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

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Disclosures

Adverum (C, R), Aerie (R), AGTC (C), Aldeyra (R), Alimera (R), Allergan (C), Apellis (C, R), B&L (C), Bayer (C, R), Bionic Vision Technologies (C), Boehringer Ingelheim (R), Kanghong (C, R), Clearside (C, R), EyePoint (C), 4D Molecular Therapeutics (C, R), Gemini (R), Genentech (C, R), Graybug (R), Gyroscope (C, R), IONIS (R), IVERIC Bio (C, R), Janssen (C, R) , Kato (C), Kodiak (C, R), LMRI (R), Nanoscope (C, R), NGM (C, R), Novartis (C, R), OccuRx (C), Ocular Therapeutix (C), ONL Therapeutics (C, O), Opthea (C, R), Oxurion (C, R), Palatin (C), PolyPhotonix (C, O), RecensMedical (C, R, O), Regeneron (C, R), REGENXBIO (C, R), Roche (C, R), Takeda (C, R), Visgenx (C, O),

C – Consultant | R - Research Support (PI) | O - Ownership (Stock Options)

Current Program Status for 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

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

Summary

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

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

All Dose Cohorts (n=46 out of 60)

RGX-314 manufactured by both BRX and HS are well-tolerated with no RGX-314-related SAEs

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

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

Results from this study support the commercial-ready BRX manufacturing process

Data cut: November 14, 2022.
BRX: Bioreactor; HS: Hyperstack

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

RGX–314 PRODUCT CANDIDATE

NAV® VECTOR **AAV8**

GENE **Anti-VEGF fab**

ROUTES OF ADMINISTRATION

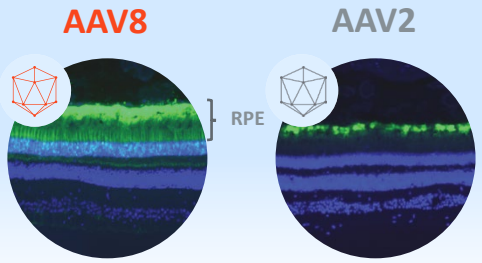
Subretinal (nAMD)

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

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

=

RGX–314: AAV8 encoding anti–VEGF fab

Potential for long-term therapeutic anti-VEGF expression

1. Vandenberghe et al. 2011 Science Translational Medicine.

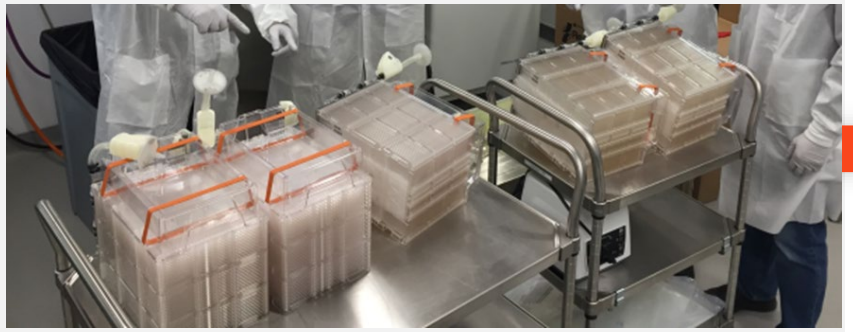
AAV: Adeno-Associated Virus

Commercial Manufacturing Process Utilizing Bioreactors for Planned Commercialization

REGENXBIO Manufacturing Innovation Center

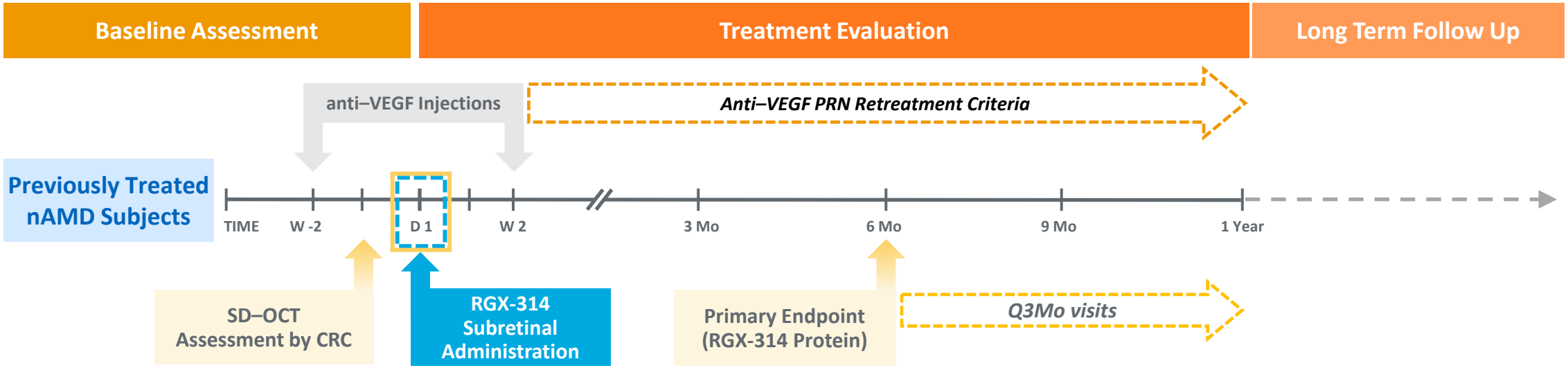
- NAVXpress™ manufacturing process is a commercial-ready, suspension cell (bioreactor) process expected to support planned commercialization of RGX-314:
  - Demonstrated robust scalability
  - Consistent high yield and product purity
  - Increased capacity to supply treatment to global patient populations
- A Phase II Pharmacodynamic (PD) study has been initiated to evaluate the clinical performance of RGX-314 manufactured from two processes:
  - Commercial-scale Process (Bioreactor, BRX) vs. Initial Clinical Research Process (Hyperstack®, HS)
- 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)	Suspension (Bioreactor, BRX)
Initial Clinical Research Process	*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**	+

