Rare Program Update

RGX-202 for the treatment of Duchenne Muscular Dystrophy
RGX-121 for the treatment of Mucopolysaccharidosis Type II

February 7, 2024

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Agenda

- **Welcome**
- **AFFINITY DUCHENNE® Phase I/II trial of RGX-202 for the treatment of Duchenne**
  - New interim results and update
- **CAMPSIITE® Pivotal trial of RGX-121 for the treatment of MPS II**
  - Topline results
  - Discussion with physicians
- **Q&A**
- **Summary of Next Rare Program Updates**

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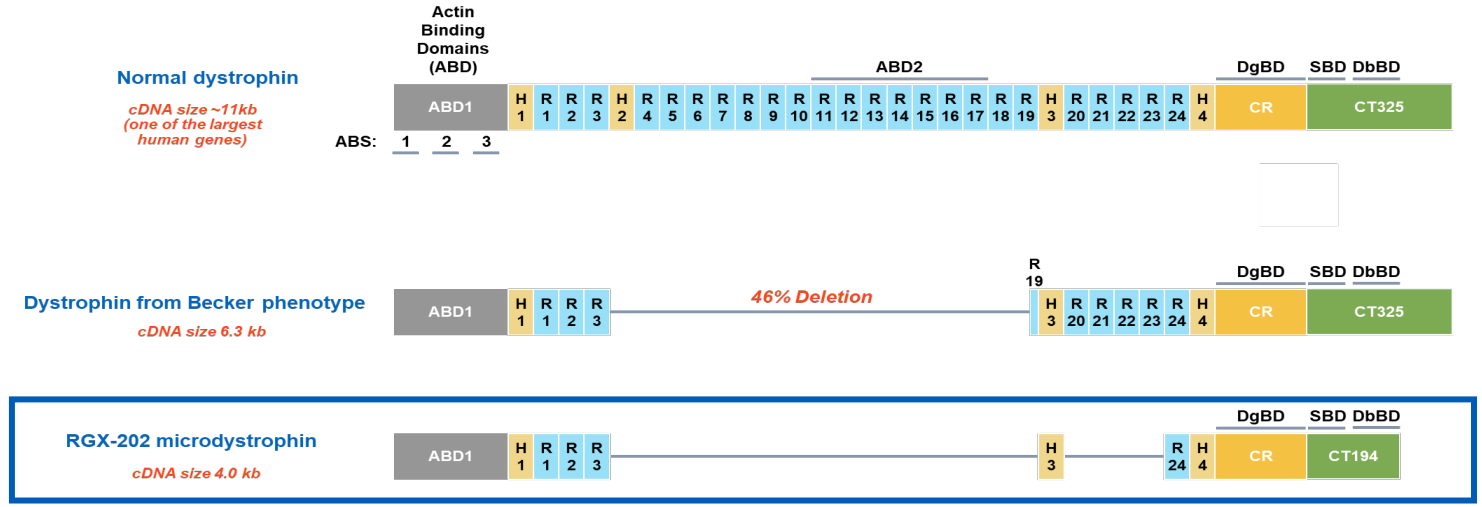
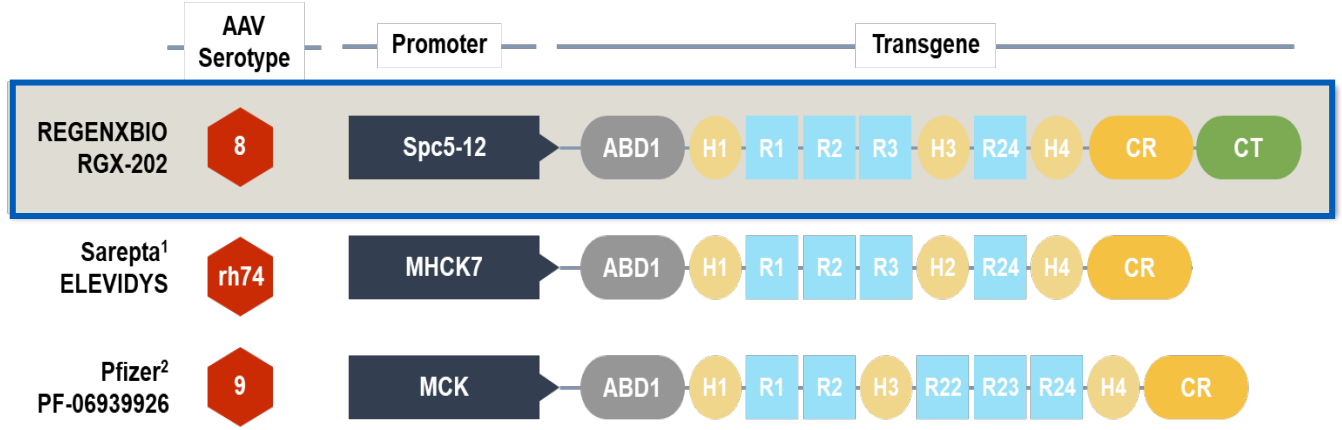
AFFINITY DUCHENNE® trial of RGX-202 for the treatment of Duchenne

