Corporate Presentation

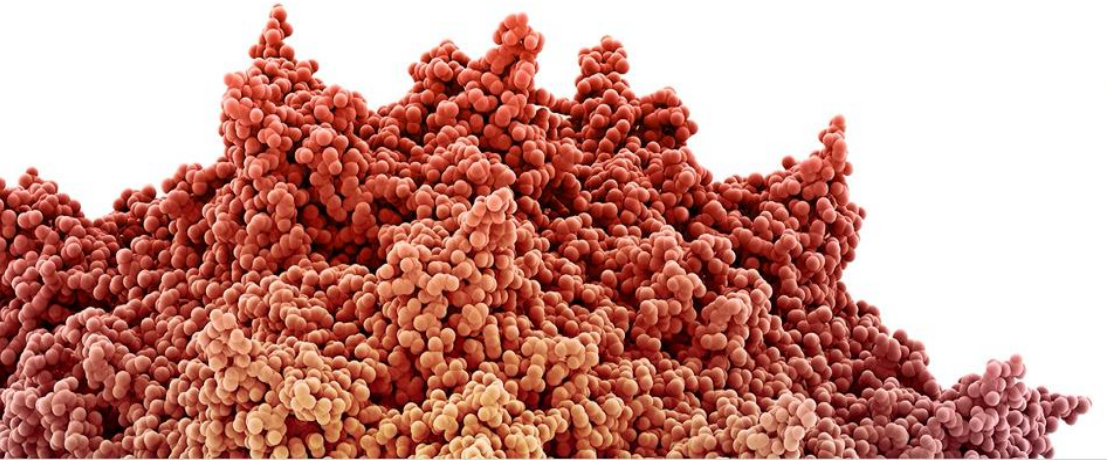
Leader in AAV Gene Therapy

3 | 2 | 2022

Forward-looking statements

This presentation includes “forward-looking statements,” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements express a belief, expectation or intention and are generally accompanied by words that convey projected future events or outcomes such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” ”assume,” “design,” “intend,” “expect,” “could,” “plan,” “potential,” “predict,” “seek,” “should,” “would” or by variations of such words or by similar expressions. The forward-looking statements include statements relating to, among other things, REGENXBIO’s future operations, clinical trials, costs and cash flow. REGENXBIO has based these forward-looking statements on its current expectations and assumptions and analyses made by REGENXBIO in light of its experience and its perception of historical trends, current conditions and expected future developments, as well as other factors REGENXBIO believes are appropriate under the circumstances. However, whether actual results and developments will conform with REGENXBIO’s expectations and predictions is subject to a number of risks and uncertainties, including the outcome of REGENXBIO’s collaboration with AbbVie and other factors, many of which are beyond the control of REGENXBIO. For a summary of certain of these risks and uncertainties, refer to the “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” sections of REGENXBIO’s Annual Report on Form 10-K for the year ended December 31, 2021 and comparable “risk factors” sections of REGENXBIO’s Quarterly Reports on Form 10-Q and other filings, which have been filed with the U.S. Securities and Exchange Commission (SEC) and are available on the SEC’s website at www.sec.gov. All of the forward-looking statements made in this presentation are expressly qualified by the cautionary statements contained or referred to herein. The actual results or developments anticipated may not be realized or, even if substantially realized, they may not have the expected consequences to or effects on REGENXBIO or its businesses or operations. Such statements are not guarantees of future performance and actual results or developments may differ materially from those projected in the forward-looking statements. Readers are cautioned not to rely too heavily on the forward-looking statements contained in this presentation. These forward-looking statements speak only as of the date of this presentation. Except as required by law, REGENXBIO does not undertake any obligation, and specifically declines any obligation, to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

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	Phase III	
Retinal Disease					
wet AMD (subretinal)	RGX-314				abbvie U.S. Equal Profit Share Ex-U.S. Tiered Royalties
wet AMD (suprachoroidal)	RGX-314				
Diabetic retinopathy (suprachoroidal)	RGX-314				
Other chronic retinal conditions					
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

REGENXBIO®

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

REGENXBIO

- Leadership and expertise in AAV and retinal gene therapy
- Strong in-house capabilities of AAV manufacturing

abbvie

- 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

First pivotal trial for nAMD is active and enrolling patients

ATMOSPHERE

Second pivotal trial for nAMD is active and enrolling patients

ASCENT

Suprachoroidal

Phase II trial in nAMD is ongoing

AAVIATE

Phase II trial for diabetic retinopathy is ongoing

ALTITUDE

REGENXBIO

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

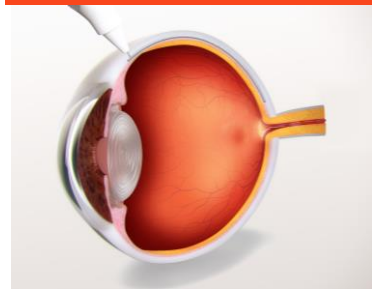
Mechanism of action

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

Routes of administration

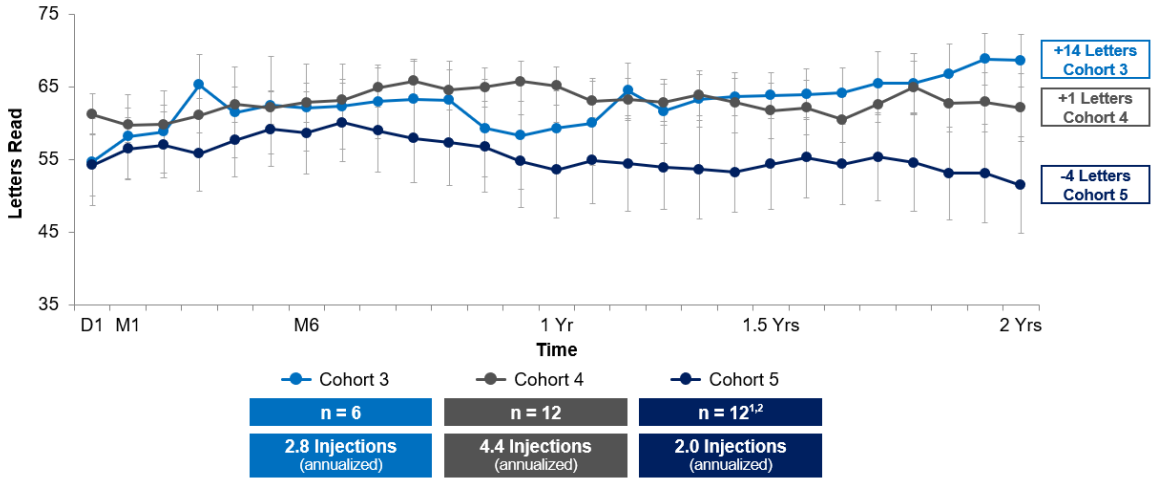
Subretinal (SR)

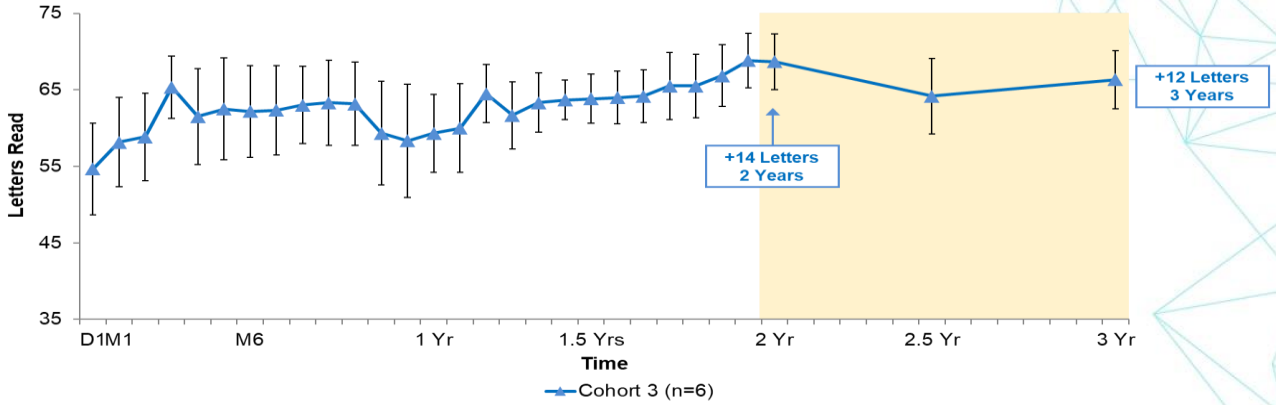
Suprachoroidal (SC)



RGX-314 Phase I/IIa Trial: Stable to Improved VA, Including VA Improvement through 3 Years in Cohort 3

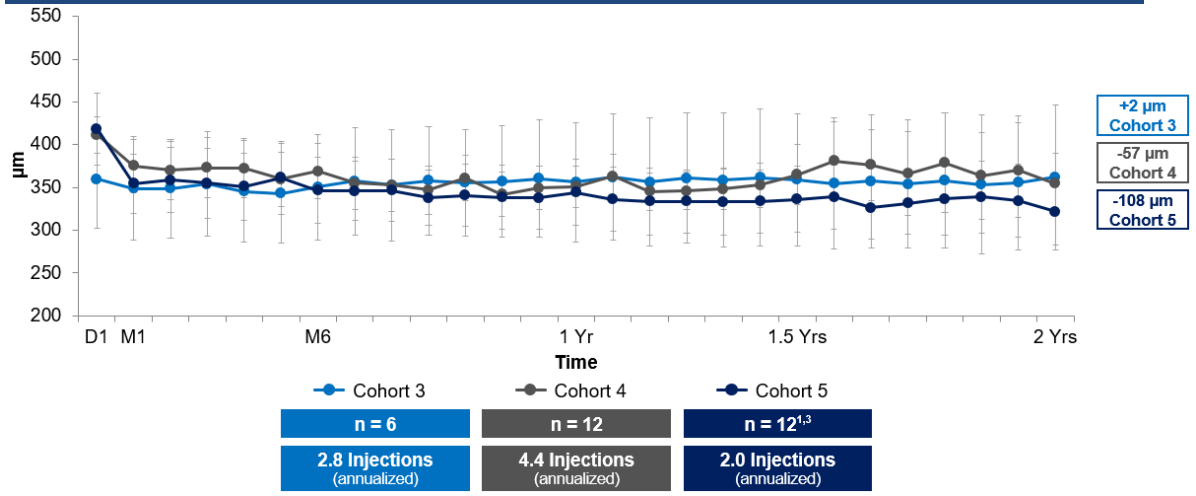
Best Corrected Visual Acuity (BCVA)



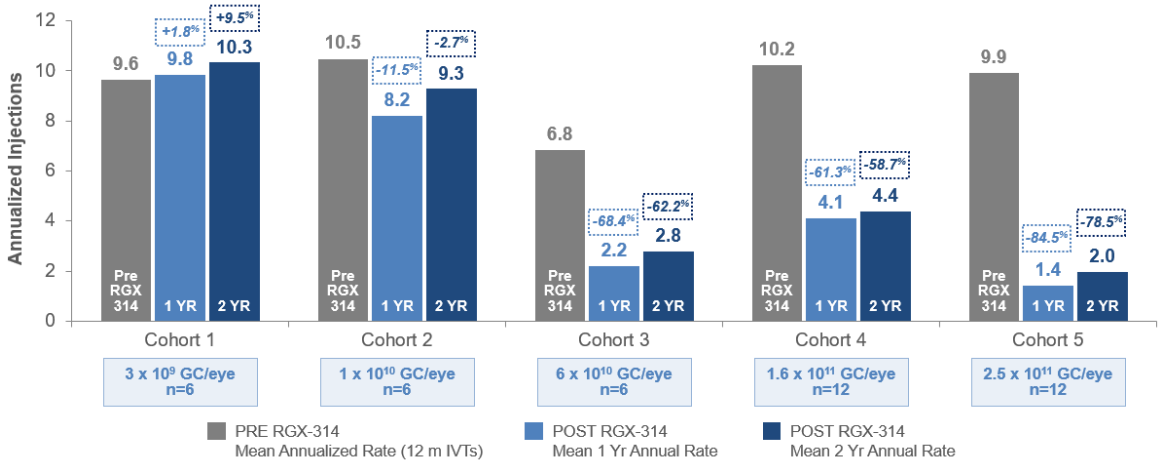


Stable to Improved Anatomy with Meaningful Reduction in anti-VEGF Injection Burden

Central Retinal Thickness (CRT) by Central Reading Center



Annualized Injection Rate[4]



REGENXBIO®

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 BCVA 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.

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

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

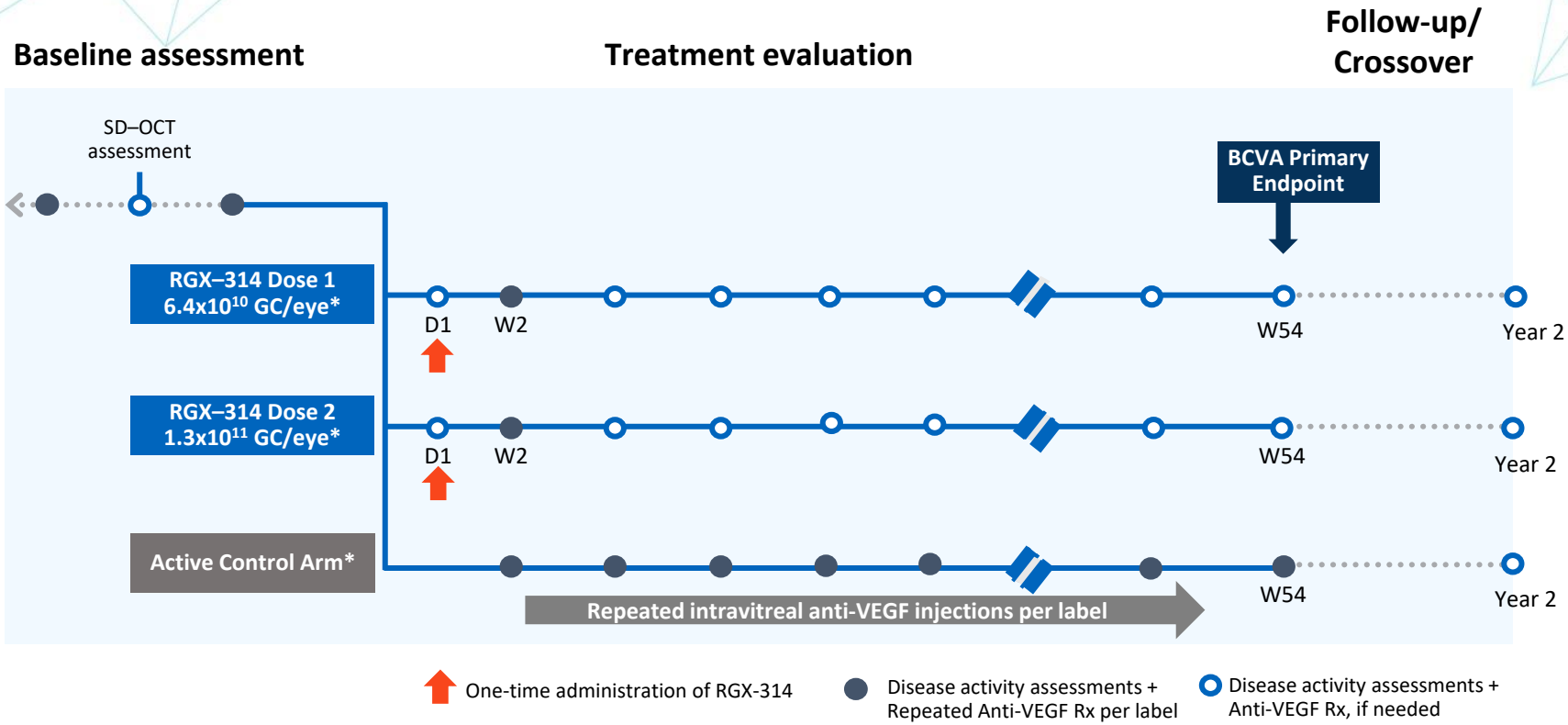
Sites: Leading retinal surgery centers across the United States and Canada