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)
$1.3x10^{11}$ GC/eye

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

DOSE 2 (Low)
$6.4x10^{10}$ GC/eye

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

ENROLLING

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

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

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

PRIMARY OBJECTIVE

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

SECONDARY OBJECTIVES

- Safety and tolerability of RGX-314
- Expression of RGX-314 protein in the eye at Month 3 and Year 1
- Effect of RGX-314 on BCVA and CRT
- Supplemental anti-VEGF injection retreatment post-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 (High Dose Cohorts)

	VARIABLE	BRX High Dose $1.3x10^{11}$ GC/eye (N=15)	HS High Dose $1.3x10^{11}$ GC/eye (N=15)	Total (N=30)
BASELINE	**Mean Age** (Years)	**76.9**	**79.3**	**78.1**
	Screening BCVA (Letters)	**60.7** (20/63)	**71.1** (20/40)	**65.9** (20/50)
	Screening OCT (Microns)	**278.1**	**282.1**	**280.1**
PRIOR THERAPY	**Months Since nAMD Diagnosis** (Mean)	**35.4**	**37.0**	**36.7**
	# Injections Since nAMD Diagnosis (Mean)	**21.2**	**23.0**	**22.1**
	# Injections in the Past Year*	**6.3**	**6.5**	**6.4**
	Average Annualized Injections in the Past Year*	**7.9**	**9.7**	**8.8**

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

- **RGX–314 was well–tolerated in all cohorts (n=46)**
- 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) were similar through 6-months and included:
    - Post-operative conjunctival hemorrhage (40% of all patients; 40% of BRX cohort and 40% of HS cohort) – 100% mild (n=12), all resolved within days to weeks
    - Post-operative inflammation[2] (30% of all patients; 27% of BRX cohort and 33% of HS cohort) – 89% mild (n=8), 11% moderate (n=1), and all resolved within days to weeks
    - Retinal pigmentary changes all occurring in periphery (13% of all patients; 13% of BRX cohort and 13% of HS cohort) – 100% mild (n=4)

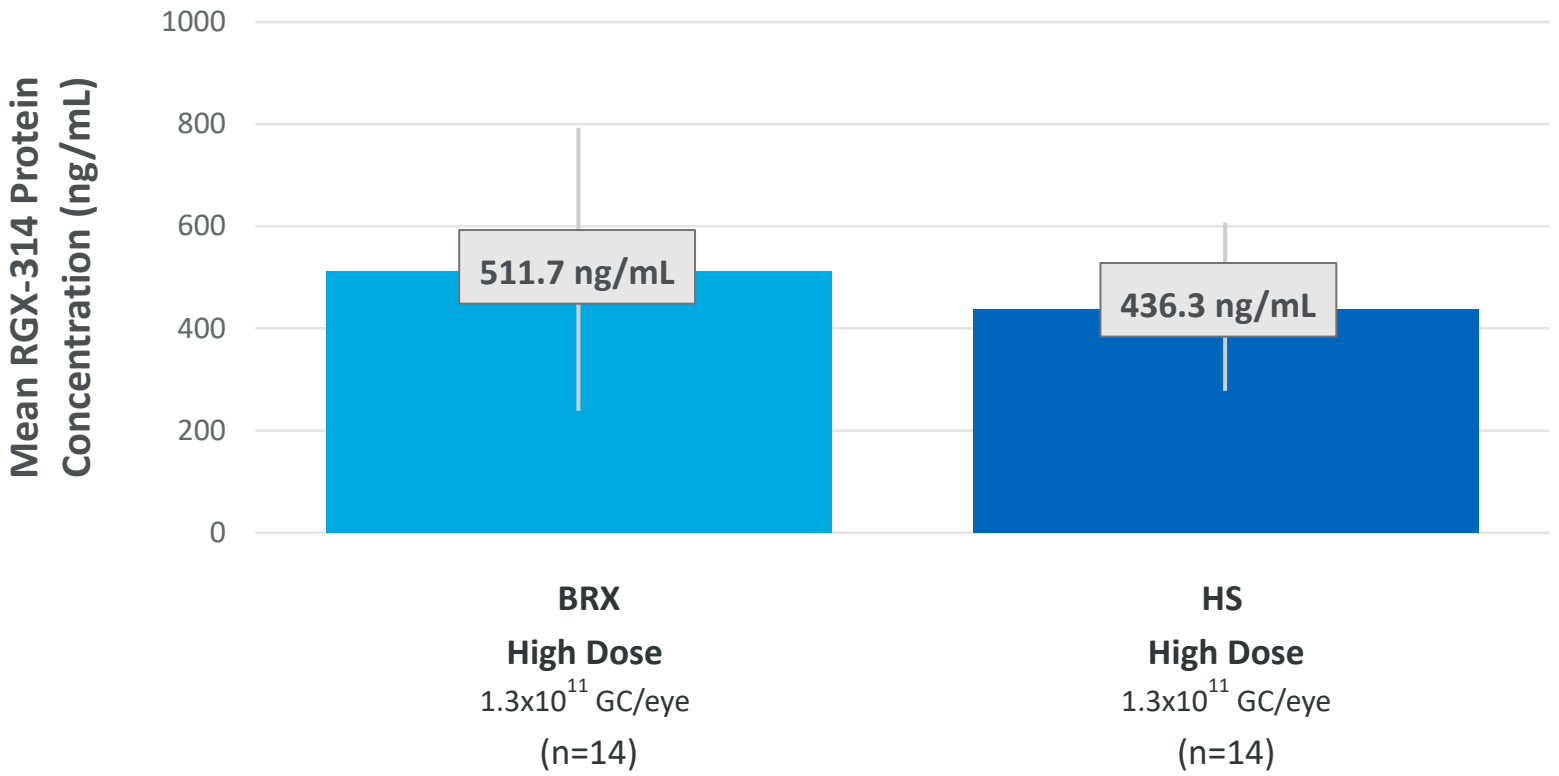
Data cut: November 14, 2022.
1. Includes AEs for total group ≥10% with onset up to 6m visit. Subjects are counted once for each Preferred Term regardless of the number of events.
2. Post-operative inflammation is defined as inflammation AEs which occurred within 30 days of subretinal procedure.
SAE: Serious Adverse Event; AE: Adverse event; BRX: Bioreactor; HS: Hyperstack

