Chugai Information Meeting on Gene Therapy for Duchenne Muscular Dystrophy

June 17, 2026

CHUGAI PHARMACEUTICAL CO., LTD.

Important Reminders

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Information regarding pharmaceuticals (including products under development) is included in this presentation, but is not intended as advertising or medical advice.

Please note that Japanese is the preferred language in expression and content, since the official language of this presentation is Japanese.

Agenda

01	Overview of Elevidys for Intravenous Infusion	Elevidys Lifecycle Leader, Chugai Pharmaceutical Co., Ltd. Yoko Sano
02	Duchenne Muscular Dystrophy (DMD): Disease and Treatment, Clinical Framework for Gene Therapy, Appropriate Use, and Clinical Positioning	Translational Medical Center National Center Hospital, National Center of Neurology and Psychiatry Hirofumi Komaki, M.D., Ph.D., Director

CHUGAI PHARMACEUTICAL

A member of the Roche group

Overview of Elevidys for Intravenous Infusion

Approval Number: 30700FZX00001000

Product approved under Type 1 Use Regulations for Living Modified Organisms

Newly Launched

Viral Vector Product

Regenerative Medical Product, Readministration Not Allowed, Conditionally and Time-Limited Approved Product

Listed on the NHI Reimbursement Price List

Elevidys® Intravenous Infusion

Elevidys delandistrogene moxeparvovec

delandistrogene moxeparvovec

® Registered Trademark

Chugai Pharmaceutical Co., Ltd.

Yoko Sano, Elevidys Lifecycle Leader

Development History

Elevidys
delandistrogene
moxeparvovec

Development History

Elevidys (generic name: delandistrogene moxeparvovec) is a gene therapy vector product developed for the treatment of Duchenne muscular dystrophy (DMD).

Elevidys was co-developed by Sarepta Therapeutics, Inc. and F. Hoffmann-La Roche Ltd., and received regulatory approval in the United States in June 2023 for the treatment of DMD. In Japan, based on results [1)] from a global Phase III clinical study in ambulatory boys with DMD aged 4 to 7 years, it received regulatory approval in May 2025 as the first gene therapy product for DMD※.

As of May 2026, it has been approved in nine countries for the treatment of ambulatory DMD.

In Europe, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommended against granting conditional approval, and the European Commission (EC) endorsed this recommendation in September 2025. Roche is planning a new global Phase III study.

※This product was designated by the Ministry of Health, Labour and Welfare on July 30, 2024, as an orphan regenerative medical product for “Duchenne muscular dystrophy” (Designation No.: (R2 Saisei) No. 16). In addition, this product is under conditional and time-limited approval, and its efficacy, effect or performance is limited to patients who meet all of the following criteria: “patients who are negative for anti-AAVrh74 antibodies,” “ambulatory patients,” and “patients aged 3 years or older and younger than 8 years.”

1) Review data at the time of approval [Multinational Phase III clinical study in patients with DMD (SRP-9001-301)]

Principles and Mechanism

Elevidys
delandistrogene
moxeparvovec

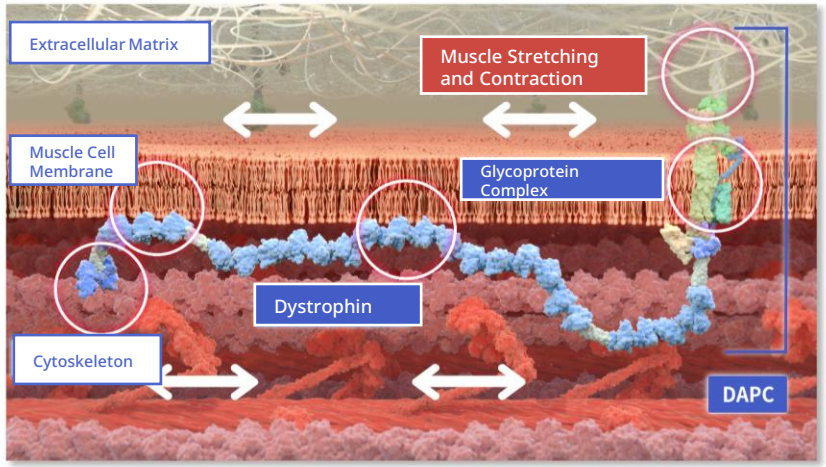
Cause of DMD

- DMD is a neuromuscular disorder caused by mutations in the dystrophin gene and follows an X-linked recessive inheritance pattern.[1)]
- When there are mutations in the dystrophin gene, “dystrophin,” the protein produced from the dystrophin gene, is absent, or abnormal dystrophin is produced. Dystrophin is expressed in various muscle tissues and forms the dystrophin-associated protein complex (DAPC), linking the cell membrane and extracellular matrix to the cytoskeleton of muscle fibers. [2)]
- When dystrophin is absent, the muscle cell membrane becomes unstable, leading to muscle cell damage and, consequently, decreased muscle strength. [3)]

(Illustration)

