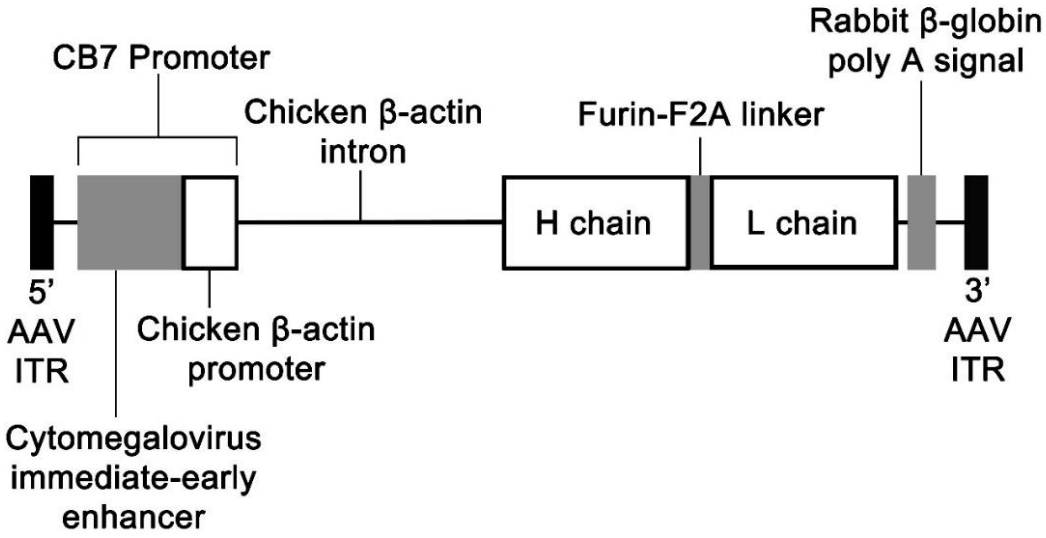
[2]Ciulla, T et al. Ophthalmology. Retina vol. 6,9(2022): 796–806.

Gene Therapy for nAMD

Different Transgenes and Delivery Routes Being Tested
Most Advanced with Regard to Development is Subretinal Injection of RGX-314

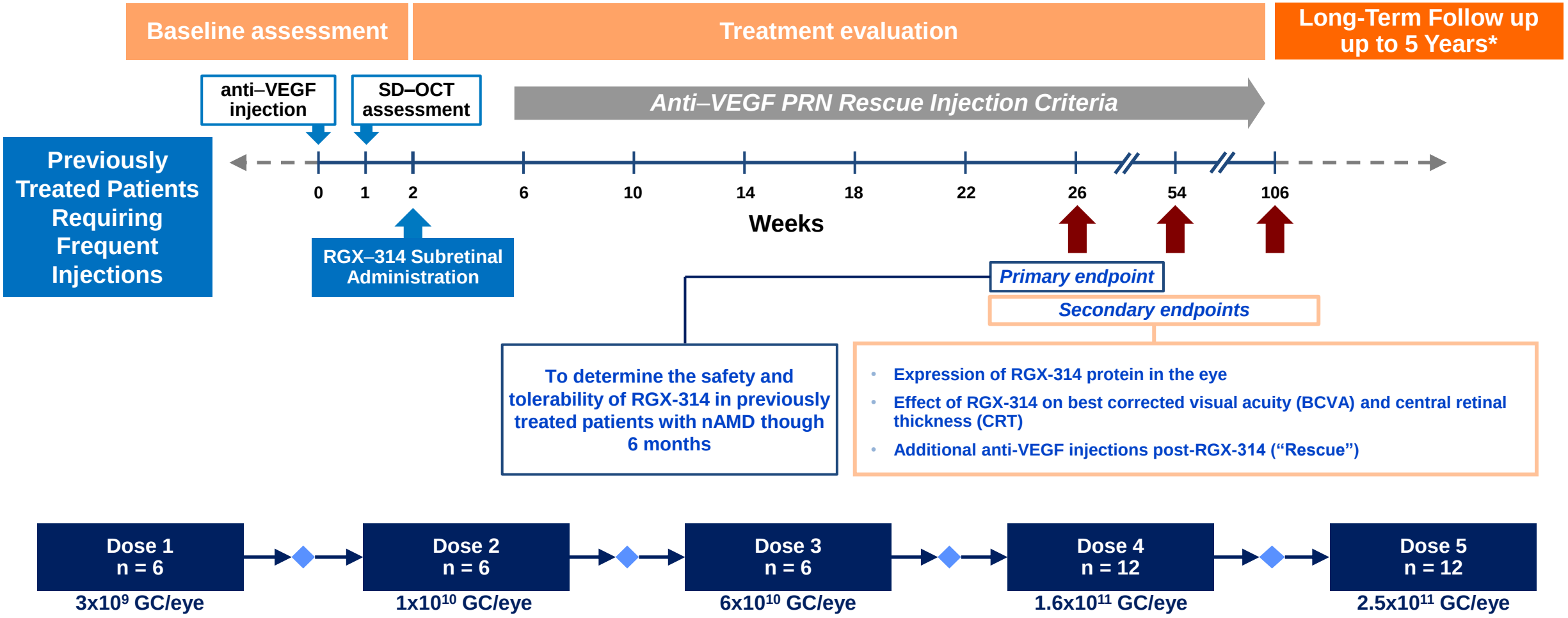


Subretinal Injection



RGX-314
AAV8 vector containing an expression construct coding for Fab similar to ranibizumab

