



Corporate Presentation

Leader in AAV Gene Therapy

3 | 30 | 2023

Forward-looking statements

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Seeking to improve lives through the curative potential of gene therapy

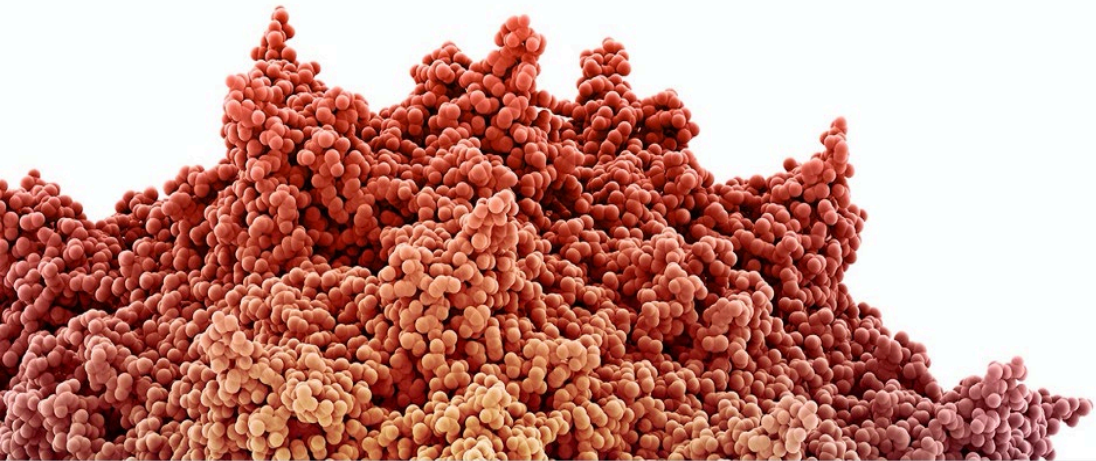
Leading pipeline of AAV Therapeutics with the potential to deliver one-time treatments

Strategic partnership with AbbVie to develop and commercialize AAV Therapeutics for retinal disease

Proprietary AAV Therapeutics manufacturing with analytics, delivery device and global supply platform

Strong balance sheet to fund operations into 2025

“5 x 25” strategy to progress 5 AAV Therapeutics from our internal pipeline and licensed programs into pivotal-stage or commercial products by 2025



REGENXBIO's internal pipeline

Indication	Development Stage				Commercial Rights
	Research	Preclinical	Phase I / II	Pivotal	
Retinal Disease					
wet AMD (subretinal)	RGX-314 SR				abbvie U.S. Equal Profit Share Ex-U.S. Tiered Royalties
wet AMD (suprachoroidal)	RGX-314 SC				
Diabetic retinopathy (suprachoroidal)	RGX-314 SC				
Other chronic retinal conditions					
<hr/>					
Batten disease (CLN2) ▲★	RGX-381				Worldwide
Neuromuscular Disease					
Duchenne muscular dystrophy ▲★	RGX-202				Worldwide
Neurodegenerative Disease					
Hunter syndrome (MPS II) ▲★■	RGX-121				Worldwide
Hurler syndrome (severe MPS I) ▲★■	RGX-111				Worldwide
Batten disease (CLN2) ▲★	RGX-181				Worldwide

- ▲ Orphan Drug Designation
- ★ Rare Pediatric Disease Designation
- Fast Track Designation
- AAV-mediated antibody delivery for chronic diseases
- Monogenic gene replacement





Retinal Diseases

Strategic partnership with AbbVie to develop and commercialize RGX-314, a potential one-time gene therapy for treatment of wet AMD and diabetic retinopathy



Leadership and expertise in AAV and retinal gene therapy



Strong in-house capabilities of AAV manufacturing



Leading eye care company



Global development and commercial infrastructure

Details of Partnership

- **\$370 million upfront payment** with up to **\$1.38 billion in additional development, regulatory and commercial milestones**
- Collaboration for the development and commercialization of RGX-314 with **equal share of profits in U.S. and REGENXBIO to receive royalties outside the U.S.**
- **REGENXBIO will lead the manufacturing of RGX-314** for clinical development and U.S. commercial supply



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: Potential best-in-class, one-time gene therapy for treatment of wet age-related macular degeneration (wet AMD)

THE DISEASE

- Blurring of central vision and progressive vision loss due to formation of leaky blood vessels in the eye
- VEGF inhibitors are standard of care to treat fluid and associated vision loss
- Frequency / uncomfortable administration of current anti-VEGF therapies affects compliance and ultimately efficacy
- >2 million patients estimated in U.S., Europe and Japan

RGX-314 PRODUCT CANDIDATE



Vector: AAV8

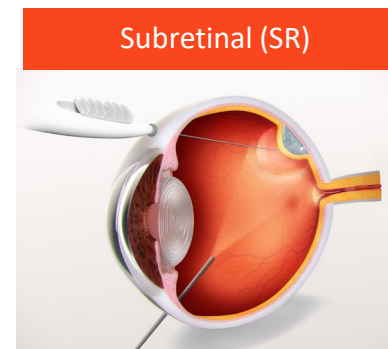


Gene: anti-VEGF Fab

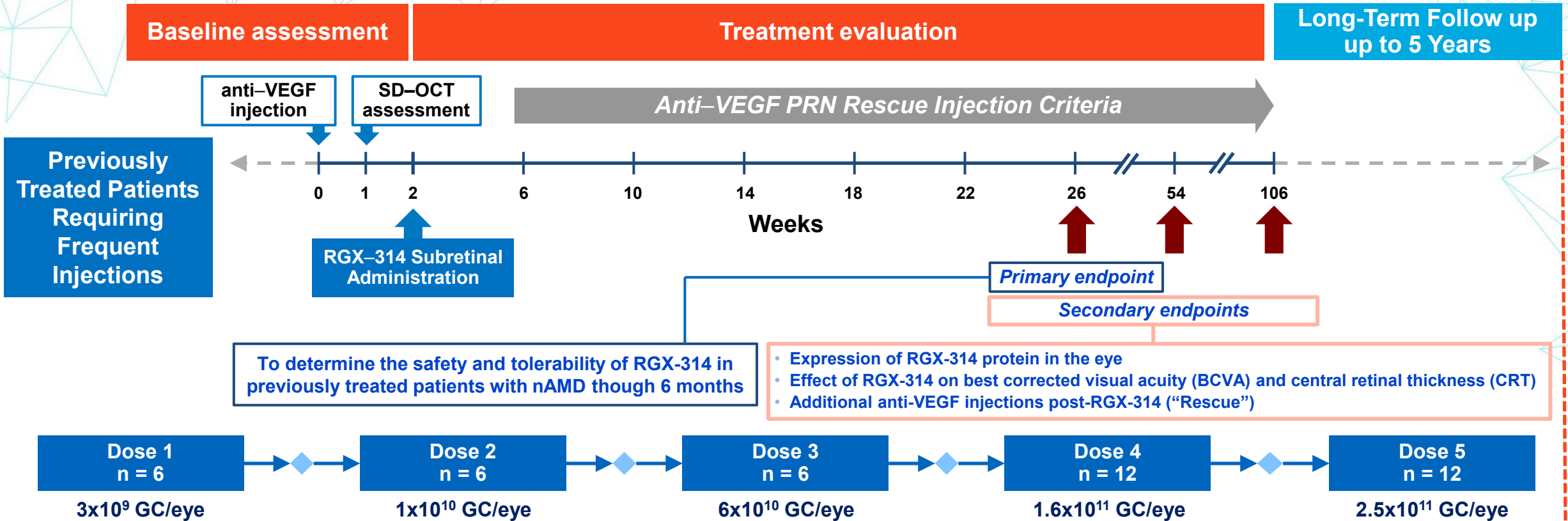
Mechanism of action

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

Routes of administration



RGX-314 Phase I/IIa and Long-Term Follow-up Trial in wAMD: Trial Design



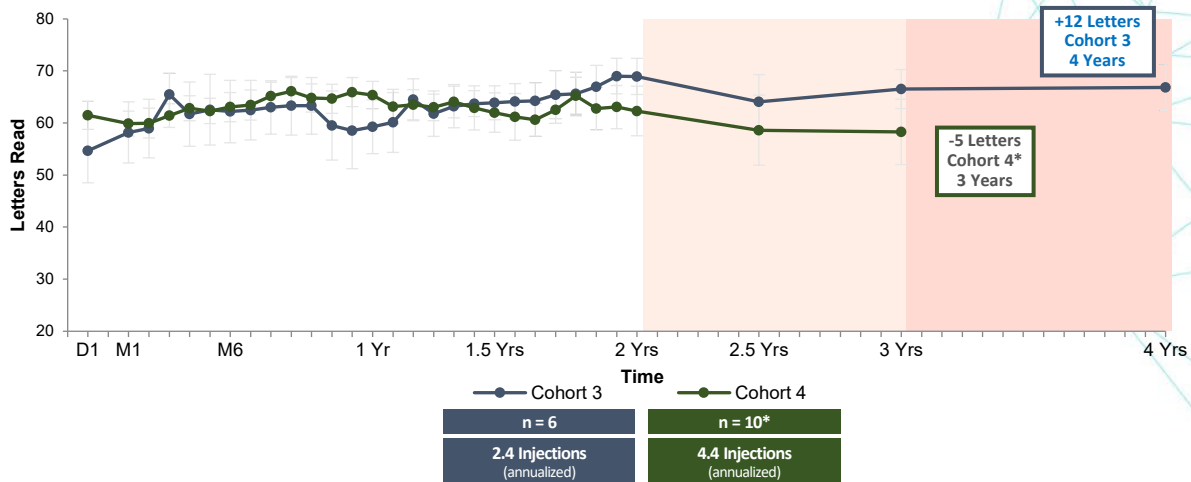
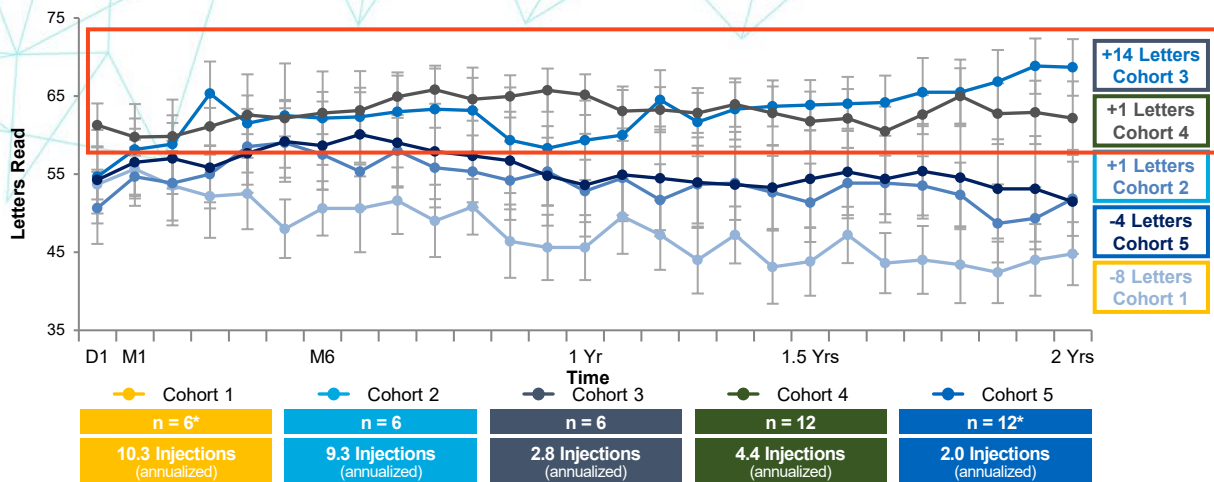
- Long Term Follow-up to 5 years post RGX-314 to assess safety and efficacy
- Patients managed per MD discretion – no protocol retreatment criteria

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
 - Number of visits and anti-VEGF injections

RGX-314 Phase I/IIa Trial into LTFU: Stable to Improved VA and Anatomy, with Meaningful Reduction in anti-VEGF Injection Burden through 4 Years in Cohort 3

Best Corrected Visual Acuity (BCVA)

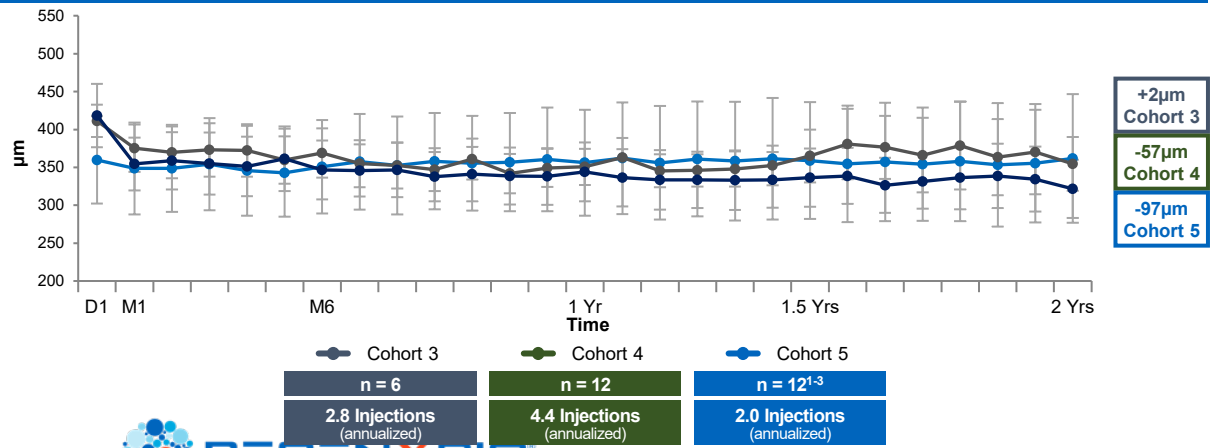


* One patient in Cohort 1 and one patient in Cohort 5 discontinued the study, both prior to visits at Week 22, and missing data post discontinuation was not used in the analysis. Another patient in Cohort 5 has missed the visits due to COVID-19 from Week 50 through Week 74 and from Week 86 through Week 94. For this patient, missing visits were imputed using last observation carried forward (LOCF). Twelve additional missing BCVA results were interpolated.

Data cut: August 29, 2022.
*One patient did not enroll in the LTFU study; one patient enrolled but did not have a study visit.

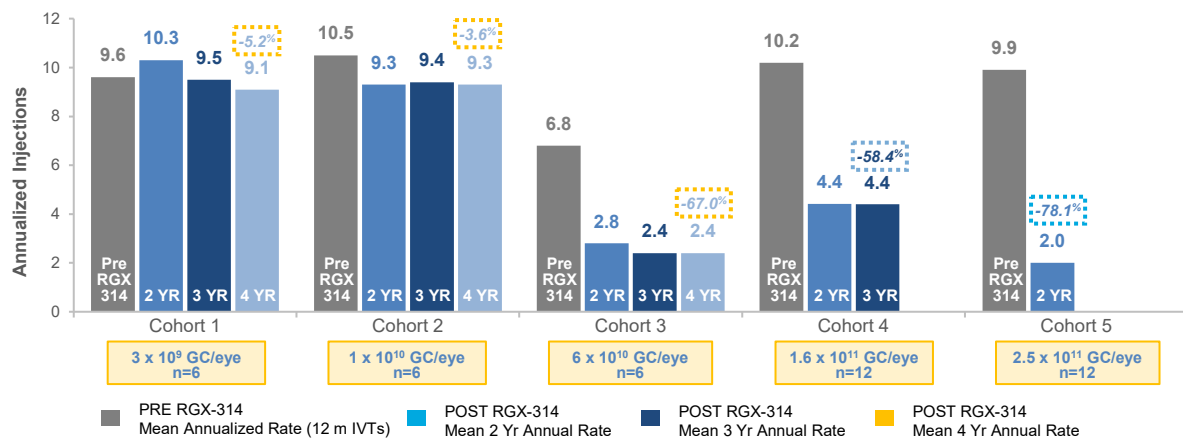
Stable to Improved Anatomy

Central Retinal Thickness (CRT) by Central Reading Center



with Meaningful Reduction in anti-VEGF Injection Burden

Annualized Injection Rate⁴



1. One patient in Cohort 5 discontinued the study prior to the Week 22 visit and missing data post discontinuation was not imputed. Another patient in Cohort 5 has missed the visits due to COVID-19 from Week 50 through Week 74 and from Week 86 through Week 94. For this patient, missing visits were imputed using last observation carried forward (LOCF). 2. Ten additional missing CRT results were interpolated. 3. Thirteen additional missing CRT results were interpolated. 4. 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 defined from RGX-314 administration to a specified cut-off date.