In the absence of mutations in the dystrophin gene

Dystrophin Expression

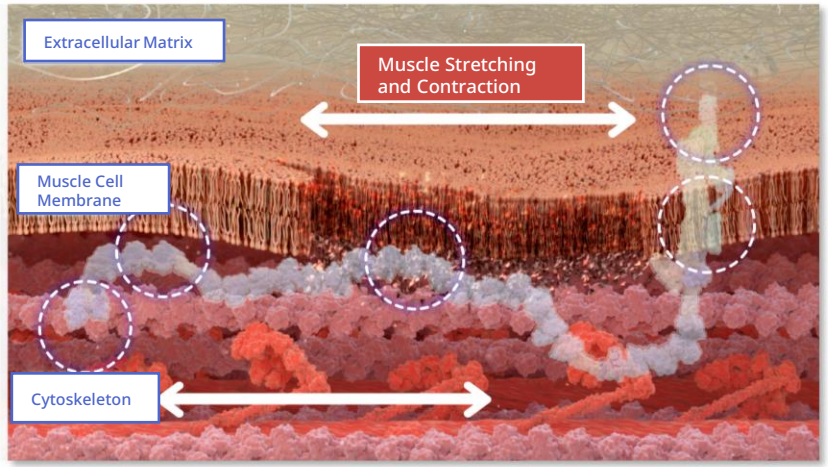


DAPC formed by dystrophin and the glycoprotein complex links the extracellular matrix and the cytoskeleton of muscle fibers, preventing damage to the muscle cell membrane during muscle stretching and contraction

Maintains the integrity of the muscle cell membrane

In patients with DMD

Dystrophin Deficiency



DAPC is not formed, the muscle cell membrane becomes unstable, and damage to the muscle cell membrane occurs during muscle stretching and contraction

Muscle weakness caused by chronic and progressive muscle inflammation

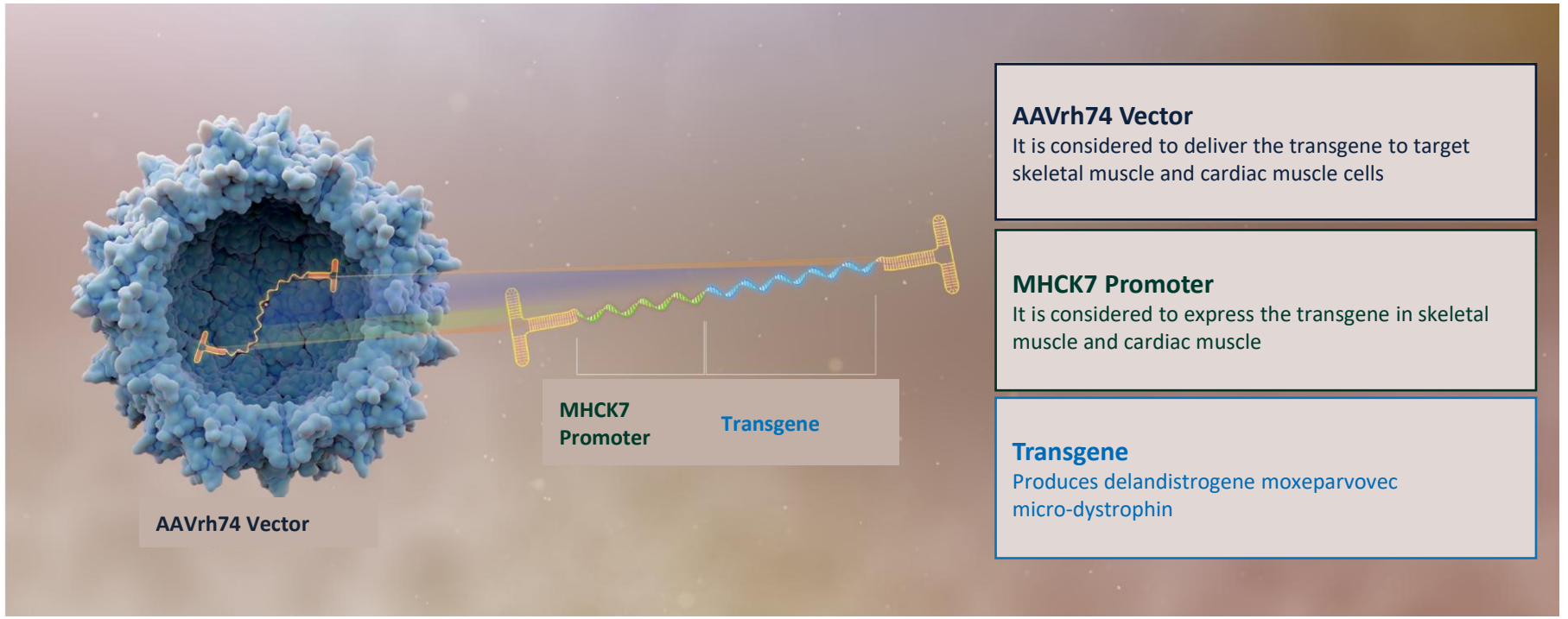
Adapted from references 1)–3)

1) Van Ruiten H, et al. EMJ. 2017; 2: 90-9.
2) Davies KE, Nowak KJ. Nat Rev Mol Cell Biol. 2006; 7: 762-73.
3) van Westering TL, et al. Molecules. 2015; 20: 8823-55. Conflict of interest: This publication includes authors who have received consulting fees from Sarepta.