New interim results and update

RGX-202 is Novel Among Current class of AAV- microdystrophins

RGX-202 expresses a new, differentiated microdystrophin with important biology that is the most similar to a natural shortened dystrophin found in boys and men that protects muscles from degenerating





RGX-202 is the only microdystrophin designed to deliver a transgene that includes the functional elements of the C-Terminal (CT) domain found in naturally occurring dystrophin.

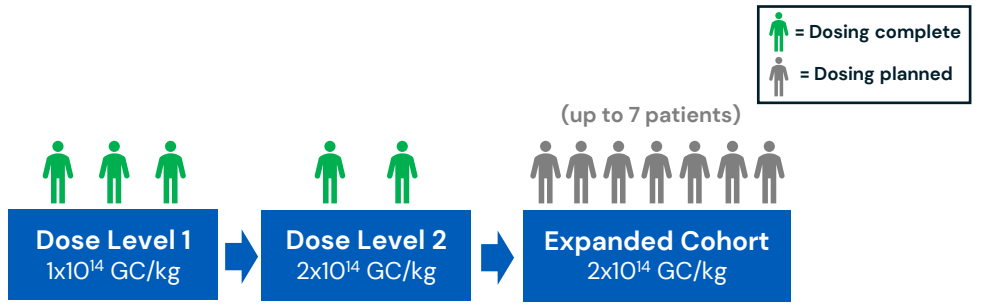
1. Harper (2002) Nat Med
2. Wang (2000) PNAS

RGX-202 Study Overview and Interim Safety

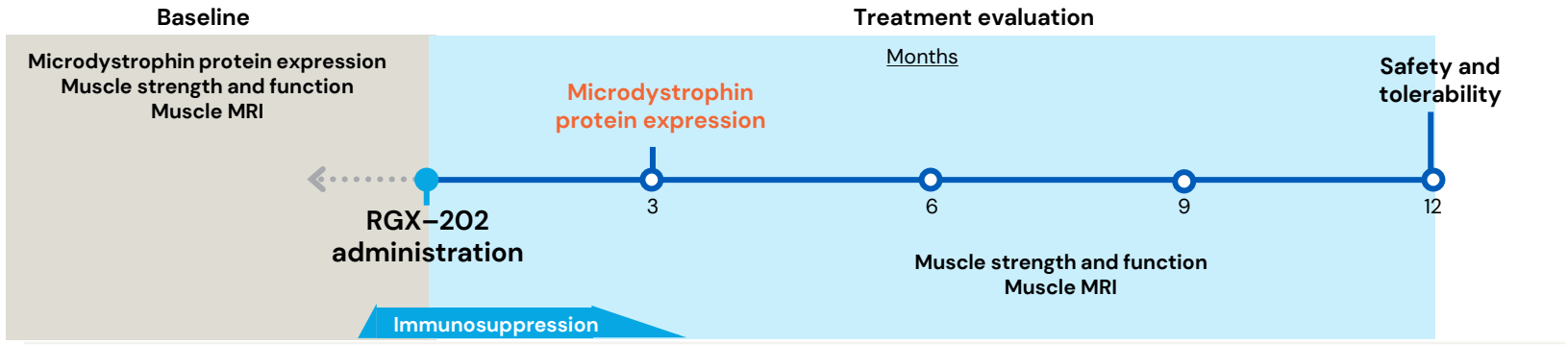
Key Eligibility Criteria

- **Boys aged 4 to 11 years**
- **Genetically confirmed DMD** (mutations in exons 18 and above)
- **100-meter walk:** able to perform it without assistive devices,
- **No pre-existing antibodies** to the gene therapy (AAV8 capsid)

Study Plan



Administration and Assessments Timeline



RGX-202 was well tolerated in five patients at both dose levels with no serious adverse events
Age at dosing: 4.4-12.1 years; Post-administration follow up: 3 weeks to 9 months