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



ATMOSPHERE

n=300 patients*

Active Control Arm: Ranibizumab 0.5mg q4w

ASCENT

n=465 patients*

Active Control Arm: Aflibercept 2.0mg q8W

REGENXBIO

*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 95 total

Route of administration: Suprachoroidal using SCS Microinjector

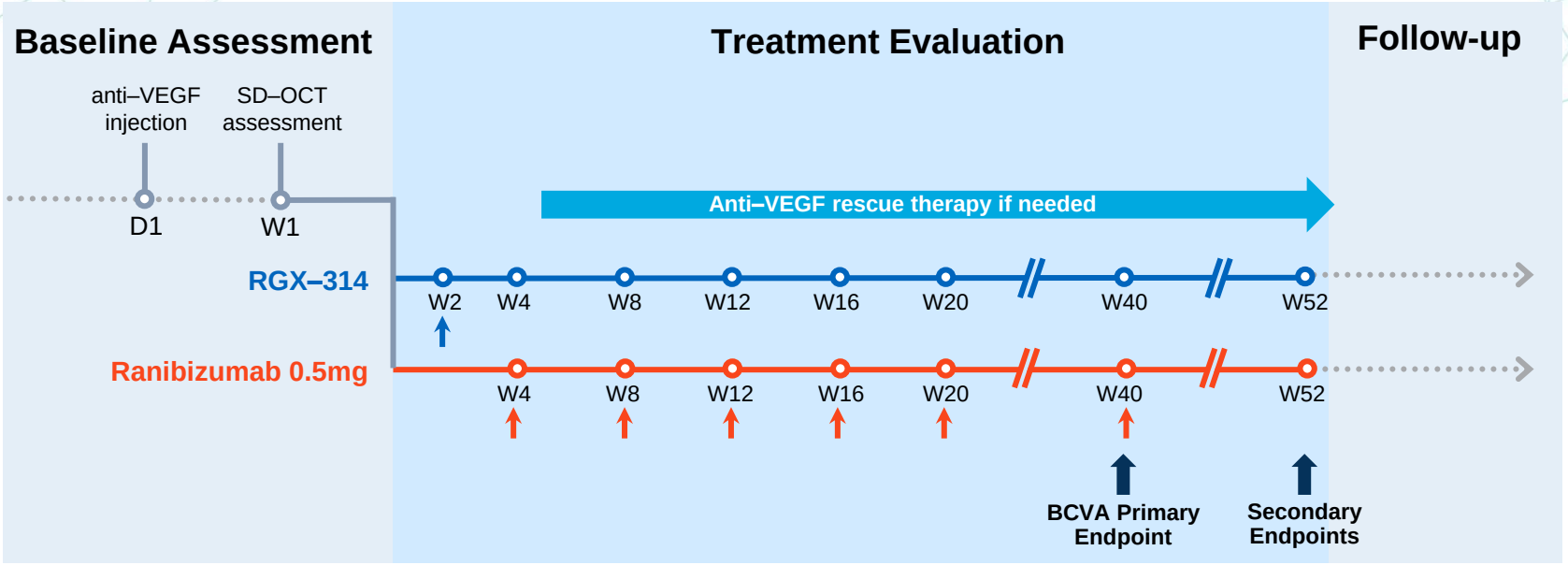
Sites: Fifteen leading retinal centers across the United States

KEY INCLUSION CRITERIA

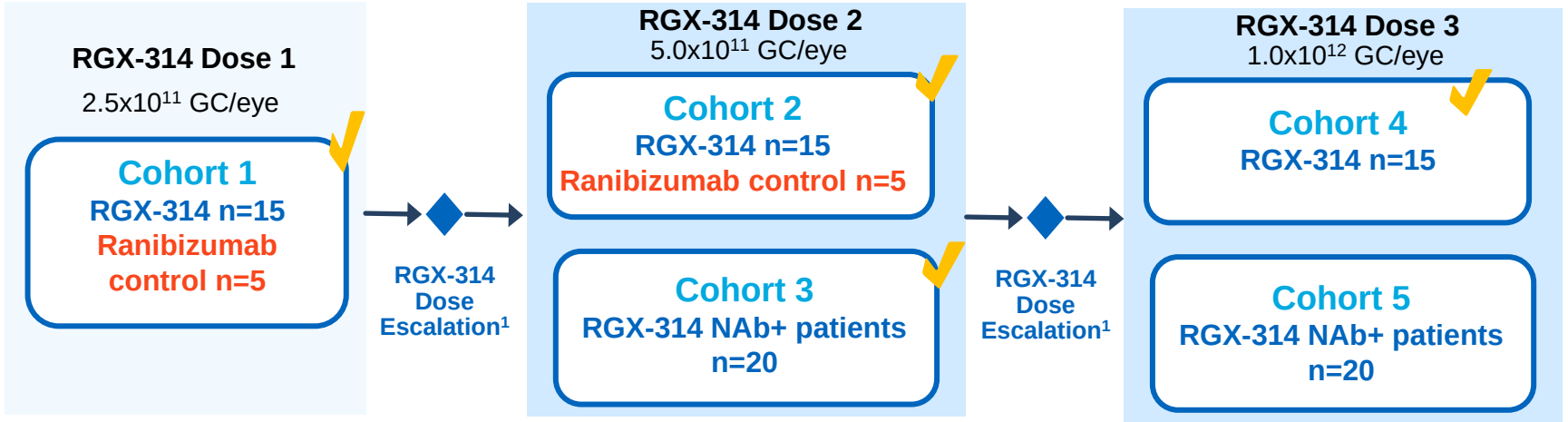
- Male or female ≥50 to 89 years of age
- Previously treated wet AMD subjects with fluid on OCT at trial entry
- Documented response to anti–VEGF at trial entry (assessed by reading center)
- BCVA between ≤ 20/25 and ≥ 20/125 (≤ 83 and ≥ 44 Early Treatment Diabetic Retinopathy Study [ETDRS] letters)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

AAVIATE® Phase II clinical trial design

Administration and follow-up timeline



Dose escalation

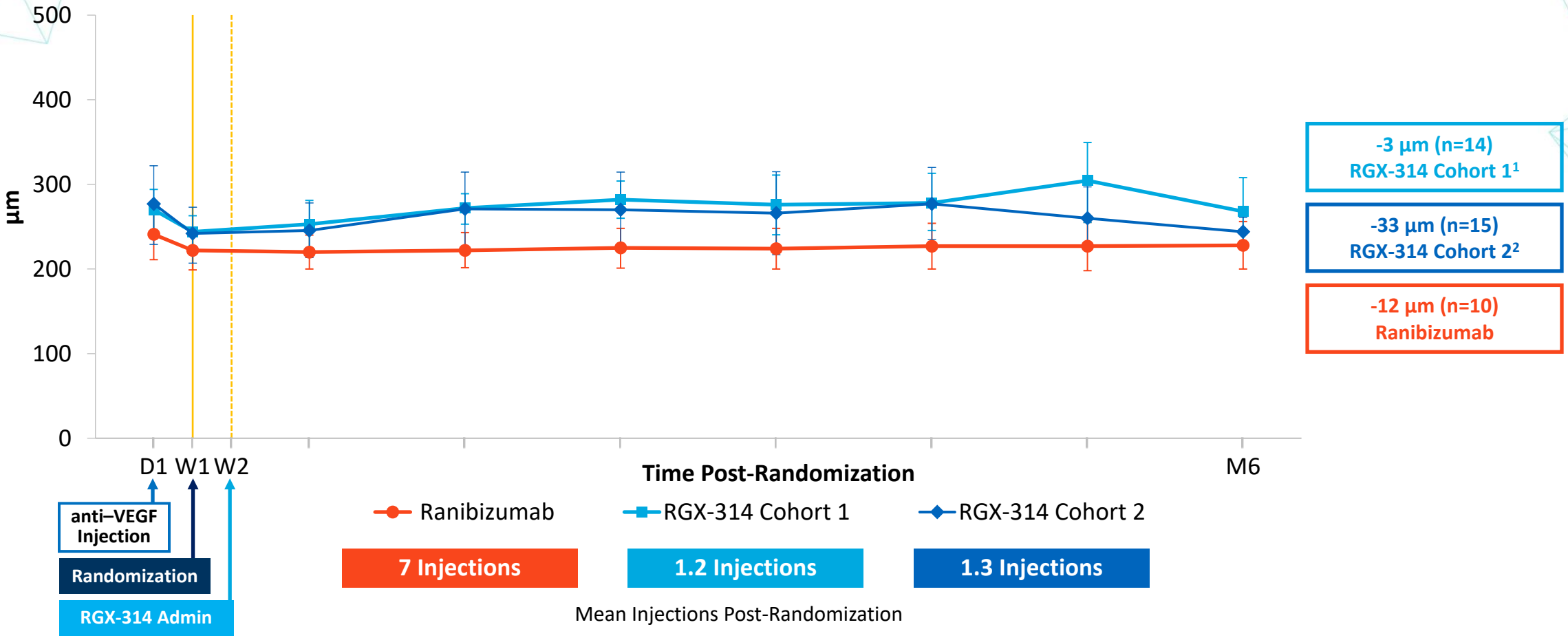


Cohort 5 currently enrolling patients

[1] Dose escalation safety review to occur two weeks after final subject in Cohort 1 has been dosed
SD-OCT = spectral domain optical coherence tomography
NAb+ = AAV8 neutralizing antibody positive

Cohorts 1 and 2: Mean CRT from Day 1 (Screening) Through Month 6

Central Retinal Thickness (CRT) 95%CI



Data cut: November 4, 2021

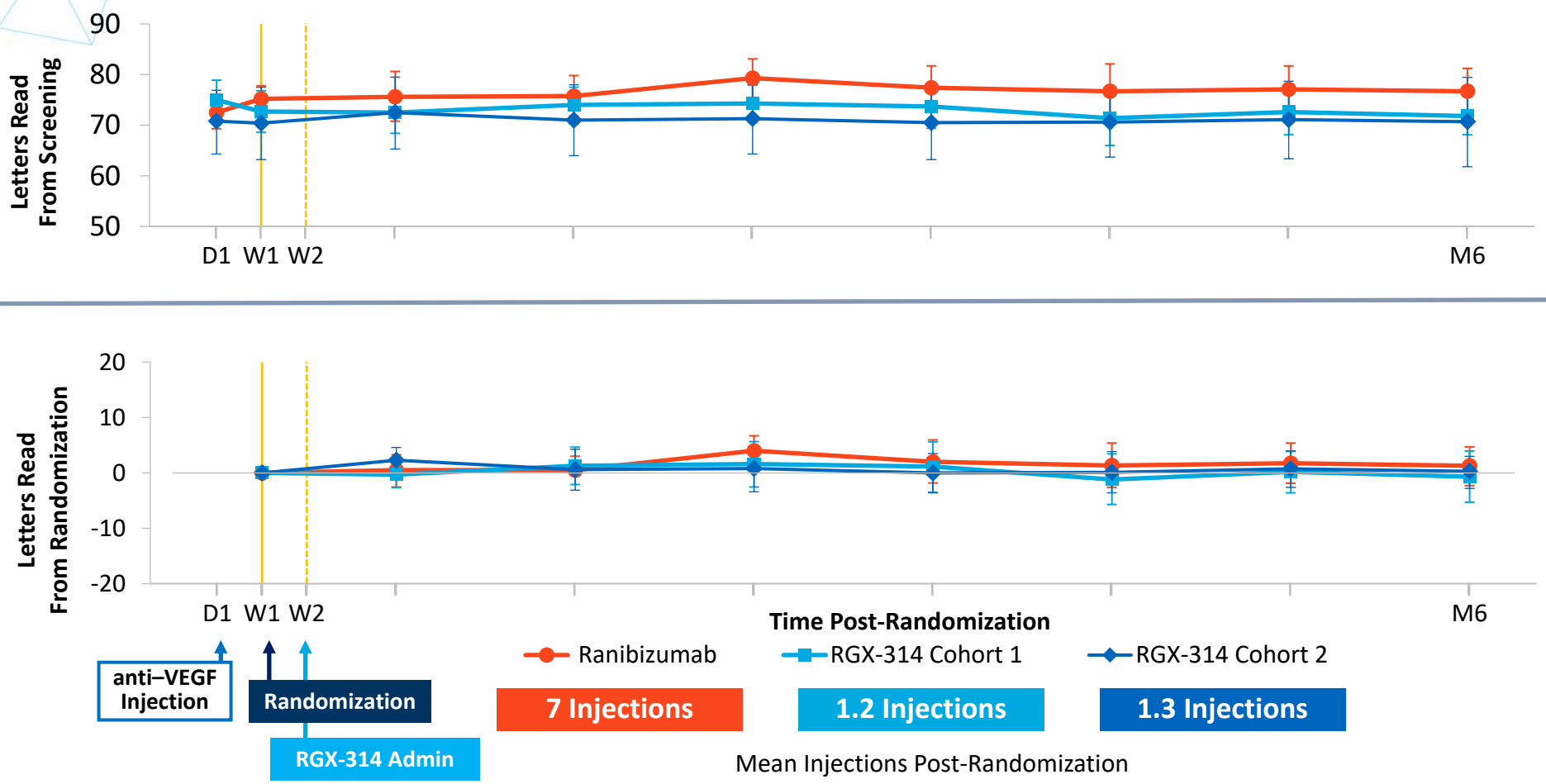
[1]One patient discontinued the study after Week 12, and only data up to week 12 is included for the subject. For one patient who has missing Weeks 8 and 28 visits, the missing data has been interpolated using the average of before and after the missing visit.

[2]For one patient who missed the Week 28 visit, the missing data has been interpolated using the average of before and after the missing visit.