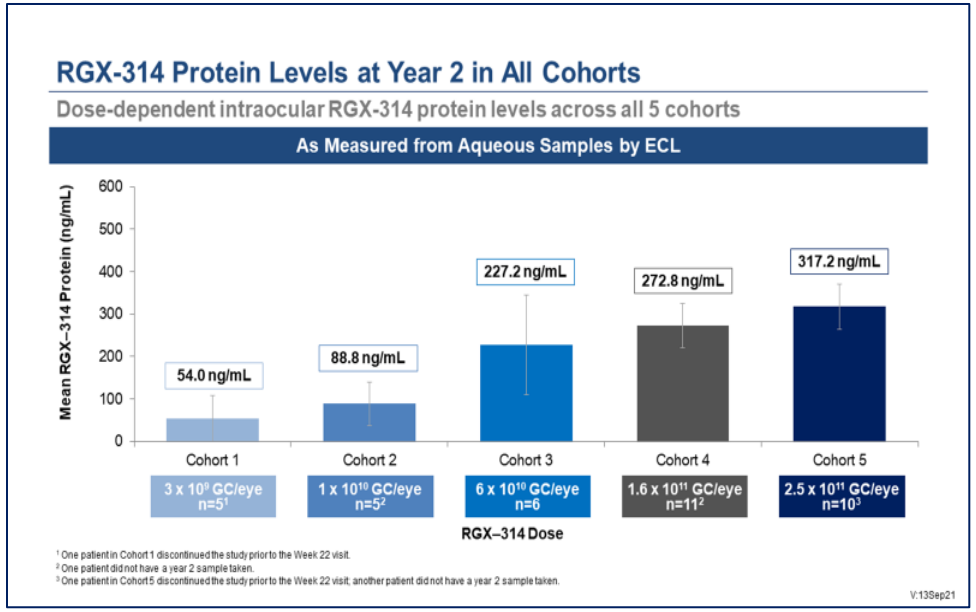
RGX-314 Phase I/IIa nAMD Study is Complete

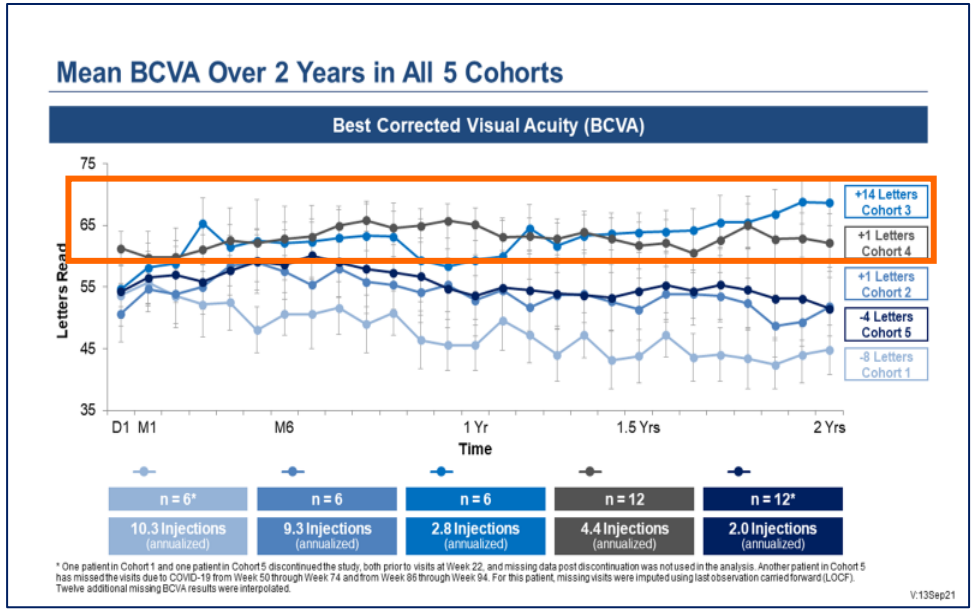


Safety review: Dose escalation safety review to occur four weeks after final patient in each cohort has been dosed
*Patients managed per MD discretion

