PBGENE-DMD gene editing treatment leads to safe and long-term functional improvement in humanized DMD-disease mouse model

Adam Mischler, Whitney Lewis, Wendy Shoop, Traci Reddick, Dan Nazarenko, Nicole Heard, Ben Morris, Haley Grimason, Krsna Rangarajan, Cheng-Wei Wang, Kalpana Kodi, Dominique Burgess, Katie Poe, Gary Owens, Jeff Smith, Cassandra Gorsuch

All authors are employees of Precision BioSciences, Inc.

PBGENE-DMD is Designed to Provide Durable Functional Muscle Improvement for the Majority of Patients with Duchenne Muscular Dystrophy

- PERMANENT GENE CORRECTION
- EVIDENCE SUPPORTING INCREASING FUNCTIONAL IMPROVEMENT
- ENDOGENOUS EXPRESSION OF FUNCTIONAL DYSTROPHIN PROTEIN
- SATELLITE CELL EDITING FOR DURABLE BENEFIT
- TREAT UP TO 60% OF PATIENTS WITH DMD[1]

Differentiated Therapeutic Approach to Permanently Correct the Root Cause of DMD

PBGENE-DMD's Novel Mechanism Results in Gene Correction and Endogenously Expressed Functional Dystrophin Protein

Permanently Correcting the Root Cause

By removing a frequently-mutated region of the dystrophin gene, PBGENE-DMD corrects the reading frame at the DNA level and is broadly applicable for up to 60% of DMD patients

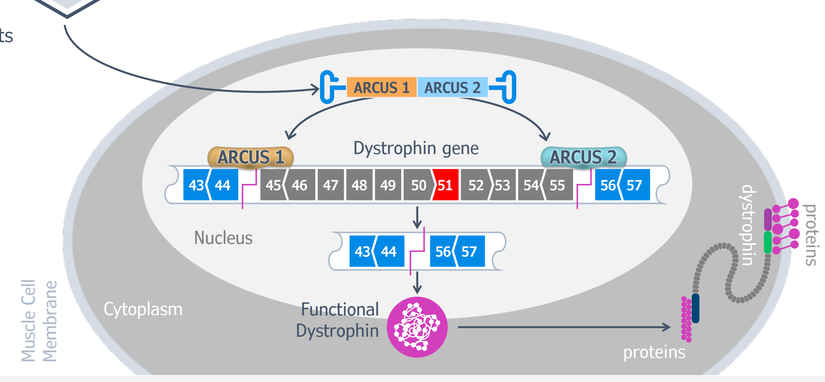
Naturally-Produced Functional Dystrophin Protein

PBGENE-DMD enables naturally-produced, near full-length, functional dystrophin closely resembling normal dystrophin

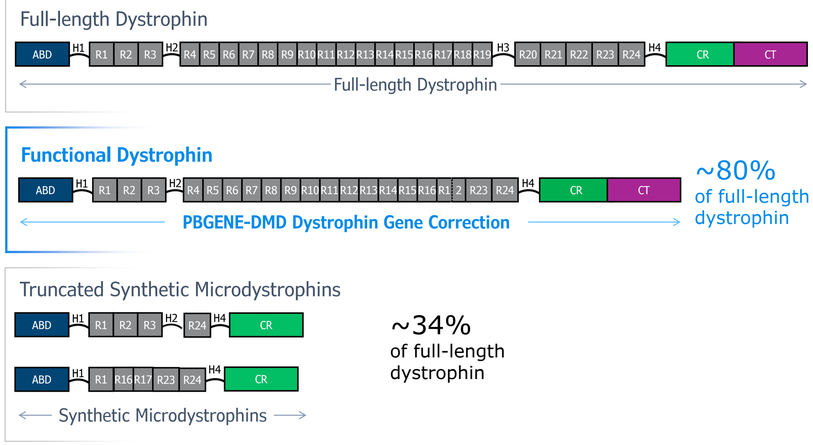
Durable Functional Muscle Improvement

PBGENE-DMD has been shown to significantly improve muscle function over time while also editing muscle satellite cells for durable therapeutic benefit

PBGENE-DMD: A single AAV encodes two ARCUS proteins designed to permanently edit a patient's own DNA sequence, resulting in natively-expressed, functional dystrophin



PBGENE-DMD Produces a Functional Dystrophin Retaining the Vast Majority of Full-length Dystrophin Protein Domains



PBGENE-DMD functional dystrophin is present in a subset of Becker patients with mild to asymptomatic phenotypes[1]

It is expected that as little as 5% expression of the functional dystrophin protein is needed to provide therapeutic benefit[2]

PBGENE-DMD Safety in GLP-Mouse Study

Study Design – 90-day study

Treatment	Dose Level (vg/kg)	Takedown (days)
PBGENE-DMD	5 x 10^{13}	7, 14, 30, 90
PBGENE-DMD	1 x 10^{14}	7, 14, 30, 90
PBGENE-DMD	1.25 x 10^{14}	7, 14, 30, 90
Vehicle	-	30, 90

Key Readouts:

- Histopathology
- Clinical Chemistry

Mice dosed at 3-4 weeks of age (equivalent to target patient population of 4-7 years old)
Disease mice are hDMDdel52/mdx, humanized DMD mouse model

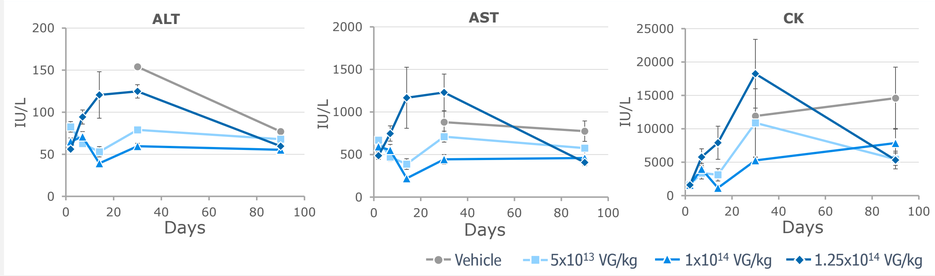
Improved Muscle Pathology After PBGENE-DMD treatment

Composite Injury Score

	Vehicle		PBGENE-DMD (1.25x10^{14} VG/kg)	
Day	30	90	30	90
Bicep Brachii	0.7	1.1	0.7	0.4
Diaphragm	1	1	0.8	0.9
Gastrocnemius	1.1	1.1	0.6	0.5
Quadriceps	1.3	1.3	0.9	0.8
Tibialis Anterior	0.4	0.6	0.3	0.3
Heart	0.4	0.1	0.1	0.1
Skeletal muscle (total)	0.9	1	0.7	0.6

Histopathologic findings for each tissue were graded subjectively and semi-quantitatively by a pathologist on a scale 0-5 (0 = unremarkable, 1 = minimal, 2 = mild, 3 = moderate, 4 = marked, 5 = severe)
Tissues were assessed for degeneration/regeneration, necrosis, mineralization and infiltrate. Composite muscle injury score averages the pathologic findings across all animals in each group for each muscle tissue.

Reduction in Serum Injury Biomarkers Following PBGENE-DMD Treatment by Dose Levels



Durable Improvements in Muscle Function with PBGENE-DMD Treatment

Study Design

Group	Mouse Model	N
PBGENE-DMD (3x10^{13} VG/kg)	Disease	10
PBGENE-DMD (1x10^{14} VG/kg)	Disease	10
Untreated	Disease	10
Untreated	Healthy	10

Key Readouts:

- Satellite Cell Imaging (ISH)
- Dystrophin Protein Restoration (WES)
- Dystrophin Positive Fibers (IF)
- Muscle Force Output

Mice dosed at 3 weeks of age (equivalent to target patient population of 4-7 years old)
Disease mice are hDMDdel52/mdx, humanized DMD mouse model
All functional readouts were conducted in vivo through Myologica

Editing Satellite Cells is Essential for Permanent Effect

In DMD where myofiber degeneration is continuous, editing satellite cells is essential for permanent therapeutic effect

Satellite cells are the resident stem cells in skeletal muscle and essential for muscle regeneration

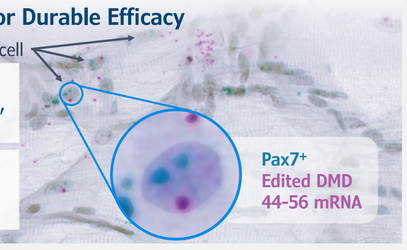
Myocytes

Myofiber

PBGENE-DMD Dystrophin Gene Correction Edits Muscle Satellite Stem Cells, Providing Potential for Durable Efficacy

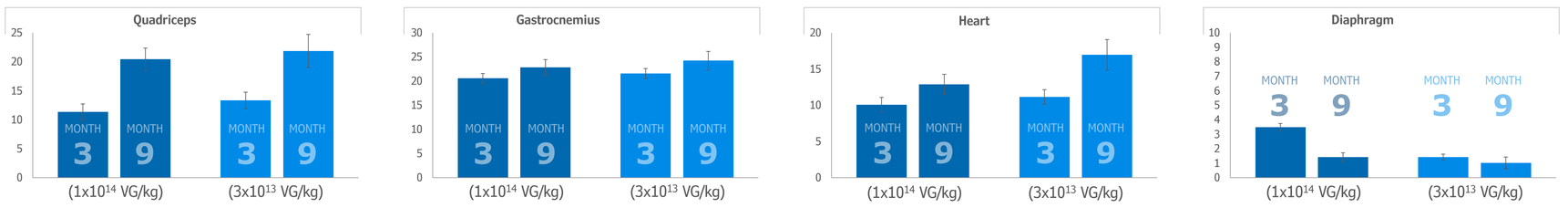
PBGENE-DMD has demonstrated *dystrophin* gene editing of satellite cells, beyond transient transduction

Observed edited dystrophin mRNA in PAX7+ cells, a marker for muscle satellite stem cells