REGENXBIO®

Cohort 1 and 2: Mean Change in BCVA Through Month 6

Best Corrected Visual Acuity (BCVA) 95% CI



+4.0 Letters (n=10) Ranibizumab

-2.8 Letters (n=14)[1] RGX-314 Cohort 1

-0.1 Letters (n=15)[2] RGX-314 Cohort 2

+1.3 Letters (n=10) Ranibizumab

+0.2 Letters (n=15)[2] RGX-314 Cohort 2

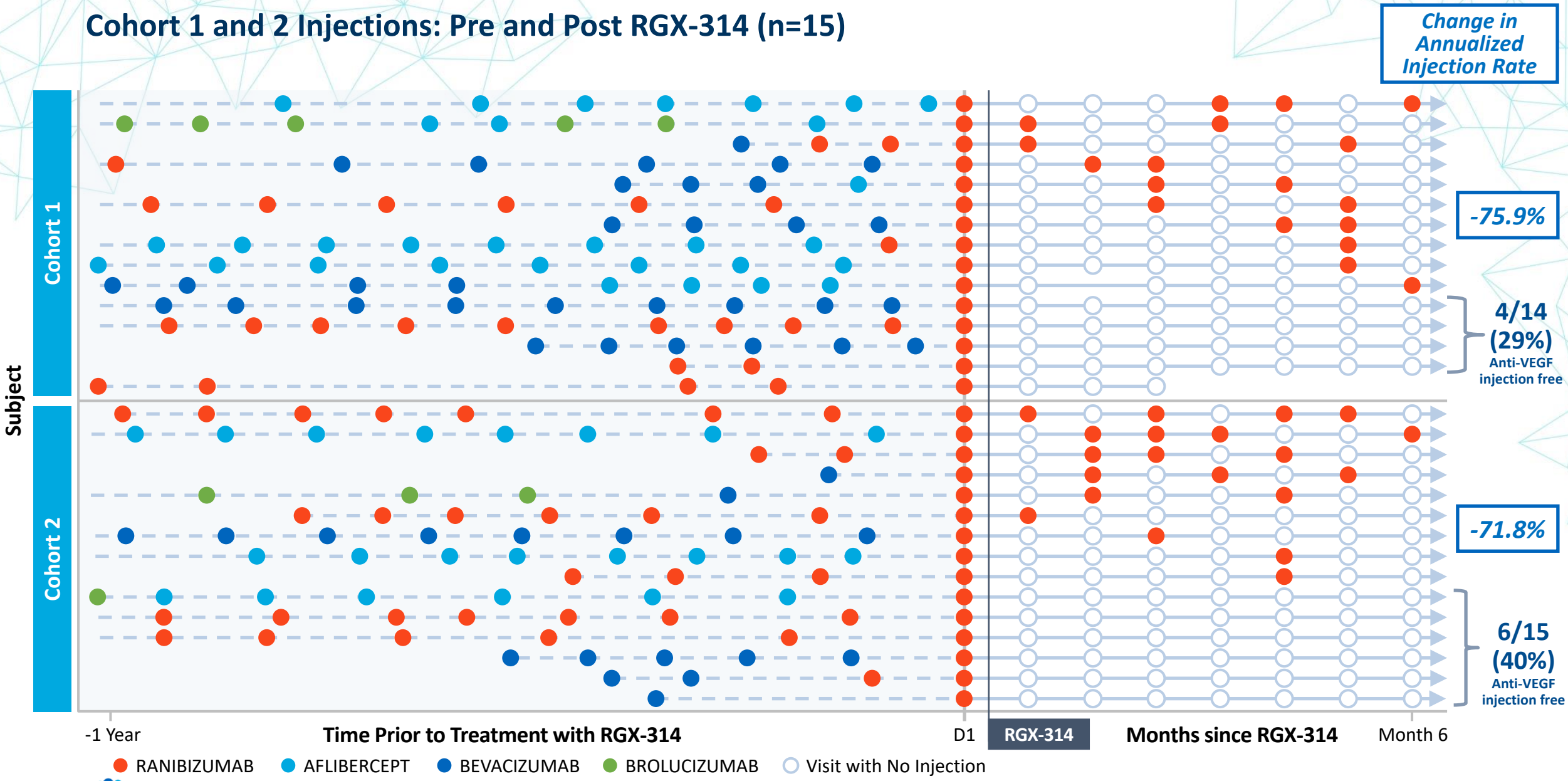
-0.6 Letters (n=14)[1] RGX-314 Cohort 1

Data cut: November 4, 2021

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

[2]For one patient who missed the Week 28 visit, the missing data has been interpolated using the average of before and after the missing visit.

Cohort 1 and 2 Injections: Pre and Post RGX-314 (n=15)



REGENXBIO

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

AAVIATE Safety Summary

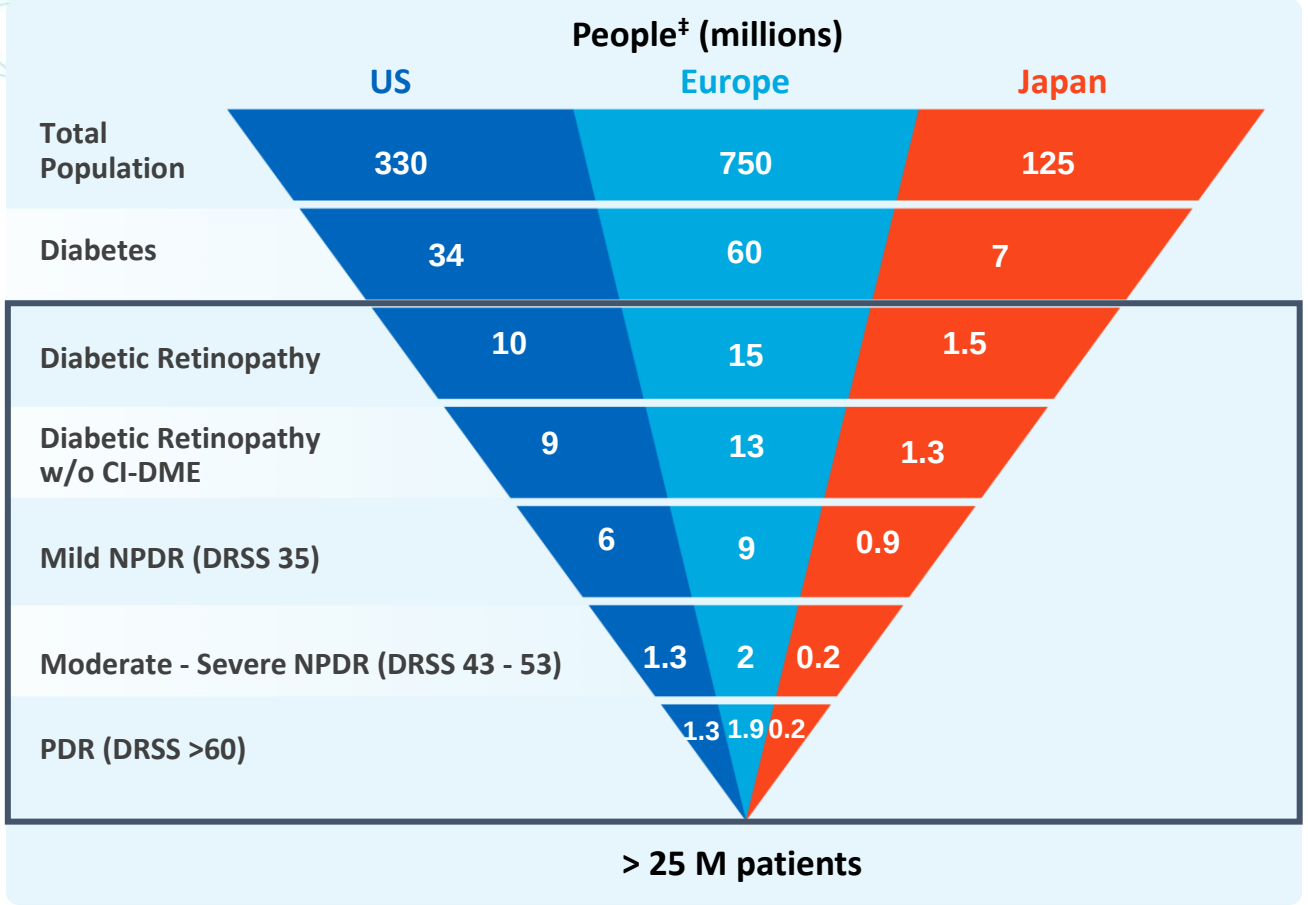
- RGX–314 was well–tolerated in Cohorts 1–3 (n=50) with follow-up ranging from 2 – 12 months
  - 4 SAEs: None considered drug-related
  - No cases of chorioretinal vasculitis or occlusion, or hypotony were observed

RGX-314 Common Ocular TEAEs[1] in the Study Eye through 6 Months:	Cohort 1 $2.5x10^{11}$ GC/eye 1 injection (N=15)	Cohort 2 $5.0x10^{11}$ GC/eye 2 injections (N=15)	Total (N=30)
Conjunctival hemorrhage	**5** (33.3%)	**3** (20.0%)	**8** (26.7%)
Intraocular Inflammation[2]	**4** (26.7%)	**3** (20.0%)	**7** (23.3%)
Worsening of nAMD[3]	**3** (20.0%)	**1** (6.7%)	**4** (13.3%)
Dry eye	**2** (13.3%)	**2** (13.3%)	**4** (13.3%)
Episcleritis[4]	**0** (0.0%)	**3** (20.0%)	**3** (10.0%)
Conjunctival hyperemia	**2** (13.3%)	**1** (6.7%)	**3** (10.0%)

Data cut: November 4, 2021

1. Includes AEs for total group ≥10% with onset up to 6m visit.
2. All mild, observed on slit lamp examination. Cohort 1: 3 patients presented with anterior cell (+0.5, +2, +2) and 1 patient presented with vitreous cell (trace). Cohort 2: 3 patients presented with anterior cell (+0.5, +1, +1). Resolved within days to weeks on topical corticosteroids.
3. All reported at one site.
4. All mild, presented 4 weeks post double injection and resolved within days to weeks on topical corticosteroid or NSAID treatment.

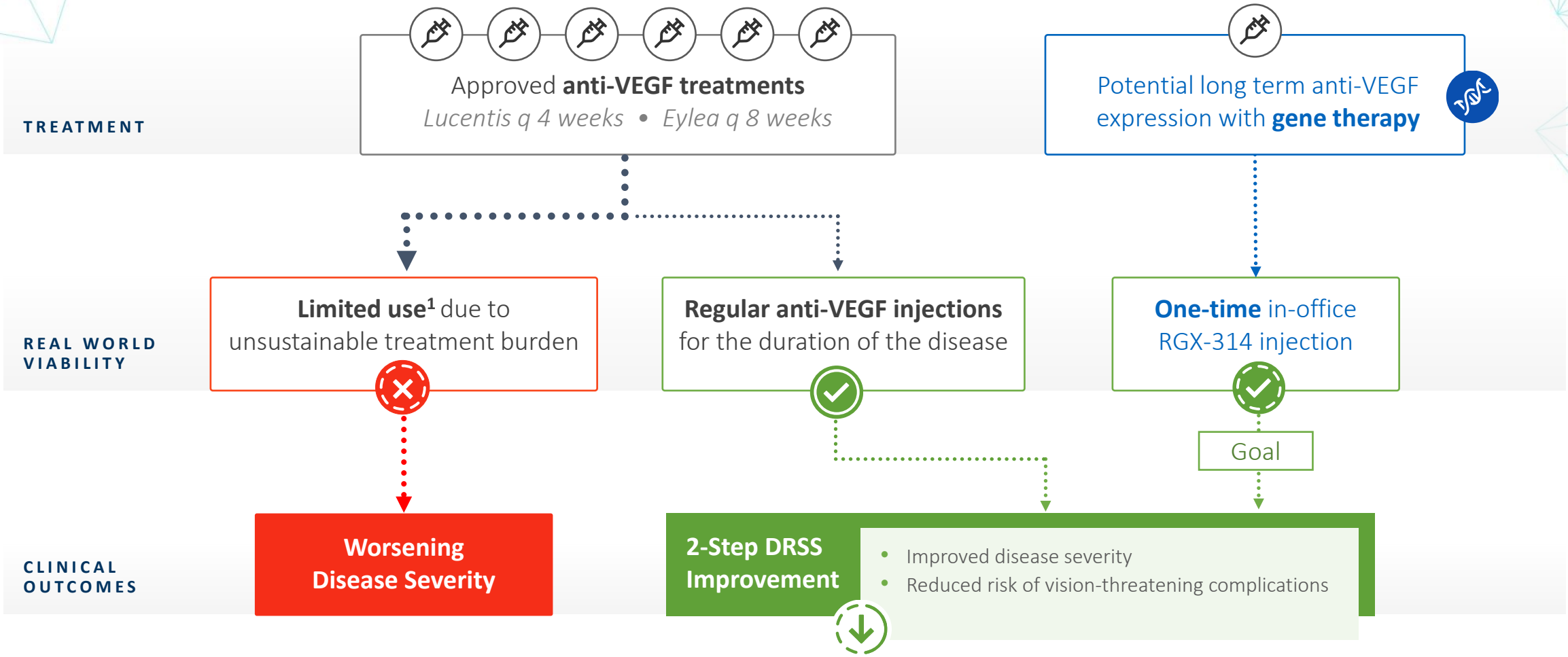
Diabetic Retinopathy is a Global Public Health Problem



- **Leading cause of blindness among working-age adults[1]**
- **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]**

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



1American Society of Retina Specialists PAT Survey 2021

VEGF: vascular endothelial growth factor | **DRSS**: diabetic retinopathy severity scale | **CI-DME**: center-involved diabetic macular edema | **PDR:** proliferative diabetic retinopathy | **ASNV**: anterior segment neovascularization

EYLEA® (aflibercept) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc. March 2021; Lucentis® (ranibizumab) Prescribing information. Genentech, Inc., March 2018

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 60 total

Route of administration: Suprachoroidal using SCS Microinjector

Sites: 18 leading retinal centers across the United States

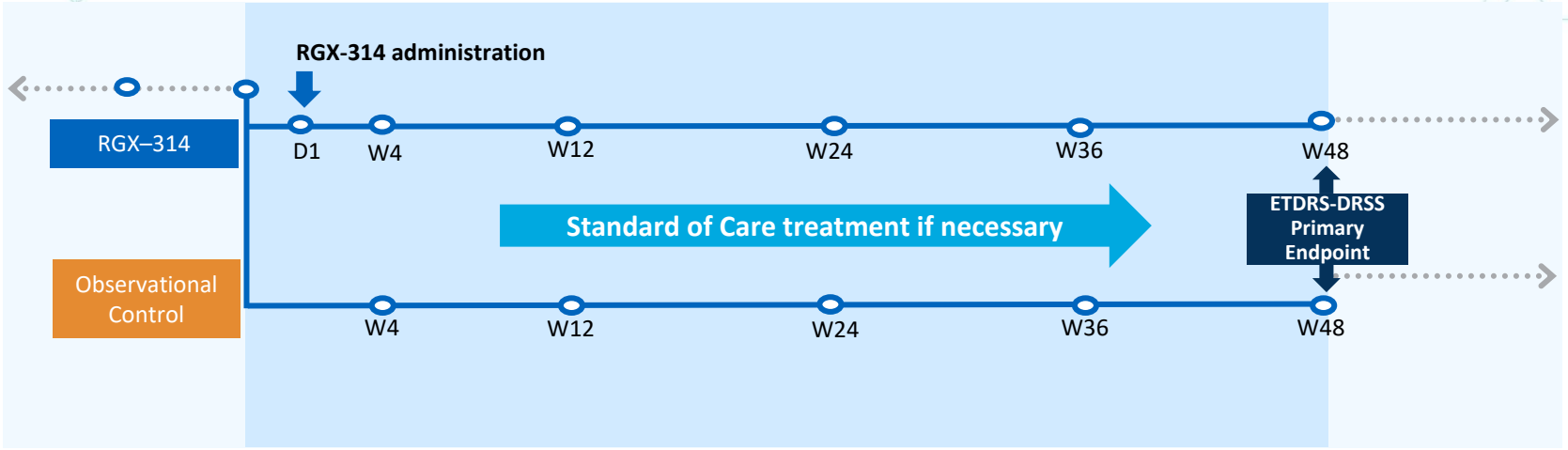
KEY INCLUSION CRITERIA

- 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 µm
- 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