RGX-314 Protein Levels are Similar Between BRX and HS High Dose Cohorts at Month 6

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

PRIMARY OBJECTIVE

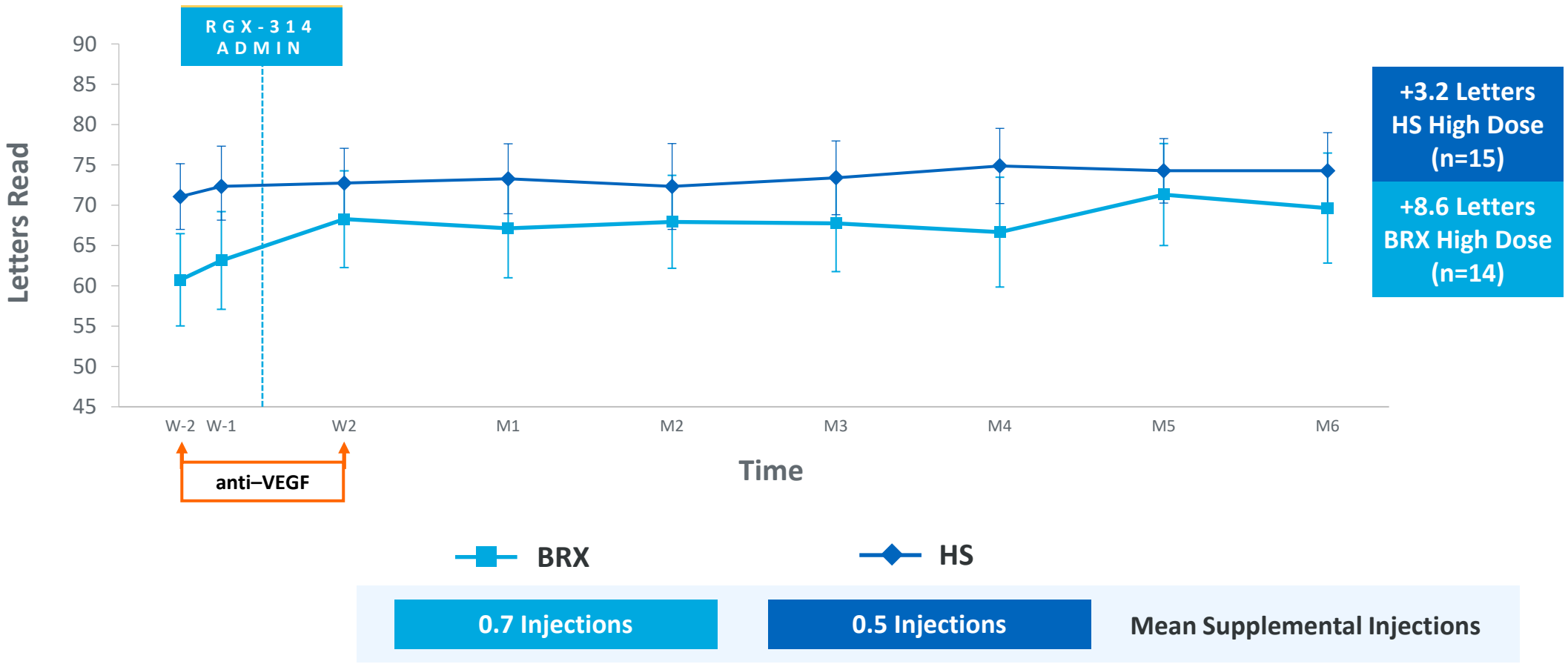
PROTEIN LEVELS



Data cut: November 14, 2022.
80% CI of the difference in 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 cohort did not provide a sample and one patient in the HS cohort provided an insufficient sample.
ECL: Electrochemiluminescence; BRX: Bioreactor; HS: Hyperstack; CI: Confidence Interval

High Dose Cohorts: Mean change in BCVA from Baseline Through Month 6

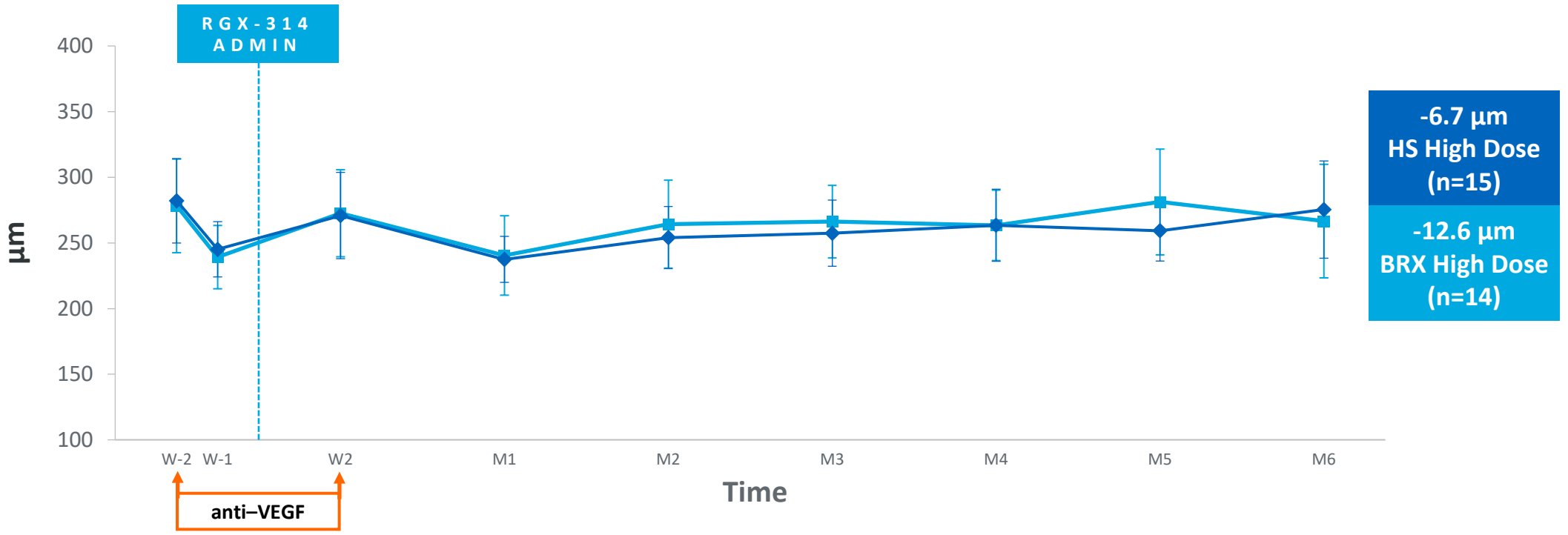
BEST CORRECTED VISUAL ACUITY (BCVA) 95% CI