Structure of Elevidys

- Elevidys (generic name: delandistrogene moxeparvovec) is a gene therapy vector product developed for the treatment of DMD.
- It is a non-replicating recombinant adeno-associated virus (recombinant Adeno-Associated Virus: rAAV) vector containing a gene[1] encoding delandistrogene moxeparvovec micro-dystrophin, a functional shortened dystrophin (hereinafter, “micro-dystrophin”), and is controlled by the α-myosin heavy chain creatine kinase 7 (MHCK7) promoter/enhancer, which optimizes expression in skeletal and cardiac muscle. [2]

(Illustration)



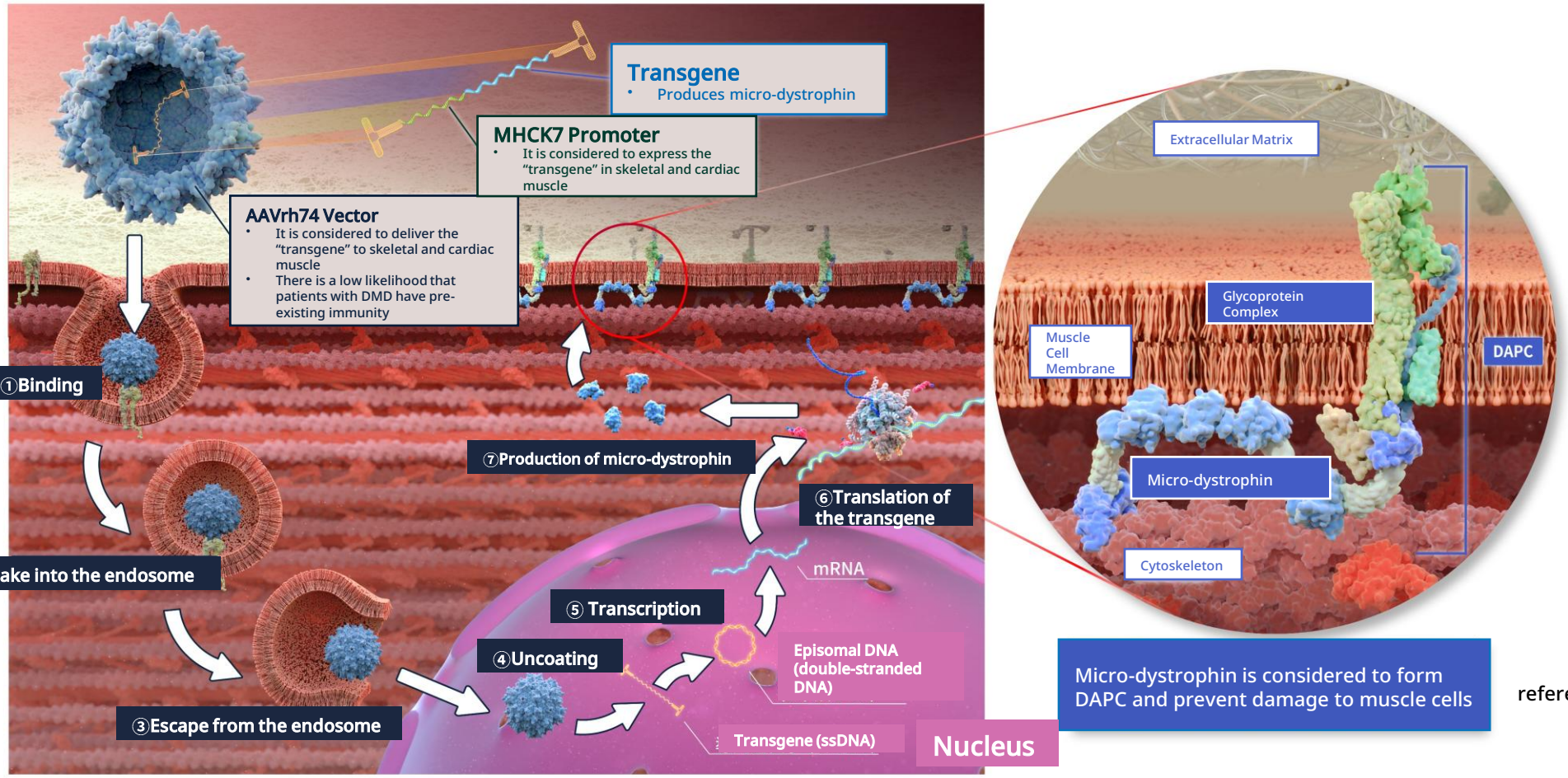
Adapted from references 3) and 4)

1) Rodino-Klapac LR, et al. Hum Mol Genet. 2013; 22: 4929-37.
2) Salva MZ, et al. Mol Ther. 2007; 15: 320-9.
3) Review data at the time of approval [Structure of delandistrogene moxeparvovec]
4) Review data at the time of approval [Overview of delandistrogene moxeparvovec]

Mechanism of Action of Elevidys

- The micro-dystrophin gene carried by Elevidys is considered to be expressed in skeletal and cardiac muscle.[1)]
- It is considered that expression of micro-dystrophin in muscle cells improves muscle function and prevents the loss of muscle strength.[2)]

(Illustration)



Adapted from references 1) and 2)

1) Review data at the time of approval [Structure of delandistrogene moxeparvovec]
2) Review data at the time of approval [Overview of delandistrogene moxeparvovec]

Basic Product Information

Elevidys
delandistrogene
moxeparvovec

Basic Information on Elevidys Intravenous Infusion
(delandistrogene moxeparvovec)

- This product is the first gene therapy for Duchenne muscular dystrophy.