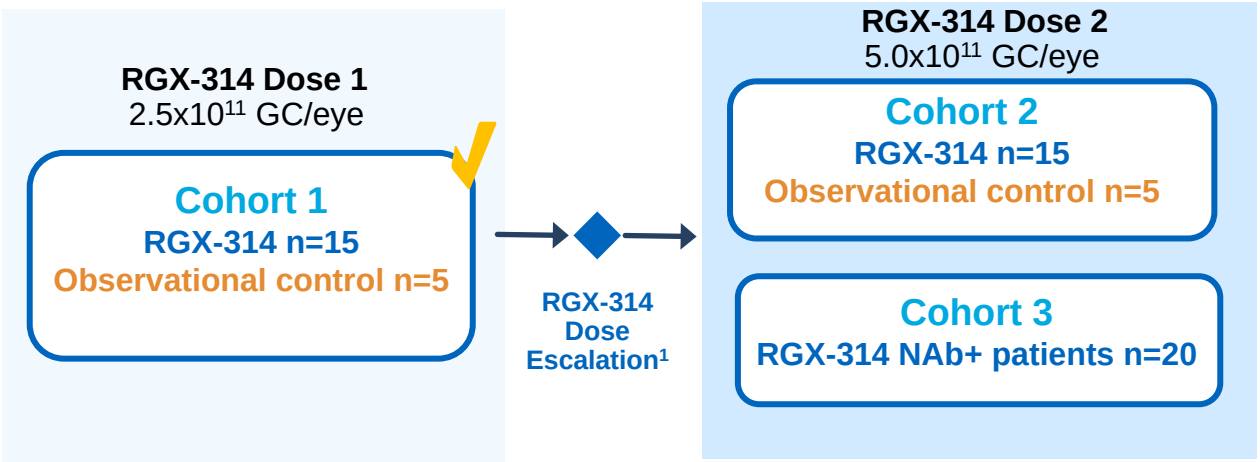
REGENXBIO

ALTITUDE™ Phase II clinical trial design

Administration and follow-up timeline



Dose escalation

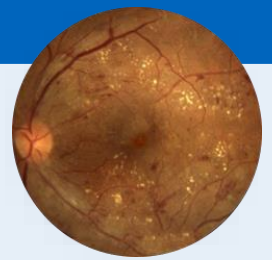
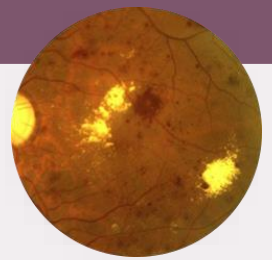


Cohorts 2 & 3 currently enrolling patients

[1] Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed

A 2-step improvement in Diabetic Retinopathy Severity Scale (DRSS) has been accepted as a pivotal endpoint by the FDA for DR clinical trials[1]

▸ INCREASING RISK OF DEVELOPING VISION THREATENING COMPLICATIONS ▸

DRSS 35 Mild NPDR	***DRSS 43*** Moderate NPDR	***DRSS 47*** Moderately Severe NPDR	***DRSS 53*** Severe NPDR	***DRSS ≥ 60*** PDR
				
• Visual symptoms mostly absent • Small bulges in blood vessels and intraretinal hemorrhages	• May experience visual symptoms • Spotted leaking of blood	• May experience visual symptoms • Leaking of blood in retina, unevenly shaped veins	• May experience visual symptoms • Widespread leaking of blood, more unevenly shaped veins	• Visual symptoms are usually present • Growth of new fragile blood vessels, in some cases leading to bleeding in the retina and center of the eye

Example of 2-step Improvement

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

REGENXBIO®

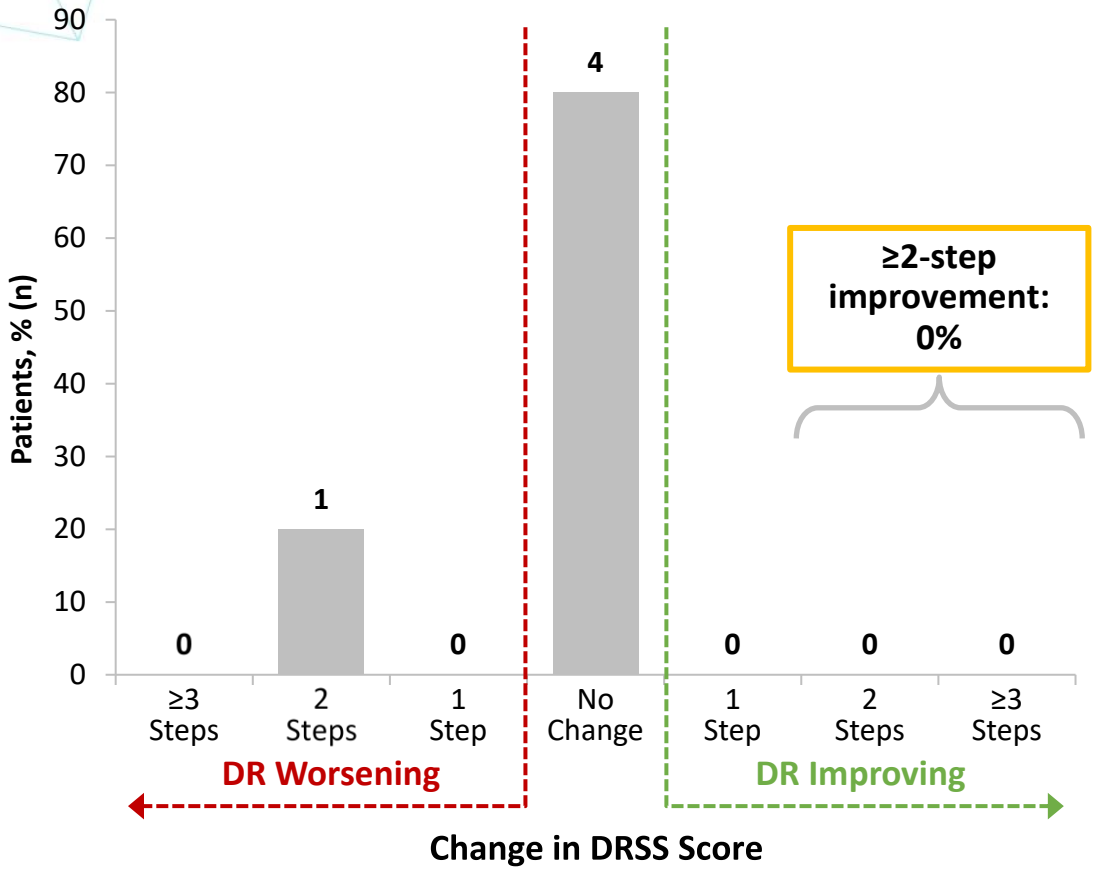
DR, diabetic retinopathy. CI-DME can occur at any stage of severity.

1. Used in the approval of EYLEA® (aflibercept) and LUCENTIS® (ranibizumab) Source: AAO PPP 2019; 2. DRSS score categorizes severity of disease in DR. ETDRS report number 12. *Ophthalmology* 1991; Images: Bakri, 2021

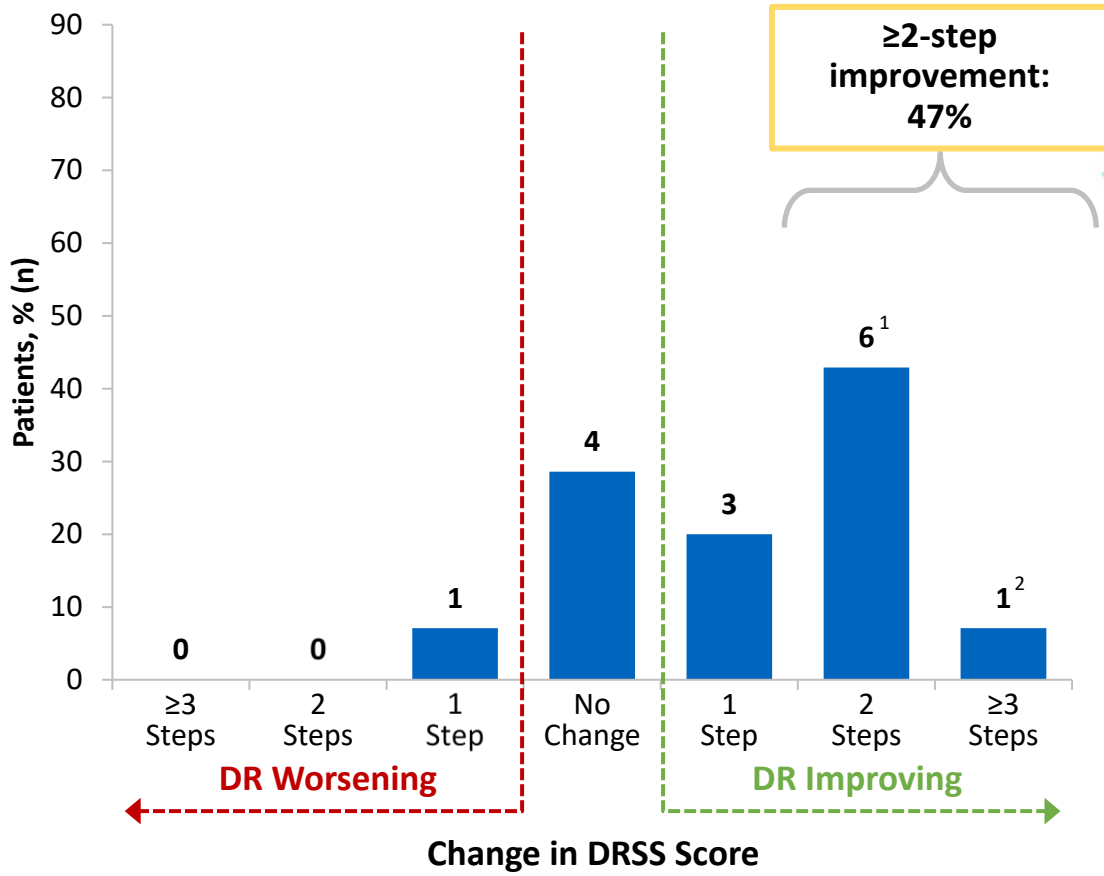
Cohort 1: Change in DRSS at Month 6

47% of RGX-314 Treated Patients Achieved a ≥2-Step Improvement in Disease Severity

Observational Control (n=5)



RGX-314 (n=15)



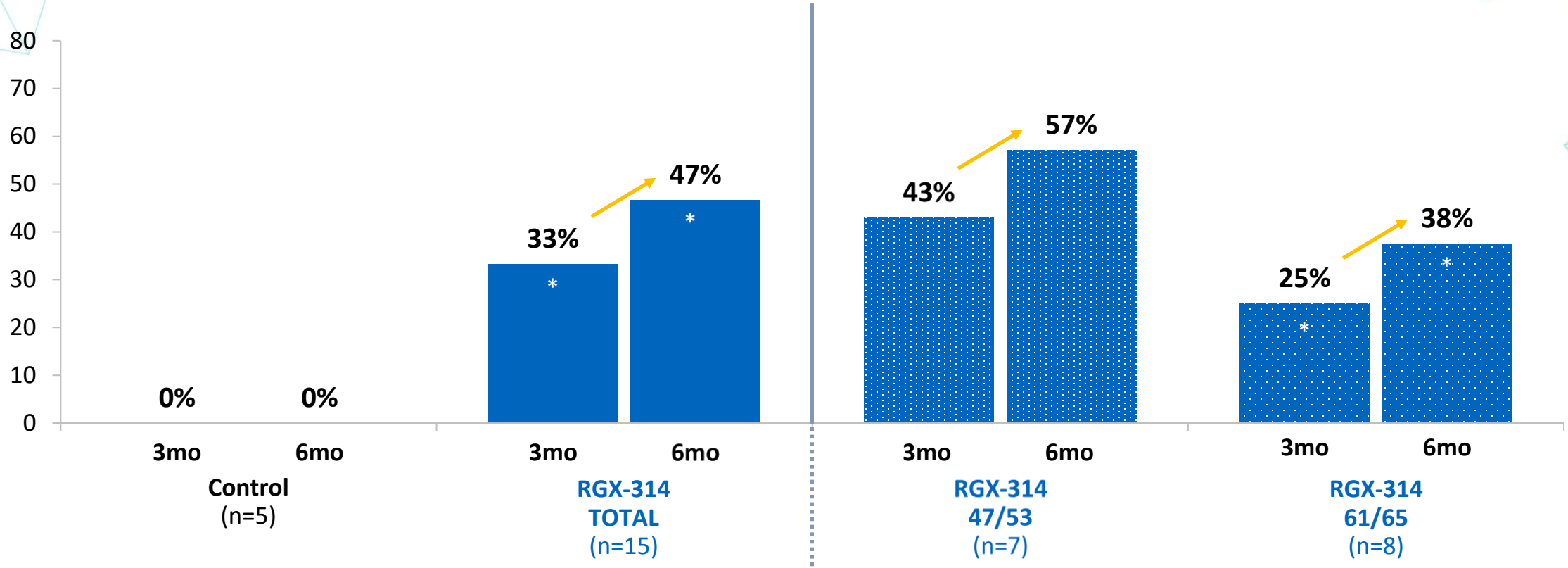
A **2-step improvement** in DRSS has been accepted as a **pivotal endpoint** by the **FDA** for **DR clinical trials**[3]

Data cut: January 18, 2022

1. One study eye (DRSS 61 at baseline) received a single Lucentis injection 8 days after RGX-314 dosing for trace vitreous hemorrhage, which was 10 weeks prior to their 3 month visit when DRSS was assessed.
2. One patient had a 4-step improvement.
3. Used in the approval of EYLEA® (aflibercept) and LUCENTIS® (ranibizumab) Source: AAO PPP 2019

