Subretinal Delivery of Investigational ABBV-RGX-314 for Neovascular AMD: A Phase II Pharmacodynamic Study

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Disclosures

Alcon - C
Alimera Sciences - C, S
Allergan - C, R, S
Apellis - S
Biogen - S
Coherus - S
EyePoint - C, S
Genentech - C, S
Iveric Bio - S
Outlook Therapeutics - C, O
RecensMedical - C
Regeneron - C, S
REGENXBIO - R

C – Consultant | R - Research Support | O - Ownership (Stock) | S - Speaker

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

ABBV-RGX-314 PRODUCT CANDIDATE

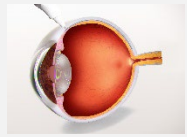
NAV® VECTOR **AAV8**

GENE **Anti-VEGF fab**

ROUTES OF ADMINISTRATION

Subretinal (nAMD)

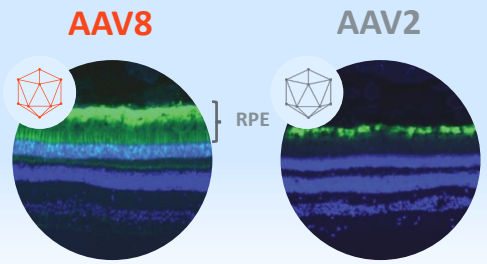
OR Suprachoroidal (nAMD/DR)



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

ABBV-RGX-314 gene encodes an anti-VEGF mAb fragment (fab)

=

ABBV-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

Current Program Status for ABBV-RGX–314

Subretinal

Phase I/IIa trial for nAMD is complete; Long-term follow-up continues

Phase II Pharmacodynamic trial for nAMD is ongoing

Two pivotal trials for nAMD are ongoing

ATMOSPHERE

ASCENT

Suprachoroidal

Phase II trial for nAMD is ongoing

AAVIATE

Phase II trial for diabetic retinopathy is ongoing

ALTITUDE

Commercial Manufacturing Process Utilizing Bioreactors for Planned Commercialization

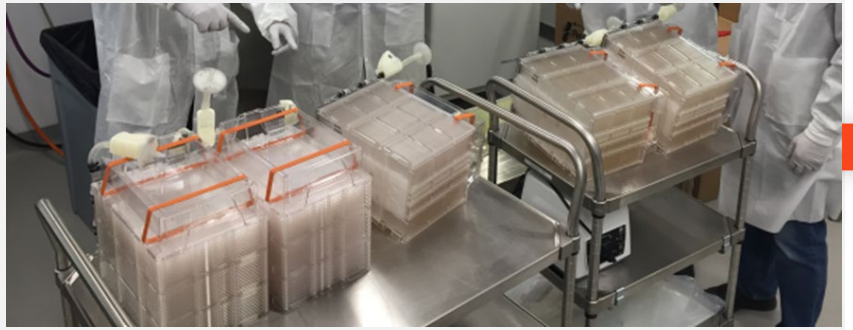
REGENXBIO Manufacturing Innovation Center

- NAVXpress™ manufacturing process is a commercial-ready, suspension cell (bioreactor) process expected to support planned commercialization of ABBV-RGX-314:
  - Demonstrated robust scalability
  - Consistent high yield and product purity
  - Increased capacity to supply treatment to global patient populations
- A Phase II Pharmacodynamic (PD) study has been initiated to evaluate the clinical performance of ABBV-RGX-314 manufactured from two processes:
  - Commercial-scale Process (Bioreactor, BRX) vs. Initial Clinical Research Process (Hyperstack®, HS)
- ABBV-RGX-314 will be manufactured for the commercial market using REGENXBIO's NAVXpress™ process at its new Manufacturing Innovation Center

Implementation of a Commercial-Ready Bioreactor Process (NAVXpress™)

Adherent (Hyperstack®, HS)