RGX-314 Phase I/IIa nAMD Study Outcomes

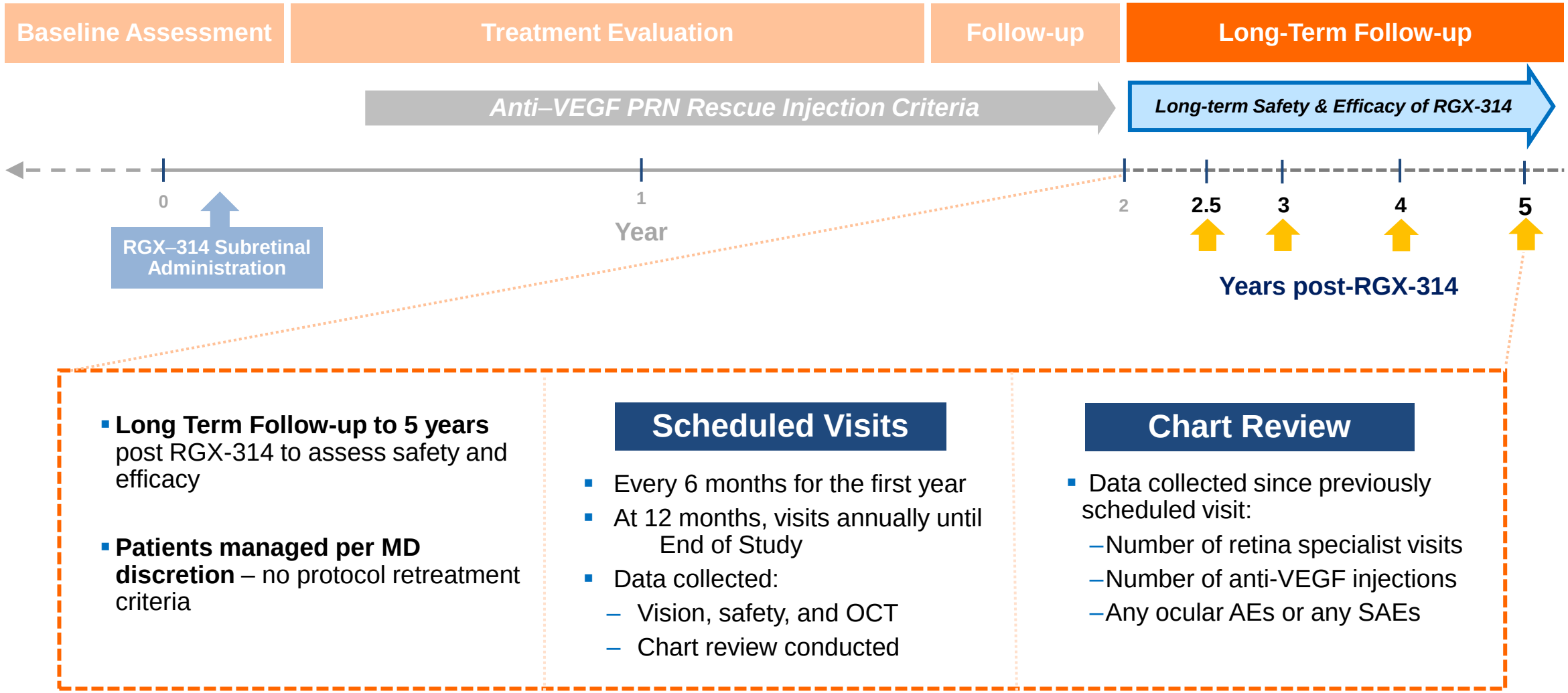
- Dose dependent increases in treatment effect were observed in the **RGX-314 Phase I/IIa study**





- After study completion, patients were encouraged to enroll in a **Long-Term Follow-up study for a total of 5 years** of follow-up post RGX-314 administration
  - Doses **similar to Cohort 3 and Cohort 4** were moved into pivotal trials
  - For Cohort 3 and 4, **16 out of 18 patients** continued in the LTFU study and have been followed **for up to 4 and 3 years**, respectively

Long-Term Follow-Up (LTFU) Study of Phase I/IIa Patients*



- **Long Term Follow-up to 5 years** post RGX-314 to assess safety and efficacy
- **Patients managed per MD discretion** – no protocol retreatment criteria

Scheduled Visits

- Every 6 months for the first year
- At 12 months, visits annually until End of Study
- Data collected:
  - Vision, safety, and OCT
  - Chart review conducted

Chart Review

- Data collected since previously scheduled visit:
  - Number of retina specialist visits
  - Number of anti-VEGF injections
  - Any ocular AEs or any SAEs