PBGENE-DMD Restores Functional Dystrophin Protein Across Key Target Muscles

Dystrophin Restoration (%) in Treated Disease Mice



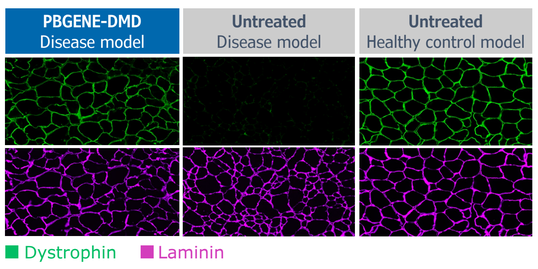
Achieved therapeutic levels of naturally-produced functional dystrophin protein within skeletal and cardiac muscle tissue

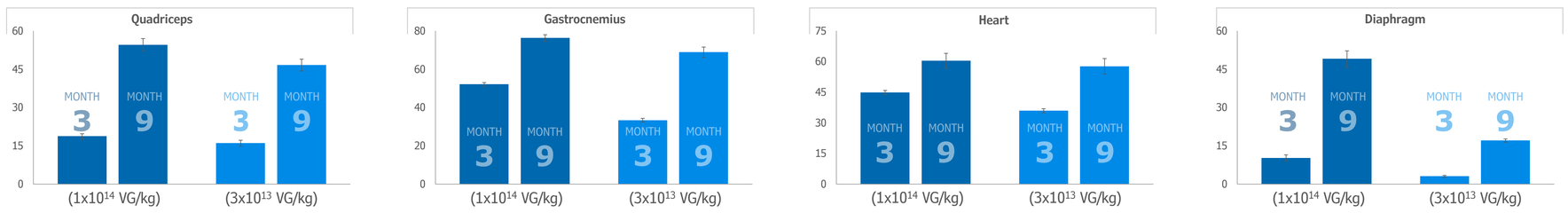
Durable and increasing dystrophin protein levels in skeletal and cardiac muscle tissue out to 9 months

Diaphragm and intercostal muscles contribute to respiratory function. We observed strong editing efficiency in the intercostals similar to other skeletal muscles (data not shown)

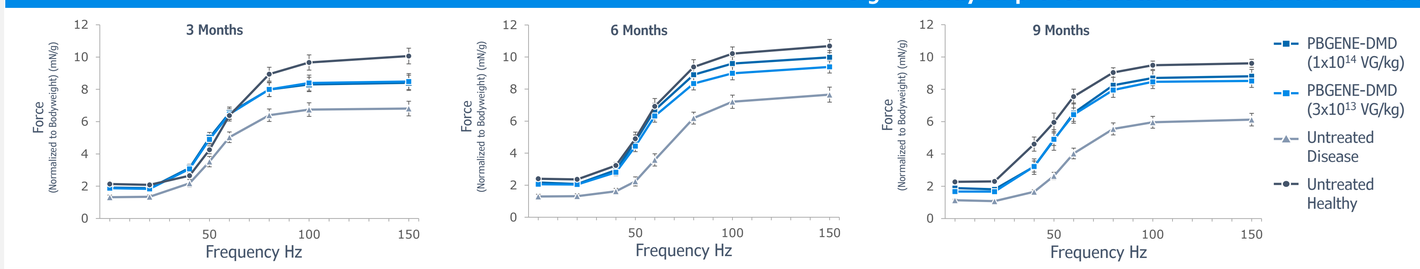
Broad and increasing levels of dystrophin-positive muscle fibers across skeletal and cardiac muscles, potentially from satellite cells

Percent of Myofibers Expressing Functional Dystrophin in Treated Disease Mice



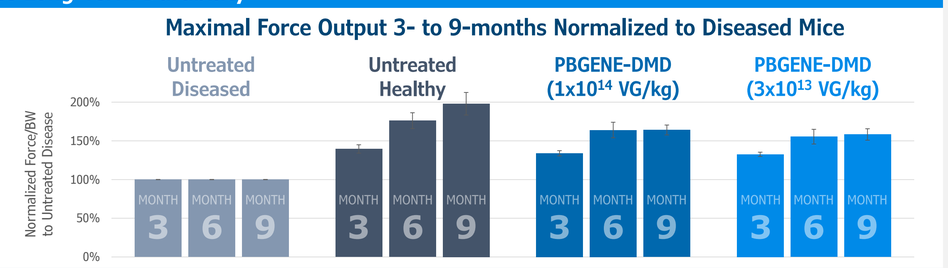


PBGENE-DMD Significantly Improves Muscle Function and Demonstrates Long-Term Durability



6-month timepoint shows an improvement in functional outcome vs. 3-month timepoint;
Improvement in muscle force output is maintained out to 9 months post PBGENE-DMD treatment

Maximal Force Output 3- to 9-months Normalized to Diseased Mice



PBGENE-DMD-treated mice maintained 81-84% of the maximal force output and 89-92% tetanic force output observed in healthy mice through 9 months

PRECISION BIOSCIENCES

1. Taglia et al. Acta Myol. 2015. (1):9-13. **2.** Feraudy et al. Ann Neurol, 2021 Feb;89(2):280-292.

MDA Clinical & Scientific Conference | 8-11 March 2026 | Orlando, FL