Data cut: November 14, 2022.
BRX: Bioreactor; HS: Hyperstack

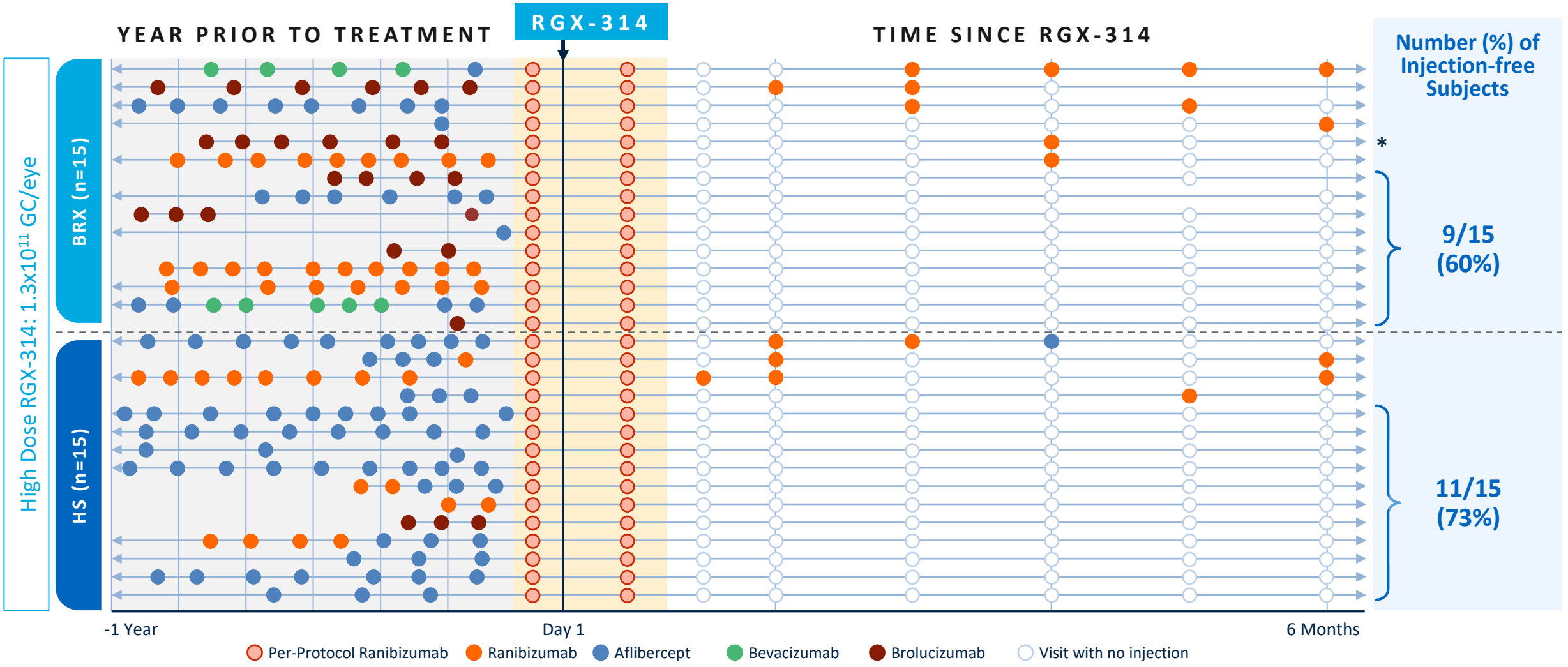
High Dose Cohorts: Mean CRT from Screening Through Month 6

MEAN CENTRAL RETINAL THICKNESS (CRT) 95% CI



Data cut: November 14, 2022.
BRX: Bioreactor; HS: Hyperstack

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

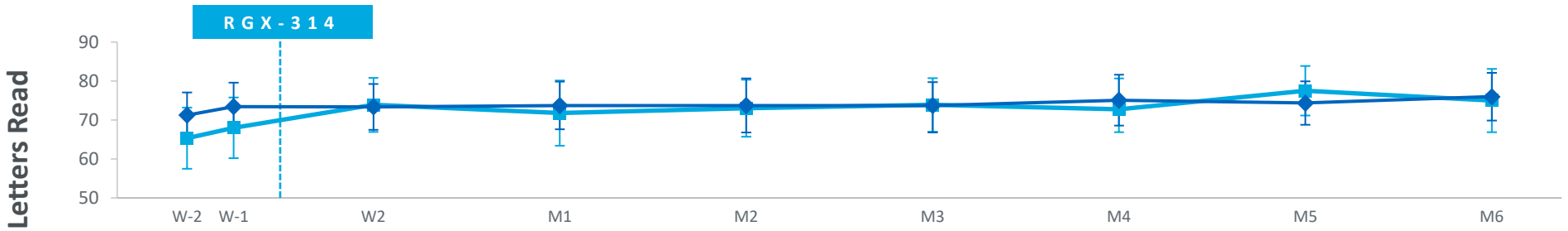


Data cut: November 14, 2022.
*Patient received an incomplete dose at time of subretinal procedure. BRX: Bioreactor; HS: Hyperstack