Drug Class	Gene therapy product; viral vector product
Efficacy or Effects	Duchenne muscular dystrophy; limited to patients who meet all of the following criteria • Patients who are negative for anti-AAVrh74 antibodies • Ambulatory patients • Patients aged 3 years or older and younger than 8 years
Dosage form	Intravenous administration (the required number of vials for each patient is enclosed in an individual package)
Dosage and administration	In general, a single intravenous infusion is administered over 60 to 120 minutes: 1.33×10^{14} vg/kg for patients weighing ≥10 kg and <70 kg, and 9.31×10^{15} vg for patients weighing ≥70 kg. This product should not be readministered. The dose of this product is calculated based on the table below*.
Orphan designation	Designated on July 30, 2024 (MHLW notification No. 0730-1); Designation No.: (R2 sai) No. 16
Other designation system	Designated intractable disease No. 113 Pediatric Chronic Disease No. 16
NHI reimbursement listing / Launch date	February 20, 2026 Price: JPY 304,972,042 per patient

Packaging

The number of vials required according to patient body weight (1 vial = 10.0 mL) is packaged in an individual box for each patient. The size of the box varies depending on the number of vials.

Although the vials are labeled in English, please refer to the Japanese-labeled package for product information.

*Table refers to the electronic package insert

Approval Conditions of Elevidys

Approval Conditions and Time Limit	Approval Conditions 1. During the period until the reapplication for marketing approval of this product after conditional and time-limited approval, post-marketing approval condition evaluation shall be conducted through clinical trials aimed at confirming the long-term efficacy and safety of this product, as well as post-marketing surveillance targeting all cases in which this product is used. 2. Necessary measures shall be taken, including dissemination of proper use guidelines developed in cooperation with relevant academic societies, to ensure that physicians with sufficient knowledge and experience in Duchenne muscular dystrophy use this product in accordance with the “Efficacy or Effects” and “Dosage and Administration” after thoroughly acquiring knowledge of the clinical trial results and adverse events of this product, at medical institutions with established systems for treating Duchenne muscular dystrophy. 3. Necessary measures shall be taken, including dissemination of the usage regulations, to ensure that this product is used in compliance with the Type 1 Use regulations approved under the “Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Act No. 97 of 2003).” Time Limit: 3 years
Expiration of Re-examination Period	Not applicable (conditionally and time-limited approved product)

Elevidys Intravenous Infusion, Electronic Package Insert, Revised February 2026 (3rd edition)

Progress of Post-Approval Safety Measure Review

Year	Date	Event and Actions
2025	May 13	◆ Conditional and time-limited approval (3 years) obtained
	June 16	◆ Report of overseas fatal cases due to acute liver failure in non-ambulatory DMD patients
	June 18	◆ Meeting of the Central Social Insurance Medical Council ✓ Requested thorough review and discussion while gathering information
	August 28	◆ Revision of the electronic package insert ✓ Acute liver failure added as a serious adverse reaction; implementation of liver function monitoring and testing specified; warnings regarding infections related to corticosteroid use added
	October 8	◆ Meeting of the Central Social Insurance Medical Council (regarding handling under the health insurance system and safety) ✓ It was agreed to discuss the handling under the health insurance system, taking into account the need for public confirmation of safety and the importance of providing thorough information.
	November 27	◆ Meeting of the Subcommittee on Safety Measures for Medical Devices and Regenerative Medical Products under the Pharmaceutical Affairs and Food Sanitation Council (Ministry of Health, Labour and Welfare) was held. ✓ As part of the discussions on safety measures, the appropriateness of information materials, the positioning of the expert panel, and the framework for collaboration with relevant academic societies were discussed.
	December 17	◆ A notification was issued by the Director of the Office of Safety Measures, Pharmaceutical Safety Division, Ministry of Health, Labour and Welfare. ✓ Notifications were sent to the presidents of the Japanese Society of Child Neurology and the Japan Society of Hepatology, requesting cooperation in emphasizing clinical experience in DMD in facility accreditation, and in establishing a system capable of ensuring appropriate emergency response and coordination.
2026	January 14	◆ Meeting of the Central Social Insurance Medical Council (regarding handling under the health insurance system and listing on the NHI price list) ✓ Safety measures jointly implemented by the Ministry of Health, Labour and Welfare, relevant academic societies, and the company were reported, and it was agreed that the reimbursement price would be reviewed by the drug pricing organization and that the product would be listed on the NHI reimbursement price list.
	February 13	◆ Meeting of the Central Social Insurance Medical Council (decision on NHI coverage and price listing for Elevidys) ✓ It was agreed that Elevidys would be covered by the NHI and listed on the NHI reimbursement price list on February 20.
	February 20	◆ Listing on the NHI reimbursement price list and launch of Elevidys on the same day