Phase I/IIa Trial: Cohorts 3–4:^a Long-term, Durable Treatment Effect Over 3 or 4 Years^{1,2}

	Cohort 3 (N=6)	Cohort 4 (N=12)
Stable or improved VA vs. baseline^b	+12 letters at 4 years +12 letters at 3 years	-5 letters at 3 years +1 letter at 2 years
Stable or improved CRT vs. baseline^c	+2 μm at 2 years	-57 μm at 2 years ^d
Reduced anti-VEGF injection burden vs. pre-RGX-314 treatment^e	2.4 injections/year 67% reduction at 4 years	4.4 injections/year 58% reduction at 3 years
Stable intraocular RGX-314 protein^f	217.8 ng/mL at 6 months 227.2 ng/mL at 2 years	643.8 ng/mL at 6 months 272.8 ng/mL at 2 years ^g

^aCohort 3: 6×10^{10} GC/eye (n=6), Cohort 4: 1.6×10^{11} GC/eye (n=12); ^bMean change in best-corrected VA from baseline; ^cMean change in CRT from baseline; ^dOne patient did not enroll in the LTFU study; one patient enrolled but did not have a study visit; ^eReduction of annualized rate of anti-VEGF injections compared to 12 months prior to RGX-314 administration; ^fMean RGX-314 protein concentration; ^gn=11 as one patient did not have a Year 2 sample.

CRT: Central Retinal Thickness; GC: Genomic Copies; VA: Visual Acuity; VEGF: Vascular Endothelial Growth Factor.

1. Campochiaro, P. Oral presentation at AAO 2022, October 1, 2022, Chicago, IL, USA. 2. 1. Ho A, et al. Oral presentation at Retina Society Annual Meeting 2021, September 29–October 2, 2021, Chicago, IL, USA.



Phase I/IIa and LTFU Trial: Safety

RGX-314 Phase I/IIa nAMD: Overall Safety*

- **RGX-314 continues to be generally well-tolerated across all doses (n=42)**
- 20 SAEs were reported in 13 patients¹; one possibly drug-related SAE reported in a patient in Cohort 5²
- Common ocular AEs³ in the study eye included:
 - Retinal pigmentary changes⁴ (69% of all patients; 87% of patients in Cohorts 3-5) – 62% mild, 2 severe (Cohort 5)⁵
 - Post-operative conjunctival hemorrhage (69% of patients) – 100% mild, majority resolved within days to weeks
 - Post-operative inflammation⁶ (36% of patients) – resolved within days to weeks, 100% mild
 - Retinal hemorrhage (26% of patients) – an anticipated event in the severe nAMD population, 91% mild
 - Post-operative visual acuity reduction (17% of patients) – majority resolved within days to weeks, 100% mild
 - Eye irritation (17% of patients – 57% mild) and eye pain (17% of patients – 86% mild)
- ***No reports of clinically-determined immune responses, drug-related ocular inflammation, or post-surgical inflammation beyond what is expected following routine vitrectomy***

RGX-314 Long-Term Follow-Up: Safety[^]

- RGX-314 continues to be generally well-tolerated in the long-term follow-up study (n=37)⁷ 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 September 13th, 2021; [^]Data cut August 29, 2022; SAE: Serious Adverse Event; AE: Adverse Event

1. Includes two deaths unrelated to RGX-314; 2. Significant decrease in vision; 3. Common ocular AEs defined by $\geq 15\%$ of patients; 4. Retinal pigmentary changes observed were hypo and hyper pigmentation on imaging occurring in the bleb area or inferior retina; 5. The two severe cases occurred at the highest dose after receiving a superior bleb. These patients developed pigmentary changes peripherally and in the macula, and had a decrease in vision; 6. Postoperative inflammation includes AC cells, flare, or inflammation. 7. Patients with at least one visit in the LTFU study

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

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

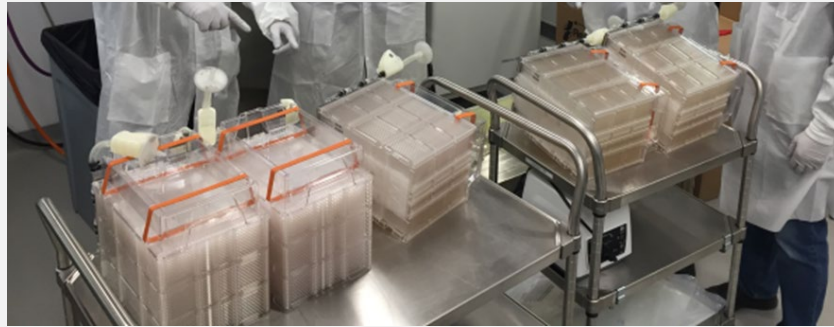
- RGX-314 manufactured by the BRX process demonstrated a similar clinical profile to the HS process

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

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 2,000L (global supply)	+
	Manual process	Highly-Automated Process	+
	Low Yield	High Yield	+

RGX-314 pivotal program for wet AMD: ATMOSPHERE® and ASCENT™ clinical trials using subretinal delivery



OBJECTIVES

Primary

- Non-inferiority in the mean change in BCVA for RGX-314 compared to repeated intravitreal injections of anti-VEGF treatment at 1 year

Secondary

- Safety and tolerability of RGX-314
- Effect of RGX-314 on vision and retinal anatomy
- Additional anti-VEGF injections post-RGX-314

Subjects: approximately 765 total

Route of administration: Subretinal

Sites: Leading retinal surgery centers across the United States and Canada

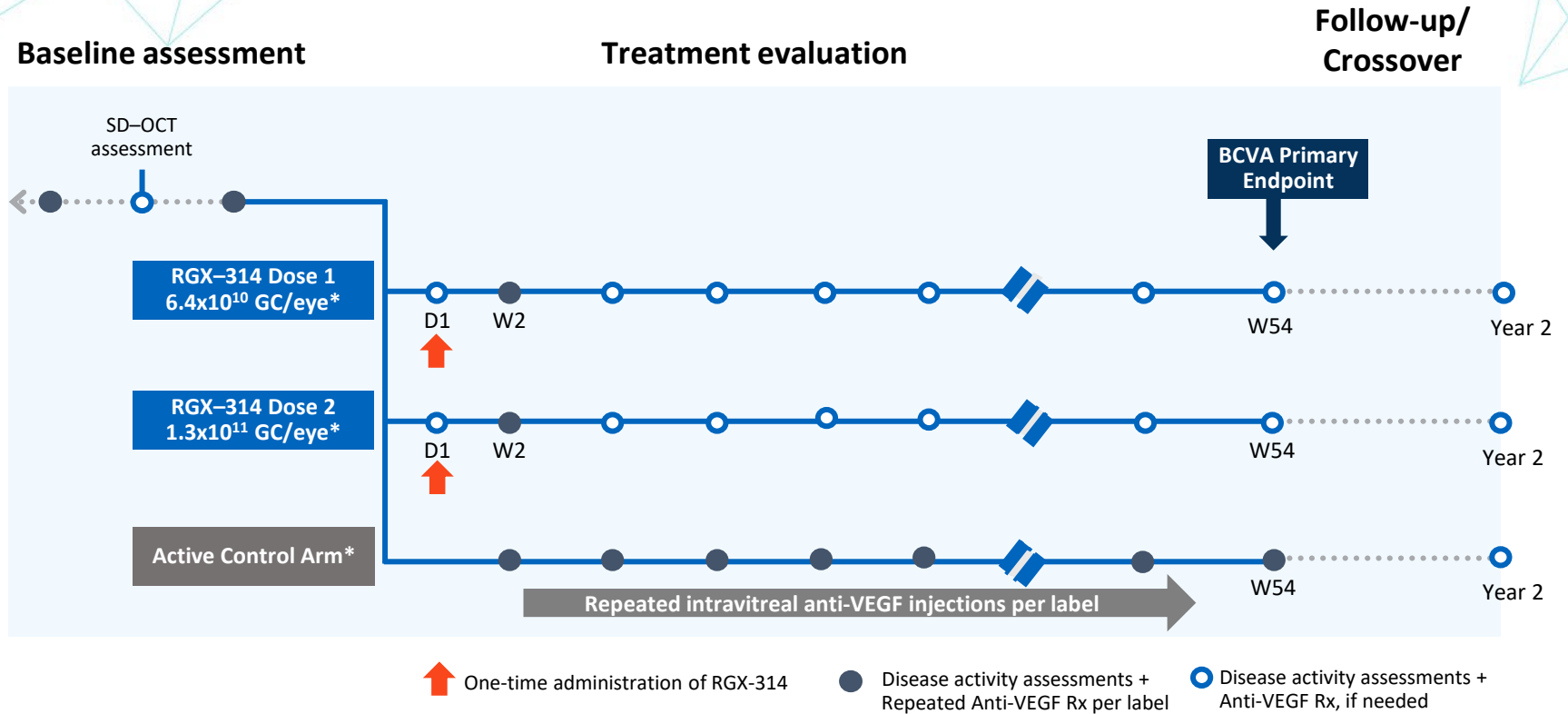


KEY INCLUSION CRITERIA

- Male or female ≥ 50 to 89 years of age
- Previously treated wet AMD subjects requiring anti-VEGF therapy
- Documented response to anti-VEGF at trial entry (assessed by SD-OCT)
- Vision of 20/32 to 20/160
- Pseudophakic (status post cataract surgery)

RGX-314 pivotal program for wet AMD: ATMOSPHERE[®] and ASCENT[™] trial designs

Administration and follow-up timeline



n=300 patients*

Active Control Arm:
Ranibizumab 0.5mg q4w



n=465 patients*

Active Control Arm:
Aflibercept 2.0mg q8W



*1:1:1 randomization

AAVIATE® Phase II clinical trial: RGX-314 for wet AMD using suprachoroidal delivery



OBJECTIVES

Primary

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

Secondary

- 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

Subjects: Up to 115 total

Route of administration: Suprachoroidal using SCS Microinjector

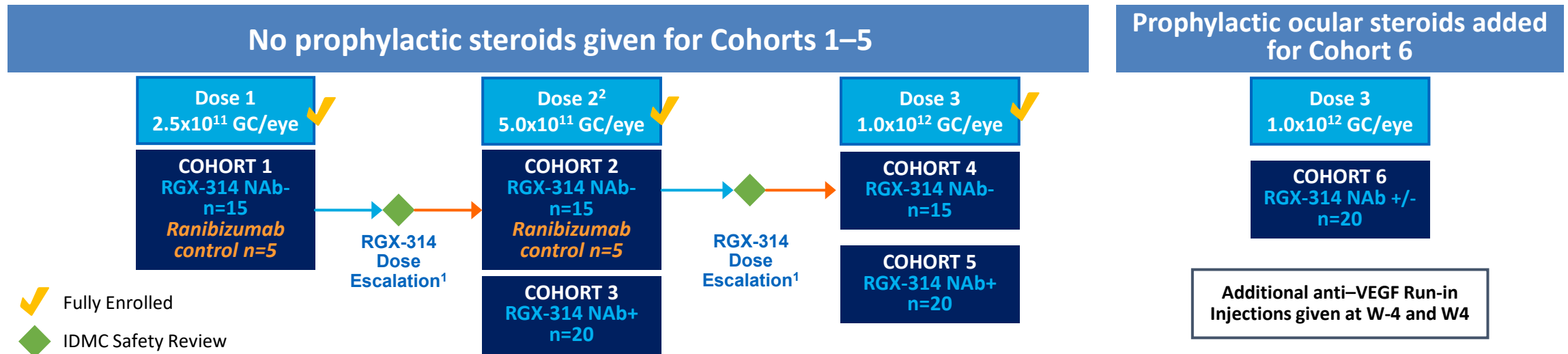
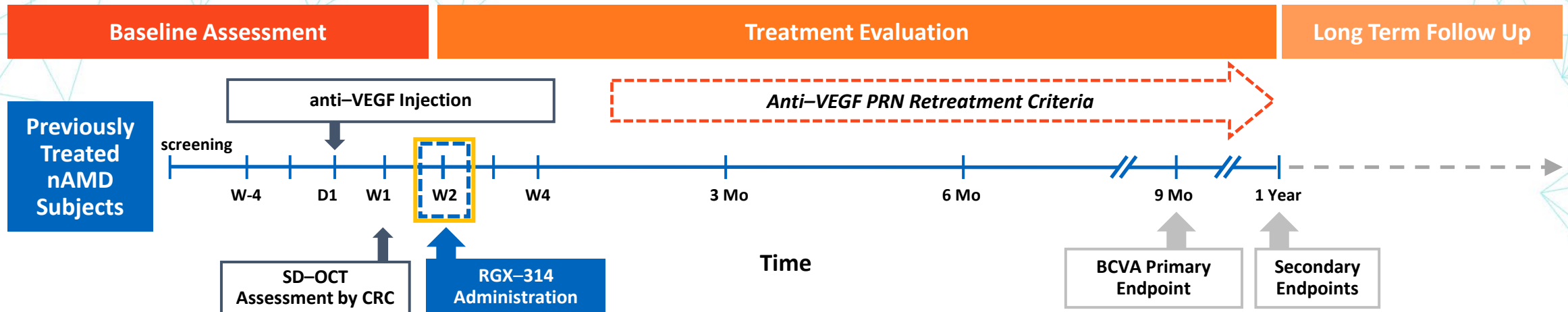
Sites: Fifteen leading retinal centers across the United States



KEY INCLUSION CRITERIA

- Male or female ≥ 50 to 89 years of age
- Previously treated wet AMD subjects with fluid on OCT at trial entry
- Documented response to anti-VEGF at trial entry (assessed by reading center)
- BCVA between $\leq 20/25$ and $\geq 20/125$ (≤ 83 and ≥ 44 Early Treatment Diabetic Retinopathy Study [ETDRS] letters) in the study eye
- Phakic or pseudophakic

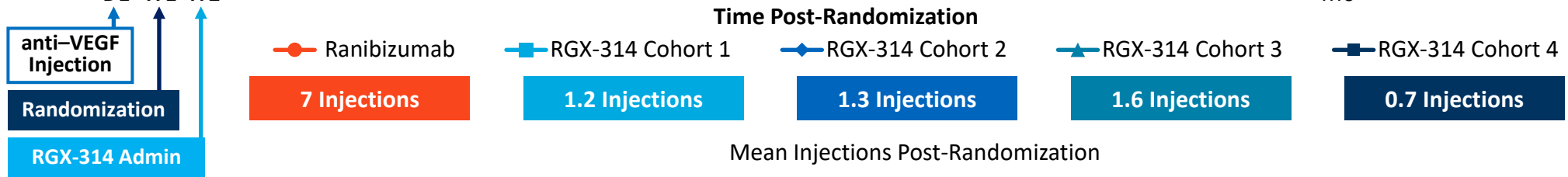
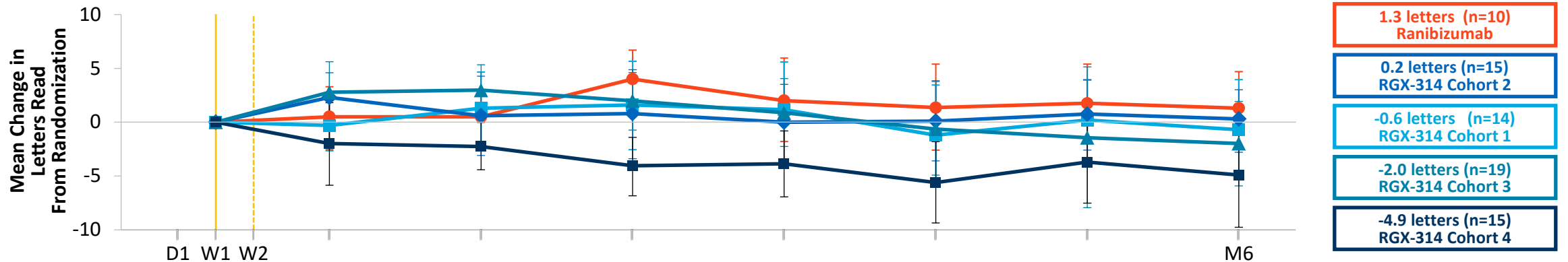
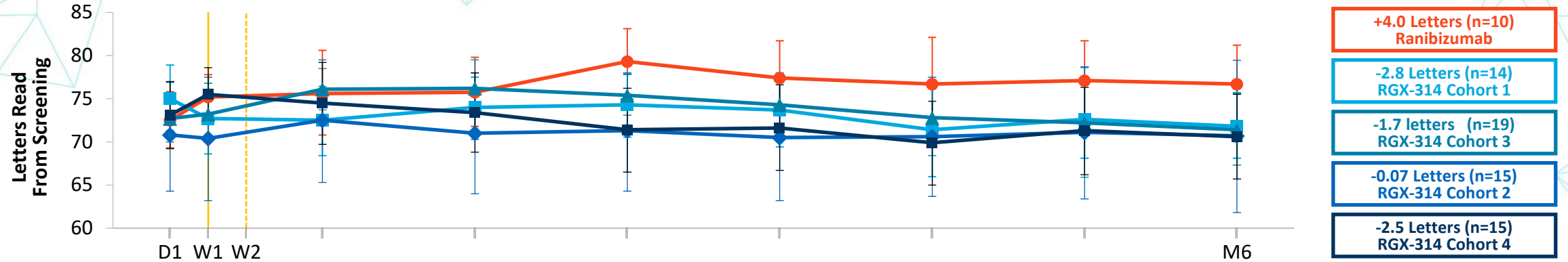
AAVIATE[®] Phase II clinical trial design



1. Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed.
 2. Subjects in Cohort 2 received two doses of 100µL, all other cohorts received one dose of 100µL.
 NAb+ = AAV8 neutralizing antibody positive; NAb- = AAV8 neutralizing antibody negative/low