Patients with ≥2 Step Improvement in Disease Severity at Months 3 and 6

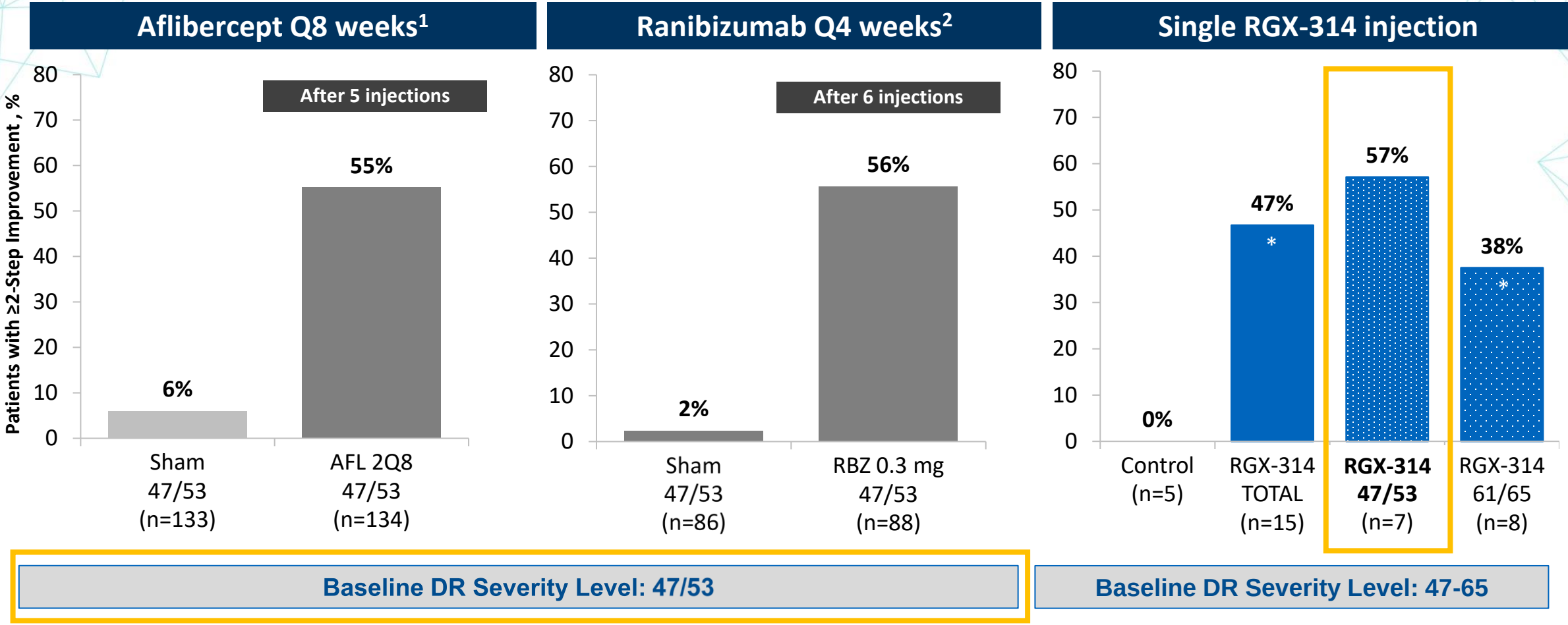
Cohort 1 RGX-314



Data cut: January 18, 2022.

*One patient had a 4-step improvement. Another 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 10 weeks prior to their 3 month visit when DRSS was assessed.

How Do ALTITUDE Cohort 1 DRSS Outcomes at 6 Months Compare to Frequent Injections of FDA-Approved Anti-VEGF?



Data cut: January 18, 2022

*One patient had a 4-step improvement. Another 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 10 weeks prior to their 3 month visit when DRSS was assessed.

1. Patients initially received 5 Q4 weeks loading doses followed thereafter by Q8 weeks dosing, per U.S. label instructions; EYLEA® (aflibercept) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc. March 2021.
2. Patients received Q4 weeks dosing of ranibizumab (RBZ), per U.S. label instructions; Wykoff CC et al. *Ophthalmology Retina*. 2018 DOI: (10.1016/j.oret.2018.06.005).

ALTITUDE Safety Summary: Cohort 1

- RGX–314 was **well-tolerated** (n=15)
  - 2 SAEs: not considered drug-related
    - Vitreous hemorrhage in an untreated *fellow eye*
    - Femur fracture
- **Common ocular TEAEs[1] in the study eye were not considered drug-related and were predominantly mild**:
  - Conjunctival hyperemia (3/15, 20%)
  - Conjunctival hemorrhage (2/15, 13%)
- One case of mild episcleritis reported 2-weeks post-dosing and resolved with topical corticosteroids
- **No intraocular inflammation** observed
  - No prophylactic corticosteroids administered
- **Stable BCVA**

	Observational Control (N=5)	Cohort 1 $2.5x10^{11}$ GC/eye (N=15)
Mean change in BCVA at M6	**-2.0 letters**	**+0.3 letters**

Data cut: January 18, 2022

1. Ocular TEAEs through 6-month visit, with common ocular TEAEs defined as ≥ 10% of RGX-314 treated study eyes.

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

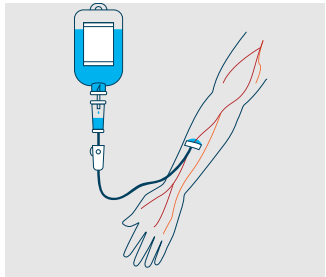
Designation: Orphan Drug Designation

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 months[1]
- 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

REGENXBIO®

[1] As assessed by muscle biospy in first 3 patients of each cohort

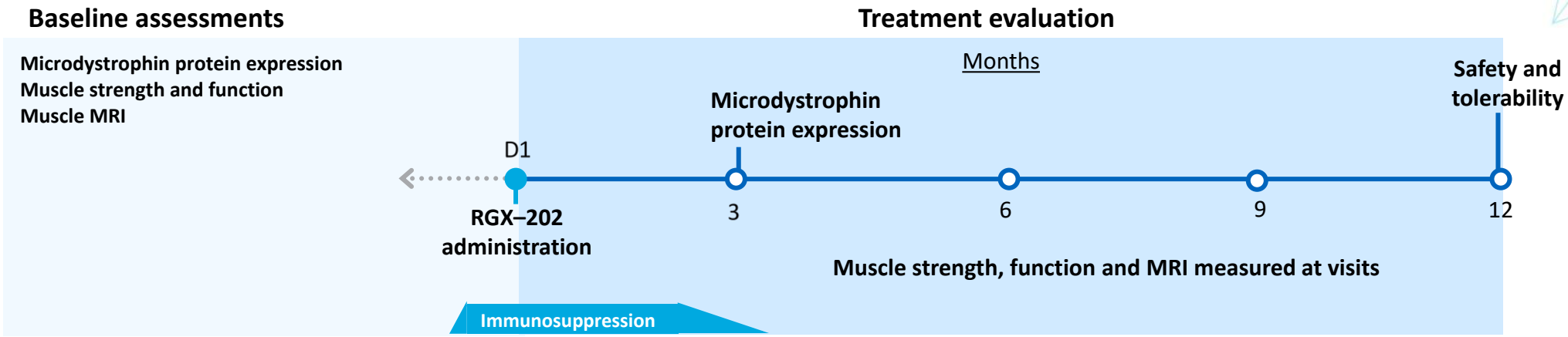
KEY INCLUSION CRITERIA and SAFETY MEASURES

- Males 4 to 11 years
- Ambulatory function
- *DMD* gene mutation between exons 18-58
- 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

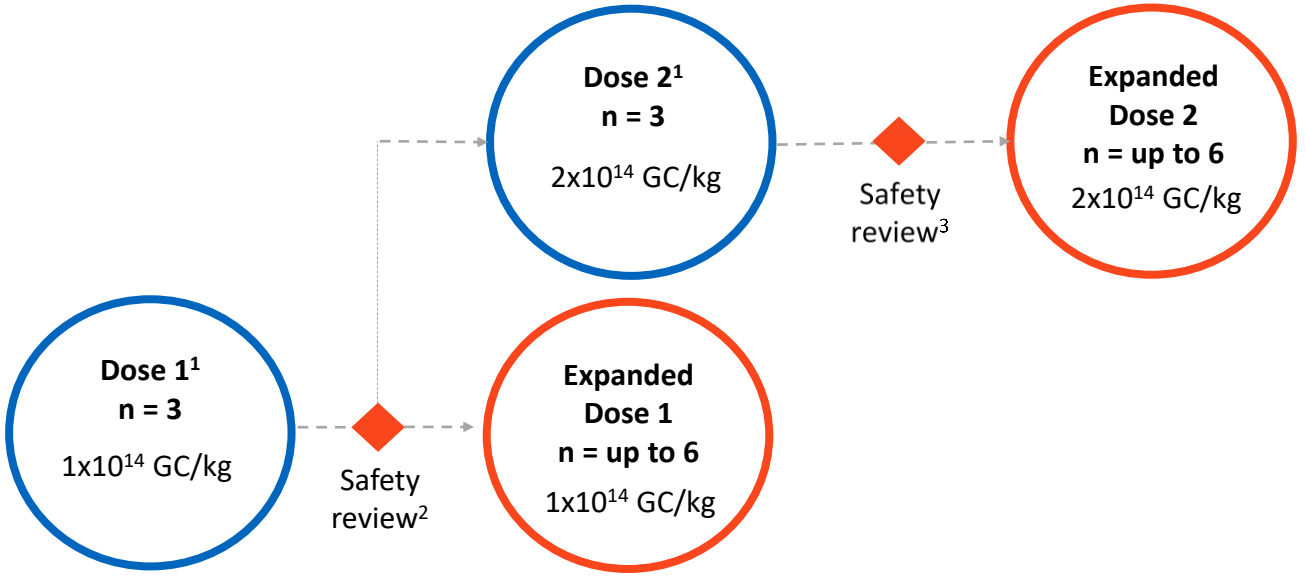
AFFINITY DUCHENNE™ clinical trial design

Administration and follow-up timeline



Dose escalation and dose expansion

Trial expected to initiate in 1H 2022

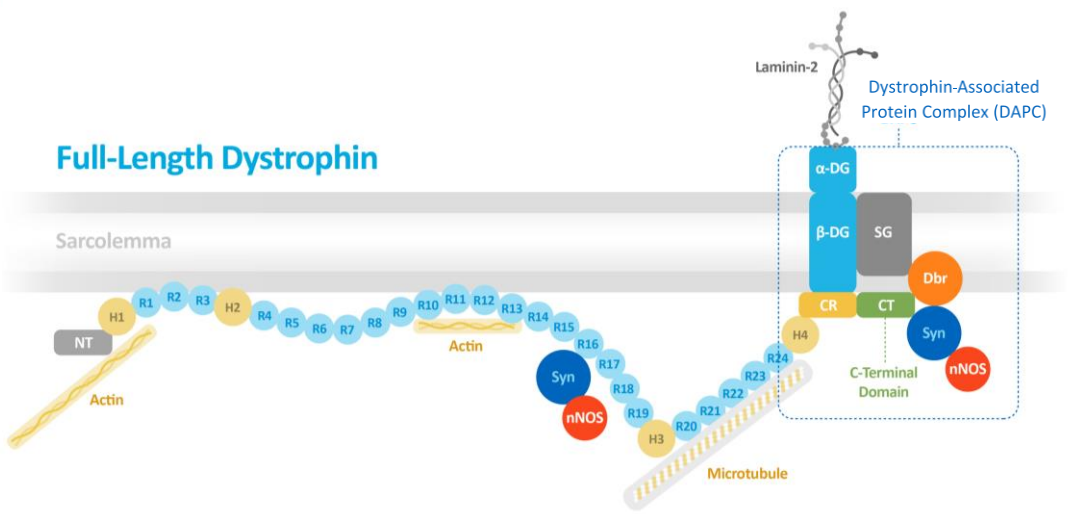


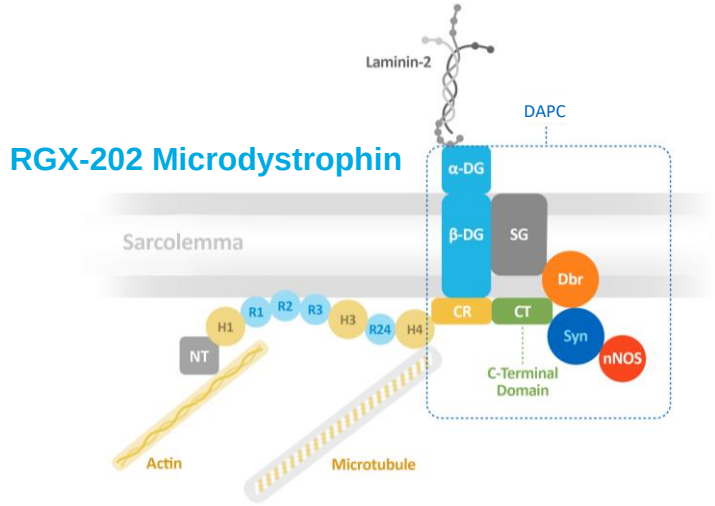
REGENXBIO®

[1]The first 3 patients in each cohort will be dosed in a staggered fashion, at least 4 weeks apart, following increasing body weight: ≤20kg, ≤30kg and ≤40kg
[2] Dose escalation safety review to occur four weeks after third patient in each cohort has been followed 4 weeks post-dosing

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

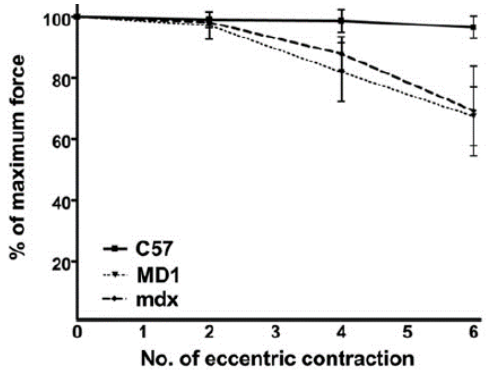
CT Domain recruits several key proteins to the muscle cell membrane (sarcolemma) including Syntrophin and Dystrobrevin, Neuronal nitric oxide synthase and other proteins[1]



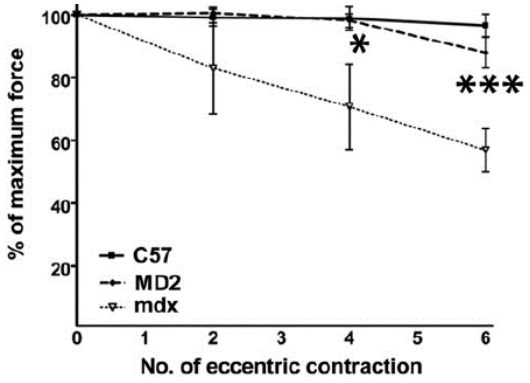


Presence of CT Domain in microdystrophin significantly improved the muscle resistance to lengthening contraction–induced muscle damage in *mdx* mice[2]

Construct without C-Terminal Domain



Construct with C-Terminal Domain



[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	ABD1 – H1 – R1 – R2 – R3 – H3 – R24 – H4 – CR – CT	4,734
Other Investigational Intervention (Example)			ABD1 – H1 – R1 – R2 – H3 – R22 – R23 – R24 – H4 – CR	