Duchenne Muscular Dystrophy (DMD): Disease and Treatment, Clinical Framework for Gene Therapy, Appropriate Use, and Clinical Positioning

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June 17, 2026, Chugai Pharmaceutical Media Seminar

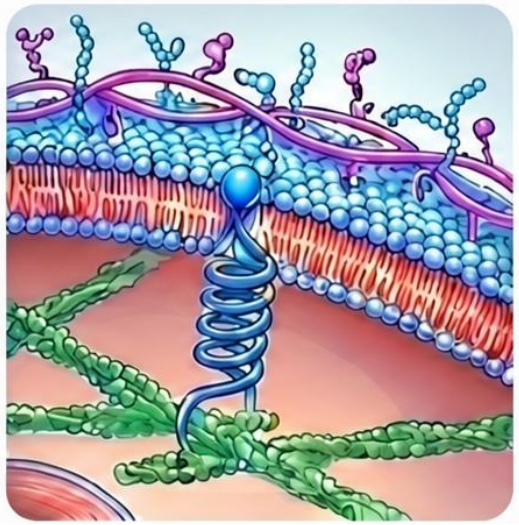
Conflict of Interest (COI) Disclosure

Presenter: Hirofumi Komaki
In relation to the content of this presentation,
the following companies have COI relationships
that should be disclosed by the lead presenter and co-presenters:

Nippon Shinyaku Co., Ltd.: Research funding, lecture fees
Chugai Pharmaceutical Co., Ltd.: Lecture fees
Sarepta Therapeutics, Inc.: Research funding
F. Hoffmann-La Roche Ltd: Consulting fees

<Illustration>

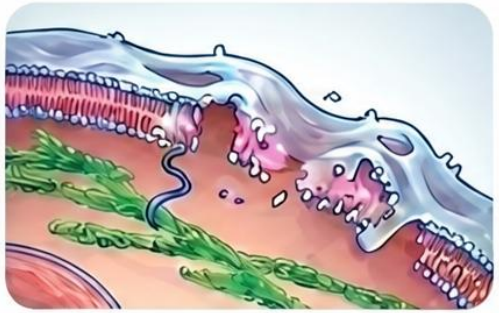
Normal Muscle Cells and the Function of Dystrophin



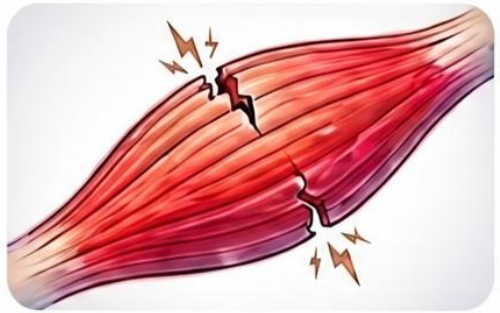
• Structural support: Links the cytoskeleton and cell membrane, providing internal reinforcement.

• Shock absorption: Reduces mechanical stress during muscle contraction and protects the membrane.

Process of Progressive Degeneration in DMD

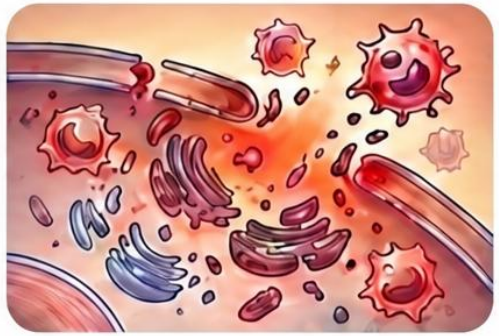


[Step 1] Loss of dystrophin and membrane fragility
Due to the absence of dystrophin, the cell membrane becomes fragile.



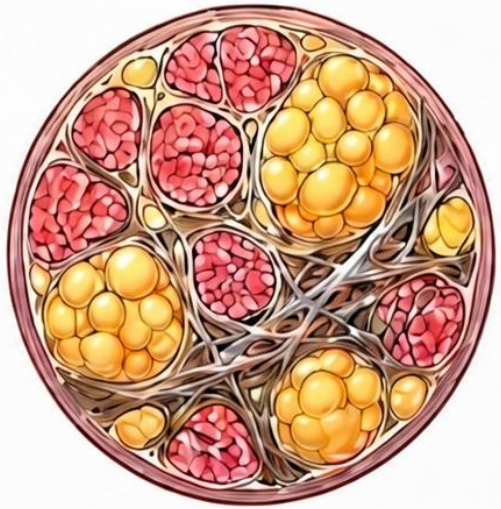
[Step 2] Cell membrane damage caused by contraction
Repeated muscle contraction leads to rupture of the weakened cell membrane.

[Step 3] Excess influx of calcium ions
Calcium ions abnormally flow into the cell through the damaged membrane.