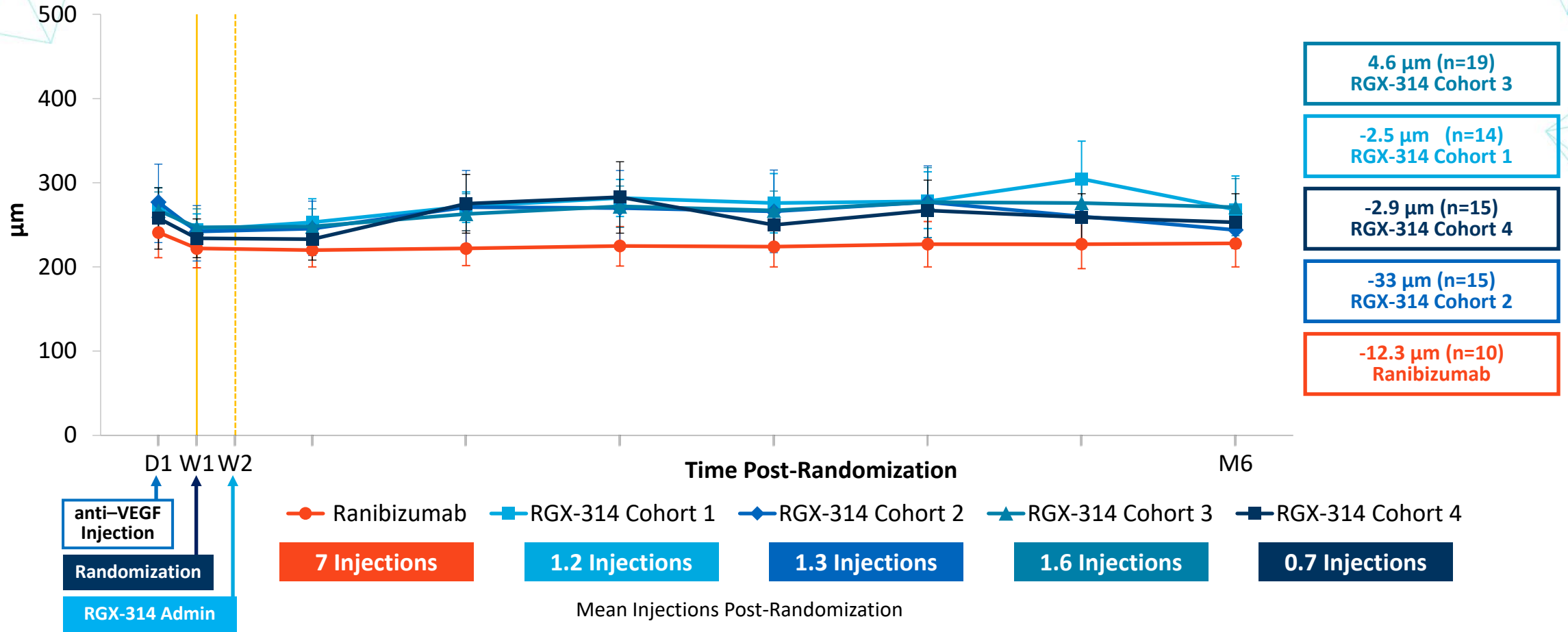
Cohorts 1-4: Mean BCVA Through Month 6

Best Corrected Visual Acuity (BCVA) 95% CI



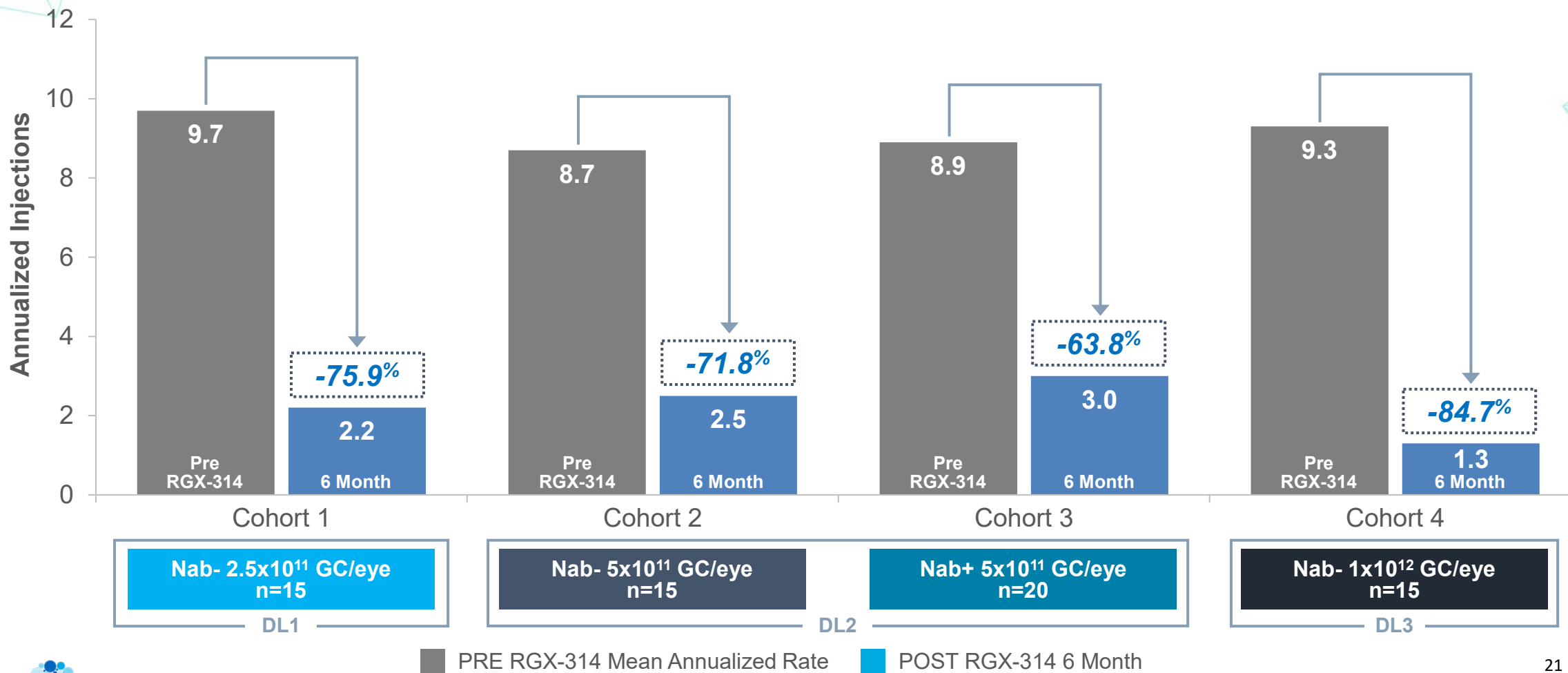
Cohorts 1–4: Mean CRT from Day 1 (Screening) Through Month 6

Central Retinal Thickness (CRT) 95%CI



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

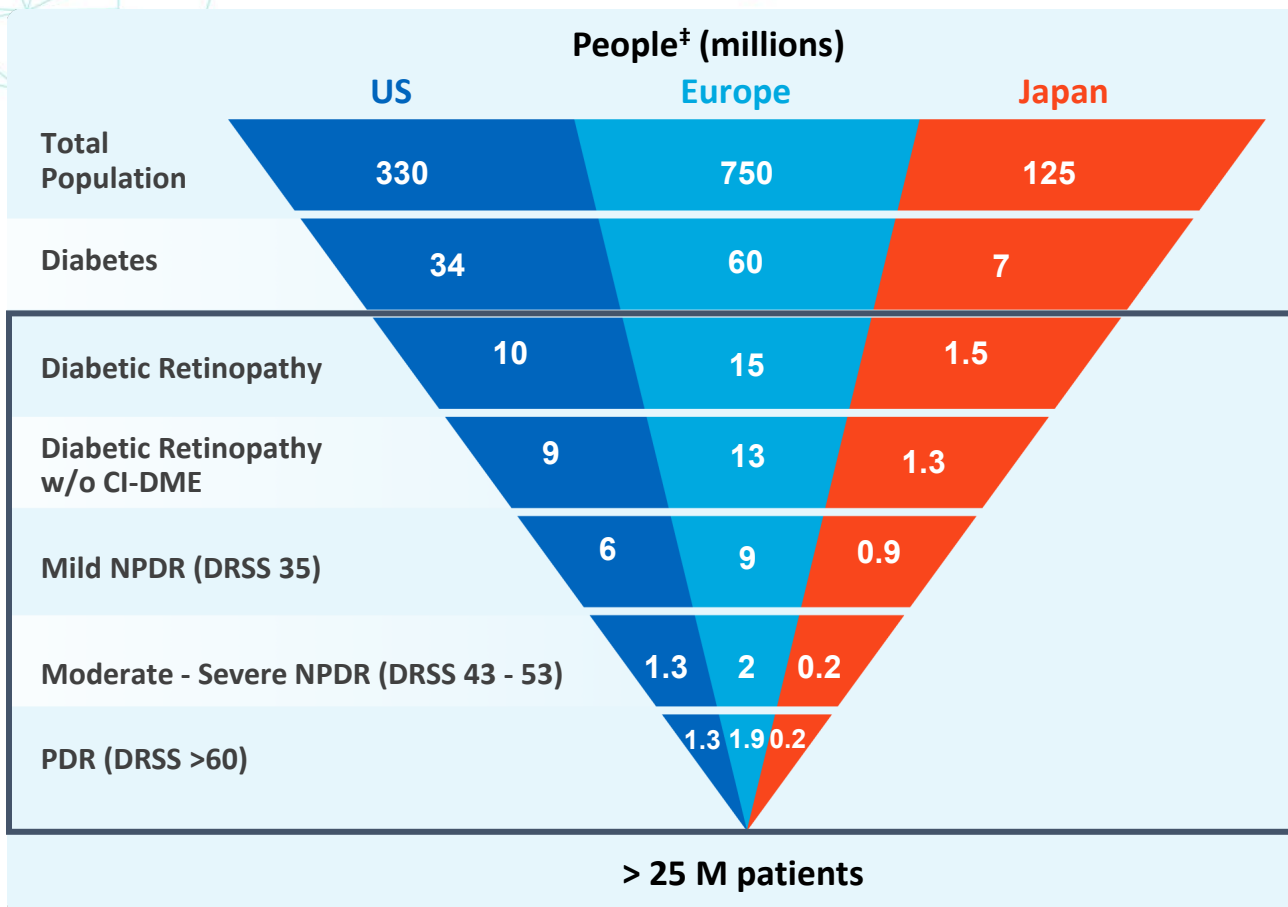
Annualized Injection Rate



- RGX-314 was well-tolerated in Cohorts 1-5 (n=85) with follow-up ranging from 1-12 months post dosing
 - 15 SAEs: None considered drug-related
 - No cases of chorioretinal vasculitis or occlusion, or hypotony were observed

Cohort 1 to 4: Common Ocular TEAEs ¹ in the Study Eye through 6 Months	Cohort 1 Dose 1 NAb- (N=15)	Cohort 2 Dose 2 NAb- (N=15)	Cohort 3 Dose 2 NAb+ (N=20)	Cohort 4 Dose 3 NAb - (N=15)	Total (N=65)
Intraocular Inflammation²	4 (26.7%)	3 (20.0%)	2 (10.0%)	6 (40.0%)	15 (23.1%)
Conjunctival Hemorrhage	5 (33.3%)	2 (13.3%)	3 (15.0%)	1 (6.7%)	11 (16.9%)
Intraocular Pressure Increased³	1 (6.7%)	2 (13.3%)	3 (15.0%)	3 (15.0%)	9 (13.8%)
Conjunctival Hyperemia	2 (13.3%)	1 (6.7%)	1 (5.0%)	3 (20.0%)	7 (10.8%)
Episcleritis⁴	0	3 (20.0%)	2 (10.0%)	2 (13.3%)	7 (10.8%)
No meaningful differences based on baseline AAV8 NAbS					

Diabetic Retinopathy is a Global Public Health Problem



Leading cause of blindness among working-age adults¹



Chronic, frequent treatment with anti-VEGF has been shown to improve DR severity and reduce risk of progression to vision threatening complications (VTCs) by > 70%²



Majority of DR patients without VTCs are not treated with anti-VEGF in the real world due to the unsustainable treatment burden of regular injections in the eye.^{3,4}

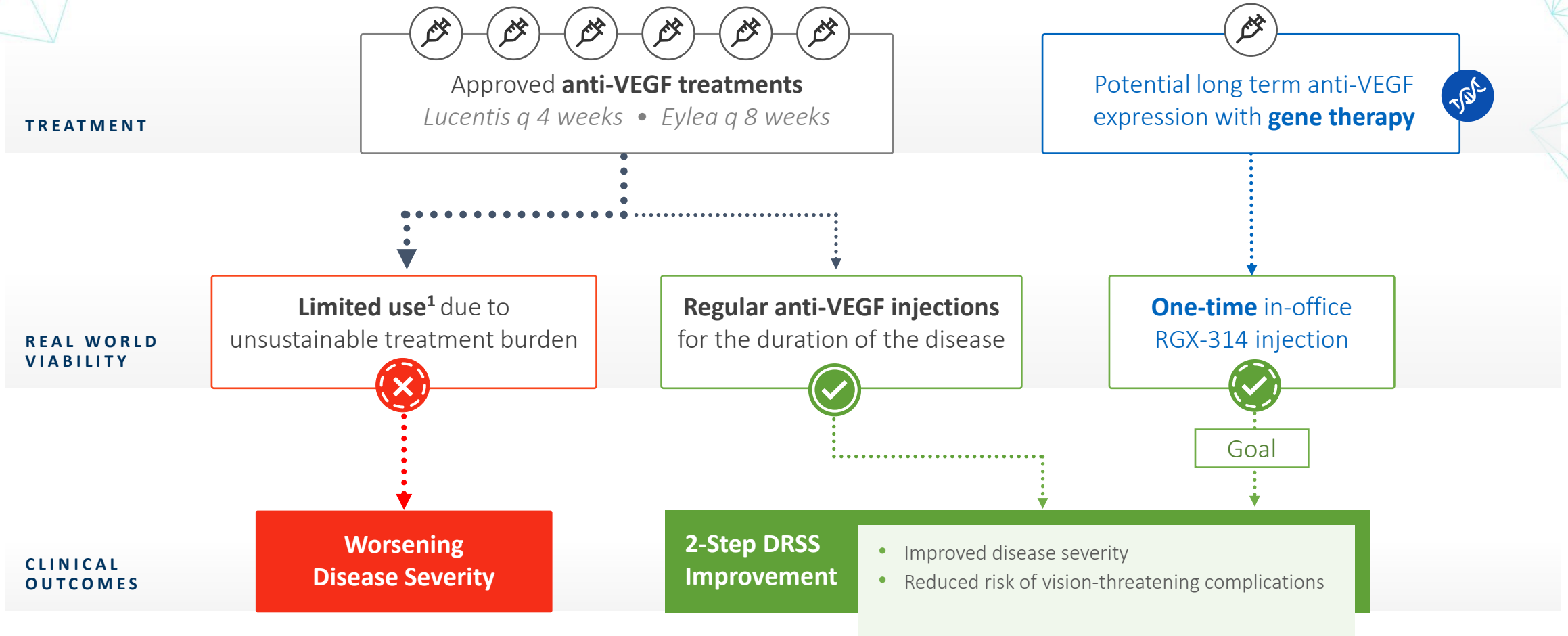


¹Lee, R., Wong, T.Y. & Sabanayagam, C. Eye and Vis 2015; ²Bakri, 2021. ASRS; ³Wykoff, CC, 2021. Diabetes Care; ⁴PAT Survey, ASRS 2021.