ABD1: Actin Binding Domain 1

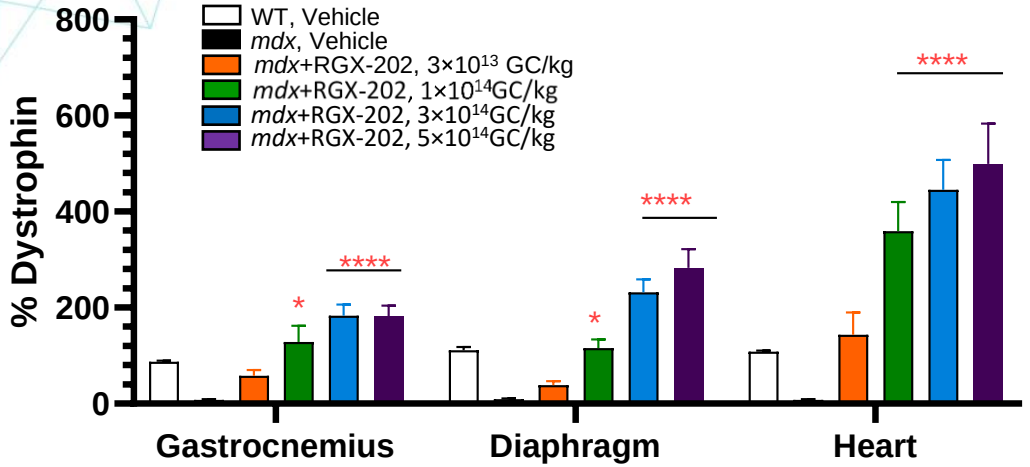
RGX-202 Features	Potential Benefits
Transgene for a novel microdystrophin includes extended coding region of dystrophin C-Terminal (CT) Domain	CT domain recruits key proteins, leading to improved muscle resistance[1]
Codon optimization and CpG content reduction	May improve gene expression, increase translational 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

REGENXBIO®

[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

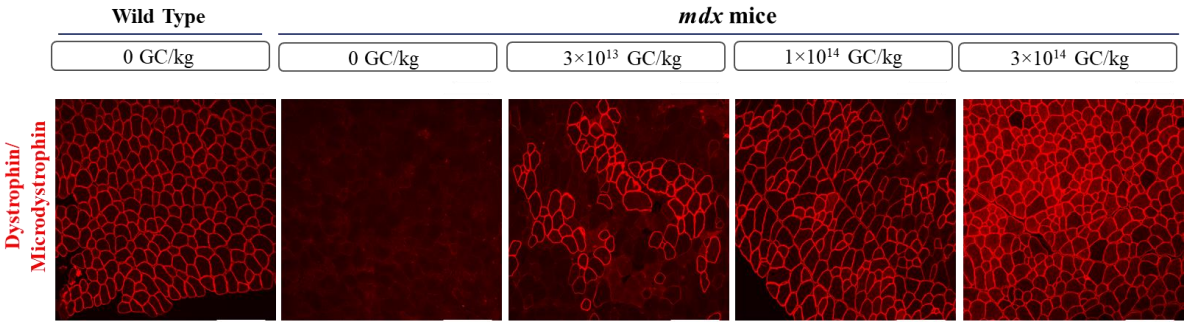
RGX-202 demonstrated robust expression of microdystrophin across skeletal and cardiac muscles along with recruitment of key proteins to the DAPC

RGX-202 Microdystrophin Expression in Muscle[1]

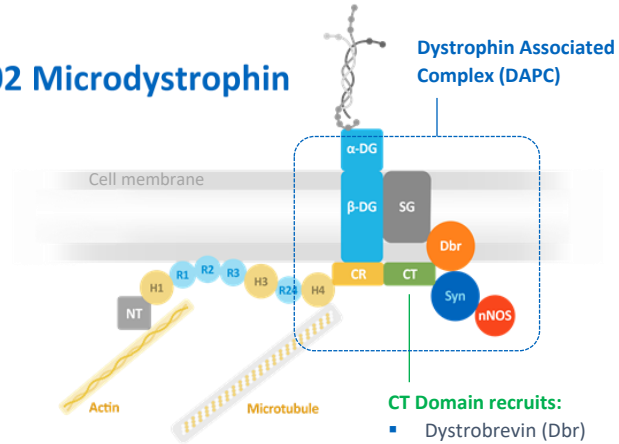


* p<0.05, **** p<0.0001 vs. vehicle control *mdx* mice

Immunohistochemistry of RGX-202 Microdystrophin in Muscle[2]



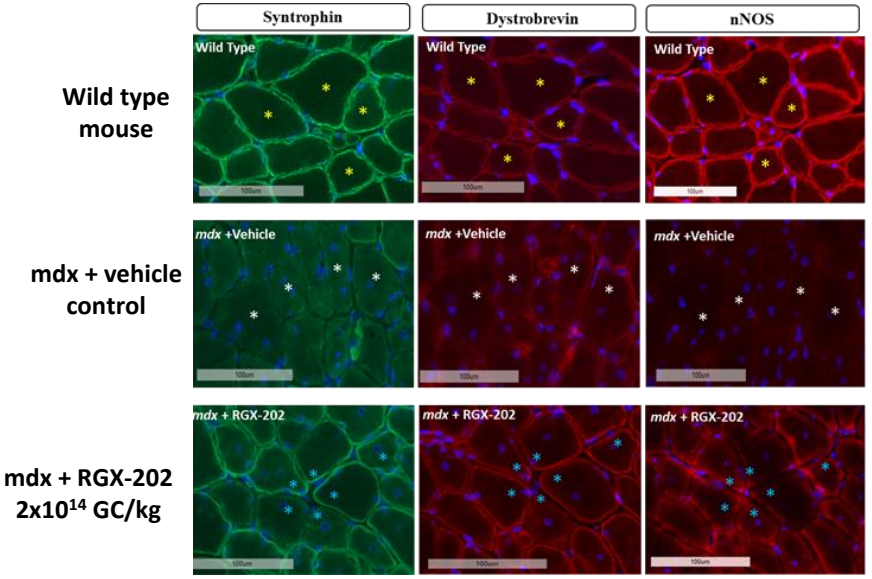
RGX-202 Microdystrophin



CT Domain recruits:

- Dystrobrevin (Dbr)
- Syntrophin (Syn)
- Neuronal Nitric Oxide Synthase (nNOS)

Immunohistochemistry of Dystrophin Protein Complex in Muscle[1]



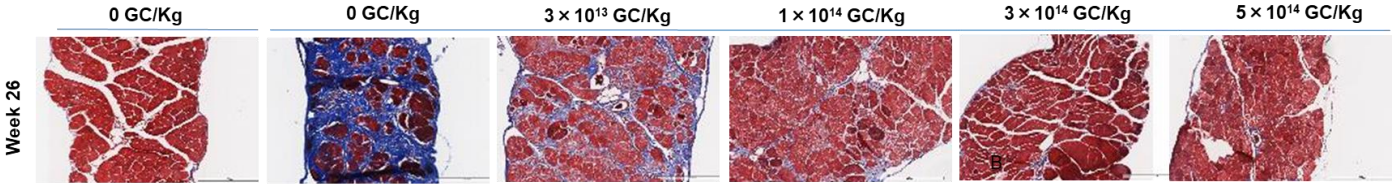
1 Kim S. et al., Poster Presented at WMS 2021 Annual Meeting, Sep 20-24, 2021

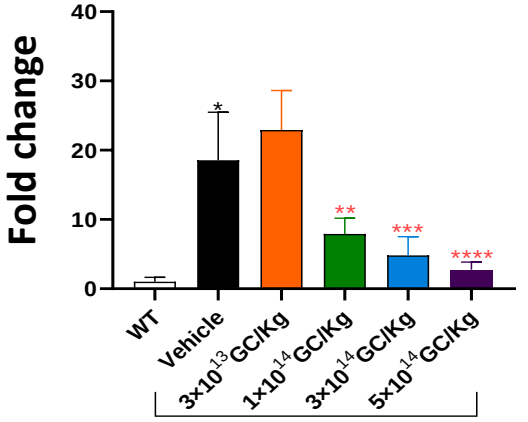
2 Data on File

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

RGX-202 demonstrated significant improvements in muscle pathology and function in *mdx* mice at doses ≥ 1x10^{14} GC/kg

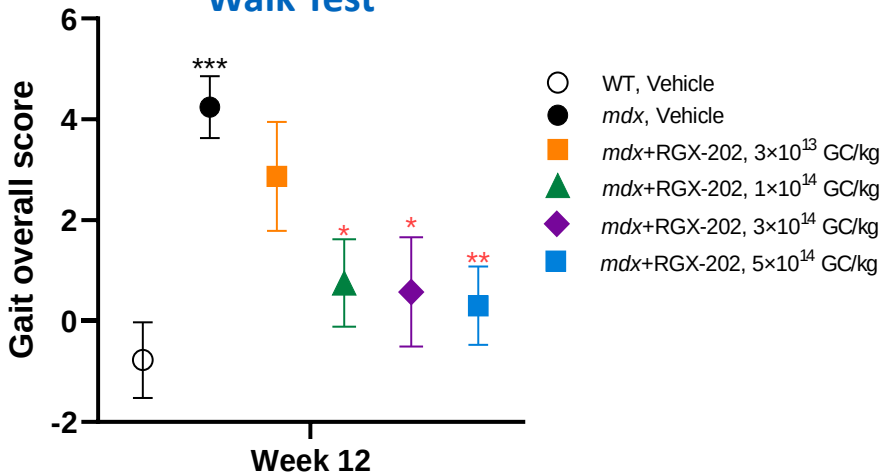
Muscle Pathology (Fibrosis)[1]





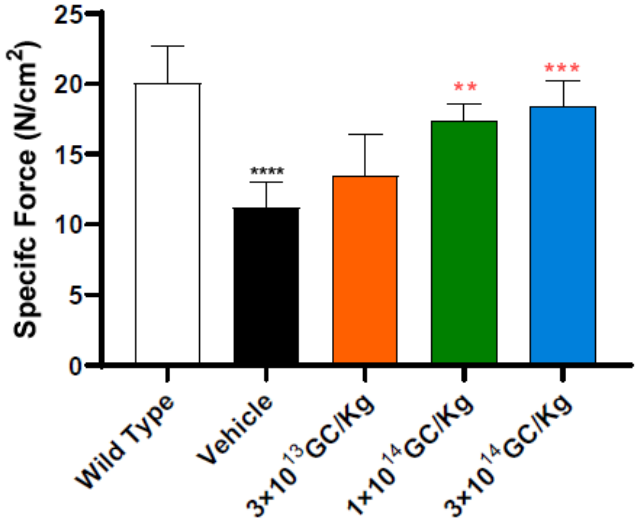
*p<0.05 vs. wild type; ** p<0.01, *** p<0.001, **** p<0.0001 vs. vehicle control *mdx* mice.

Walk Test[1]



*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 ± SEM

Muscle Force[2]



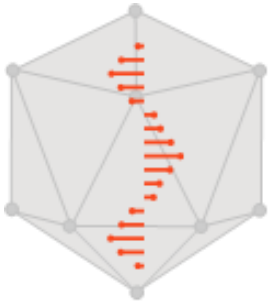
*p<0.05, **** p < 0.0001, vs. wild type vehicle. *p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001 vs. mdx vehicle, Comparisons are by 1-way ANOVA or Tukey or 2-way ANOVA and Tukey

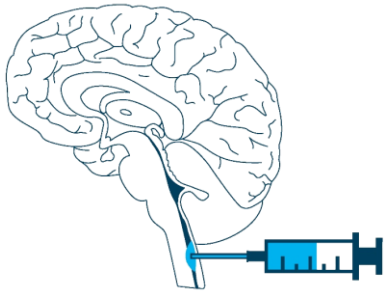
REGENXBIO®

1 Kim S. et al., Poster Presented at WMS 2021 Annual Meeting, Sep 20-24, 2021
2 Data on File

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	▪ 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	▪ 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	▪ 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	▲ Orphan Drug Designation ★ Rare Pediatric Disease Designation ■ Fast Track Designation	▲ Orphan Drug Designation ★ Rare Pediatric Disease Designation ■ Fast Track Designation	▲ Orphan Drug Designation ★ Rare Pediatric Disease Designation

RGX–121 Phase I/II clinical trial 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

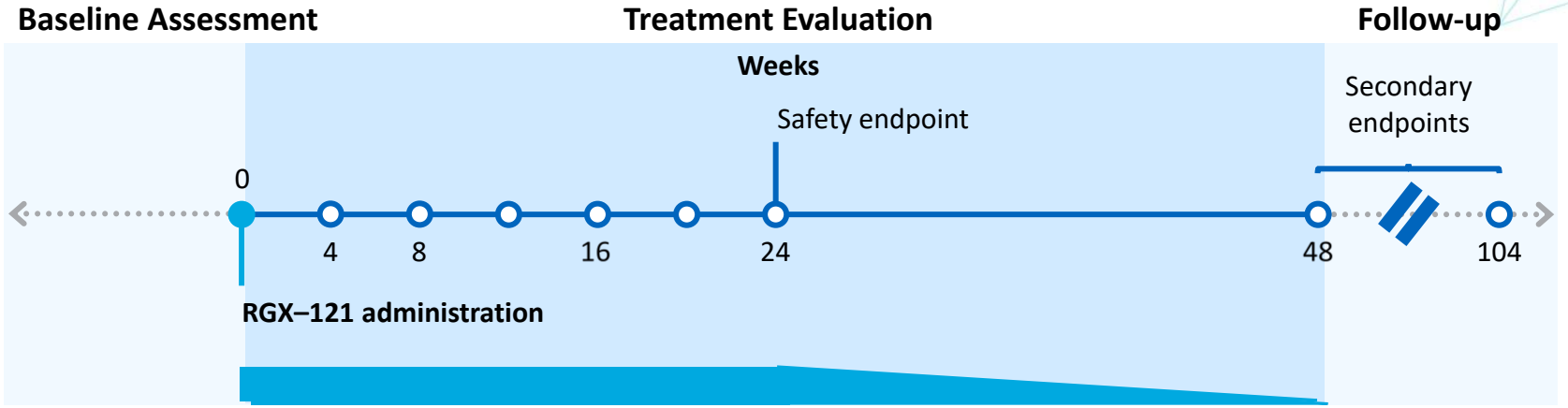
KEY INCLUSION CRITERIA

- 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

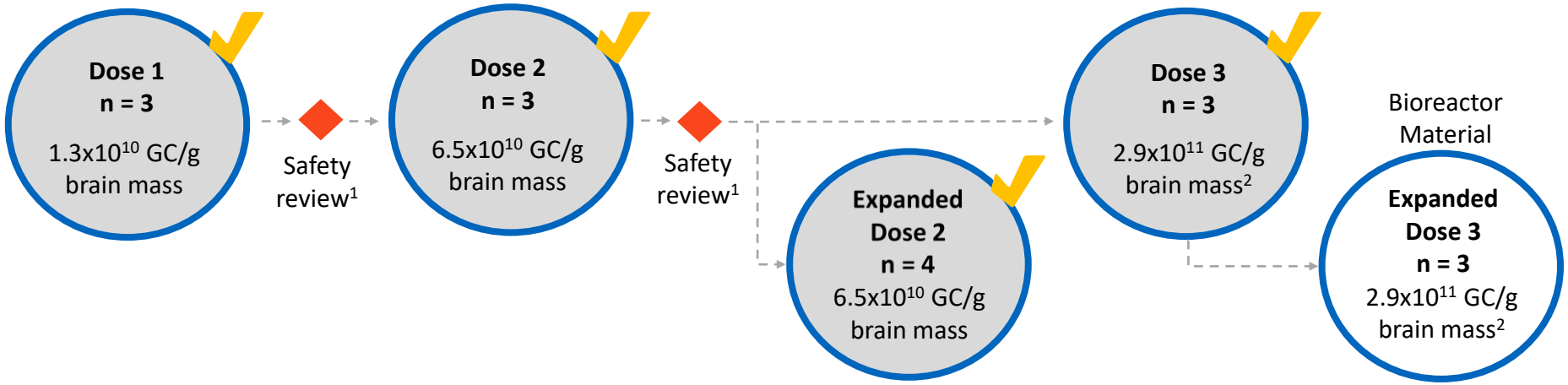
REGENXBIO

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

Administration and follow-up timeline



Dose escalation



Primary Dose 3 cohort completed in October 2021
Dose 3 expansion cohort using bioreactor material (commercial process) planned to start in Q1 2022

REGENXBIO®

* Dose Level 3 previously reported as 2.0 x10^{11} GC/g of brain mass of RGX-121 based on Poly-A-specific PCR assay. This is equivalent to 2.9x1011 GC/g of brain mass of RGX-121 using transgene-specific PCR assay.