High Dose Cohorts: Subjects with No Anti-VEGF Injections over 6 Months

Subjects with no supplementary injections showed stable to improved vision with stable anatomy

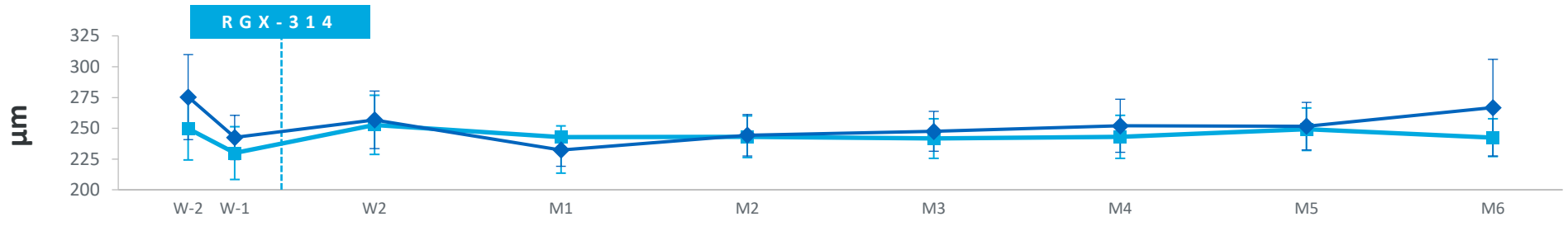
MEAN BEST CORRECTED VISUAL ACUITY (BCVA) 95% CI



+4.7 Letters
HS High Dose (n=11)

+9.7 Letters
BRX High Dose (n=9)

MEAN CENTRAL RETINAL THICKNESS (CRT) 95% CI



-8.5 µm
HS High Dose (n=11)

-7.2 µm
BRX High Dose (n=9)

anti–VEGF

Time

BRX — **8.4 Injections**

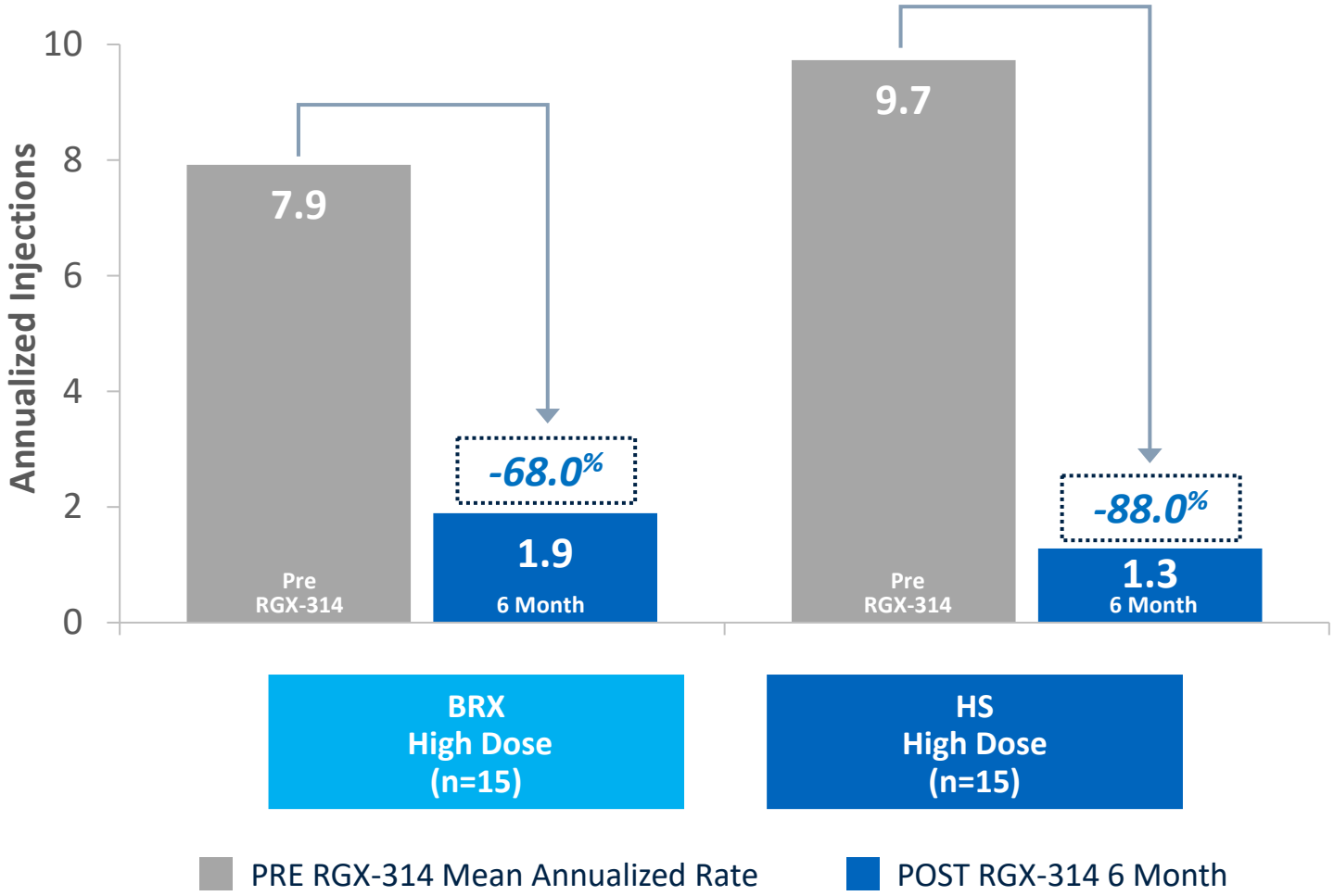
HS — **9.1 Injections**

Average Prior Annualized Injection Rate

Data cut: November 14, 2022.
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.