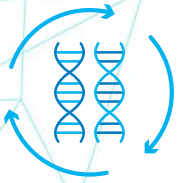
PDR = Proliferative Diabetic Retinopathy, DRSS = Diabetic Retinopathy Severity Scale. NPDR = Non-proliferative Diabetic Retinopathy, CI-DME = Center-Involved Diabetic Macular Edema, VEGF = vascular endothelial growth factor

*Figures have been rounded. *Patients with DME were excluded from the total DM population based on its prevalence (Varma, 2014 for US and Holekamp, 2016 for Europe and Japan), then each stage was estimated based on Wykoff, 2021. References: Lee, R., Wong, T.Y. & Sabanayagam, C.. Eye and Vis 2015; United Nations WPP, 2019; CDC, National Diabetes Statistics Report; ⁴Zhang X et al. JAMA; World Health Organization, 2021; Li, JQ, 2019. Eur J Ophthalmology. Eur Heart J; International Diabetes Foundation, 2020; Tanaka, 2014. Int J Epidemiology; Flaxel CJ, 2020. Ophthalmology; Bakri, 2021. ASRS; Gross JG (Protocol S), JAMA Ophthalmol 2018; Leng ASRS, Khurana ASRS, Obed 2018, Green 2020; Wykoff, CC, 2021. Diabetes Care; Varma, R, 2014. Jama Ophthalmology; Holekamp, NM, 2016. Am J Managed Care

A single in-office injection of RGX-314 has the potential to provide long-term foundational anti-VEGF therapy to prevent progression of diabetic retinopathy and associated vision-threatening complications



ALTITUDE® Phase II clinical trial in DR



OBJECTIVES

Primary

- Evaluate proportion of patients with ≥ 2 step improvement in severity on the Diabetic Retinopathy Severity Scale (DRSS) at 1 year

Secondary

- Safety and tolerability of RGX-314
- Development of DR-related ocular complications
- Need for additional standard of care interventions

Subjects: Up to 80 total

Route of administration: Suprachoroidal using SCS Microinjector

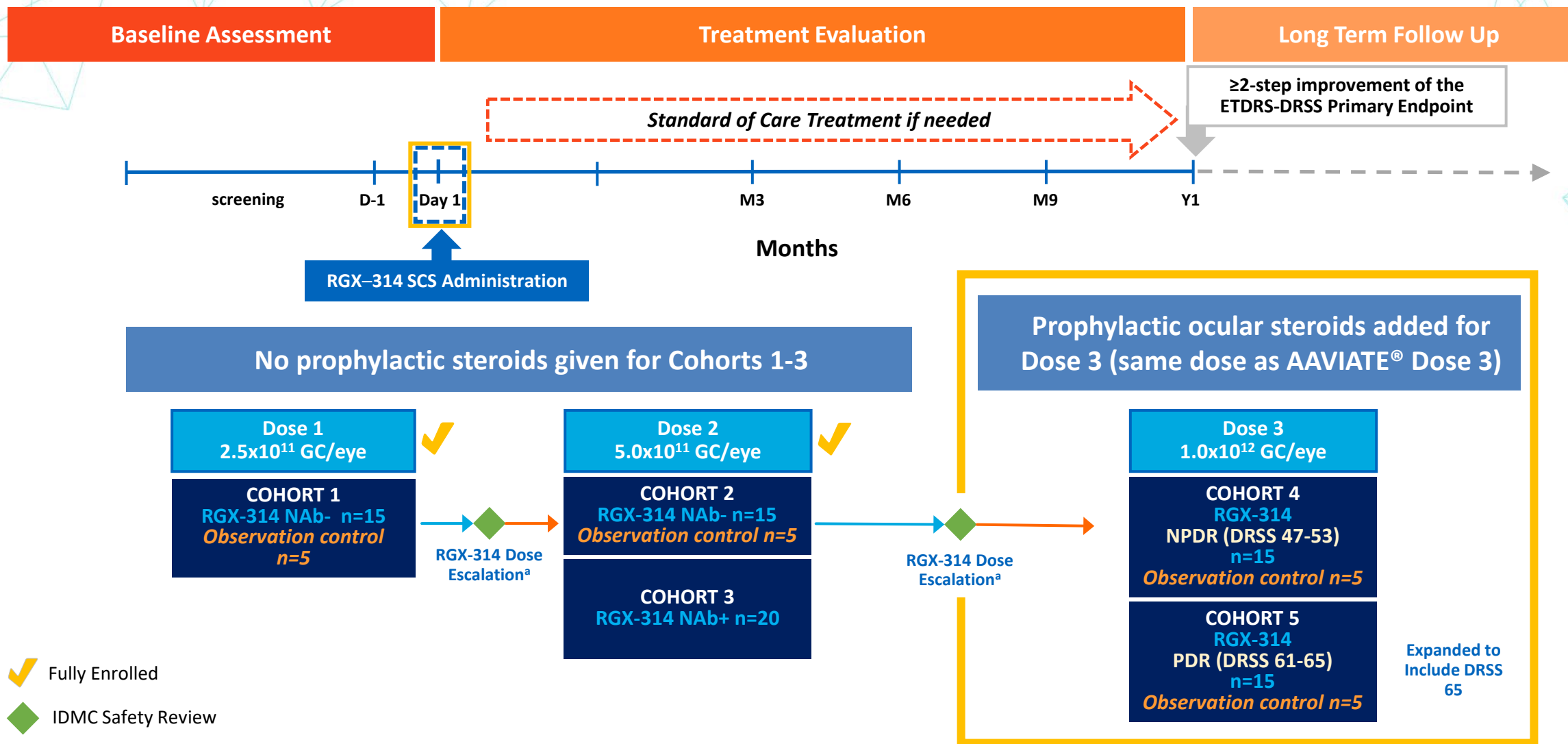
Sites: 18 leading retinal centers across the United States



KEY INCLUSION CRITERIA

- Male or female ≥ 25 to 89 years of age with DR secondary to diabetes mellitus Type 1 or Type 2
- Moderately severe NPDR, severe NPDR, or Mild PDR (DRSS levels 47-61)
- No active CI-DME, CST $< 320 \mu\text{m}$
- Vision of 20/40 or better (≥ 69 Early Treatment Diabetic Retinopathy Study [ETDRS] letters) in the study eye
- No anti-VEGF injection(s) in prior 6 months

RGX-314 ALTITUDE Study Design



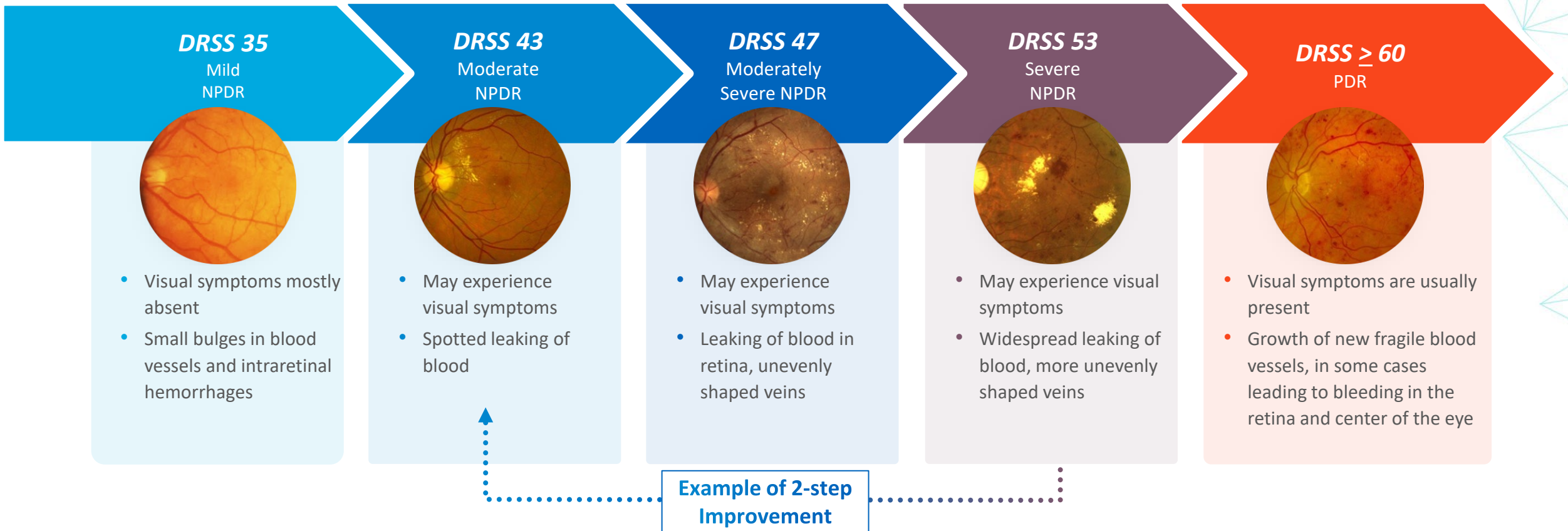
a. Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed.

SCS: Suprachoroidal Space; NAb+ = AAV8 neutralizing antibody positive; NAb- = AAV8 neutralizing antibody negative/low; Y1 = 48 weeks; NPDR: Non-proliferative Diabetic Retinopathy; PDR: Proliferative Diabetic Retinopathy



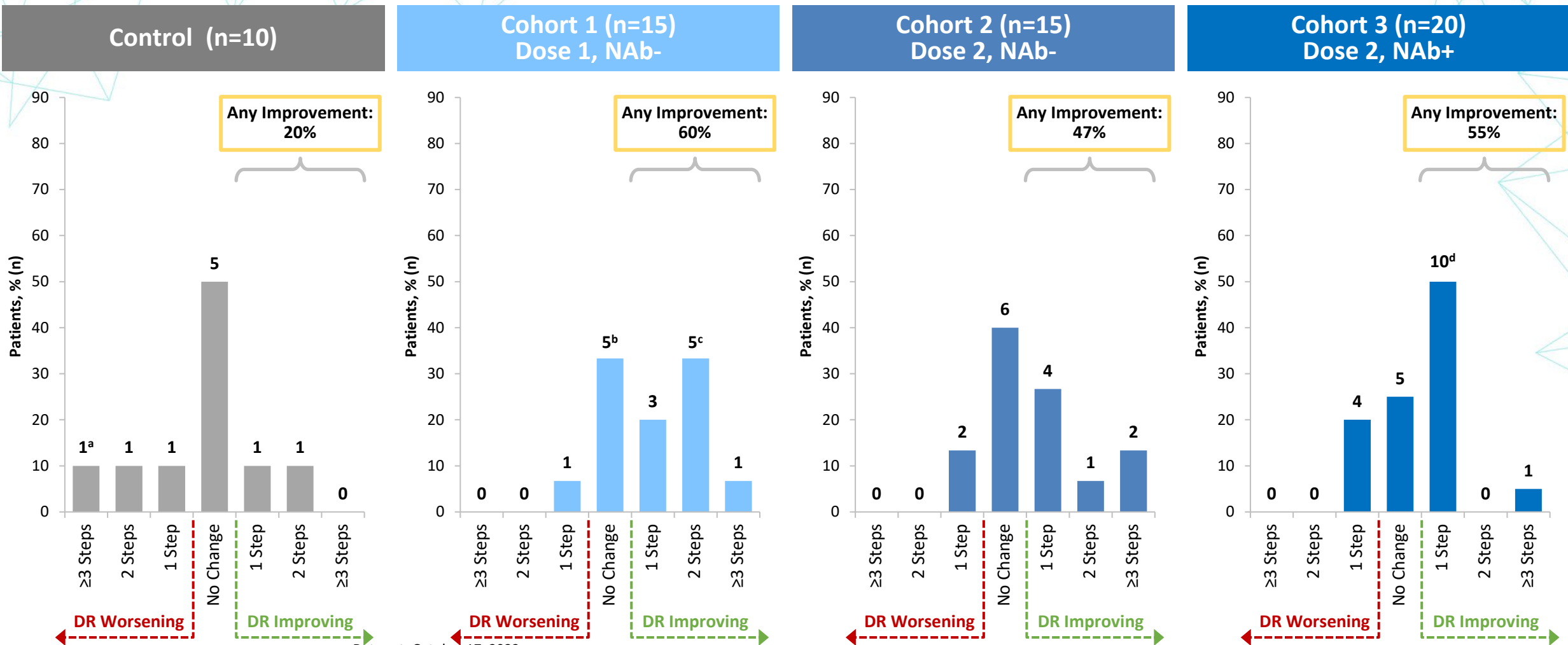
A 2-step improvement in Diabetic Retinopathy Severity Scale (DRSS) has been accepted as a pivotal endpoint by the FDA for DR clinical trials¹

► INCREASING RISK OF DEVELOPING VISION THREATENING COMPLICATIONS ►



DR disease severity is measured using the Diabetic Retinopathy Severity Scale ²

Change in DRSS at Month 6



Data cut: October 17, 2022.

a. One observation control patient received two Lucentis injections in the study eye for vitreous hemorrhage (4-step worsening to DRSS 71 [severe PDR] at 6 months).

b. During an interim central reading center masked adjudication, 1 patient's DRSS grades at baseline and 6 months were updated from Grade 47 and Grade 35, respectively, to Grade 61 since prior interim data release.

c. One patient received a single Lucentis injection in the study eye (DRSS 61 at baseline) 8 days after RGX-314 dosing for trace vitreous hemorrhage, which was 22 weeks prior to their 6 month visit when DRSS was assessed.

d. One patient missed their 6-month visit, so their 3-month results were used.



- **RGX-314 was well-tolerated in Cohorts 1-3 (n=50)**
 - 5 SAEs: None considered drug-related
 - No cases of chorioretinal vasculitis or occlusion, or hypotony were observed

Cohorts 1 to 3: Common Ocular TEAEs^a and Intraocular Inflammation in the Study Eye through 6 Months	Cohort 1 Dose 1 NAb- (N=15)	Cohort 2 Dose 2 NAb- (N=15)	Cohort 3 Dose 2 NAb+ (N=20)	Total (N=50)
Conjunctival hyperemia	4 (26.7%)	5 (33.3%)	4 (20.0%)	13 (26.0%)
Conjunctival hemorrhage	3 (20.0%)	2 (13.3%)	1 (5.0%)	6 (12.0%)
Episcleritis^b	1 (6.7%)	1 (6.7%)	4 (20.0%)	6 (12.0%)
Intraocular Inflammation^c	0 (0.0%)	3 (20.0%)	0 (0.0%)	3 (6.0%)
No meaningful differences based on baseline AAV8 NAbs				

- **Stable BCVA through 6 Months in Cohorts 1-3 (n=50)**

Data cut: October 17, 2022.

a. Common TEAEs include AEs for total group ≥10% with onset up to 6m visit.

b. All cases were mild (grade 1) and are resolved or resolving on topical corticosteroids.

c. All cases were mild (range +0.5 to +1) and most presented 2-6 weeks post injection, predominantly as anterior cells on slit lamp examination. Resolved on topical corticosteroids.

SAE: Serious Adverse Event; TEAE: Treatment Emergent Adverse Event.

Rare diseases



RGX-202 for treatment of Duchenne muscular dystrophy (Duchenne)

THE DISEASE

- Duchenne is caused by mutations in the *DMD* gene which encodes dystrophin, a protein involved in muscle contraction and strength
- Without dystrophin, muscles throughout the body degenerate and become weak, eventually leading to loss of movement and independence, required support for breathing, cardiomyopathy and premature death
- Affects 1 in 3,500 to 5,000 male births worldwide
- RGX-202 has received Orphan Drug Designation and Rare Pediatric Disease Designation by the FDA

RGX-202 PRODUCT CANDIDATE



Vector: AAV8



Transgene: microdystrophin

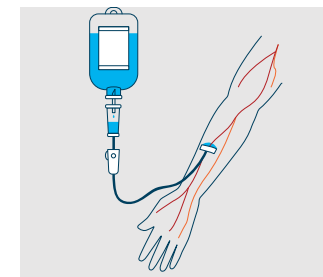
Designation: Orphan Drug Designation

Mechanism of action

Delivers a transgene for a novel microdystrophin that includes the functional elements of the C-Terminal domain found in naturally occurring dystrophin

Route of administration

Intravenous to target muscle



AFFINITY DUCHENNE™ Phase I/II clinical trial



OBJECTIVES

Primary

- Safety and tolerability of RGX-202 in patients with Duchenne

Secondary and Exploratory

- Microdystrophin protein expression levels in muscle at 3 months¹
- Muscle strength and functional assessments, including North Star Ambulatory Assessment
- Muscle MRI

Subjects: Up to 18 total

- 2 dose cohorts of 3 patients each
- Option to dose up to 6 additional patients in each cohort in dose expansion phase

Sites: US sites, with additional sites in Canada and Europe expected to follow



¹ As assessed by muscle biopsy in first 3 patients of each cohort



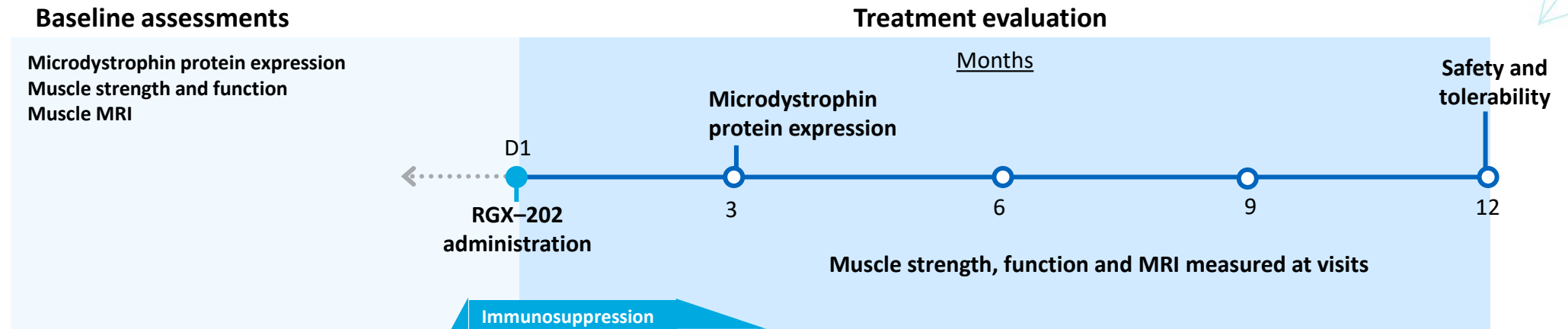
KEY INCLUSION CRITERIA and SAFETY MEASURES

- Males 4 to 11 years
- Ambulatory function
- *DMD* gene mutation between exons 18 and above
- Negative for anti-AAV8 antibodies

-
- Comprehensive, short-term, prophylactic immunosuppression regimen
 - Prednisolone, Sirolimus and Eculizumab initiated prior to RGX-202 administration, to proactively mitigate potential complement-mediated immunologic responses