[Step 4] Muscle cell necrosis and chronic inflammation
Excess calcium induces cell death, and inflammation persists.

Irreversible Tissue Degeneration



• Fibrosis and fatty infiltration: Regeneration of muscle cells cannot keep up, and the tissue is replaced by connective tissue and fat.

• Decreased muscle strength: Reduction in muscle mass leads to progressive and severe muscle weakness.

Source: Ali ABB et al. Front Physiol. 2023;14:1183101. Mareedu S et al. Front Physiol. 2021;12:647010.
Prepared by the presenter with reference to the above sources

Major Symptoms of DMD

- In DMD, symptoms begin to appear around 2 to 4 years of age, motor function peaks at around 5 years of age under the natural course, and loss of ambulation generally occurs around 10 years of age.[1)]
- Without treatment, the life expectancy is estimated to be in the teenage years.
- The life expectancy of patients with DMD is still only around 30 years of age[2)], and there is a need for fundamental disease-modifying treatment.

※The types, severity, and progression of symptoms vary depending on the patient's condition and treatment status.

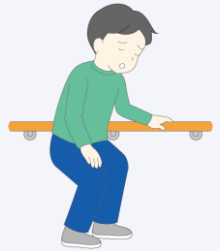
Up to around 4 years of age (developmental stage)

- Unable to run, prone to falling
- Delayed motor development

Around 5–7 years of age (early ambulatory stage)

- Pseudohypertrophy of the calf muscles
- Toe walking
- Gowers' sign is observed
- Waddling gait is observed

Around 8–10 years of age (late ambulatory stage)



- Walking ability declines
- A wheelchair may be required in some situation

Around 11–18 years of age (early non-ambulatory stage)

- Loss of ambulation
- Decreased motor function of the upper limbs
- Respiratory and cardiac function decline

Around 18 years of age and older (late non-ambulatory stage)

- Progressive deterioration of respiratory and cardiac function

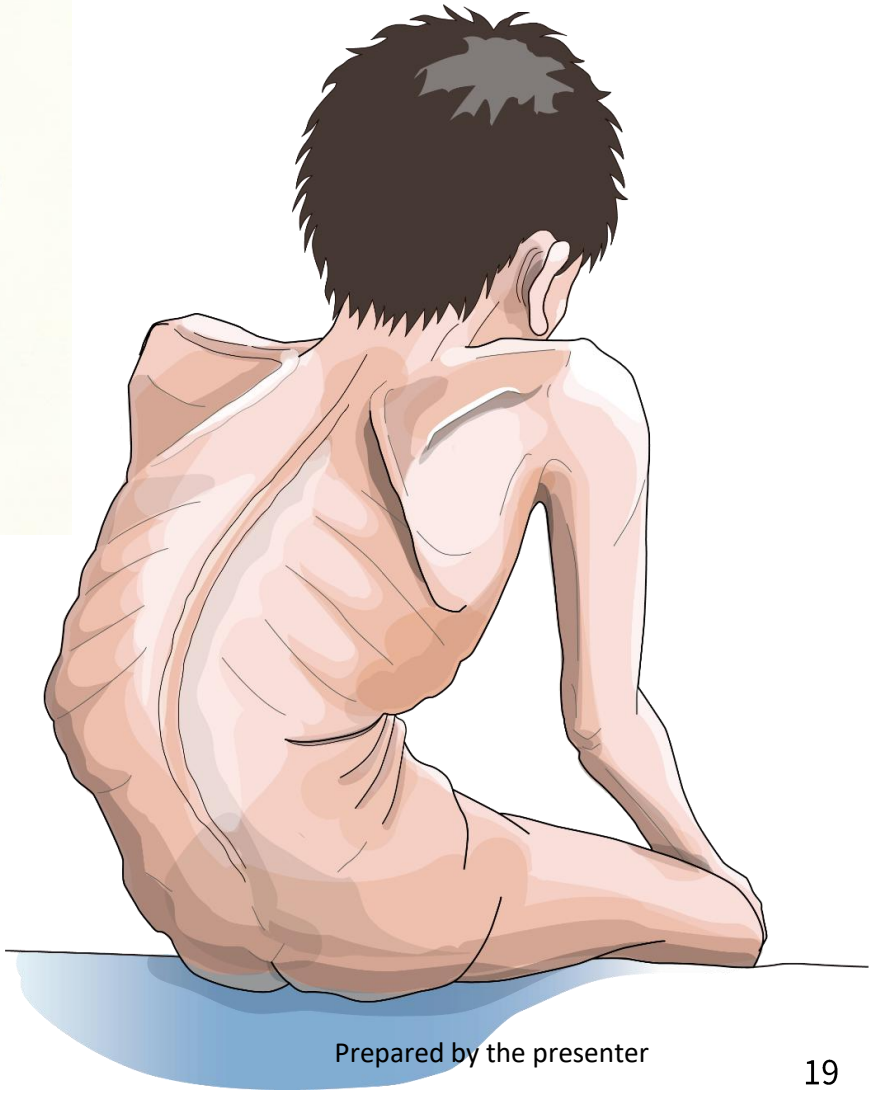
Adapted from references 1) and 3)

1) Pediatric Chronic Disease Information Center. No. 47 Duchenne Muscular Dystrophy. https://www.shouman.jp/disease/details/11_21_047/ (Accessed June 10, 2026)
2) Bushby K, Connor E. Clin Investig (Lond). 2011; 1: 1217-35.
3) Uchiyama K (ed.). Standard Pediatrics, 8th Edition. Igaku-Shoin; 2013.