Initial Clinical Research Process

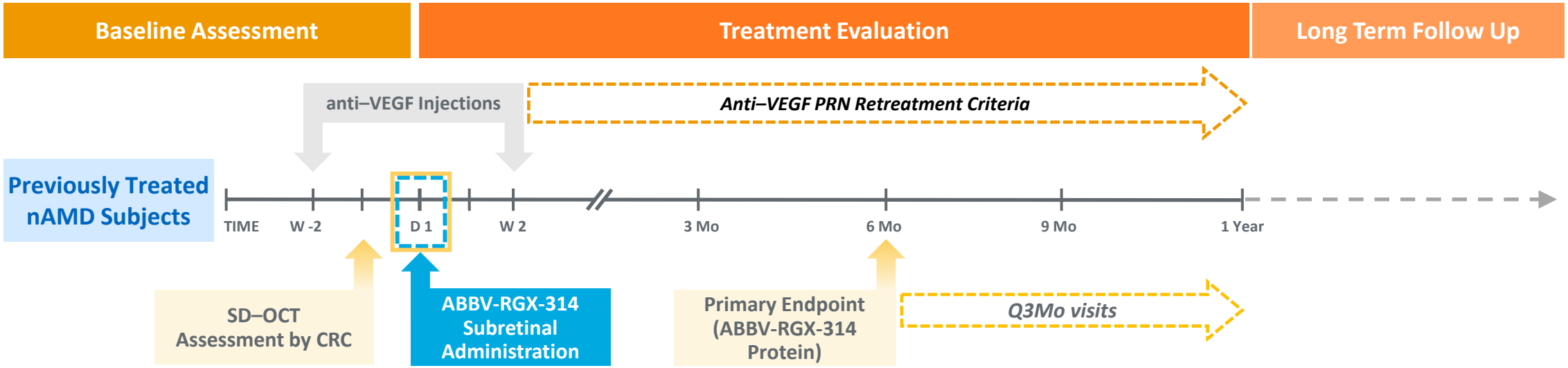


Suspension (Bioreactor, BRX)

Commercial-Ready Process

Cell Culture	**HEK293 cell line and triple transfection**		≈
Purification	**Chromatography (same steps, different scales)**		≈
Product Quality	**Analytical Comparability Demonstrated**		≈
Productivity	**Small Scale**	**Scalable to 2000L (global supply)**	+
	Manual process	**Highly-Automated Process**	+
	Low Yield	**High Yield**	+

ABBV-RGX-314 Phase II Clinical Trial in nAMD: A Pharmacodynamic (PD) Study



No prophylactic steroids given beyond routine vitrectomy SOC

✓ Fully Enrolled

DOSE 1 (High)
1.3×10^{11} GC/eye

BRX ✓ ABBV-RGX-314 n=15 → HS ✓ ABBV-RGX-314 n=15

DOSE 2 (Low)
6.4×10^{10} GC/eye

BRX ✓ ABBV-RGX-314 n=15 → HS ✓ ABBV-RGX-314 n=15

Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed.
BRX: Bioreactor; HS: Hyperstack; SOC: standard of care

ABBV-RGX-314 Phase II Clinical Trial in nAMD: A Pharmacodynamic Study

Bridging study will support planned commercialization of ABBV-RGX-314 manufactured by the BRX process

PRIMARY OBJECTIVE

- Expression of ABBV-RGX-314 protein in the eye at Month 6

SECONDARY OBJECTIVES

- Safety and tolerability of ABBV-RGX-314
- Expression of ABBV-RGX-314 protein in the eye at Month 3 and Year 1
- Effect of ABBV-RGX-314 on BCVA and CRT
- Supplemental anti-VEGF injection retreatment post-ABBV-RGX-314
- Time to first supplemental anti-VEGF

RETREATMENT CRITERIA

- Based on worsening vision and/or fluid due to nAMD

SUBJECTS: UP TO 60 TOTAL

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

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
- BCVA between 20/30 and 20/160 (78 and 40 Early Treatment Diabetic Retinopathy Study [ETDRS] letters) in the study eye
- Exclude any subfoveal atrophy or fibrosis
- Pseudophakic (status post cataract surgery)

Baseline Characteristics

	VARIABLE	BRX High Dose $1.3x10^{11}$ GC/eye (N=15)	HS High Dose $1.3x10^{11}$ GC/eye (N=15)	BRX Low Dose $6.4x10^{10}$ GC/eye (N=15)	Overall Mean (N=45)
BASELINE	**Mean Age** (Years)	76.9	79.3	77.7	78.0
	Screening BCVA (Letters)	60.7 (20/63)	71.1 (20/40)	65.7 (20/50)	65.8 (20/50)
	Screening OCT (Microns)	278.1	282.1	258.4	272.9
PRIOR THERAPY	**Months Since nAMD Diagnosis** (Mean)	35.4	37.1	56.1	42.9
	# Injections Since nAMD Diagnosis (Mean)	21.2	23.0	34.2	26.1
	# Injections in the Past Year*	6.3	6.5	7.3	6.7
	Average Annualized Injections in the Past Year*	7.9	9.7	8.2	8.6

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 Week -2)/365.25).
* Includes anti-VEGF injection at screening visit 1 (Week -2).
BRX: Bioreactor; HS: Hyperstack

Safety Summary

- **ABBV-RGX–314 was well–tolerated in all cohorts (n=60)**
- 5 SAEs reported in 4 patients, none considered drug-related
- Common AEs[1] in the study eye in the High Dose cohorts (BRX: n=15 and HS: n=15) and Low Dose BRX Cohort (n=15) were similar through 6-months and included:
    - Post-operative conjunctival hemorrhage (38% of all patients; 40% of BRX-HD cohort, 47% of HS-HD cohort, and **27% of BRX-LD**) – 100% mild (n=17), all resolved within days to weeks
    - Post-operative inflammation[2] (31% of all patients; 27% of BRX-HD cohort, 33% of HS-HD cohort, and **33% of BRX-LD cohort**) – 86% mild (n=12), 14% moderate (n=2), and all resolved within days to weeks
    - Retinal pigmentary changes all occurring in periphery (13% of all patients; 13% of BRX-HD cohort, 13% of HS-HD cohort, and **13% of BRX-LD cohort**) – 100% mild (n=6)