RGX–121 Phase I/II Clinical Trial: Safety Update and Cohorts 1, 2, and 3 Data Summary

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

---

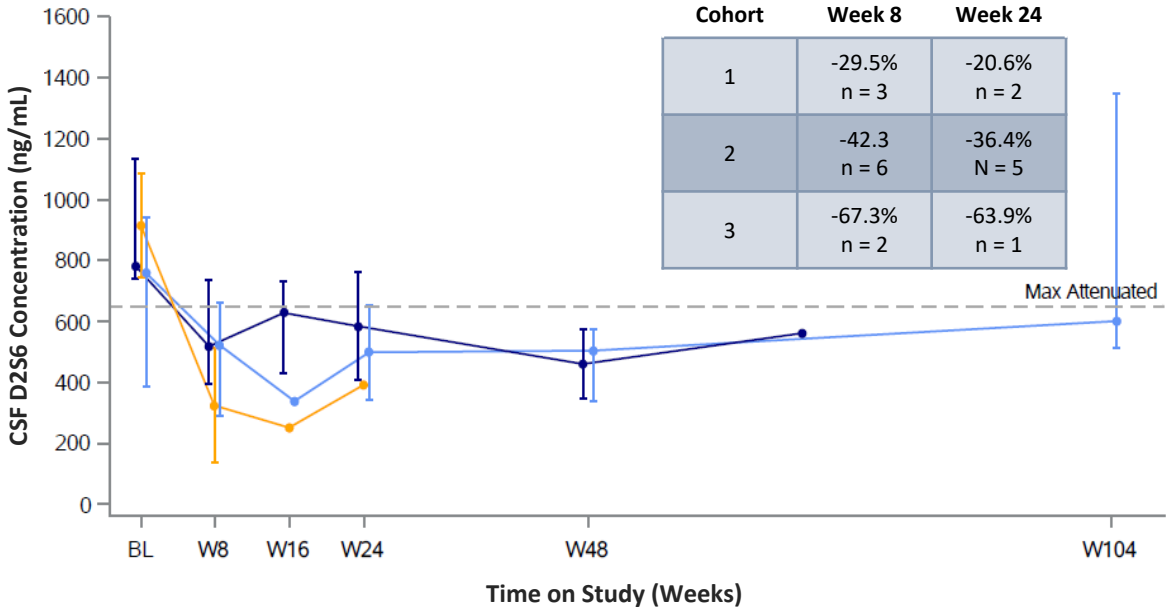
- **CNS biomarker and neurodevelopmental assessments indicate encouraging RGX-121 profile**
  - Dose-dependent reductions in CSF biomarkers demonstrated across 3 Cohorts
  - Cohort 3 CSF D2S6, a component of HS closely correlated with severe MPS II, approached normal levels
  - Improvements in neurodevelopmental function and caregiver reported outcomes in Cohorts 1 and 2 demonstrated CNS activity up to 2 years after RGX-121 administration

---

- **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

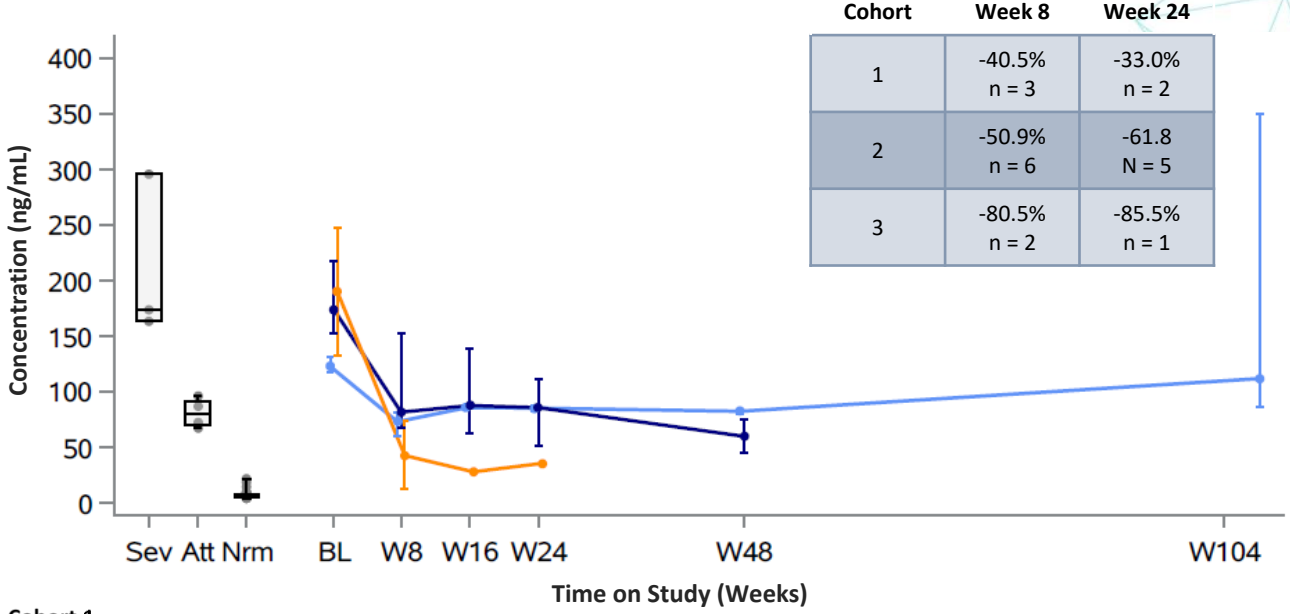
RGX–121 Phase I/II Clinical Trial: CSF HS and D2S6 measurements showed dose-dependent reductions in Cohorts 1-3 with Cohort 3 participants approaching normal levels in D2S6

Heparan sulfate (HS) in cerebral spinal fluid, Median*



Cohort	Week 8	Week 24
1	-29.5% n = 3	-20.6% n = 2
2	-42.3 n = 6	-36.4% N = 5
3	-67.3% n = 2	-63.9% n = 1

HS D2S6 disaccharide in cerebral spinal fluid, Median*



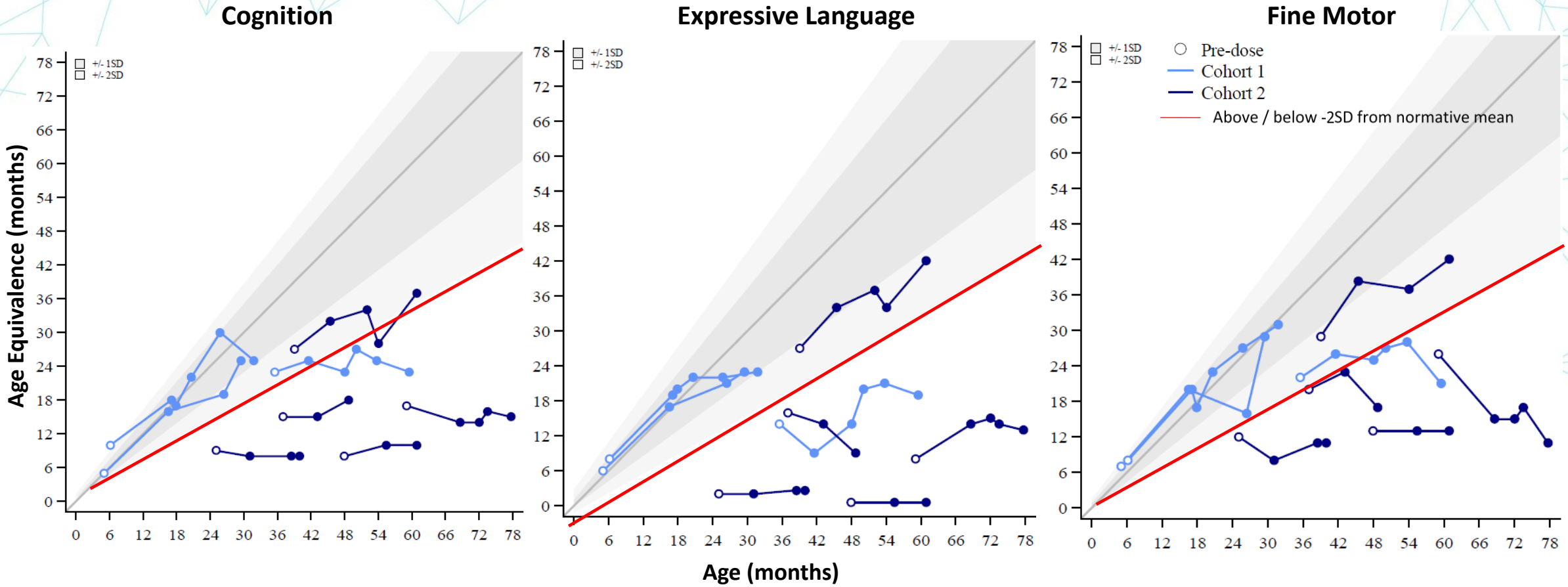
Cohort	Week 8	Week 24
1	-40.5% n = 3	-33.0% n = 2
2	-50.9% n = 6	-61.8 N = 5
3	-80.5% n = 2	-85.5% n = 1

Cohort 1
Cohort 2
Cohort 3

Data cut: December 20, 2021
* CNS related clinical event (ventriculoperitoneal shunt infection) took place on Day 522 post RGX-121 administration in this Cohort 1 patient that was deemed unrelated to study drug
† Median CSF HS concentration +/- Q1 and Q3 per cohort.
Normative data are based on 29 normal samples. The ages for 9 normative samples range from 1 month to 21 years old.
Severe defined as IQ < 70. The ages of 3 severe samples range from 4 years 8 months to 10 years old.
Attenuated defined as IQ ≥ 70. The ages of 4 attenuated samples range from 11 years to 29 years old.

RGX–121 Phase I/II clinical trial: Neurodevelopmental Function

Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III)



- 3 participants with cognitive function above -2 SD at baseline remained within 2 SD at the last assessment on the cognition, expressive language and fine motor subtests
- Minimal skill acquisition was demonstrated in participants with cognitive function below -2 SD at baseline

REGENXBIO®

Data cut: December 20, 2021

Participants separated by baseline function on cognitive subtest above and below -2 SD from the normative mean (red line)

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

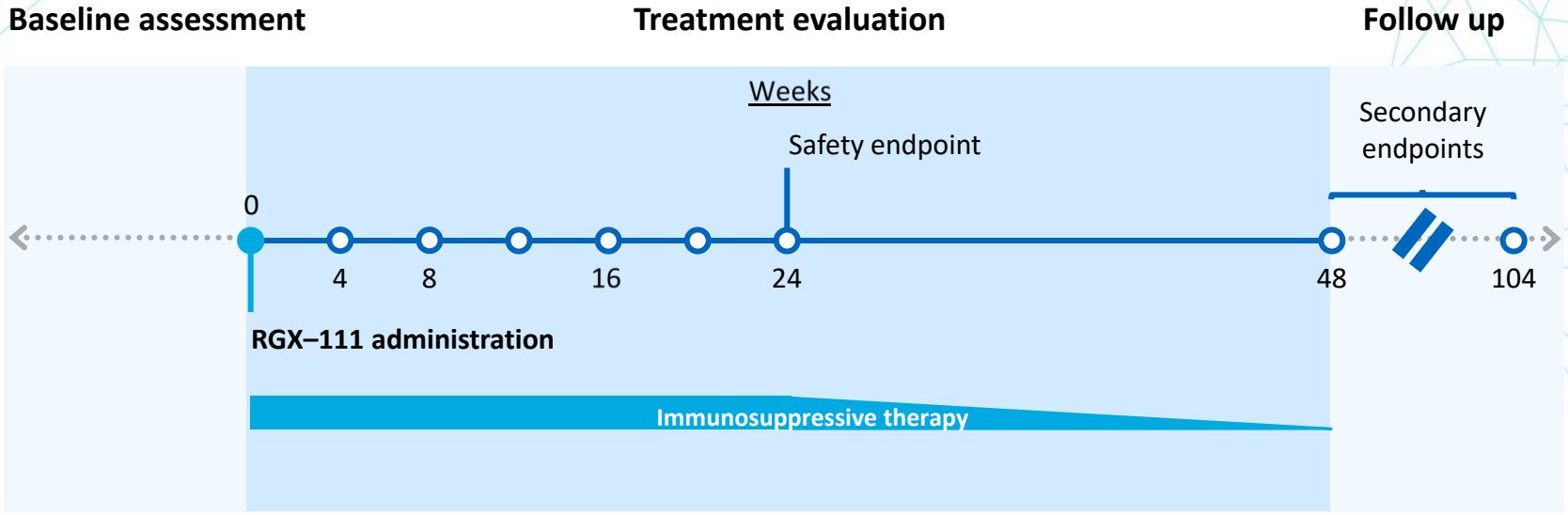
KEY INCLUSION CRITERIA

- 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

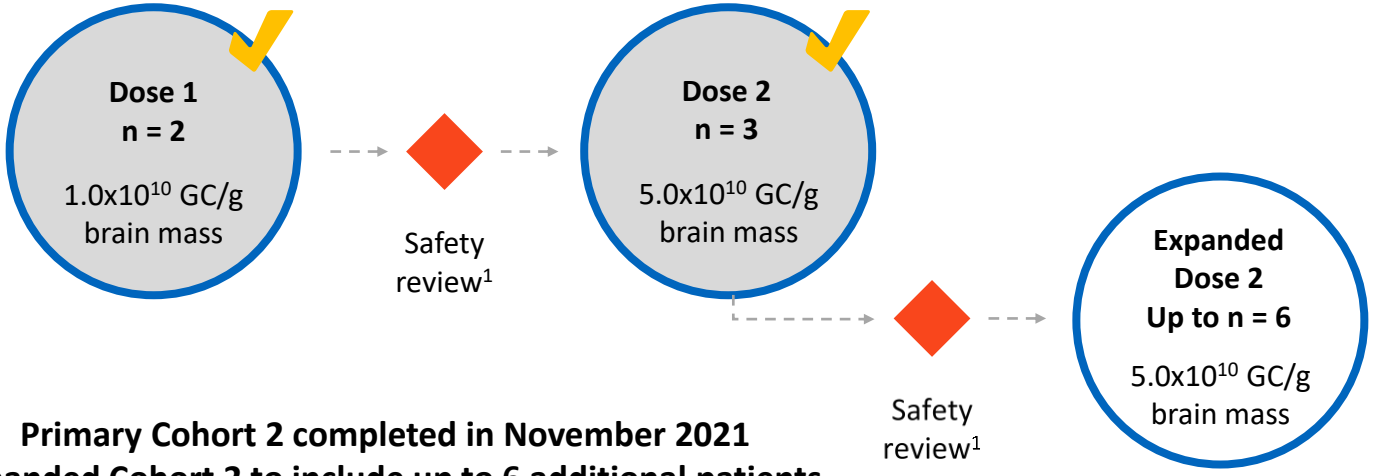
REGENXBIO

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

Administration and follow-up timeline



Dose escalation



Primary Cohort 2 completed in November 2021
Expanded Cohort 2 to include up to 6 additional patients