Patient 3 Interim Efficacy Data

- **Robust RGX-202 microdystrophin expression was observed at three months, with comparable results obtained via Western Blot and LC-MS**
- **Decrease in creatinine kinase (CK) levels at 10 weeks**

RGX-202 Microdystrophin Expression

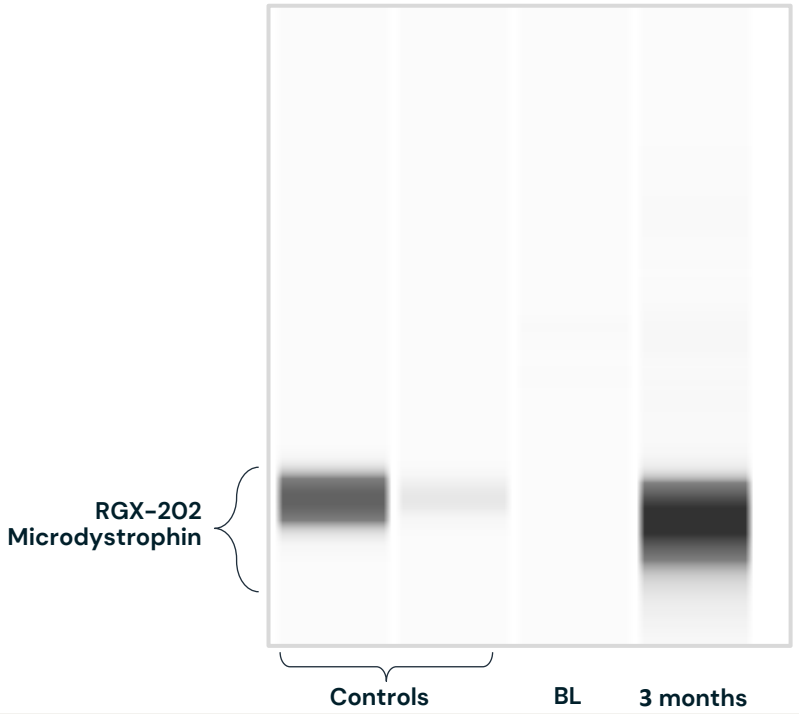
RGX-202 Microdystrophin (% Normal Control)	Patient 3 (6.6 yo, 26.8 kg)
Western blot (Jess method)	83.4

CK levels

	Avg Baseline	Week 10
CK Levels (U/L)	16,014	1,094
% Reduction	93%	

Elevated CK levels are associated with muscle injury and are uniformly elevated in patients with Duchenne

Western Blot (Jess)



LC-MS

Microdystrophin expression adjusted for muscle content
Control was level of wild-type (normal) dystrophin in normal muscle, and baseline was below the limit of quantification
Muscle biopsies are collected from bicep at baseline and 3 months post RGX-202 administration
Data cut date of February 6, 2024

Interim Efficacy Results Summary

Dose Level 1 (n=3)

- Robust RGX-202 microdystrophin expression observed
- Serum CK levels meaningfully decreased, representative of improvement in muscle disease
- RGX-202 microdystrophin localization to the sarcolemma supports the expected distribution in muscle tissue

Patient	Age at Dosing (years)	Weight at Dosing (kg)	Western blot (Jess method), RGX-202 Microdystrophin (% Normal Control)	CK Levels, week 10 (% reduction from baseline)
1	4.4	17.8	38.8	-43
2	10.5	28.3	11.1	-44
3	**6.6**	**26.8**	**83.4**	**-93**

Microdystrophin expression adjusted for muscle content
Control was level of wild-type (normal) dystrophin in normal muscle, and baseline was below the limit of quantification
Muscle biopsies are collected from bicep at baseline and 3 months post RGX-202 administration
Elevated CK levels are associated with muscle injury and are uniformly elevated in patients with Duchenne
Data cut date of February 6, 2024

CAMPSIITE® Trial of RGX-121 for the treatment of MPS II

Topline pivotal results

RGX-121 Gene Therapy for MPS II

High Unmet Need in MPS II

- MPS II is also known as Hunter Syndrome
- Inherited, X-linked recessive disease
- Caused by a deficiency of an enzyme called iduronate-2-sulfatase (I2S) which results in excess accumulation of glycosaminoglycans (GAGs)
- Causes systemic and CNS symptoms
- Reduced ability to eliminate GAGs in the brain, especially D2S6, leads to neurodegeneration, and early death
    - At least two-thirds of patients exhibit neuronopathic (CNS symptoms) MPS II
- Standard of care includes IV enzyme replacement therapy (ERT), which does not address CNS disease involvement