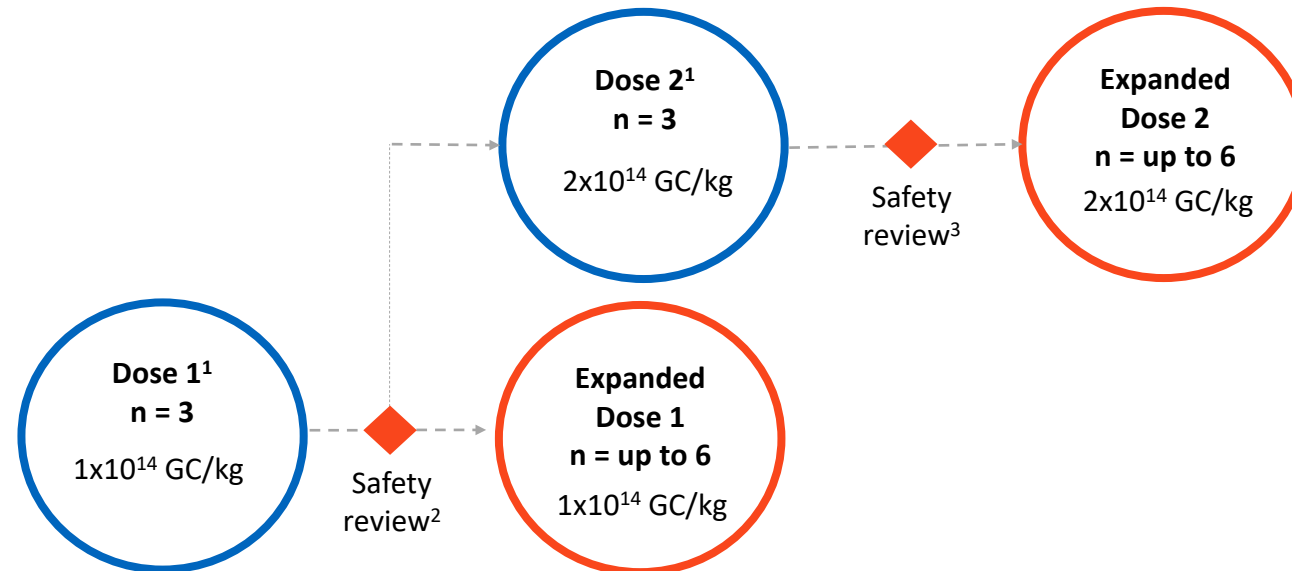
AFFINITY DUCHENNE™ clinical trial design

Administration and follow-up timeline



Dose escalation and dose expansion

Trial expected to initiate in 1H 2023

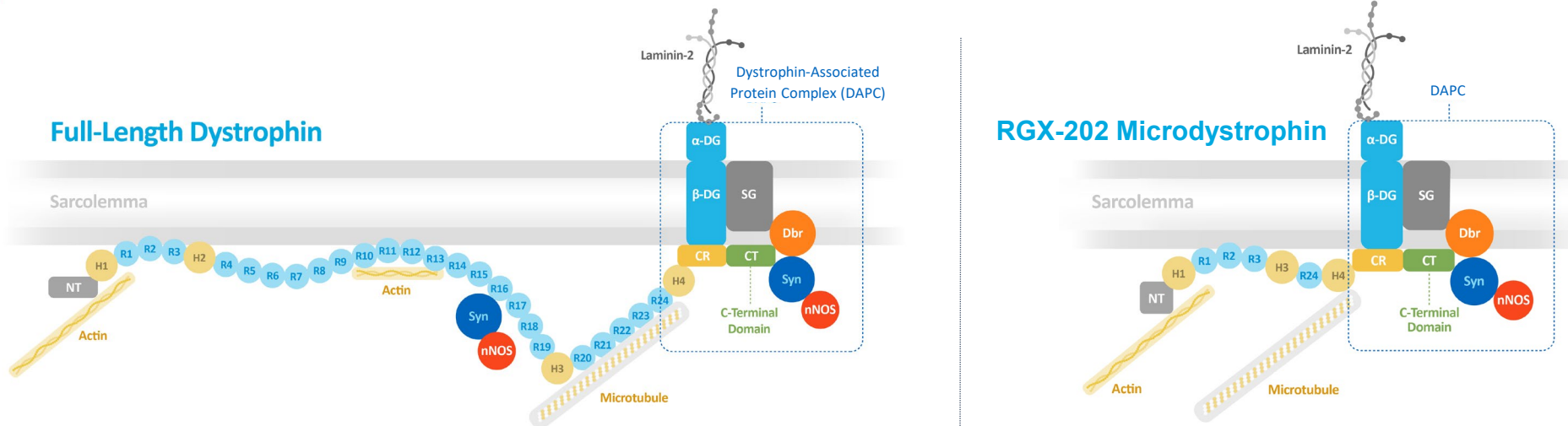


¹The first 3 patients in each cohort will be dosed in a staggered fashion, at least 4 weeks apart, following increasing body weight: ≤ 20 kg, ≤ 30 kg and ≤ 40 kg

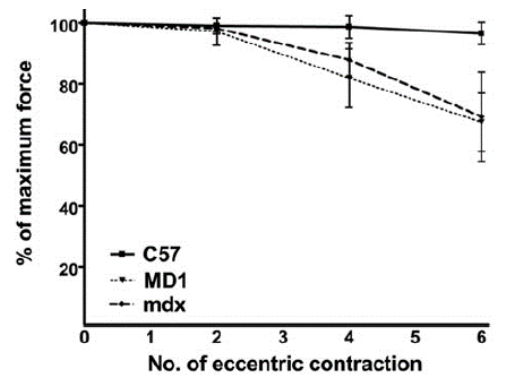
²Dose escalation safety review to occur four weeks after third patient in each cohort has been followed 4 weeks post-dosing

RGX-202 microdystrophin is designed to retain key elements of full-length dystrophin

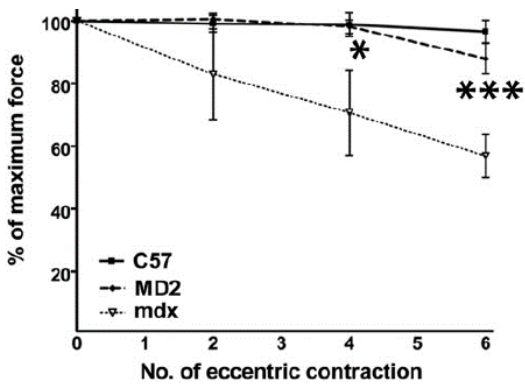
CT Domain recruits several key proteins to the muscle cell membrane (sarcolemma) including Syntrophin and Dystrobrevin, Neuronal nitric oxide synthase and other proteins¹



Construct without C-Terminal Domain



Construct with C-Terminal Domain



Presence of CT Domain in microdystrophin significantly improved the muscle resistance to lengthening contraction-induced muscle damage in *mdx* mice²





¹ Allen et al, *Physiological Review*, 2016

² Koo et al, *Human Gene Therapy*, 2011

Syn: Syntrophin; Dbr: Dystrobrevin; CR: Cystein rich domain; nNOS: Neuronal nitric oxide synthase; DG: Dystroglycan; H: hinge; R: repeat

RGX-202 program has several features that provide potential benefits

	Capsid	Promoter	Microdystrophin transgene design	Transgene Size (bp)
RGX-202	AAV8	Spc5-12		4,734
Other Investigational Intervention (Example)				

ABD1: Actin Binding Domain 1

RGX-202 Features

Potential Benefits

Transgene for a novel microdystrophin includes extended coding region of dystrophin C-Terminal (CT) Domain	CT domain recruits key proteins, leading to improved muscle resistance ¹
Codon optimization and CpG content reduction	May improve gene expression, increase translational efficiency and reduce immunogenicity ²
NAV [®] AAV8 vector and Spc5-12 muscle specific promoter	Designed to support the delivery and targeted expression of genes throughout skeletal and heart muscle ^{3, 4, 5}
Commercial-scale cGMP material already produced	Material to be used in AFFINITY DUCHENNE™

¹ Koo et al, *Human Gene Therapy*, 2011

² Faust, et al. *Journal of Clinical Investigation*, 2013

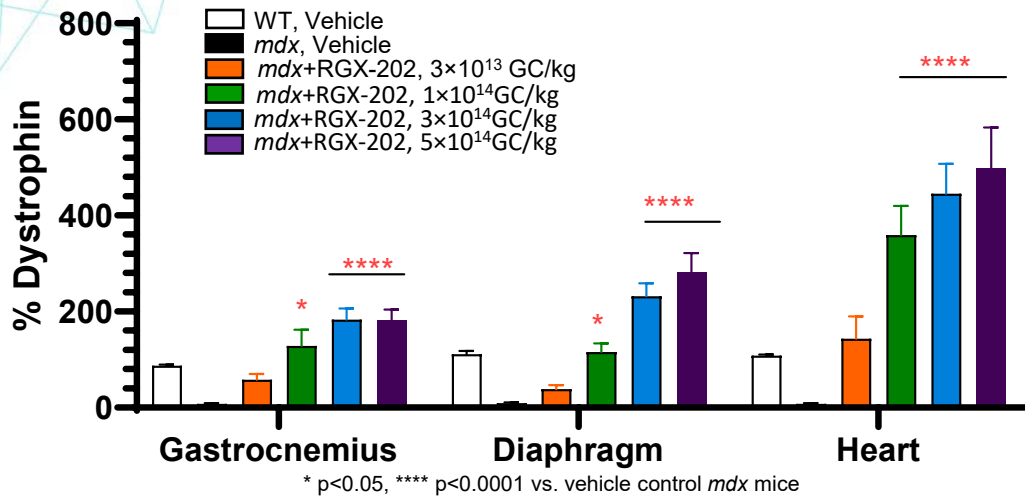
³ Le Guiner, et al. *Nature Communications*, 2017

⁴ Mack, et al. *Molecular Therapy*, 2017

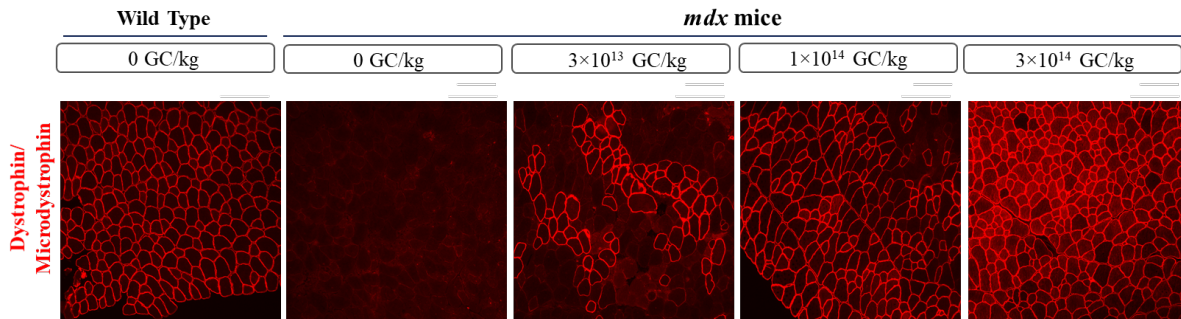
⁵ Shieh, et al. ASGCT 2019

RGX-202 demonstrated robust expression of microdystrophin across skeletal and cardiac muscles along with recruitment of key proteins to the DAPC

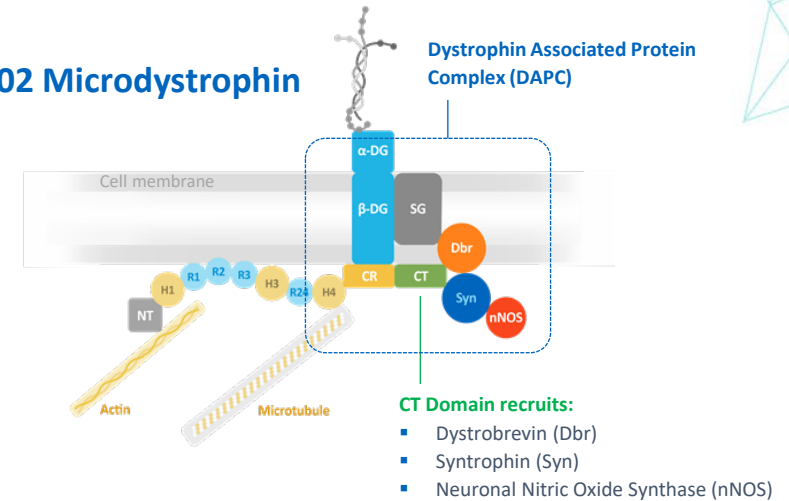
RGX-202 Microdystrophin Expression in Muscle¹



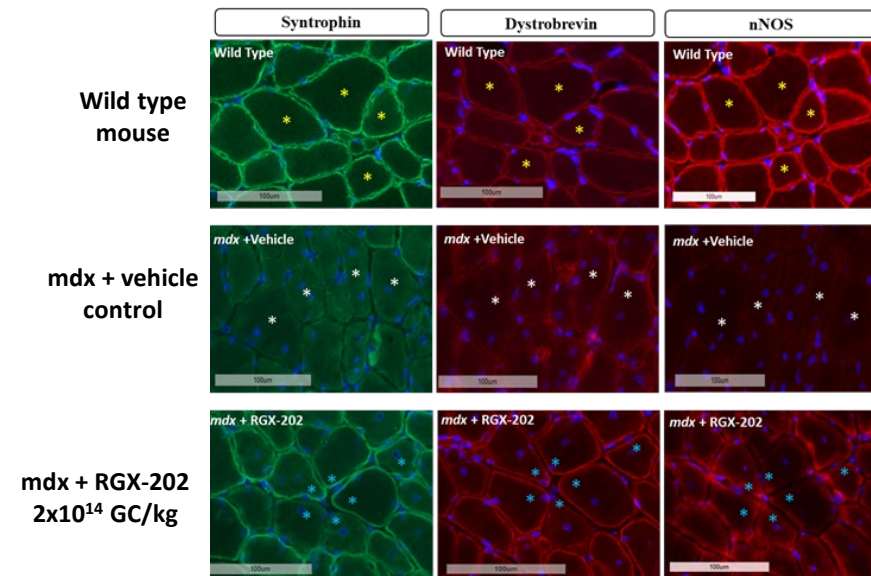
Immunohistochemistry of RGX-202 Microdystrophin in Muscle²



RGX-202 Microdystrophin

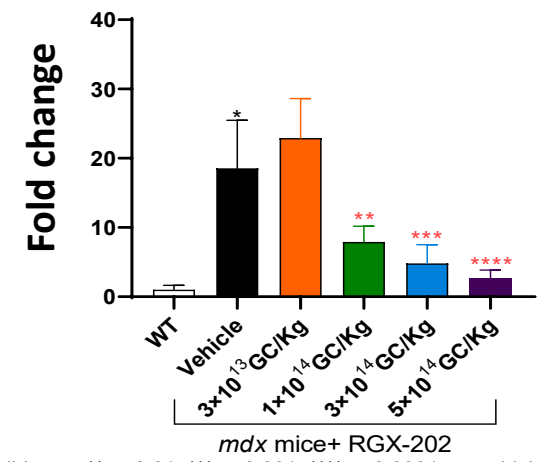
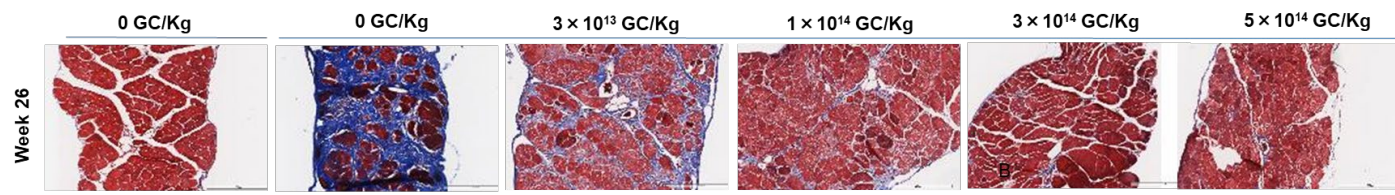


Immunohistochemistry of Dystrophin Protein Complex in Muscle¹

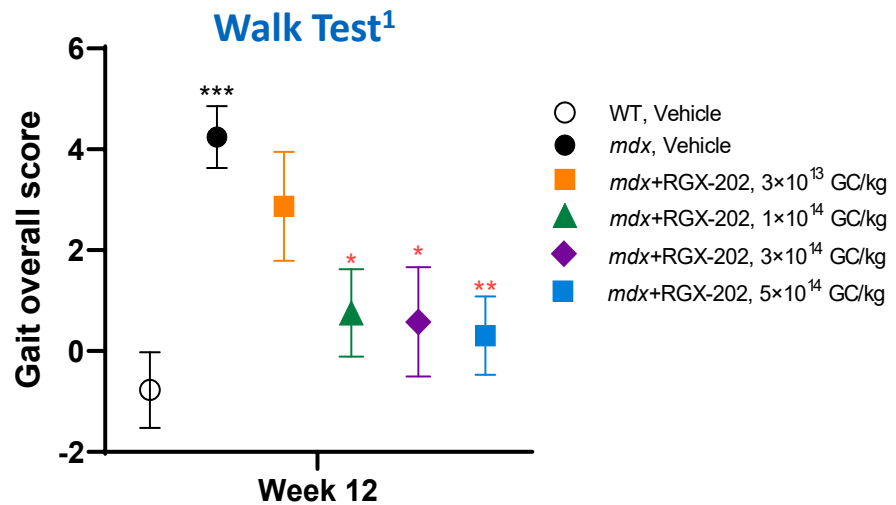


RGX-202 demonstrated significant improvements in muscle pathology and function in *mdx* mice at doses $\geq 1 \times 10^{14}$ GC/kg

Muscle Pathology (Fibrosis)¹

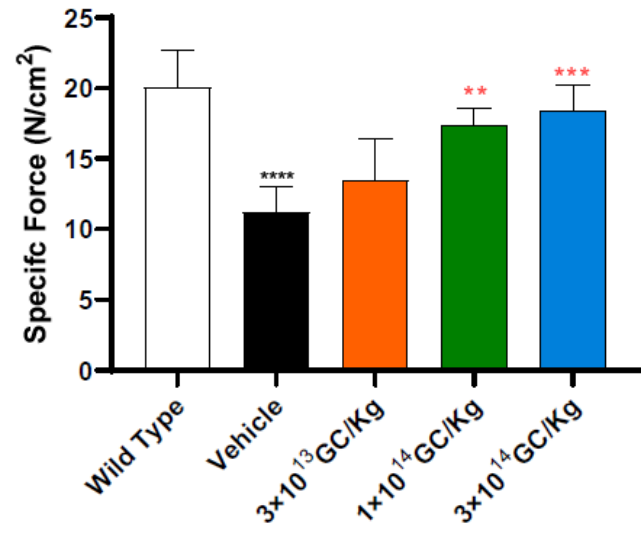


*p<0.05 vs. wild type; ** p<0.01, *** p<0.001, **** p<0.0001 vs. vehicle control *mdx* mice.