Mean Change in Annualized Injection Rate PRE and POST RGX-314 in High Dose Cohorts

Annualized Injection Rate



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BRX: Bioreactor; HS: Hyperstack

Patient Case*

*These slides present results from an individual patient and are not indicative of outcomes experienced by all patients in this trial

PRIOR TO RGX-314

PATIENT A

High Dose (BRX)

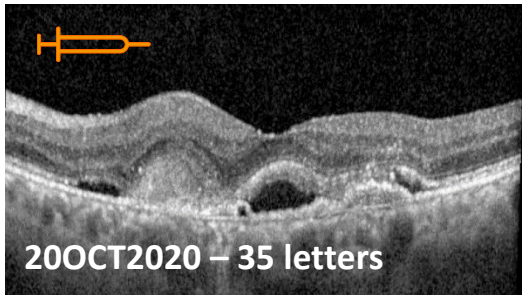
AGE	STUDY EYE
84 yrs.	OS

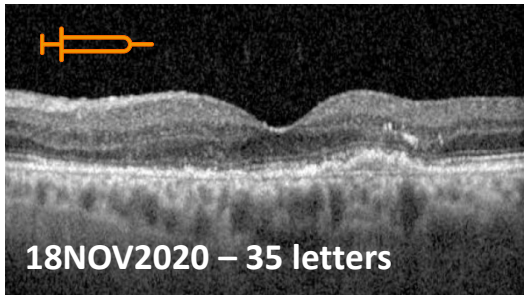
YEARS SINCE nAMD DIAGNOSIS	0.9
# ANTI-VEGF INJECTIONS IN YEAR PRIOR TO RGX-314	11
# SUPPLEMENTAL INJECTIONS	0