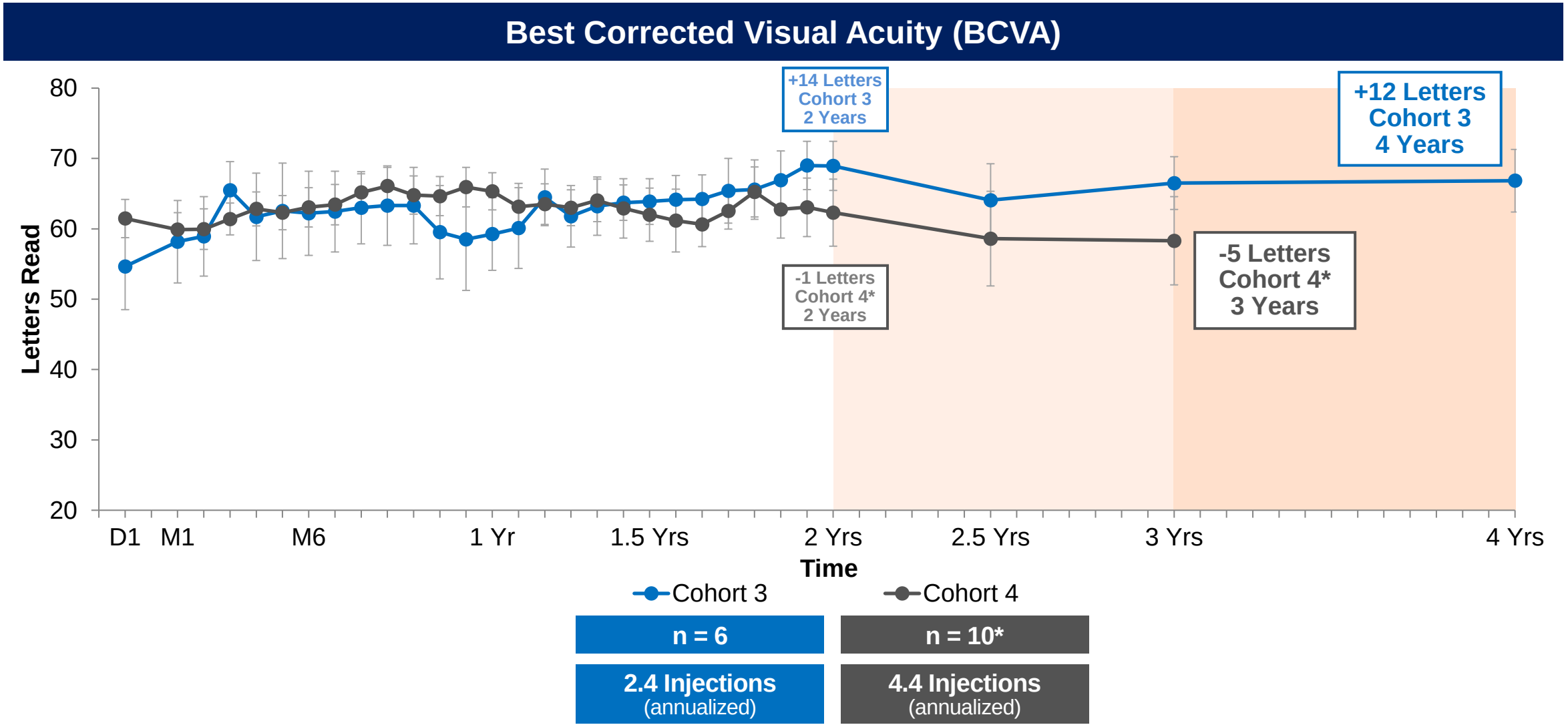
*The majority of subjects rolled over from the Phase I/IIa study into the LTFU study (N=37 out of 42)

RGX-314 Long-Term Follow-Up Study: Safety

- RGX–314 continues to be generally well-tolerated in the long-term follow-up study (n=37*) with 2.5–5 years of follow-up
- 9 SAEs were reported in 4 patients, and none were considered drug-related
- Drug-related ocular AEs:
  - Cohort 1–4: no new events
  - Cohort 5: one case of significant vision decrease during the long-term follow-up study, in a patient that had macular pigmentary changes after a superior bleb in the Phase I/IIa study

Data cut August 29, 2022.
SAE: Serious Adverse Event; AE: Adverse Event.
*Patients with at least one visit in the LTFU study