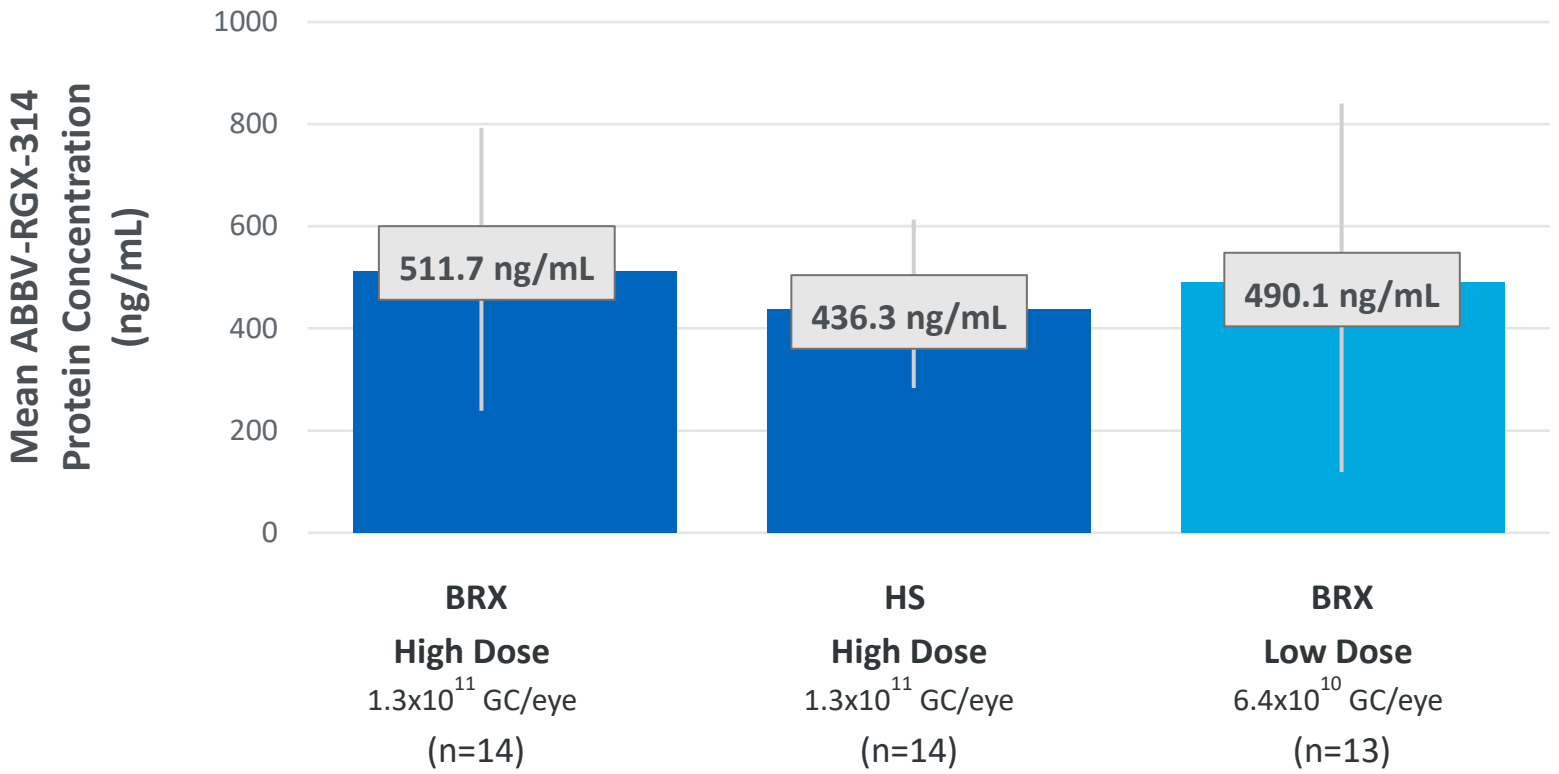
Data cut: May 8, 2023.
1. Includes AEs for total group ≥10% with onset up to 6m visit. Subjects are counted once for each Preferred Term regardless of the number of events.
2. Post-operative inflammation is defined as inflammation AEs which occurred within 30 days of subretinal procedure.
SAE: Serious Adverse Event; AE: Adverse event; BRX: Bioreactor; HS: Hyperstack

ABBV-RGX-314 Protein Levels are Similar Between Cohorts at Month 6

As Measured from Aqueous Samples by ECL 6 Months post-ABBV-RGX-314

PRIMARY OBJECTIVE

PROTEIN LEVELS



Data cut: May 8, 2023.