< Illustration >

Gowers sign

Scoliosis, muscle atrophy



Prepared by the presenter

Establishment of Current Multidisciplinary Treatment (Base Treatment)

Achievement of social participation, education, and employment

Respiratory Management	Physical Function Management	Pharmacological Therapy	Systemic Management
Appropriate introduction of non-invasive positive pressure ventilation (NPPV) and regular monitoring. Respiratory rehabilitation including lung expansion exercises.	Range-of-motion training, posture management (seating), and preventive interventions for contractures and scoliosis.	Objective prolongation of the ambulatory period through steroid administration.	Cardiac care using ACE inhibitors and other therapies. Nutritional guidance and evaluation of swallowing function.

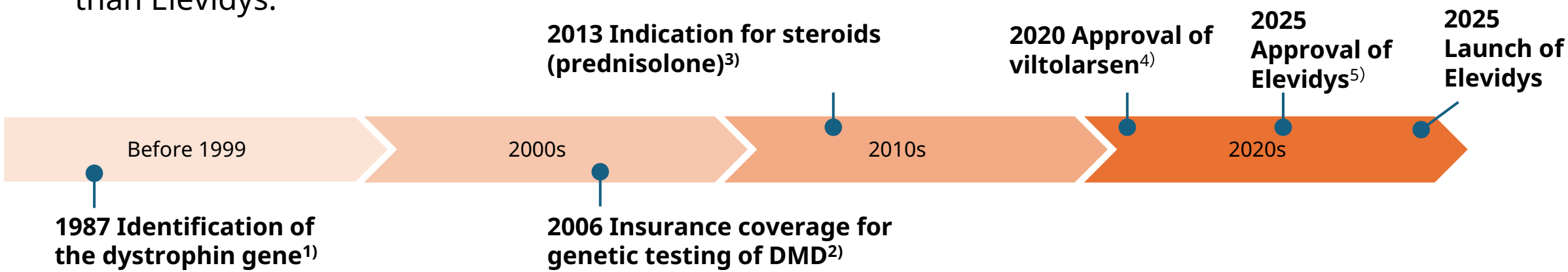
Proactive and comprehensive multidisciplinary team (MDT) care is functioning as the current standard of care (base treatment).

NPPV（non invasive positive pressure ventilation,）, ACE inhibitors (angiotensin-converting enzyme inhibitors)

1) McDonald CM, et al. Lancet. 2018;391(10119):451-461. 2) Matthews E, et al. Cochrane Database of Systematic Reviews. 2016 May 5;2016(5):CD003725. 3) The Japanese Society of Neurology et al. (supervisors). Clinical Practice Guidelines for Duchenne Muscular Dystrophy 2014 4) Birnkrant DJ, et al. Lancet Neurol. 2018;17(3):251-267. Prepared by the presenter with reference to these sources

DMD Treatment in Japan (as of June 2026)

- As of June 2026, steroids and viltolarsen are used as existing pharmacological treatments other than Elevidys.



Steroids (prednisolone)

- Reported efficacy for skeletal muscle disorders (e.g., prolonged ambulation and maintenance of respiratory function)[6)]
- Generally initiated when motor function reaches its peak[6)]
- Indication (excerpt): "Duchenne muscular dystrophy"[7)]
- Dosage and administration (excerpt): "In general, prednisolone is orally administered at a daily dose of 5–60 mg in 1–4 divided doses in adults. The dosage may be adjusted according to age and symptoms.[7)]

Viltolarsen

- An antisense oligonucleotide that binds to exon 53 of dystrophin pre-mRNA and induces exon 53 skipping, thereby enabling expression of functional dystrophin[4)]
- Indication: "Duchenne muscular dystrophy with confirmed deletions in the dystrophin gene amenable to exon 53 skipping"[4)]
- Dosage and administration (excerpt): "Usually, viltolarsen is administered intravenously at 80 mg/kg once weekly over 1 hour."[4)]

1) Takeda S, Suzuki T. MD Frontier. 2021; 1: 52–5.
2) Central Social Insurance Medical Council, General Meeting (575th), Agenda. December 22, 2023. Individual Items (No. 19). https://www.mhlw.go.jp/content/12404000/001181965.pdf (Accessed June 10, 2026).
3) Guideline Development Committee for Duchenne Muscular Dystrophy. Clinical Practice Guidelines for Duchenne Muscular Dystrophy 2014. Nankodo; 2014.
4) Viltepso Intravenous Infusion 250 mg, Electronic Package Insert, Revised November 2021 (4th edition).5) Intractable Disease Information Center. Muscular Dystrophy (Designated Intractable Disease No. 113) (November 2024). https://www.nanbyou.or.jp/entry/4522 (Accessed June 10, 2026).
6) Predonin Tablets 5 mg, Electronic Package Insert, Revised March 2026 (6th edition).