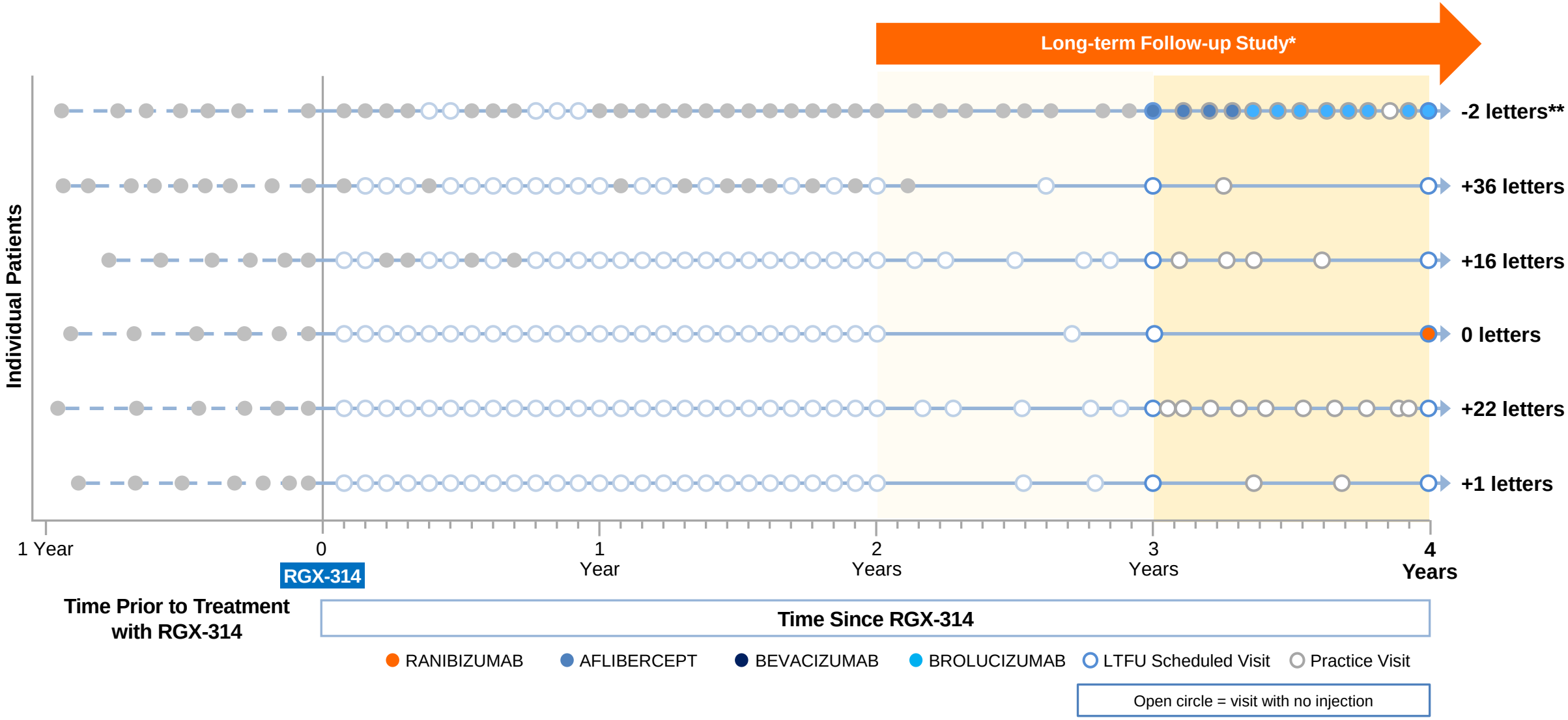
Long-Term Follow-Up: Mean BCVA for Cohorts 3 and 4



Data cut: August 29, 2022.

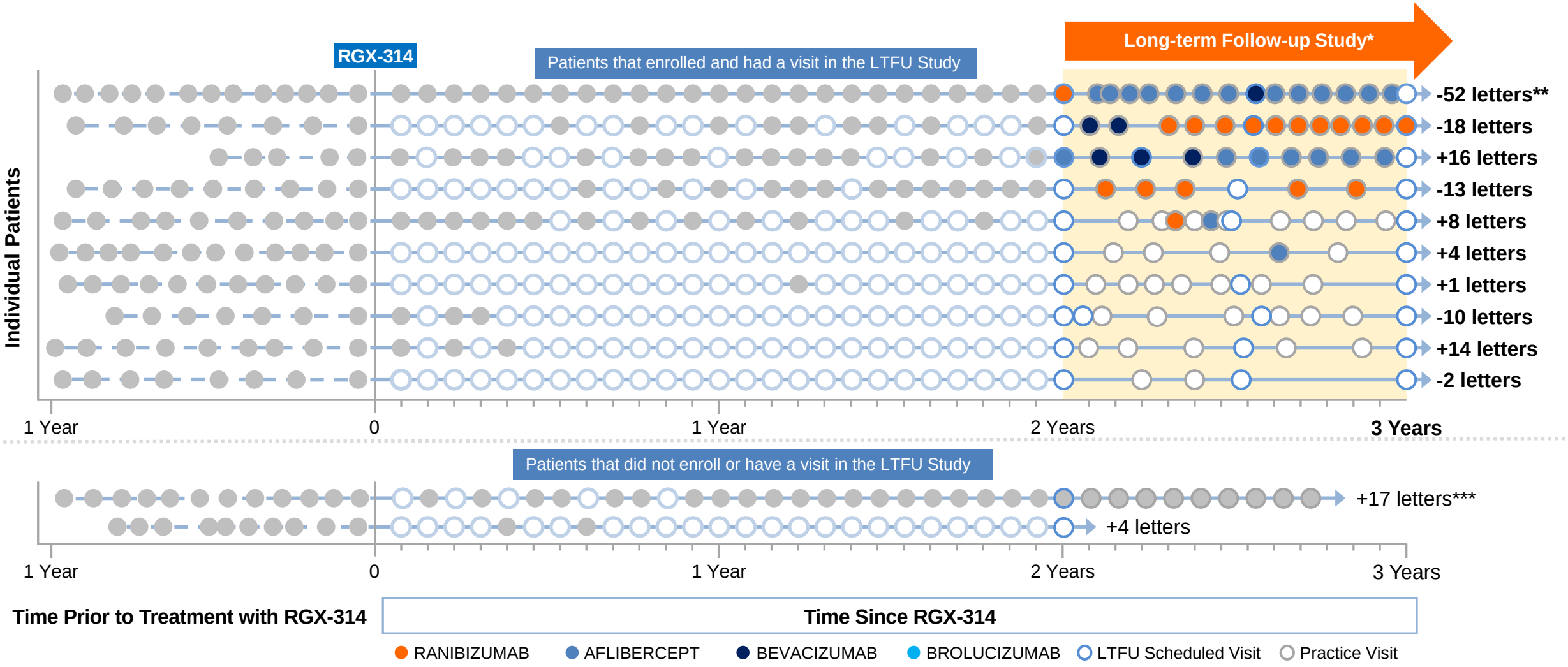
*One patient did not enroll in the LTFU study; one patient enrolled but did not have a study visit.