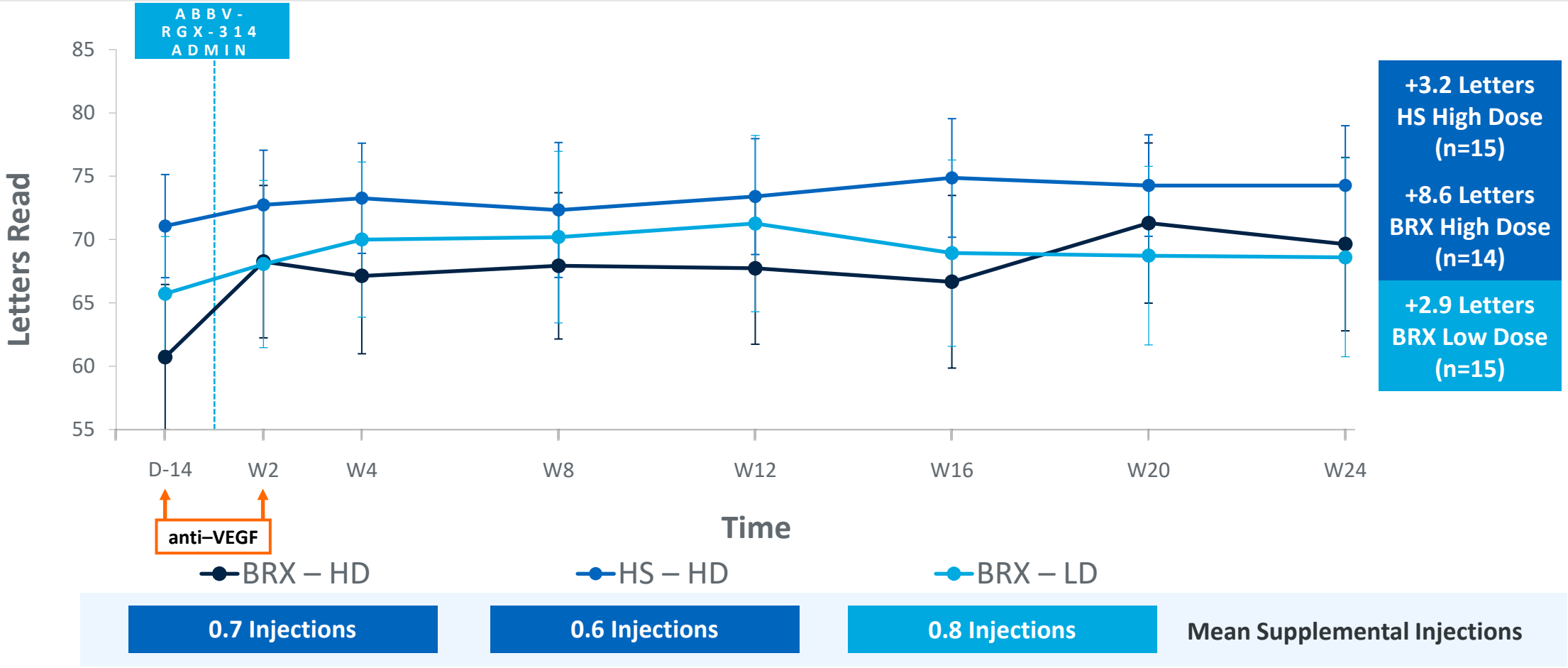
80% CI of the difference in ABBV-RGX-314 manufactured by BRX and HS (-38, 189) are calculated as specified in the protocol and overlaps 0, indicating that there is no statistical difference.

One patient in the BRX-HD cohort did not provide a sample, one patient in the HS-HD cohort provided an insufficient sample, and two patients in the BRX-LD cohort did not have data available as of the data cut.

ECL: Electrochemiluminescence; BRX: Bioreactor; HS: Hyperstack; CI: Confidence Interval