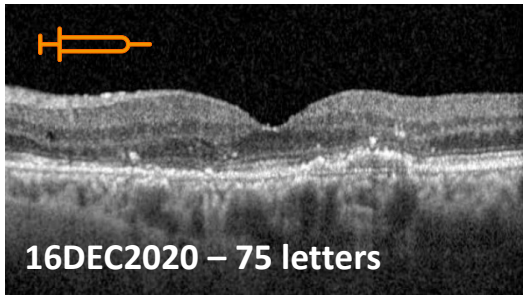
Ranibizumab Injection

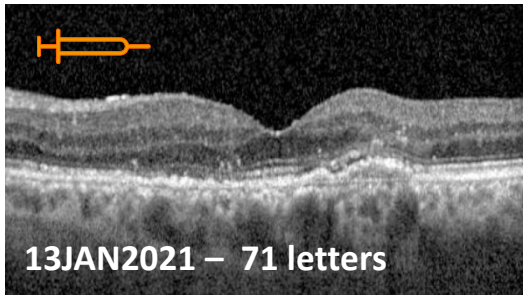
BRX: Bioreactor; HS: Hyperstack

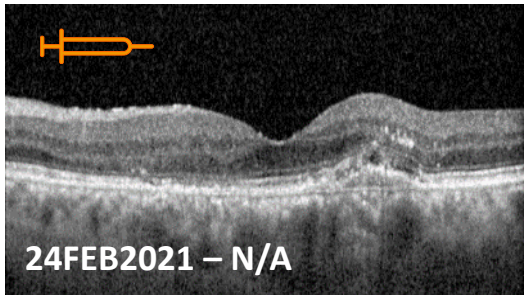
PRIOR HISTORY

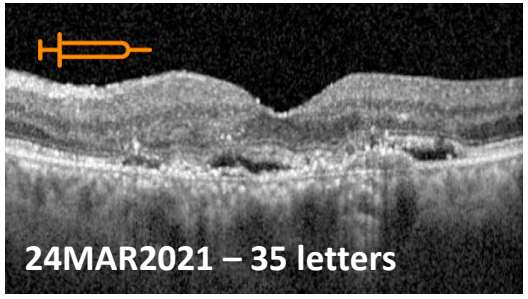


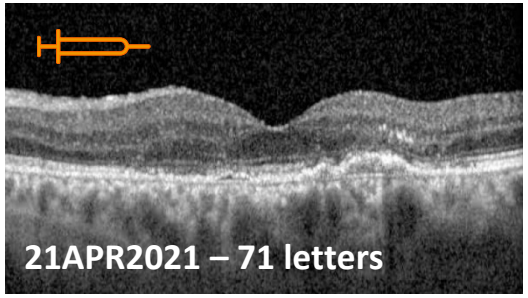


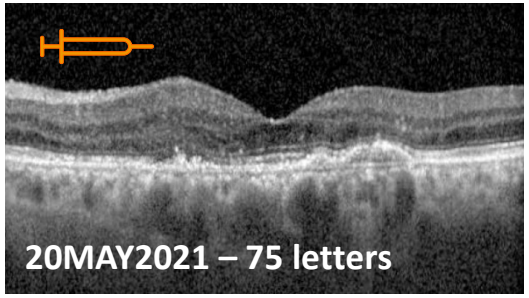


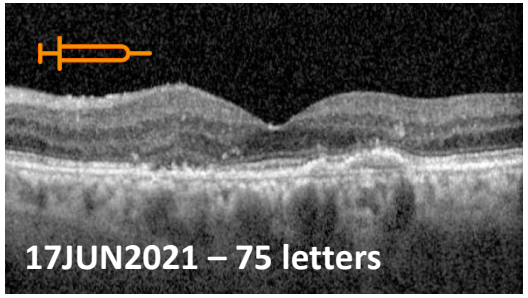


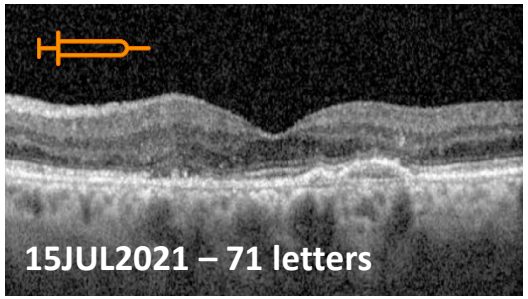


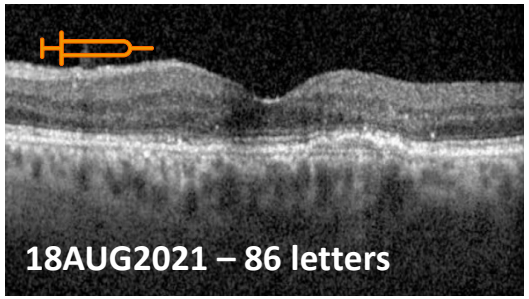












PATIENT A

High Dose (BRX)

AGE	STUDY EYE
84 yrs.	OS

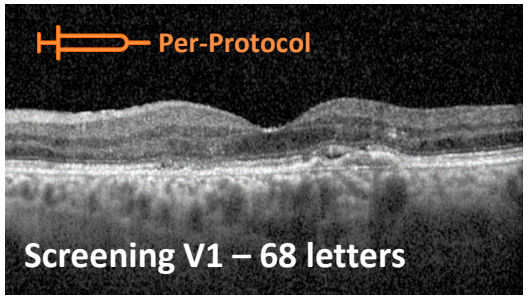
YEARS SINCE nAMD DIAGNOSIS	0.9
# ANTI-VEGF INJECTIONS IN YEAR PRIOR TO RGX-314	11
# SUPPLEMENTAL INJECTIONS	0