Cohort 3 Injections and Change in BCVA Over 4 Years



*Retreatment per MD discretion in clinical practice.
**Patient received incomplete dose at time of subretinal procedure.

Cohort 4 Injections and Change in BCVA Over 3 Years



*Retreatment per MD discretion in clinical practice.

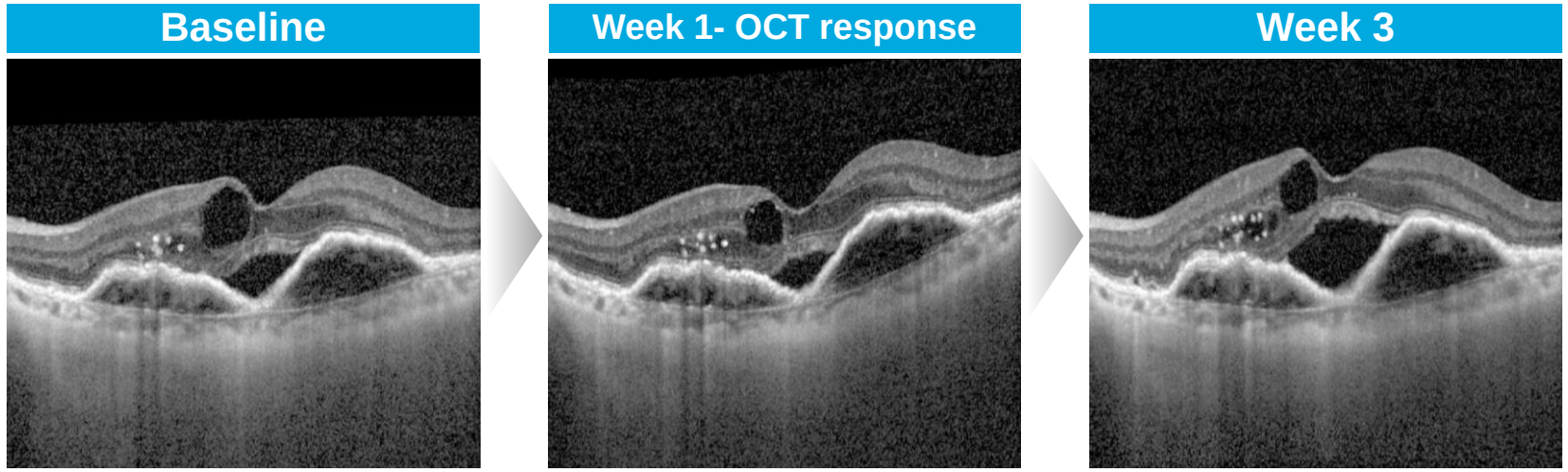
**This 77-year-old female with refractory wAMD had persistent fluid despite monthly anti-VEGF injections for 18 months prior to entering the study. She had continued disease activity during the study despite continued anti-VEGF injections and developed hemorrhage and subretinal fibrosis causing vision loss.

***Patient enrolled in the LTFU study but did not have a study visit. BCVA is Last Observation Carried Forward from the Phase I/IIa study.

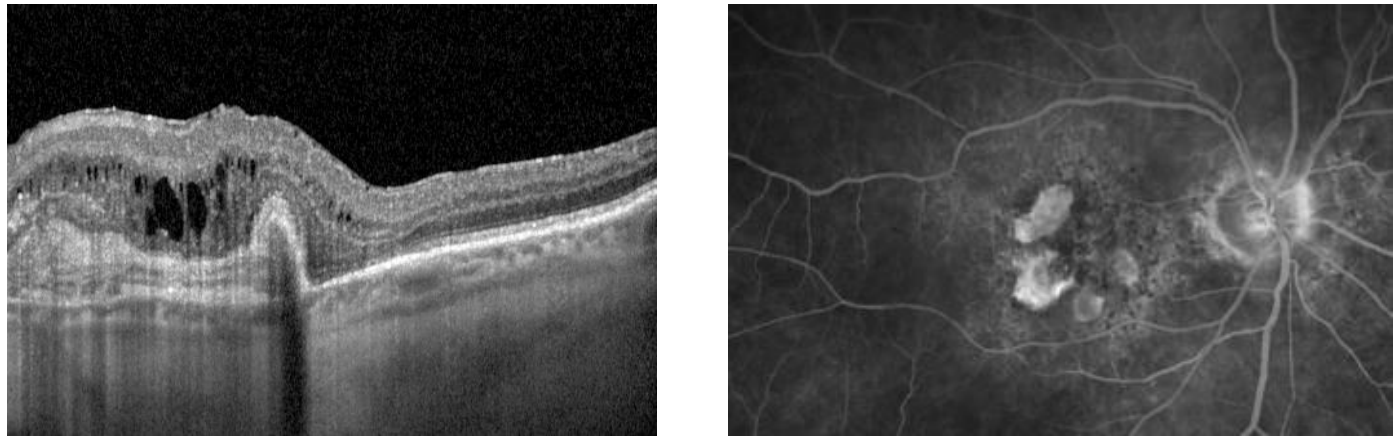
Key Learning: Exclude Subjects with Uncontrolled and End-Stage Disease in Pivotal Trials