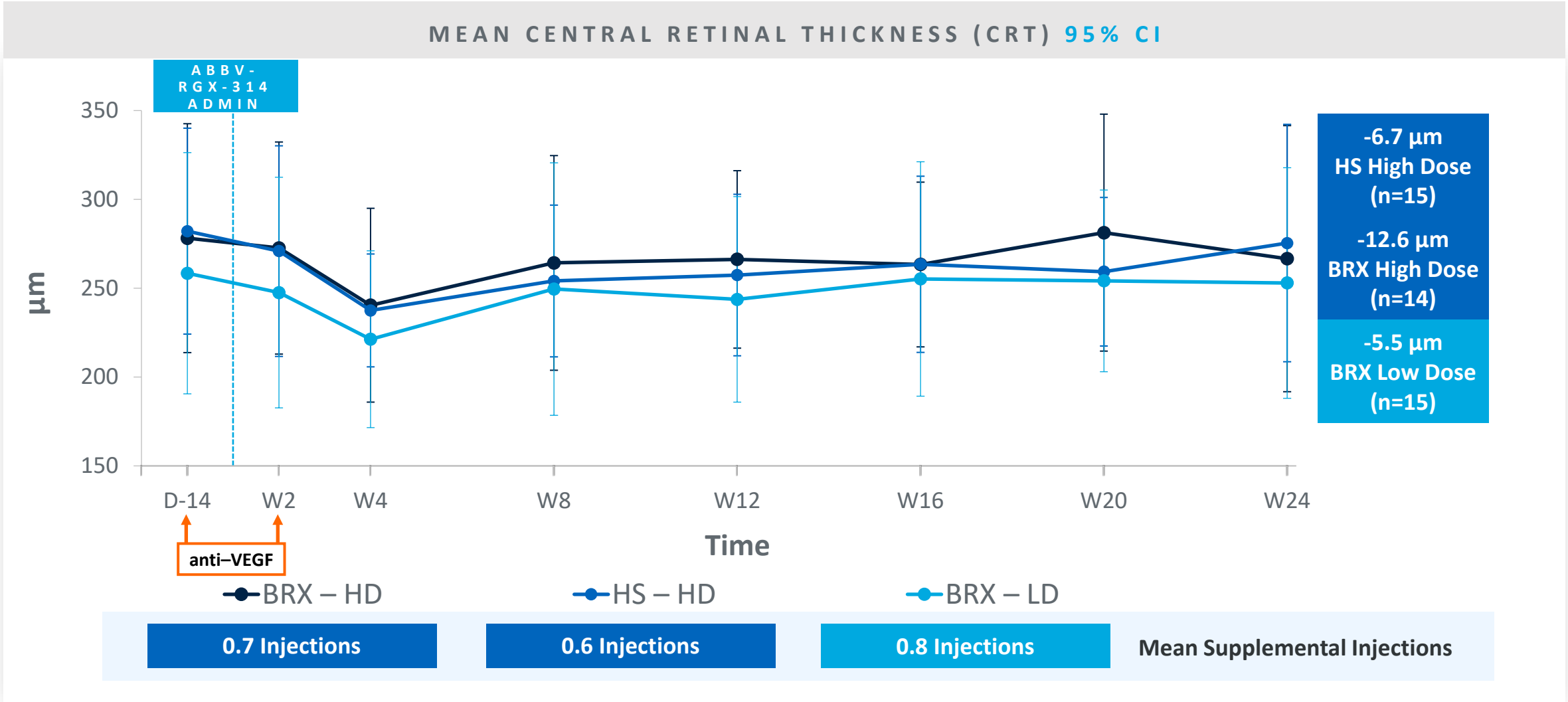
Both Dose Levels Demonstrated Stable to Improved BCVA Through Month 6

MEAN BEST CORRECTED VISUAL ACUITY (BCVA) 95% CI



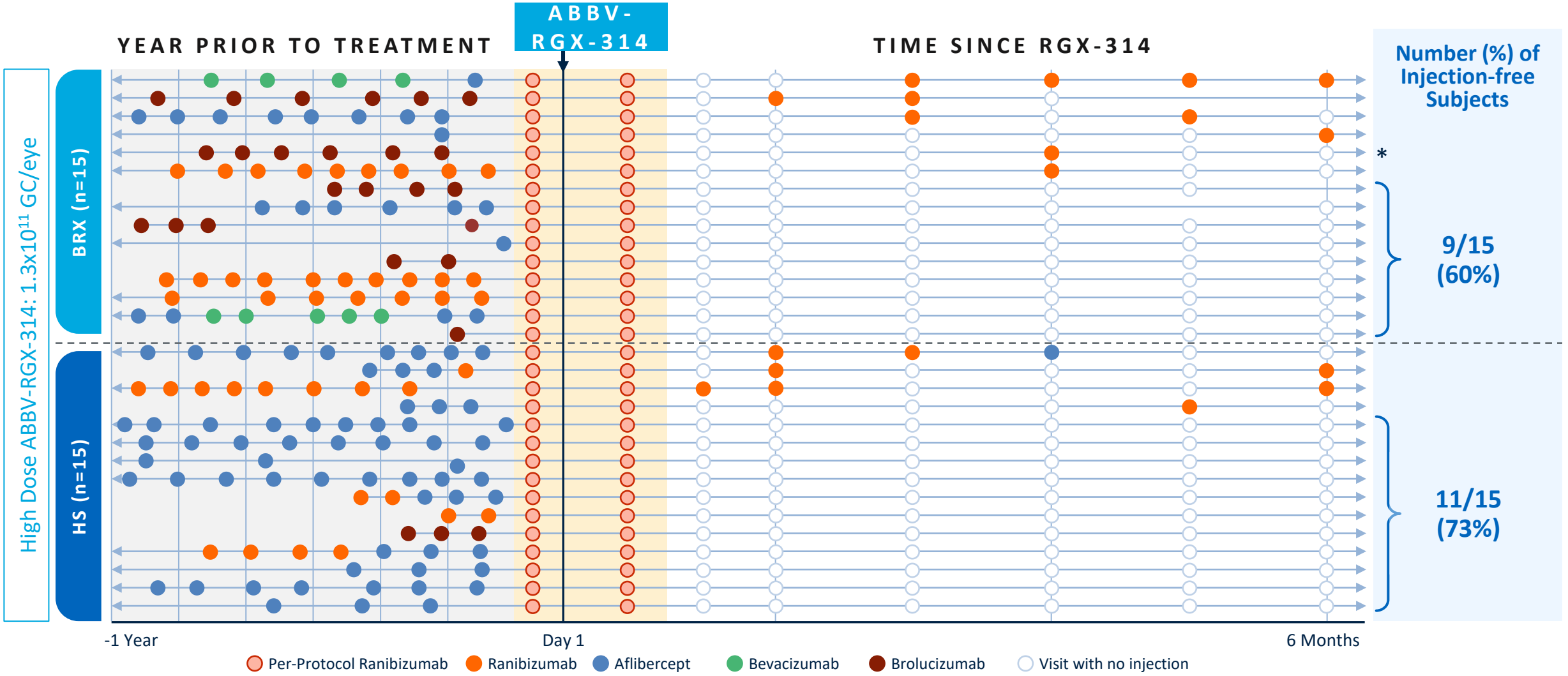
Data cut: May 8, 2023.
BRX: Bioreactor; HS: Hyperstack.