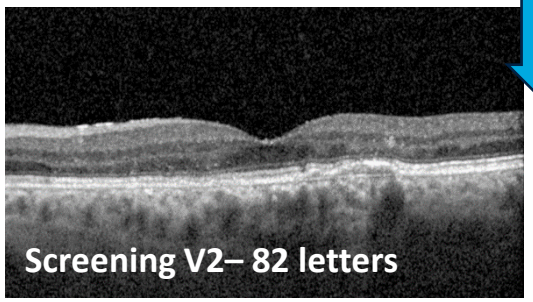
Ranibizumab Injection

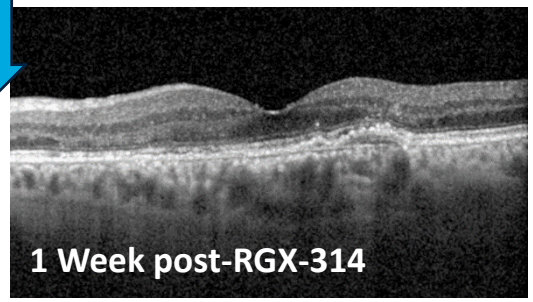
BRX: Bioreactor; HS: Hyperstack

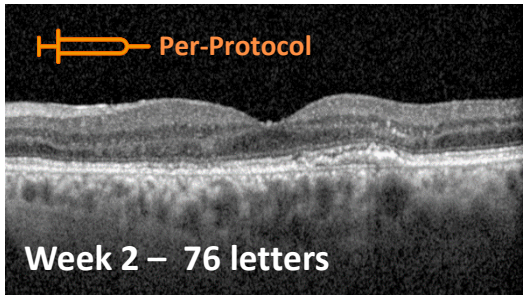
On Study

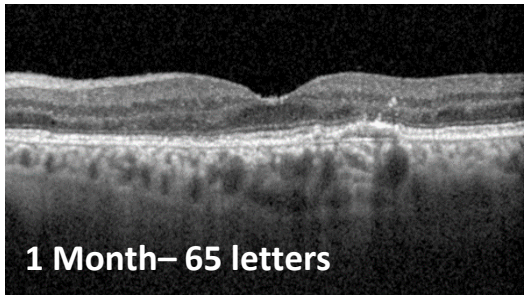
RGX-314

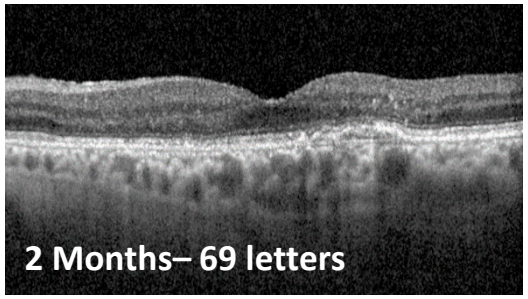


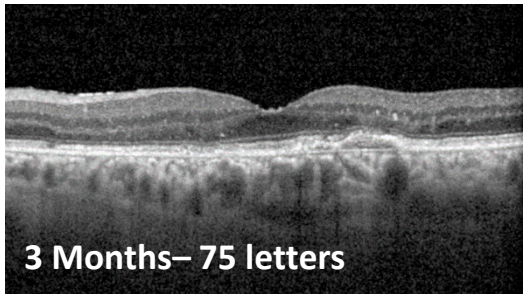


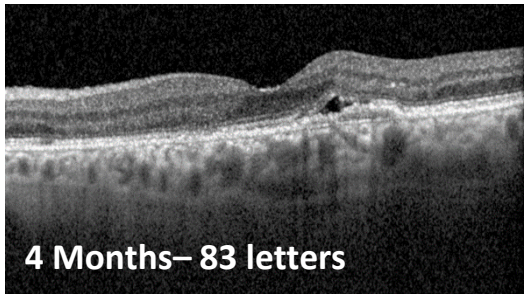


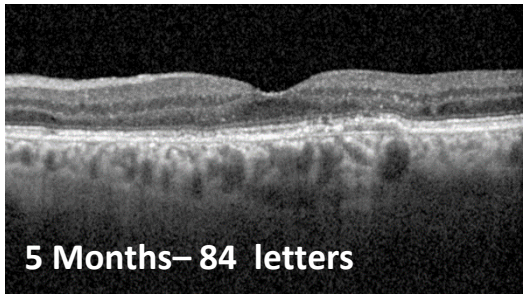




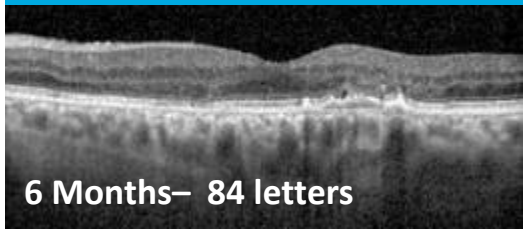








+16 LETTERS



PRIOR YEAR

PATIENT A

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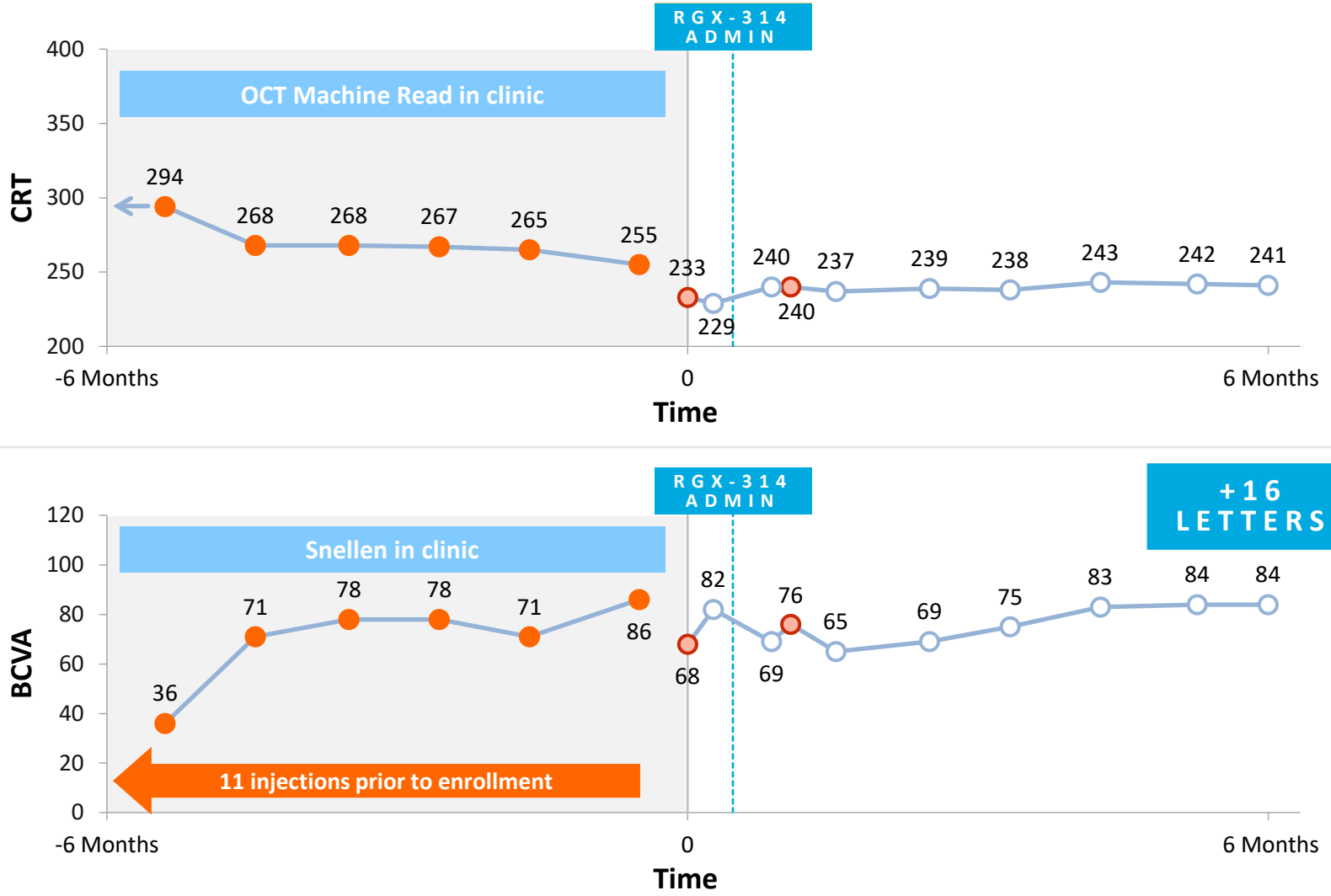
YEARS SINCE nAMD DIAGNOSIS	0.9
# ANTI-VEGF INJECTIONS IN YEAR PRIOR TO RGX-314	11
# SUPPLEMENTAL INJECTIONS	0

BRX: Bioreactor; HS: Hyperstack

Central Retina Thickness (CRT) AND Best Corrected Visual Acuity (BCVA)*



Ranibizumab Per-Protocol Ranibizumab Visit with no injection

*CRTs on-study are measured by Central Reading Center, and on-study BCVAs are ETDRS letters.

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

Summary

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

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

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

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

- Common AEs[1] in the study eye in High Dose Cohorts BRX (n=15) and HS (n=15) were similar
- Similar and expected RGX-314 protein level expression
- Both cohorts demonstrated stable to improved BCVA and retinal thickness
- Majority of patients were injection-free in both cohorts, with meaningful reductions in anti-VEGF injection burden

Results from this study support the commercial-ready BRX manufacturing process

Data cut: November 14, 2022.
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.
BRX: Bioreactor; HS: Hyperstack