RGX-314 Phase I/IIa: Characteristics of Patients to be Excluded in Pivotal Trials

Patients with Very Large Central Retinal Thickness (CRT)

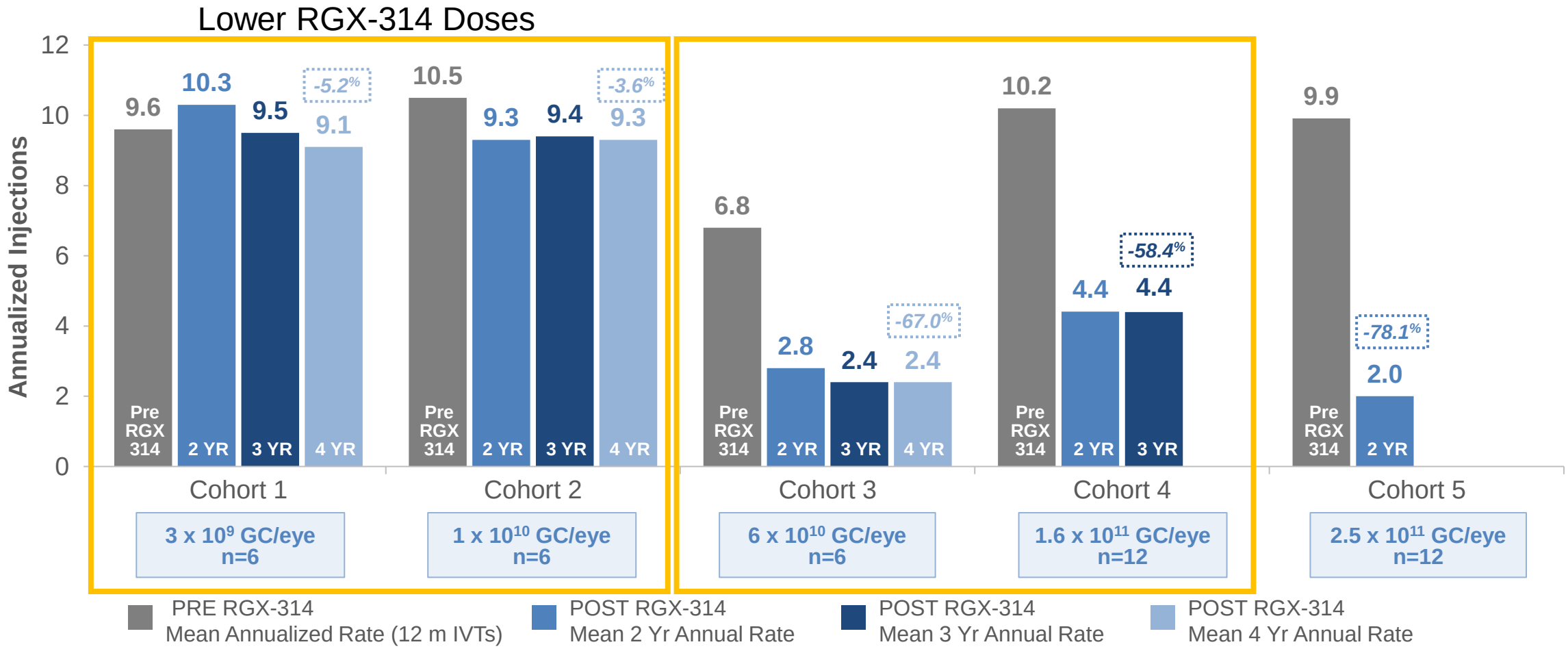


Baseline Subfoveal Fibrosis, Subfoveal Atrophy



Mean Change in Annualized Injection Rate PRE and POST RGX-314 in Cohorts 1–5 Over 4 Years