Both Dose Levels Demonstrated Stable to Improved CRT Through Month 6



Data cut: May 8, 2023.
BRX: Bioreactor; HS: Hyperstack.

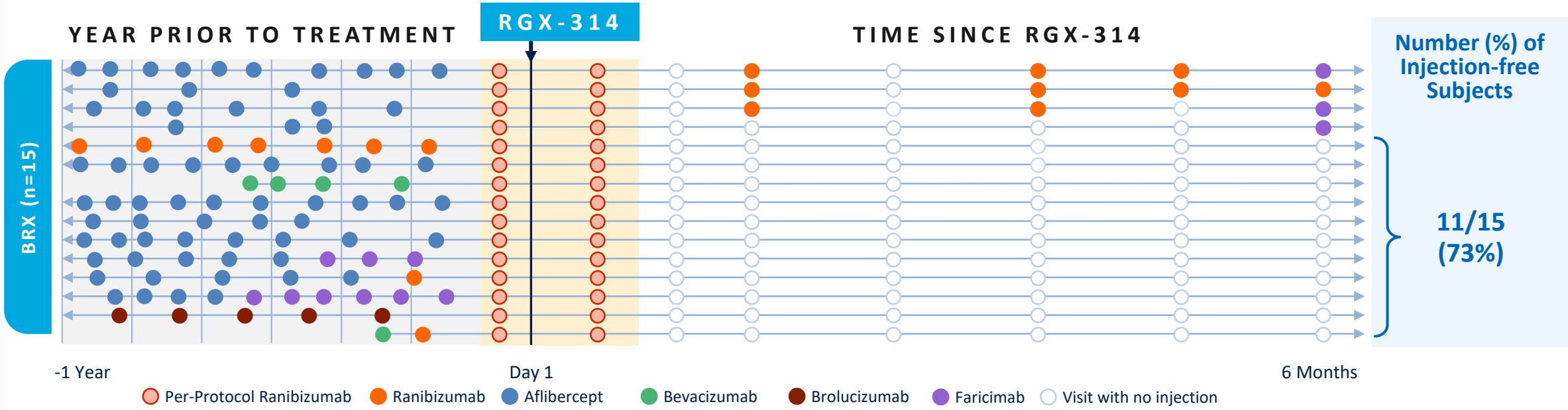
High Dose Cohort Injections: Pre and Post ABBV-RGX-314 (n=30) – 6 Month Data



Data cut: May 8, 2023.
*Patient received an incomplete dose at time of subretinal procedure. BRX: Bioreactor; HS: Hyperstack