Potential of RGX-121 for MPS II

AAV9 Vector
+ *IDS* Transgene

FDA Designations:

- ▲ Orphan Drug Designation
- ★ Rare Pediatric Disease Designation
- ■ Fast Track Designation
- ✚ Regenerative Medicine Advanced Therapy Designation

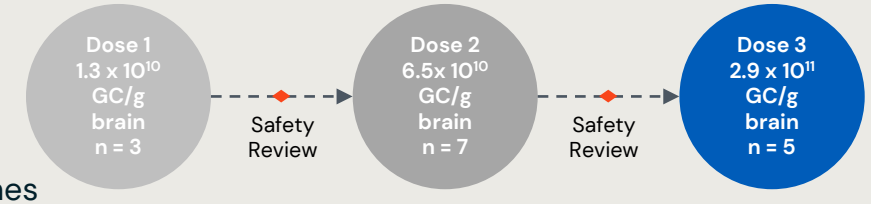
- Direct delivery of new gene to cells in the CNS for the restoration of full and normal functioning I2S enzyme
- Goal to reduce excess GAGs and prevent CNS disease progression
- CSF D2S6 levels have been shown to distinguish between neuronopathic and attenuated (no CNS symptoms) MPS II
- RGX-121 development program is using CSF D2S6 as a surrogate endpoint reasonably likely to predict clinical benefit
- RGX-121 effect may also reach other tissues and potentially reduce or eliminate need for IV ERT

D2S6 is a trisulfated disaccharide component of heparan sulfate.

CAMPSIITE® Phase I/II/III Study Design

CAMPSIITE Part 1, Dose Finding

- 15 neuronopathic patients dosed
  - ≥ 4 months to < 5 years
- Endpoints:
  - Safety
  - CSF D2S6
  - Neurodevelopment
  - Caregiver-reported outcomes
  - Systemic biomarkers
- Option to discontinue IV ERT at W52*

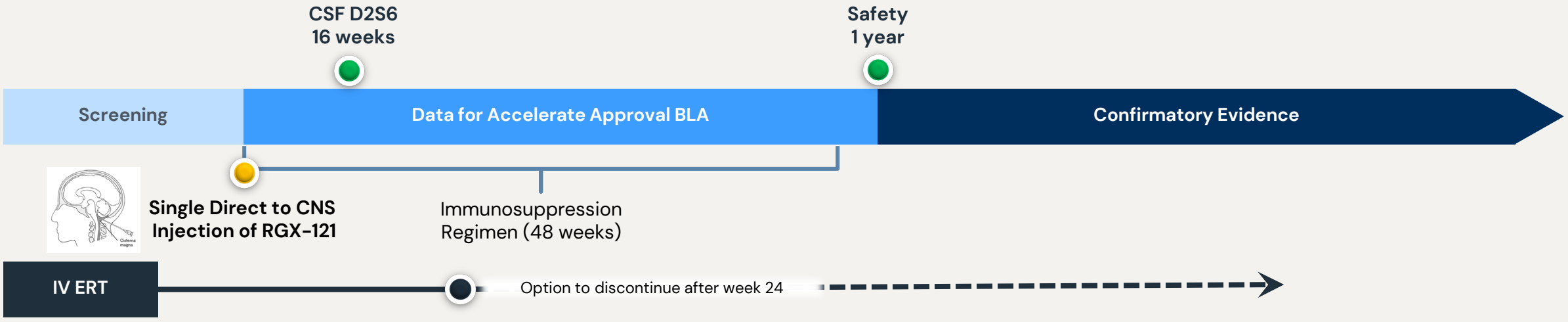


Pivotal Dose

CAMPSIITE Part 2, Pivotal

- 10 neuronopathic patients dosed
  - ≥ 4 months to < 5 years
- Primary Endpoint:
  - Proportion of patients with CSF D2S6 below maximum attenuated level at W16
- Secondary Endpoints
  - Neurodevelopment
  - Caregiver-reported outcomes
  - Systemic biomarkers
  - Safety

Pivotal Design



GC= genome copies
*Option to discontinue was changed to 24 weeks in May 2022 via protocol update

CAMPSIITE Part 1 – Updates

RGX-121 was well tolerated in 15 patients across 3 dose levels

CSF D2S6 levels were reduced to attenuated levels, approached normal levels at pivotal dose