*p < 0.05, *** p < 0.001 vs. wild type vehicle (RM two-way ANOVA, Sidak's post hoc); * p < 0.05, ** p < 0.01 vs. *mdx* vehicle (Mixed effects model ANOVA, Dunnett's post hoc). Data are presented as mean \pm SEM

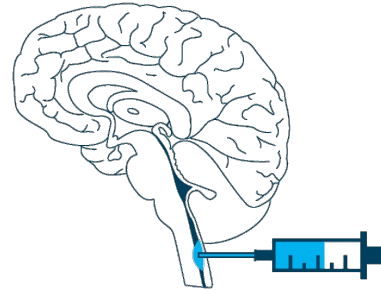
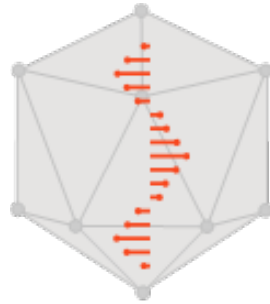
Muscle Force²



*p<0.05, **** p < 0.0001, vs. wild type vehicle. *p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001 vs. *mdx* vehicle. Comparisons are by 1-way ANOVA or Tukey or 2-way ANOVA and Tukey

REGENXBIO's neurodegenerative disease franchise

AAV9 vector



Intracisternal
Delivery

	RGX-121 for MPS II	RGX-111 for MPS I	RGX-181 for CLN2 Disease
Disease	<ul style="list-style-type: none"> Reduced ability to process glycosaminoglycans (GAGs), leading to neurodegeneration and early death X-linked recessive disease Available treatment is inadequate to treat neurodegeneration More than 500 patients born annually worldwide 	<ul style="list-style-type: none"> Reduced ability to process GAGs, leading to neurodegeneration and early death Autosomal recessive disease Available treatment is inadequate to treat neurodegeneration; stem cell transplant partially effective More than 500 patients born annually worldwide 	<ul style="list-style-type: none"> Reduced ability to process cellular waste peptides, leading to seizures, vision loss, neurodegeneration and early death Autosomal recessive disease Available treatment requires frequent ICV infusions of ERT, shown to stabilize some but not all disease manifestations Approximately 500 patients born annually worldwide
Gene	IDS Gene Replacement	IDUA Gene Replacement	TPP1 Gene Replacement
FDA Designations	<ul style="list-style-type: none"> ▲ Orphan Drug Designation ★ Rare Pediatric Disease Designation ■ Fast Track Designation 	<ul style="list-style-type: none"> ▲ Orphan Drug Designation ★ Rare Pediatric Disease Designation ■ Fast Track Designation 	<ul style="list-style-type: none"> ▲ Orphan Drug Designation ★ Rare Pediatric Disease Designation

CAMPSIITE™ Part 1: Phase I/II clinical trial of RGX-121 in MPS II



OBJECTIVES

Primary

- To determine the safety and tolerability of RGX–121 in severe MPS II subjects who have or are at high risk of developing neurocognitive deficits

Secondary

- Effect of RGX–121 on biomarkers of I2S activity in CSF, serum and urine
- Effect of RGX–121 on neurocognitive deficits

Subjects: Approximately 16 patients

Sites: Leading U.S. and international lysosomal storage disease centers

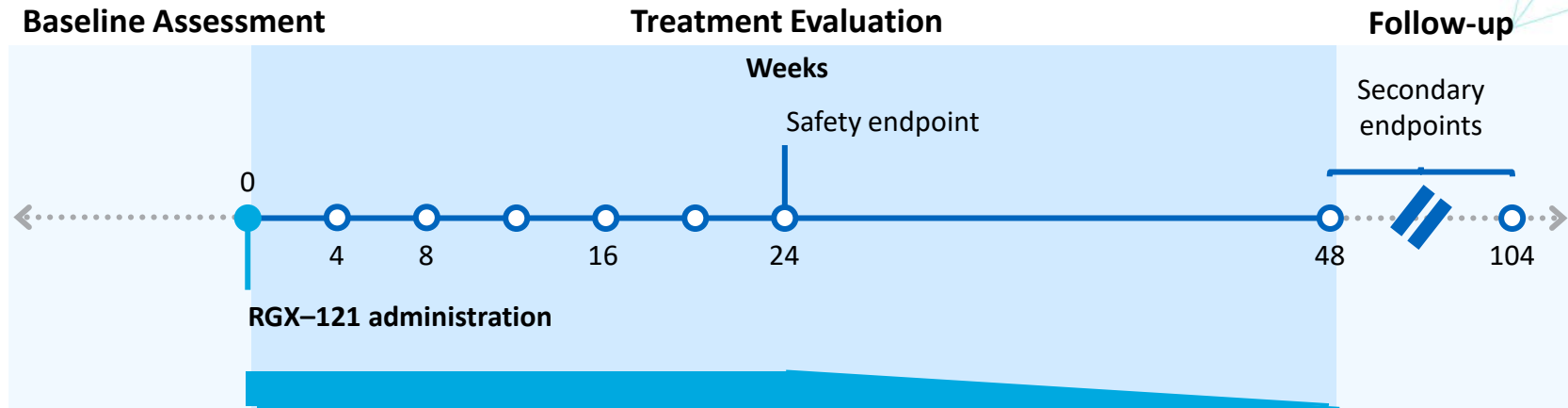


KEY INCLUSION CRITERIA

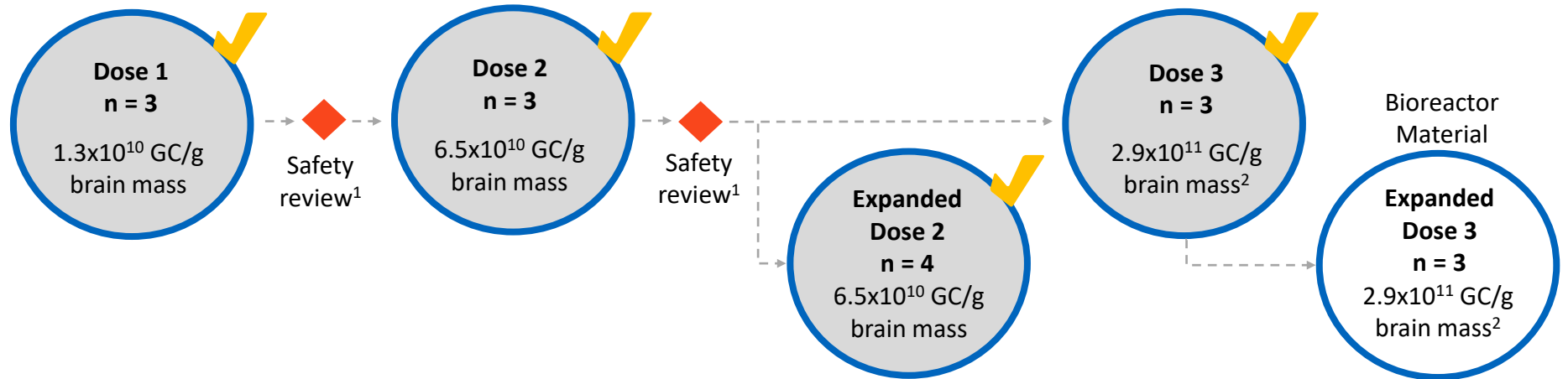
- Male subjects ≥ 4 months to < 5 years of age
- Meeting one of the following criteria:
 - Diagnosis of MPS II and a score ≤ 77 on neurocognitive testing
 - Diagnosis of MPS II and a decline of ≥ 1 standard deviation on consecutive intelligent quotient testing
 - Having a relative diagnosed with severe MPS II who has the same IDS mutation as the subject
 - Having documented mutation(s) in *IDS* that is known to result in a neuronopathic phenotype
- No contraindications for intracisternal or intracerebroventricular injection and immunosuppressive therapy

RGX-121 Phase I/II Clinical Trial: Administration and Dose Escalation

Administration and follow-up timeline



Dose escalation



Primary Dose 3 cohort completed

Dose 3 expansion cohort currently enrolling using bioreactor material (commercial process)



* Dose Level 3 previously reported as 2.0×10^{11} GC/g of brain mass of RGX-121 based on Poly-A-specific PCR assay. This is equivalent to 2.9×10^{11} GC/g of brain mass of RGX-121 using transgene-specific PCR assay.

RGX-121 Phase I/II Clinical Trial: Summary of Results

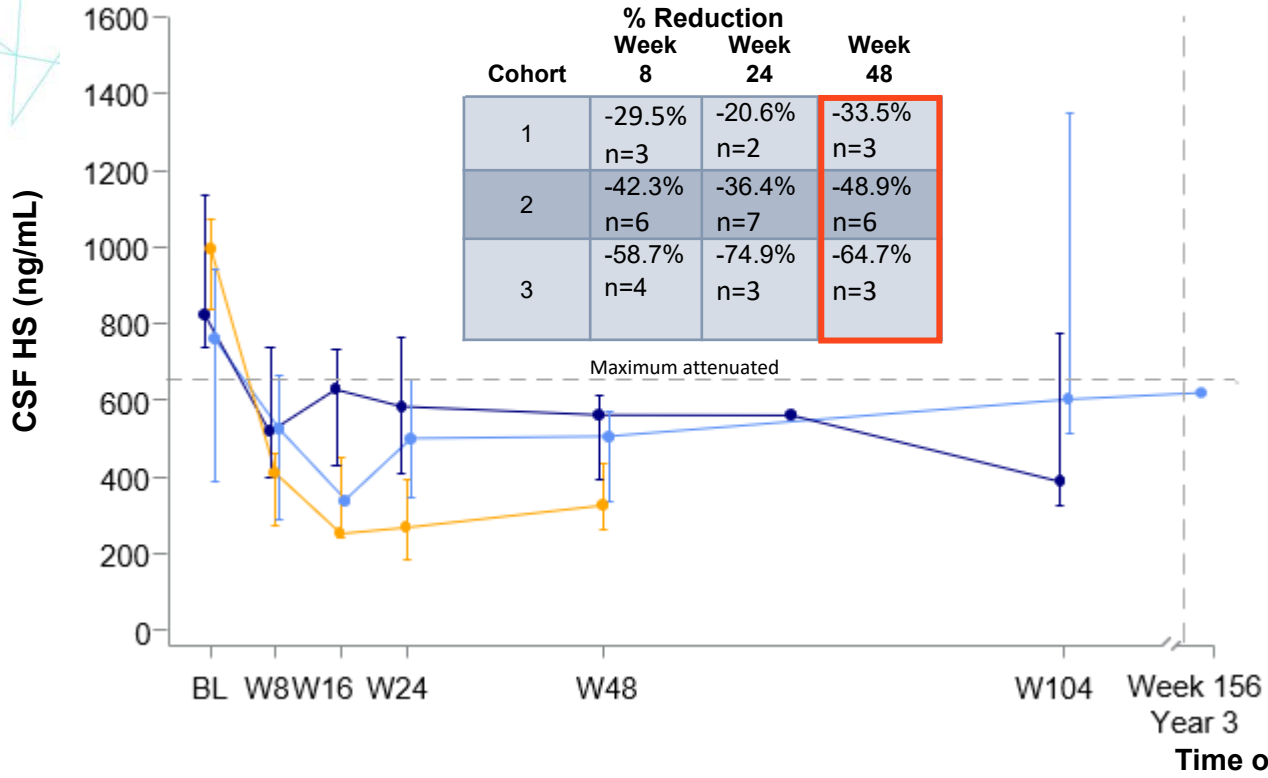
- **Well-tolerated following one-time RGX-121 administration¹**
 - 15 patients dosed in 3 Cohorts with no SAEs related to study drug

- **CNS: CSF GAGs and neurodevelopmental assessments indicate encouraging RGX-121 profile^{1,2}**
 - Dose-dependent reductions in CSF biomarkers demonstrated across cohorts²
 - Cohort 3 CSF HS D2S6, a component of HS closely correlated with severe MPS II, approached normal levels at 48 weeks¹
 - Neurodevelopmental and daily activity skill acquisition was observed up to 3 years after RGX-121 administration
 - Treatment response appeared to be dependent on the extent of neurologic deficits at baseline

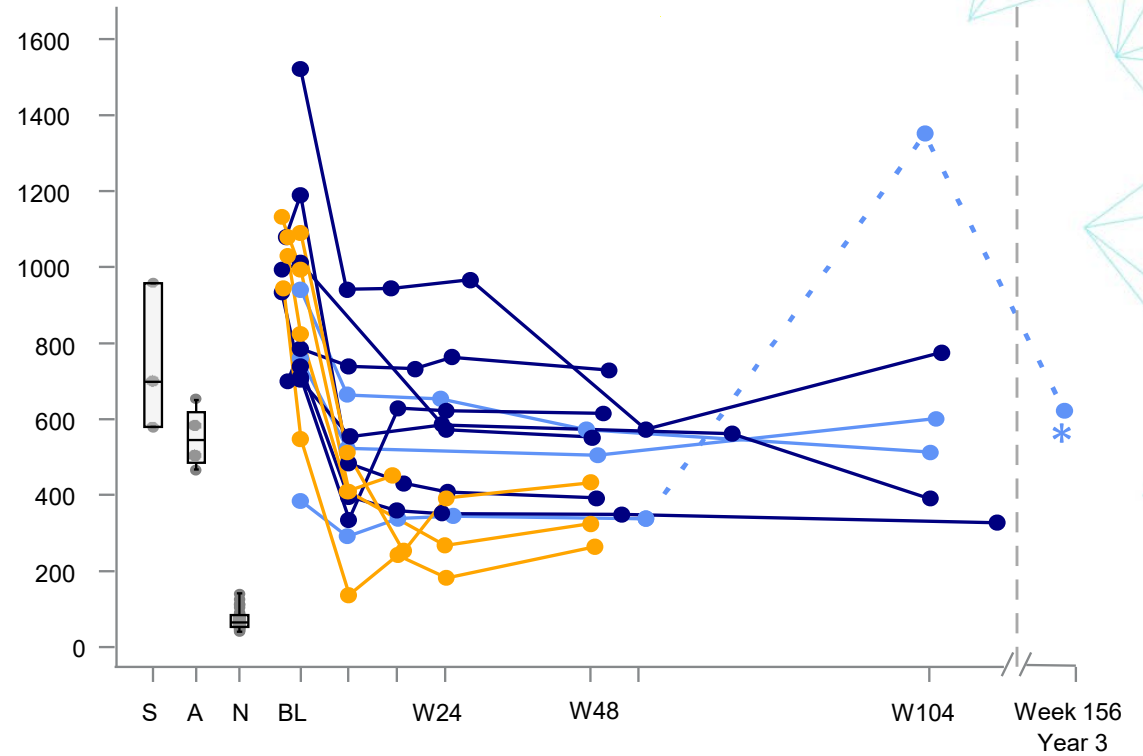
- **Systemic: Evidence of enzyme expression and biomarker activity after CNS RGX-121 administration***
 - Majority of participants demonstrated increases in plasma I2S concentration
 - Urine GAG measures showed evidence of systemic effect of RGX-121 independent of ERT treatment

Cerebrospinal Fluid (CSF) GAGs: Heparan Sulfate (HS)

Cohorts (median[†])



Individual Participants



— Cohort 1 n = 3
— Cohort 2 n = 7
— Cohort 3 n = 4

- Week 48 CSF HS measurements continued to show dose-dependent reductions in Cohorts 1-3
- 13 of 14 participants in all three cohorts demonstrated decreased CSF HS from baseline at last time point available*



* CNS related clinical event (ventriculoperitoneal shunt infection) deemed unrelated to study drug took place on Day 522 post RGX-121 administration in this Cohort 1 participant

[†] Median CSF HS concentration +/- Q1 and Q3 per cohort.