REGENXBIO®

[1]Dose escalation safety review to occur eight weeks after final subject in cohort has been dosed

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

- **Well tolerated following one-time RGX-111 administration**
  - A total of 6 participants dosed with RGX-111 with no SAEs related to study drug

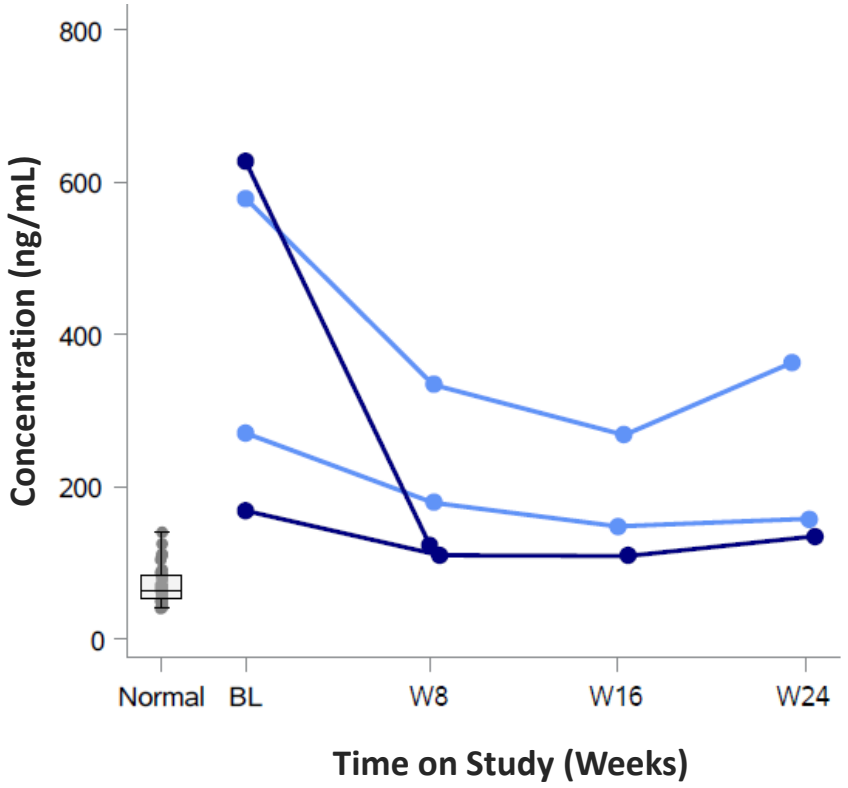
- **CNS biomarker and neurodevelopmental assessments indicate encouraging RGX-111 CNS profile**
  - CSF HS reduction and IDUA enzyme activity indicate CNS biological activity
  - Participants showed continued skill acquisition within 2 SD of normative mean on the cognition, expressive language and fine motor subtests at last assessment
  - Single patient IND participant at 42 months of age demonstrated higher age equivalent scores than available natural history data 20 months after RGX-111 administration

- **Emerging evidence of systemic biomarker activity after CNS administration of RGX-111**
  - Plasma I0S6 reductions observed following RGX-111 administration
  - Low levels of urinary GAGs maintained in all participants

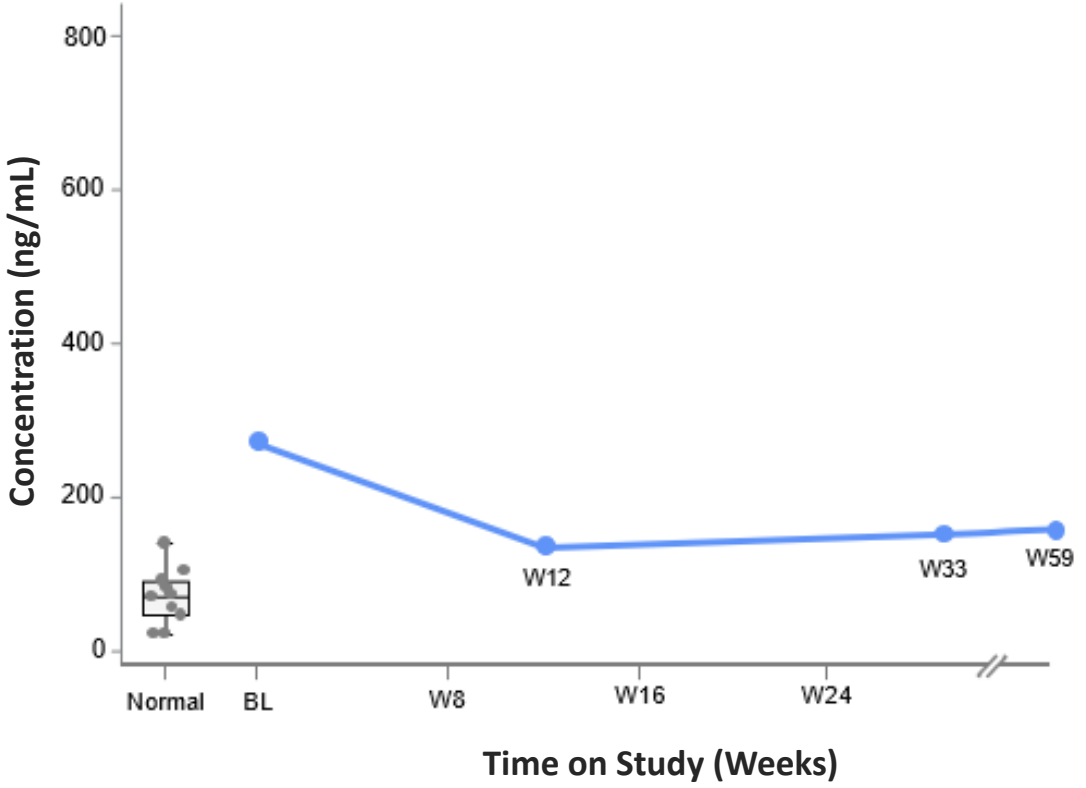
Data cut December 20, 2021
Single Patient IND: Patient dosed at 20 months of age at Dose 1

RGX–111 Phase I/II Clinical Trial and Single Patient IND: Biomarker Assessments Indicate Encouraging RGX-111 CNS Profile

Heparan sulfate (HS) in cerebral spinal fluid
Phase 1/2 Trial



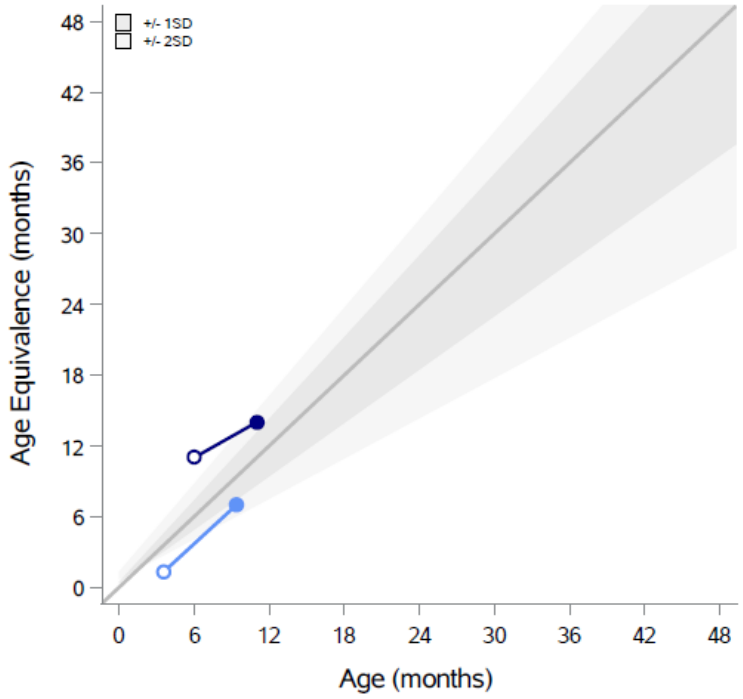
Heparan sulfate (HS) in cerebral spinal fluid
Single Patient IND



Decreased CSF heparan sulfate in all participants through last time point available

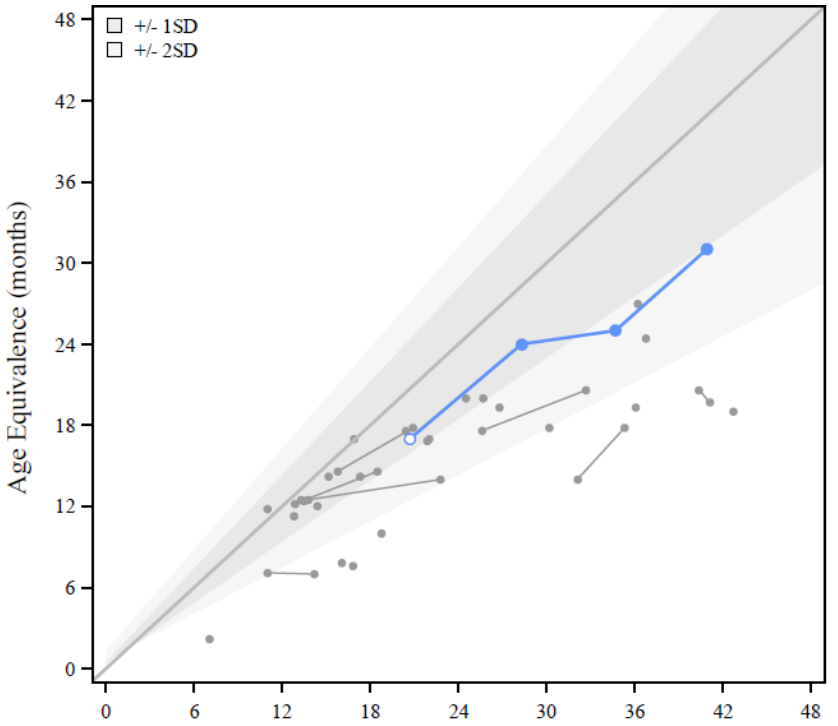
RGX–111 Phase I/II Clinical Trial and Single Patient IND: Neurodevelopmental Assessments Indicate Encouraging RGX-111 CNS Profile

Phase I/II trial neurodevelopment



All participants showed continued skill acquisition within 2 SD of normative mean on the cognition subtest at last assessment

Single patient IND neurodevelopment



Single patient IND participant at 42 months of age demonstrated higher age equivalent scores than available natural history data 20 months after RGX-111 administration*

Data cut: December 20, 2021

* Natural history data (Shapiro et al., 2018) gathered using BSID-II; RGX-111 single patient IND data gathered using BSID-III

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
- Higher gene transfer
- Longer-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

NOVARTIS	astellas	Lilly	Pfizer	BAYER
Takeda	ultragenyx	uniQure	lysogene	ESTEVE

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

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
- cGMP manufacturing facility expected to be operational in H1 2022; will enable production at bioreactor scales up to 2,000L
- Integrated approach will allow 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	FOXKISER, MSD
Olivier Danos, Ph.D.	EVP and Chief Scientific Officer	Biogen, cnrs
Vit Vasista	EVP and Chief Financial Officer	PRTM, MSD
Steve Pakola, M.D.	EVP and Chief Medical Officer	aerpio, amakem THERAPEUTICS
Curran Simpson	EVP, Chief Operations and Technology Officer	gsk, Human Genome Sciences
Ram Palanki, Pharm.D.	EVP, Commercial Strategy and Operations	Santen, Genentech A Member of the Roche Group
Patrick Christmas, J.D.	EVP, Chief Legal Officer	Lumara Health™, WELLSTAT THERAPEUTICS
Laura Coruzzi, Ph.D., J.D.	EVP, Intellectual Property	JONES DAY
Shiva Fritsch	EVP, Chief People Officer	NOVAVAX, Human Genome Sciences

Financial results and guidance

2021 FY financials as of 12/31/21 (mm)

Revenue:	$470.3
R&D expense:	$181.4
G&A expense:	$79.3
Net income:	$127.8
Basic share count:	42.8

2021 FY financial highlights

Ended 2021 with **$849.3 million in cash, cash equivalents and marketable securities**
Under terms of the partnership with AbbVie, REGENXBIO **received a $370 million upfront payment in Q4 2021, with potential to receive up to $1.38 billion in milestones**
Aggregate net proceeds of $216.1 million received from follow-on offering of common stock completed in January 2021

Program guidance and anticipated milestones

RGX–314	**Subretinal wet AMD:** 2 pivotal trials ongoing: ATMOSPHERE™ currently enrolling patients; ASCENT™ active and screening patients **Suprachoroidal wet AMD:** Cohort 5 enrollment ongoing, expected completion in 1H 2022 **Suprachoroidal DR:** Cohorts 2&3 enrollment ongoing, expected completion in 1H 2022
RGX-202	IND cleared; AFFINITY DUCHENNE™ expected to initiate in 1H 2022
RGX–121	**Phase I/II trial in patients up to 5 years old**: Cohort 3 expansion expected to start Q1 2022 **Phase I/II trial in pediatric patients over 5 years old**: ongoing
RGX–111	Phase I/II trial Cohort 2 expansion expected to enroll in 1H 2022

Financial guidance:

Based on its current operating plan, REGENXBIO expects its balance in cash, cash equivalents and marketable securities of $849.3 million as of December 31, 2021, to fund its operations, including the completion of its internal manufacturing capabilities and clinical advancement of its product candidates, into 2025.

Thank You