Annualized Injection Rate*

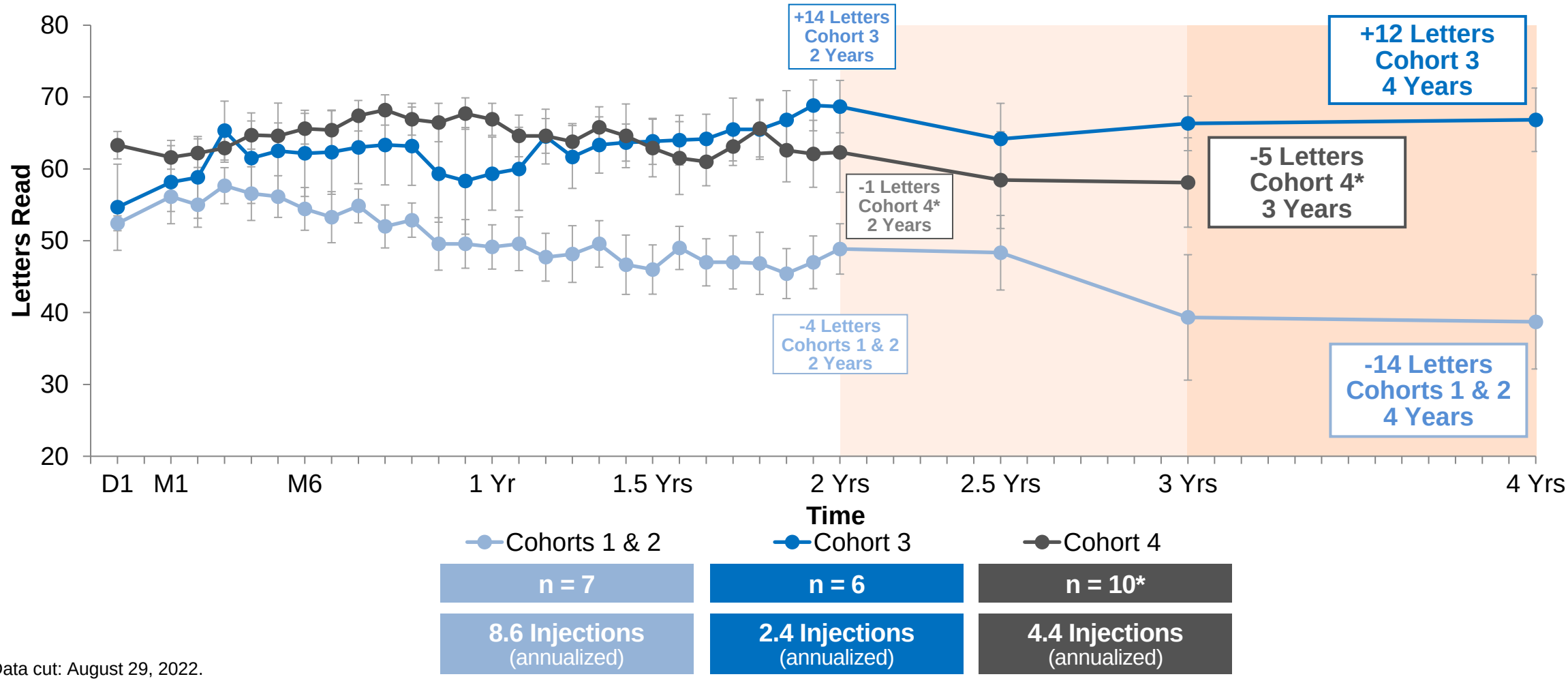


Retreatment Criteria: Any CNV-related increased, new, or persistent fluid; Vision loss of ≥5 letters associated with fluid; New ocular hemorrhage.

*Prior annual rate is (Total # of prior IVTs in 1 year)/(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. Analysis included all 42 patients from the Phase I/IIa study.

Mean Change in BCVA for Cohort 3 and 4 Compared to Lower Doses (Cohort 1 & 2 combined)

Cohorts 1 and 2 lost vision despite regular injections



Data cut: August 29, 2022.

Completer definition: For C1, C2, and C3, they will be patients who completed 4 years. For C4, they are patients who completed 3 years.

*One patient did not enroll in the LTFU study; one patient enrolled but did not have a study visit.

Interim Conclusions from the RGX-314 Subretinal Long-Term Follow-Up Study

- Subretinal RGX-314 continues to be **generally well-tolerated** in a Long-Term Follow-Up Study (n=37*) and will continue to be followed for a total of 5 years
- No new drug-related ocular AEs were reported in the last year of follow-up for Cohorts 3 and 4

- With a **single** injection of RGX-314, **patients demonstrate a long-term, durable treatment effect** for Cohort 3 over 4 years and Cohort 4 over 3 years
  - Stable to improved visual acuity
  - Meaningful reductions in anti-VEGF injection burden

Two pivotal trials for nAMD are now active and enrolling patients

ATMOSPHERE ASCENT

Data cut August 29, 2022.
*Patients with at least one visit in the LTFU study

RGX-314 Subretinal nAMD Phase I/IIa – LTFU Study Group

- **Robert Avery, MD** (Santa Barbara, CA)
- **David Brown, MD** (Houston, TX)
- **Peter Campochiaro, MD** (Baltimore, MD)
- **Stephen Huddleston, MD** (Memphis, TN)
- **Jeff Heier, MD** (Boston, MA)
- **Allen Ho, MD** (Philadelphia, PA)
- **Arshad Khanani, MD** (Reno, NV)
- **Albert Maguire, MD** (Philadelphia, PA)
- **Dante Pieramici, MD** (Santa Barbara, CA)
- **Charles Wykoff, MD PhD** (Houston, CA)