Low Dose Cohort Injections: Pre and Post ABBV-RGX-314 (n=15) – 6 Month Data

Low Dose ABBV-RGX-314: 6.4×10^{10} GC/eye

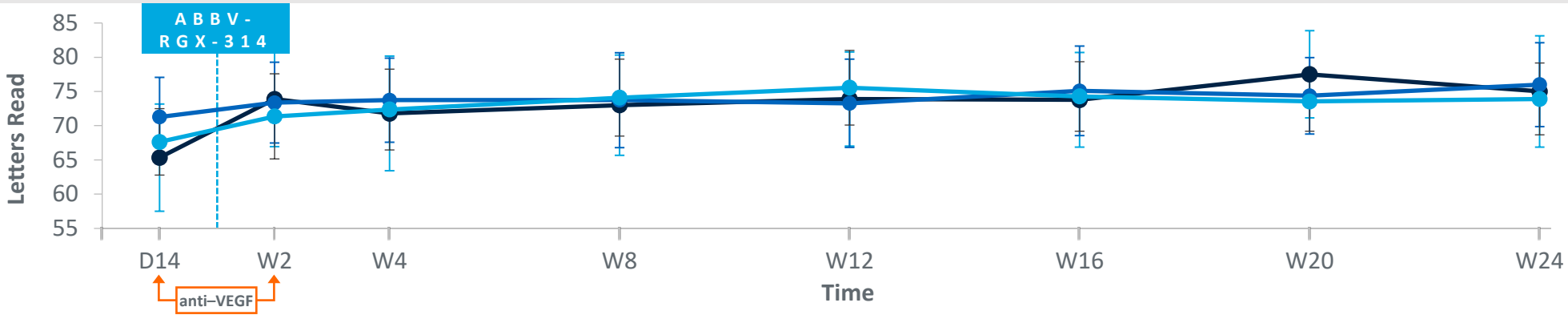


Data cut: May 8, 2023.
BRX: Bioreactor; HS: Hyperstack

Subjects with No Supplemental Anti-VEGF Injections over 6 Months

Subjects in both dose levels showed stable to improved vision and anatomy

MEAN BEST CORRECTED VISUAL ACUITY (BCVA) 95% CI

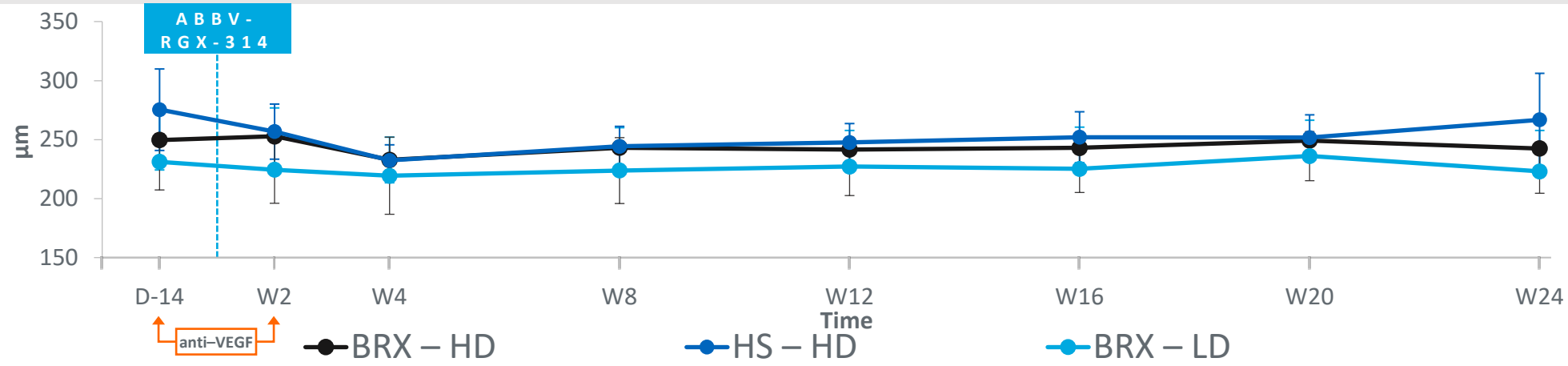


+4.7 Letters
HS High Dose (n=11)

+9.7 Letters
BRX High Dose (n=9)

+6.3 Letters
BRX Low Dose (n=11)

MEAN CENTRAL RETINAL THICKNESS (CRT) 95% CI



-8.5 µm
HS High Dose (n=11)

-7.2 µm
BRX High Dose (n=9)