Normative data are based on 29 normal samples. The ages for 9 normative (N) samples range from 1 month to 21 years old.

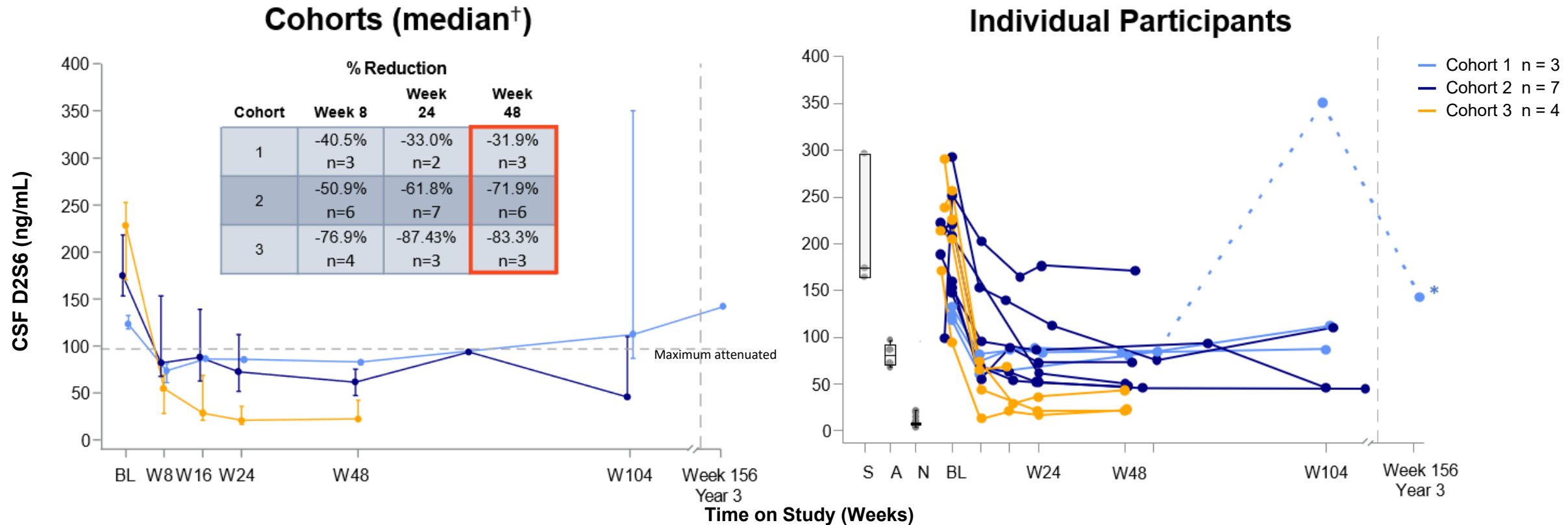
Severe (S) defined as IQ < 70. The ages of 3 severe samples range from 4 years 8 months to 10 years old.

Attenuated (A) defined as IQ ≥ 70. The ages of 4 attenuated samples range from 11 years to 29 years old.

Data cut January 3, 2023

CSF GAGs: HS D2S6

D2S6 is a Correlate of Neuropathology Phenotype in Severe MPS II¹⁻³



- Week 48 CSF HS D2S6 measurements continued to show dose-dependent reductions across cohorts, with Cohort 3 participants approaching normal levels
- 13 of 14 of participants in all three cohorts demonstrated decreased CSF HS D2S6 from baseline at last time point available*
- Measurable CSF I2S protein concentration in 10 of 11 Cohort 2 & 3 participants after RGX-121 administration

1. Holley (2011) J Biol Chem 2. Wilkinson (2012) PLoS One 3. Gleitz (2018) EMBO Mol Med

* CNS related clinical event (ventriculoperitoneal shunt infection) deemed unrelated to study drug took place on Day 522 post RGX-121 administration in this Cohort 1 participant

[†] Median CSF D2S6 concentration +/- Q1 and Q3 per cohort.

Normative data are based on 29 normal samples. The ages for 9 normative (N) samples range from 1 month to 21 years old.

Severe (S) defined as IQ < 70. The ages of 3 severe samples range from 4 years 8 months to 10 years old.

Attenuated (A) defined as IQ ≥ 70. The ages of 4 attenuated samples range from 11 years to 29 years old.

Neurodevelopmental Function

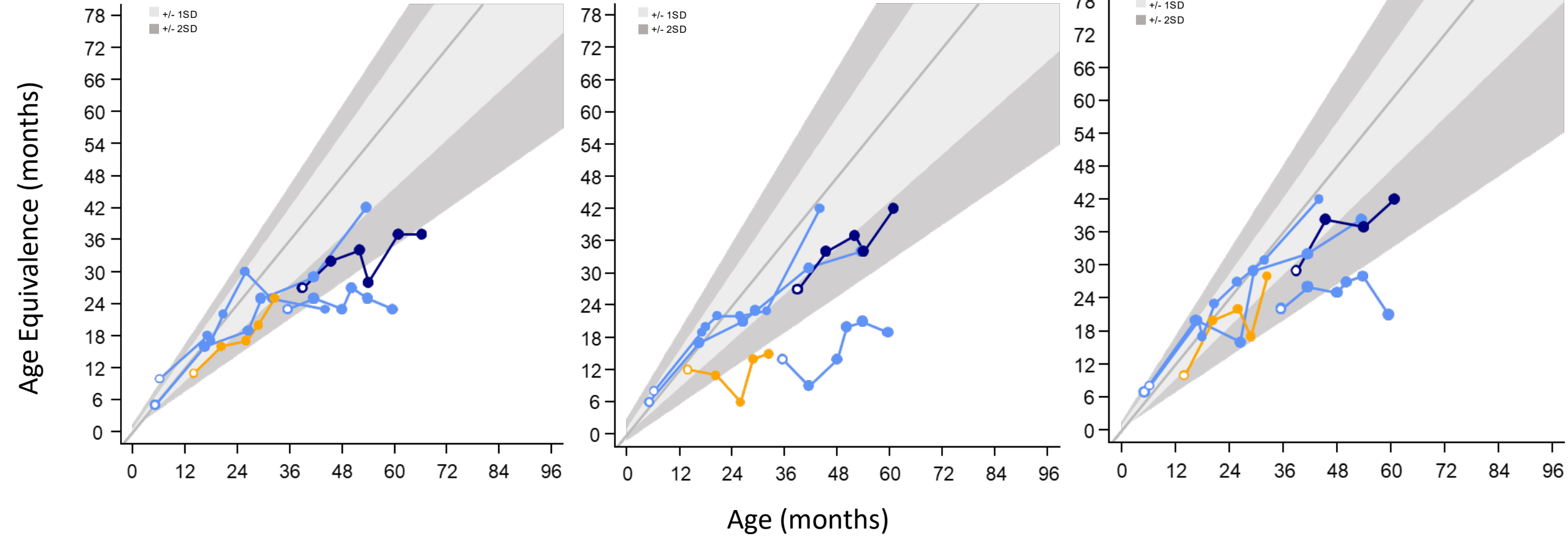
Baseline BSID-III Cognitive Function $\geq -2SD$

- Cohort 1
- Cohort 2
- Cohort 3

Cognition

Expressive Language

Fine Motor



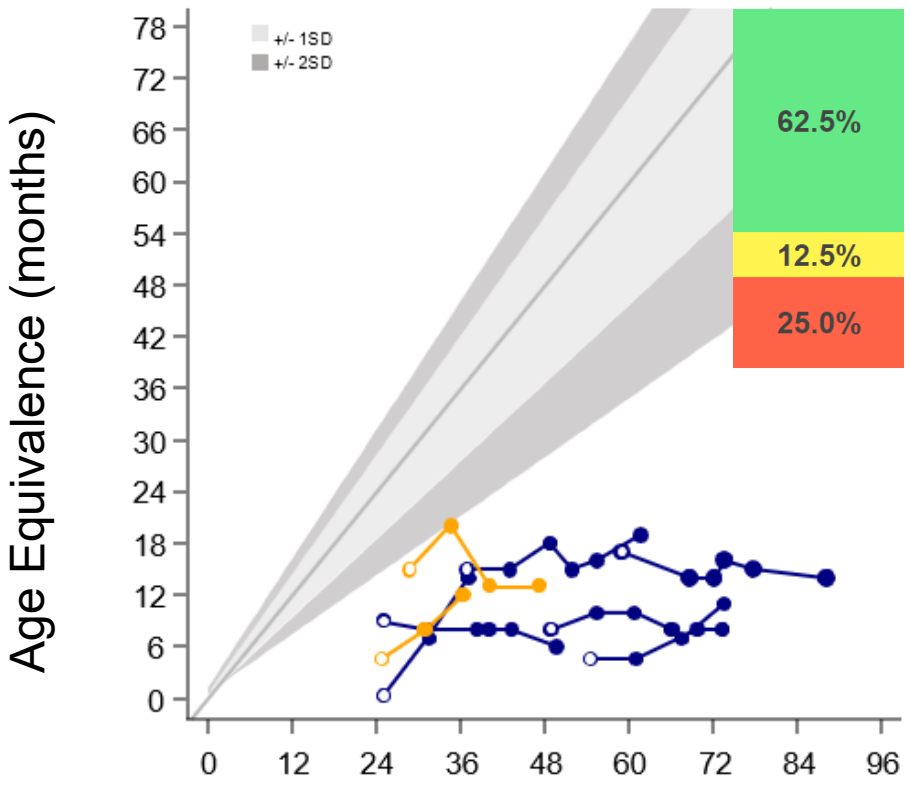
The majority of participants with baseline function $\geq -2SD$ have developmental function that remained within that range on at least 2 domains

Includes participants (n = 5) with > 6 months of follow-up

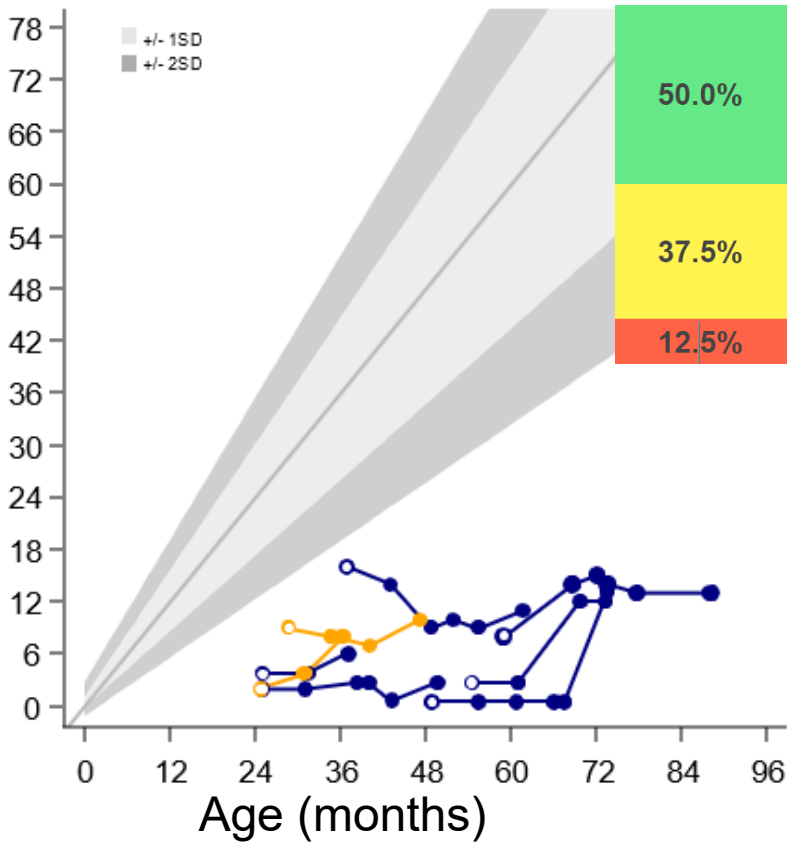
Neurodevelopmental Function

Baseline BSID-III Cognitive Function Below -2 SD

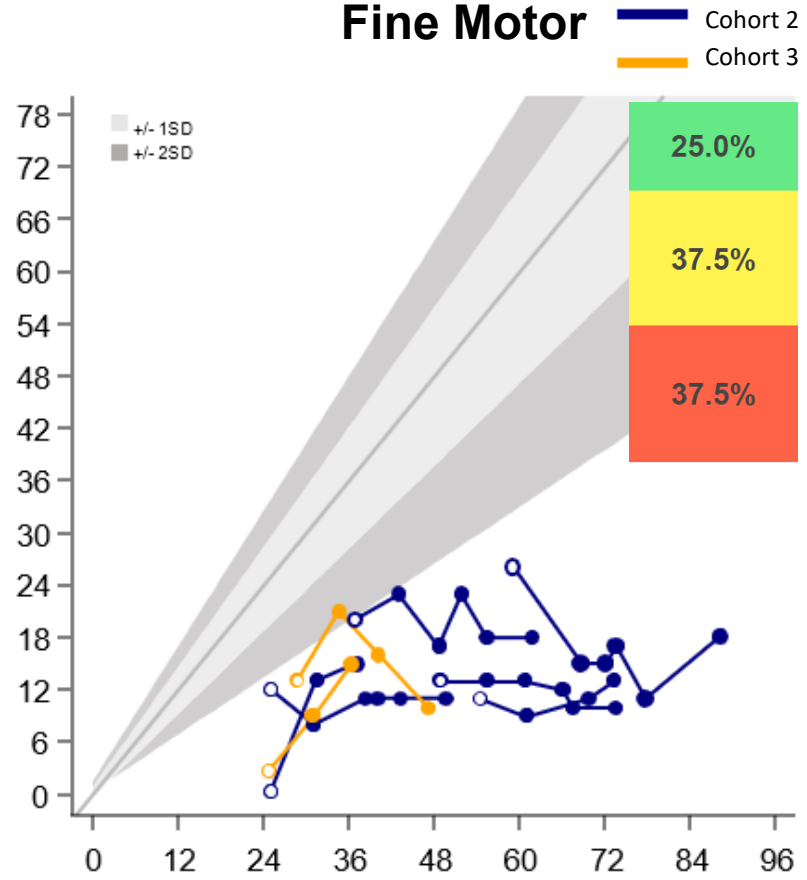
Cognition



Expressive Language



Fine Motor

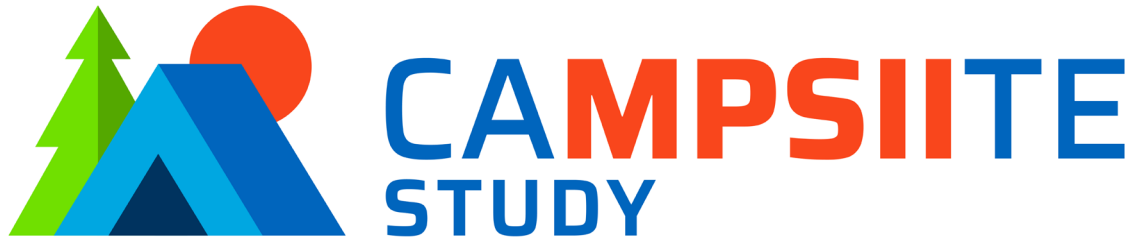


The majority of participants with baseline function below -2SD stabilized or had an increase of ≥ 3 mo in AEq on cognitive, expressive, language or fine motor subtests

Includes participants (n = 8) with > 6 months of follow-up

Change from baseline (CFB) is defined as: Increase ■ ≥ 3 mo AEq; Stabilization ■ $-3 < \text{CFB} < 3$ mo AEq; Decrease ■ ≤ -3 mo AEq

Announcing RGX-121 pivotal program: CAMPSIITE™ Part 2: Phase III Trial



- Enrolling boys with neuronopathic MPS II, aged 4 months up to five years
- Expected to enroll up to 10 patients to support the BLA filing utilizing the accelerated approval pathway
- Trial supports potential enrollment of additional patients
- Participants will receive 2.9×10^{11} GC/g of brain mass, the same dose being evaluated in Cohort 3 of the Phase I/II trial
- Trial will collect GAGs in CSF and neurodevelopmental data, and caregiver reported outcomes
- The pivotal program is using commercial-scale cGMP material from REGENXBIO's proprietary, high-yielding suspension-based manufacturing process, name NAVXpress™
- CAMPSIITE is a global trial which is expected to include sites in the United States, Brazil, and Canada

RGX-111 Phase I/II clinical trial in MPS I



OBJECTIVES

Primary

- To determine the safety and tolerability of RGX-111 in MPS I subjects with neurocognitive deficits

Secondary

- Effect of RGX-111 on biomarkers of IDUA activity in CSF, serum and urine
- Effect of RGX-111 on neurocognitive deficits