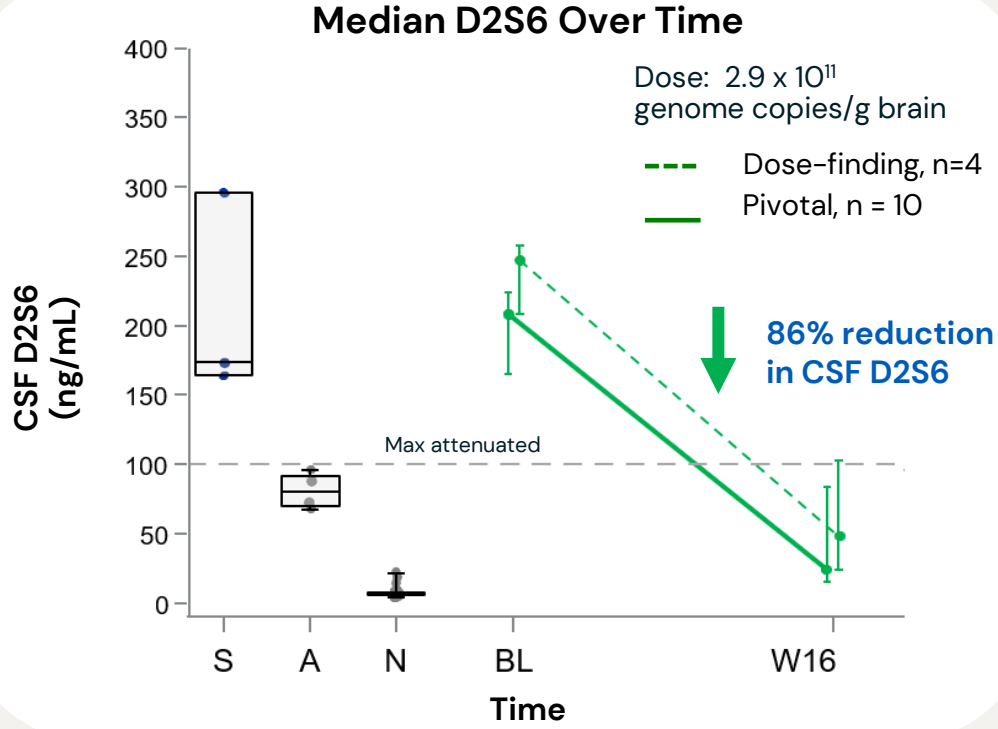
Neurodevelopmental skill acquisition was observed up to 4 years after RGX-121 administration

Investigators are choosing to discontinue IV ERT or allow participants to remain IV ERT naïve

CAMPSIITE Part 2 – Pivotal Trial Primary Endpoint Achieved

Primary Endpoint:
Proportion of Patients with CSF D2S6 below maximum attenuated level at W16

- Primary endpoint reached with statistical significance (p value of 0.00016)*
  - 8 of 10 pivotal patients demonstrated reductions in CSF D2S6 to below maximum attenuated levels
  - Other 2 pivotal patients also exhibited robust reductions in CSF D2S6 (55%, 85%)



Meaningful reductions in CSF D2S6, approaching normal levels

10 participants dosed as of July 31, 2023
Data cut January 3, 2024

* Response rate was compared to the margin of 20% (two-sided p value of 0.00016)
Median CSF D2S6 concentration +/- Q1 and Q3 per cohort.
(S) Severe (A) Attenuated (N) Normative

CAMPSIITE Pivotal – Summary and Next Steps

RGX-121 was well tolerated in 10 patients at pivotal dose

- Pivotal trial met CSF D2S6 primary endpoint with statistical significance
- CSF D2S6 is surrogate endpoint reasonably likely to predict clinical benefit for CNS disease
- Results support plans to file BLA in H2 2024 utilizing the Accelerated Approval pathway

Q&A

Accelerating Rare Disease Treatments in 2024

RGX-202 for treatment of Duchenne

Cohort 2 Complete + NEW Biomarker Results
Robust RGX-202 microdystrophin expression

Pivotal Topline:
CSF D2S6 primary endpoint reached with statistical significance (p value of 0.00016)*

Cohort 2 Biomarker Results:
DL2 safety supports expansion with parallel enrollment

Pivotal Dose Selection:
Make pivotal dose determination

Functional Results:
Initial strength and function assessment data for both dose levels

Pivotal Initiation:
RGX-202 microdystrophin as surrogate endpoint for clinical benefit

BLA Filing:
Using accelerated approval

RGX-121 for treatment of MPS II