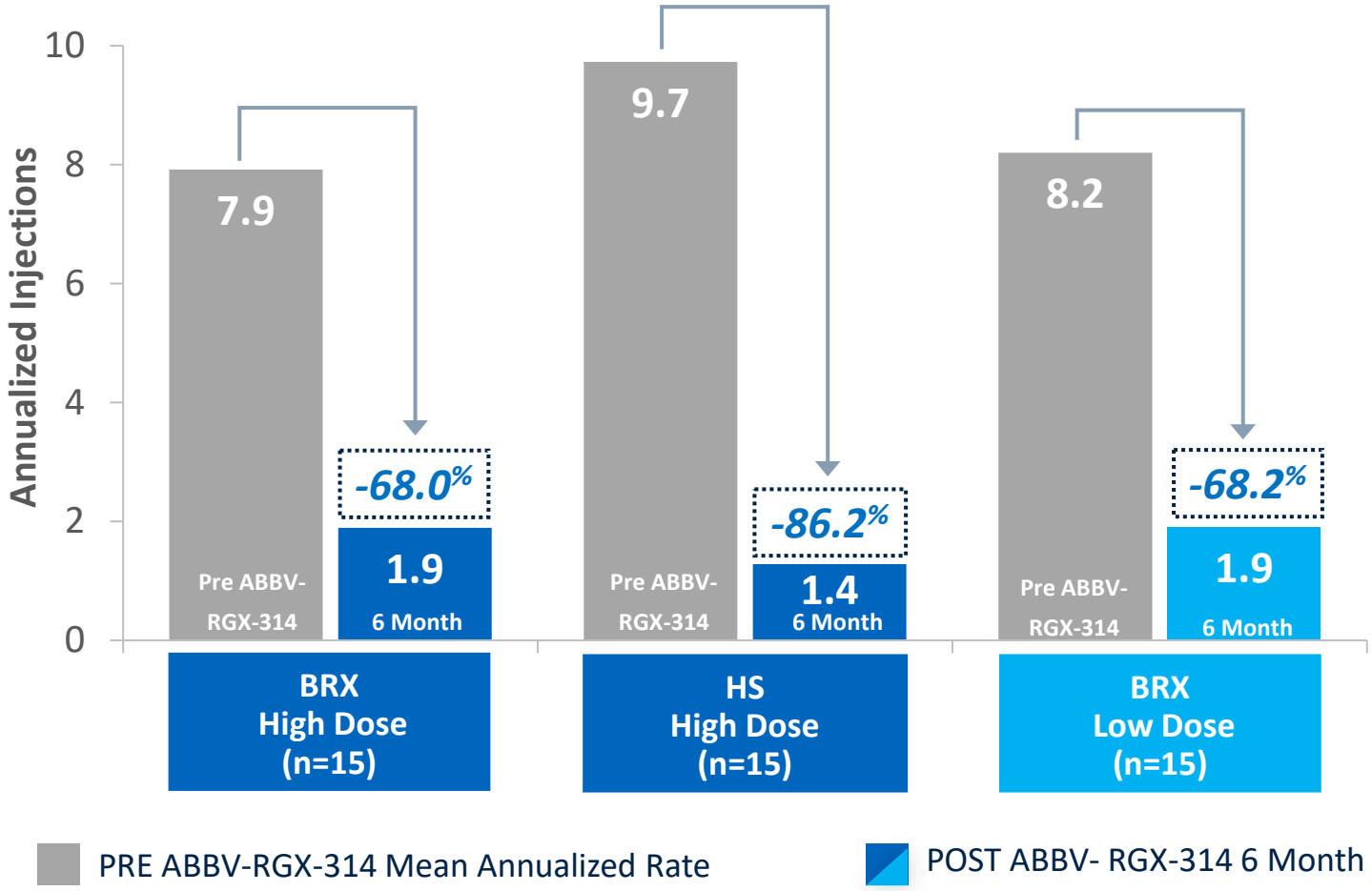
-8.1 µm
BRX Low Dose (n=11)

8.4 Injections	9.1 Injections	8.9 Injections	Average Prior Annualized Injection Rate

Data cut: May 8, 2023.
Average annualized injections in the past year is: (Total # of prior injections)/(minimum(366 days, Duration between first injection and Week -2)/365.25) and includes anti-VEGF injection at screening visit 1 (Week -2).
BRX: Bioreactor; HS: Hyperstack.

Subjects in Both Dose Levels Had Meaningful Reduction in Anti-VEGF Injection Burden Through Month 6

Annualized Injection Rate



Data cut: May 8, 2023.
Average annualized injections in the past year is: (Total # of prior injections)/(minimum(366 days, Duration between first injection and Week -2)/365.25) and includes anti-VEGF injection at screening visit 1 (Week -2).
BRX: Bioreactor; HS: Hyperstack

ABBV-RGX-314 Phase II Subretinal Pharmacodynamic (PD) nAMD Study

Summary

Commercial-ready, bioreactor (BRX) manufacturing process is expected to support future commercialization of ABBV-RGX-314

A Phase II PD nAMD study was conducted to evaluate ABBV-RGX-314 from the planned commercial process (BRX) vs. the initial clinical research process (Hyperstack®, HS):

All Subjects Dosed (n=60)

ABBV-RGX-314 manufactured by both BRX and HS (both dose levels) are well-tolerated with no ABBV-RGX-314-related SAEs

High Dose (BRX and HS; n=30) and Low Dose (BRX; n=15) Cohorts through Month 6

ABBV-RGX-314 manufactured by the BRX process demonstrated a similar clinical profile to the HS process:

- Common AEs[1] in the study eye were similar
- Similar and expected ABBV-RGX-314 protein level expression
- All cohorts demonstrated stable to improved BCVA and retinal thickness
- Majority of patients were injection-free in all cohorts, with meaningful reductions in anti-VEGF injection burden

Initial study results support the dose levels and cGMP commercial-ready material being evaluated in the ongoing ATMOSPHERE and ASCENT pivotal trials

Data cut: May 8, 2023.

1. Includes AEs for total group ≥10% with onset up to 6m visit. Subjects are counted once for each Preferred Term regardless of the number of events.