SUBJECTS: Up to 11 total

SITES: Leading U.S. and lysosomal storage disease centers

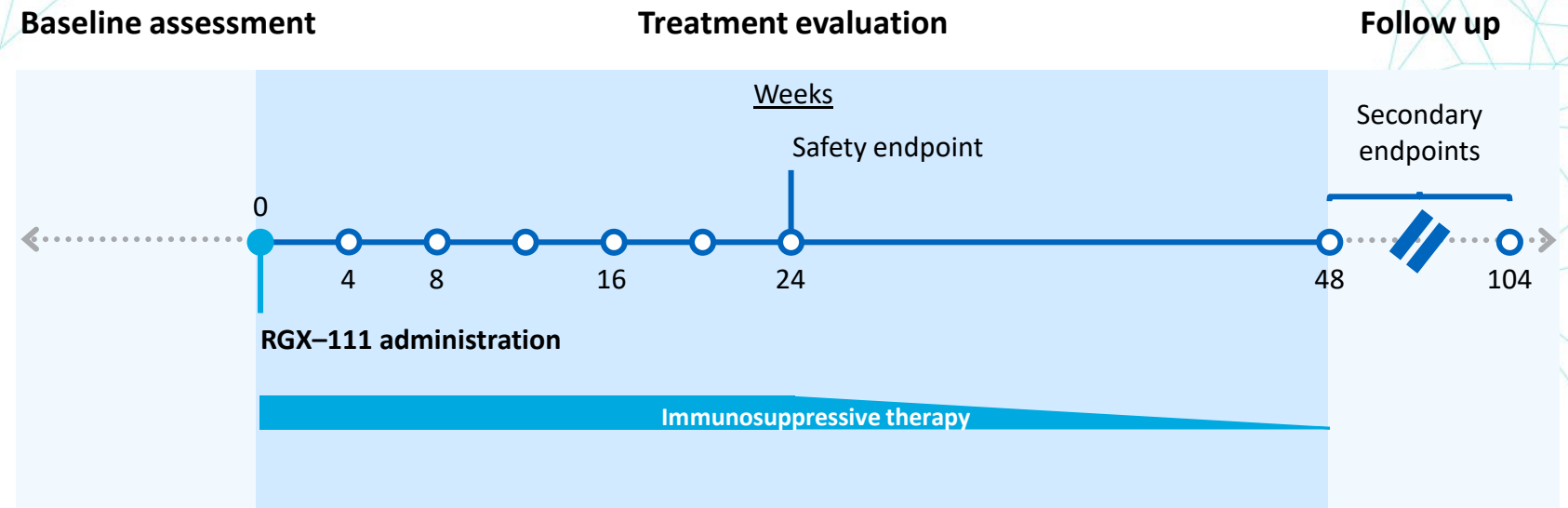


KEY INCLUSION CRITERIA

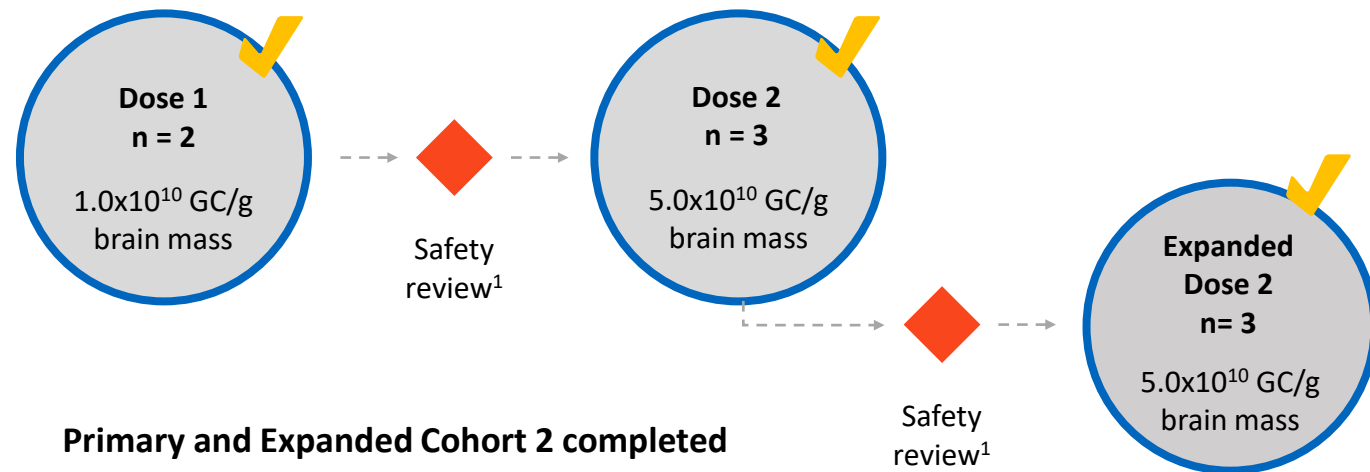
- Male or female ≥ 4 months of age
- Documented evidence of CNS involvement due to MPS I or documented diagnosis of MPS I
 - A score of ≥ 1 standard deviation below mean on intelligent quotient testing or in one domain of neuropsychological function
 - A decline of ≥ 1 standard deviation on sequential testing
 - Having documented biallelic mutation in *IDUA* predictive of severe MPS I or a relative diagnosed with severe MPS I
- No contraindications for intracisternal or intracerebroventricular injection or immunosuppressive therapy

RGX-111 Phase I/II Clinical Trial: Administration and Dose Escalation

Administration and follow-up timeline



Dose escalation



RGX-111 Phase I/II Clinical Trial and Single Patient IND Summary

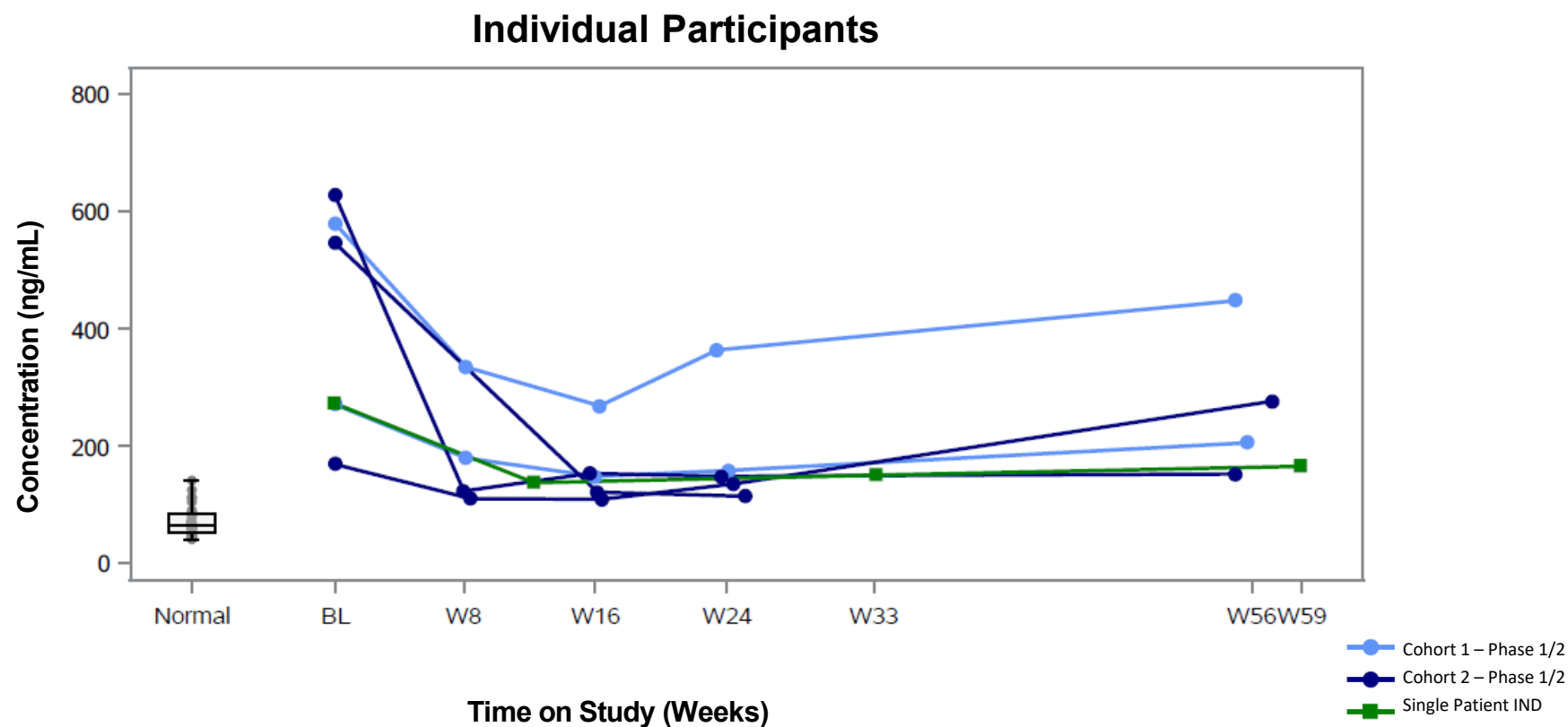
- **Well tolerated following one-time RGX-111 administration**
 - A total of 8 Phase I/II trial participants and a single patient IND participant dosed with RGX-111 with no SAEs related to study drug

- **CNS biomarker and neurodevelopmental assessments indicate encouraging RGX-111 CNS profile**
 - CSF HS reduction and IDUA enzyme activity indicate CNS biological activity
 - Majority of participants showed continued skill acquisition within 2 SD of normative mean on the cognition, expressive language and fine motor subtests at last assessment
 - Cognitive function in a Phase I/II trial participant and the single IND participant was higher than the age equivalent scores in the available natural history

- **Emerging evidence of systemic biomarker activity after CNS administration of RGX-111**
 - Plasma IOS6 reductions observed following RGX-111 administration
 - Low levels of urinary GAGs maintained in all participants

Cerebrospinal Fluid (CSF) GAGs

Heparan Sulfate (HS)



- Decreased CSF heparan sulfate in majority of participants through last time point available
- Measurable CSF IDUA enzyme activity* in 4 of 5 participants in the Phase I/II trial and in the single patient IND participant

Neurodevelopmental Function

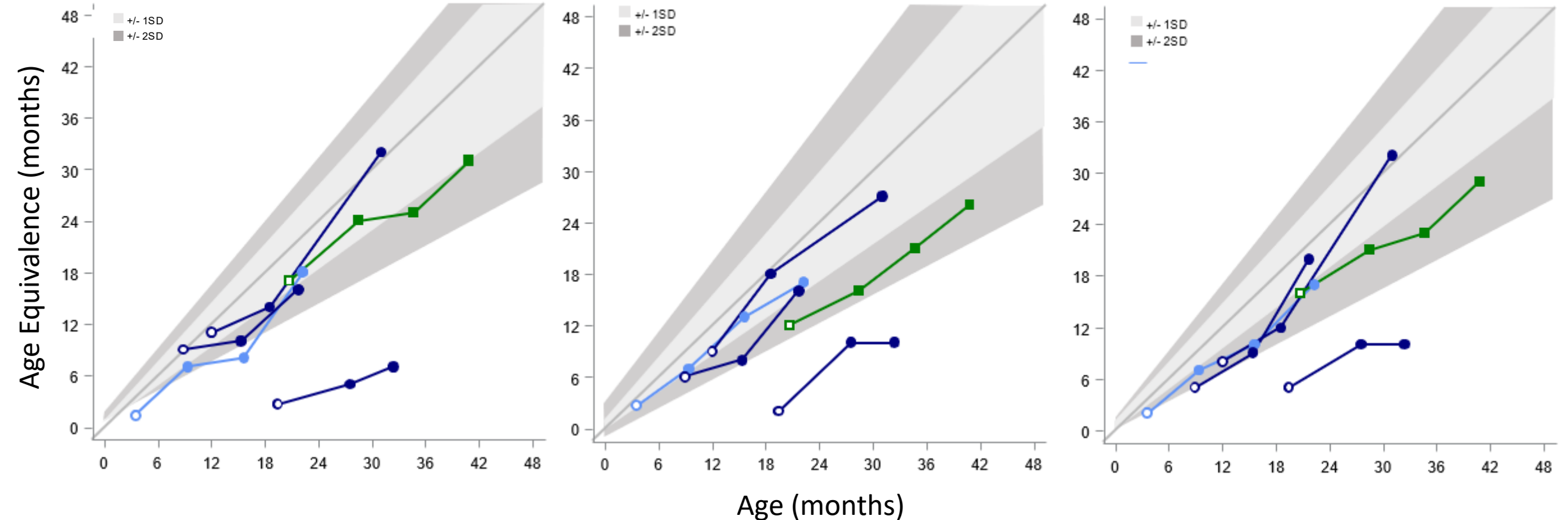
BSID-III

● Cohort 1 – Phase I/II
● Cohort 2 – Phase I/II
■ Single Patient IND

Cognition

Expressive Language

Fine Motor



All participants show continued developmental skill acquisition on all subtests
 At last assessment, 4 of 5 participants have function \geq -2 SD of normative mean on the cognition, expressive language and fine motor subtests

NAV[®] Technology Platform



The NAV[®] Technology Platform is based on a *broad and deep IP portfolio*

Exclusive rights to more than **100 patents** and **patent applications worldwide**

- AAV7, AAV8, AAV9, AAVrh10
- Over 100 other novel AAV sequences
- Sequences that are at least 95% identical to these capsids

Key features of REGENXBIO's NAV[®] Technology Platform

- Broad and novel tissue selectivity
- Improved manufacturability
- High gene transfer
- Long-term gene expression



 The NEW ENGLAND
JOURNAL of MEDICINE

Long-Term Safety and Efficacy of Factor IX Gene Therapy in Hemophilia B

 The NEW ENGLAND
JOURNAL of MEDICINE

Single-Dose Gene-Replacement Therapy for Spinal Muscular Atrophy

REGENXBIO's NAV[®] Technology Platform has been widely adopted

Multiple clinical stage programs being developed by NAV Technology Licensees across a broad range of therapeutic areas



REGENXBIO | Industry leader in AAV production and manufacturing

Deep in-house knowledge of vector characterization and strength in technical operations

3,000 ft² in-house GLP pilot plant with 3 X 200L bioreactor capacity
18,000 ft² of fully-operational advanced manufacturing and analytics lab space
30+ batches of cGMP bulk drug substance product covering multiple programs



Flexible, large-scale cGMP capacity



Potential for candidate selection to clinical material in 12 months



Robust suspension cell culture-based production



Integrated process optimization to enable scale and quality



Analytical capabilities to ensure quality for patients



Key highlights of REGENXBIO's new headquarters

- Corporate, research and manufacturing headquarters opened in May 2021
- **REGENXBIO Manufacturing Innovation Center fully operational**, enabling production at bioreactor scales up to 2,000L using NAVXpress™ suspension platform process
- Integrated approach allows for more efficient development and manufacturing of product candidates





Team and Conclusion

The REGENXBIO team

Name	Position	Prior Affiliations	
Ken Mills	President, CEO & Co-Founder; Director		
Olivier Danos, Ph.D.	EVP and Chief Scientific Officer		
Vit Vasista	EVP and Chief Financial Officer		
Steve Pakola, M.D.	EVP and Chief Medical Officer		
Curran Simpson	EVP, Chief Operations and Technology Officer		
Ram Palanki, Pharm.D.	EVP, Commercial Strategy and Operations		
Patrick Christmas, J.D.	EVP, Chief Legal Officer		
Laura Coruzzi, Ph.D., J.D.	EVP, Intellectual Property		
Shiva Fritsch	EVP, Chief People Officer		

Financial results and guidance

FY 2022 financial results (millions)

Revenue:	\$113
R&D expense:	\$242
G&A expense:	\$85
Net loss:	\$280
Basic share count (12/31/22):	43.3

FY 2022 financial highlights

Ended 2022 with **\$565 million** in cash, cash equivalents and marketable securities

Financial guidance:

REGENXBIO expects its balance in cash, cash equivalents and marketable securities of \$565 million as of December 31, 2022 to fund its operations into 2025. This cash runway guidance is based on the Company's current operational plans and excludes the impact of any payments that may be received from AbbVie upon the achievement of development or commercial milestones under our RGX-314 collaboration.

Program guidance and anticipated milestones

RGX-314	<p>Subretinal wet AMD: 2 pivotal trials ongoing: ATMOSPHERE[®] and ASCENT[™] currently enrolling patients</p> <p>Suprachoroidal wet AMD: Enrollment in Cohort 6 on track to be complete by 1H 2023, data update expected 2H 2023</p> <p>Suprachoroidal DR: Enrollment in Cohorts 4 and 5 on track to be complete by 1H 2023, data update expected 2H 2023</p>
RGX-202	<p>Phase I/II AFFINITY DUCHENNE[™] Trial: Active and recruiting patients, expected to report initial trial data 2H 2023</p> <p>AFFINITY BEYOND[™] Seroprevalence trial: Active and recruiting patients</p>
RGX-121	<p>Phase I/II/III CAMPSIITE[™] Trial: Active and enrolling patients; expected to file BLA in 2024 using accelerated approval pathway</p> <p>Phase I/II trial in pediatric patients over 5 years old: Ongoing</p>
RGX-111	<p>Phase I/II trial: Enrollment complete, on track to manufacture commercial-scale cGMP material using the NAVXpress[™] platform process in the first half of 2023 to support continued development</p>



Thank You