Entering the Era of Disease Modification: Evolution of DMD Treatment

Untreated Era

Life expectancy up to 20 years.

Establishment of Standard of Care (SoC)

Prolonged survival (28.1 years or more) with steroids, respiratory management, and spinal stabilization surgery.

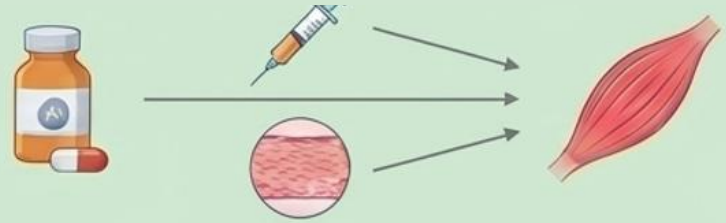
Current Stage (The New Era)

Implementation of personalized treatment based on genetic testing (exon skipping and gene therapy).

New Therapeutic Approaches

B Exon Skipping

C Untreated various modalities including anti-inflammatory therapies



Comprehensive disease modification through multiple approaches, including immunomodulation, anti-inflammatory drugs, and anti-fibrotic therapies.

Key Insight: We have entered an era that requires an integrated perspective evaluating not only efficacy but also safety, immunological aspects, and patient quality of life (QOL).

1) The Japanese Society of Neurology et al. (supervisors). Clinical Practice Guidelines for Duchenne Muscular Dystrophy 2014 2) Birnkrant DJ, et al. Lancet Neurol. 2018;17(3):251-267. 3) Ishikawa Y, et al. Neuromuscular Disorders. 2011;21(1):47-51. 4) Komaki H. Brain Dev. 2025 Oct;47(5):104397.
Prepared by the presenter with reference to the above sources

Medical Background for the Need for Gene Therapy

Outcomes of Multidisciplinary Treatment

Management and Prolongation
through Existing Treatments

- Objective prolongation of life expectancy through respiratory and cardiovascular care.
- Prolongation of the ambulatory period through the use of steroids and other treatments.
- Delay of complications (contractures and scoliosis) through rehabilitation.
- Expansion of opportunities for social participation after adulthood.

Establishment of symptomatic approaches that delay disease progression and manage complications.

Limitations of Existing Treatments

Fundamental Issues
as a Progressive Disease

- The mutation in the dystrophin gene, which is the underlying cause, remains.
- It is difficult to completely prevent continuous muscle fiber damage associated with daily activities.
- Progression of irreversible tissue replacement from skeletal muscle to cardiac and respiratory muscles.

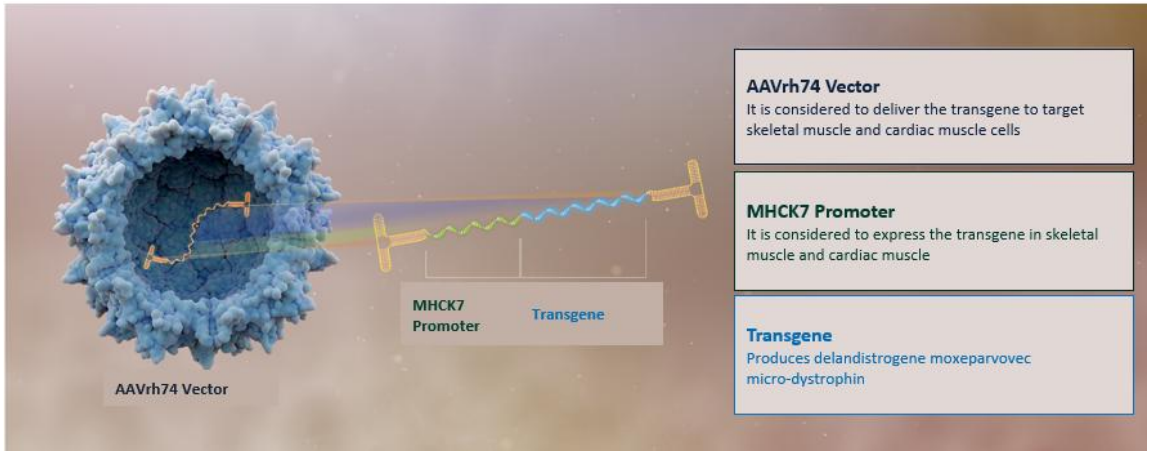
The biological mechanism of disease "progression" itself cannot be halted.

Conclusion: While continuing symptom management (base treatment), the introduction of next-generation therapies that directly target the underlying cause (dystrophin deficiency) has been a long-standing challenge in clinical practice.

1) McDonald CM, et al. Lancet. 2018;391(10119):451-461. 2) Matthews E, et al. Cochrane Database of Systematic Reviews. 2016 May 5;2016(5):CD003725. 3) The Japanese Society of Neurology et al. (supervisors). Clinical Practice Guidelines for Duchenne Muscular Dystrophy 2014 4) Birnkrant DJ, et al. Lancet Neurol. 2018;17(3):251-267. Prepared by the presenter with reference to the above sources

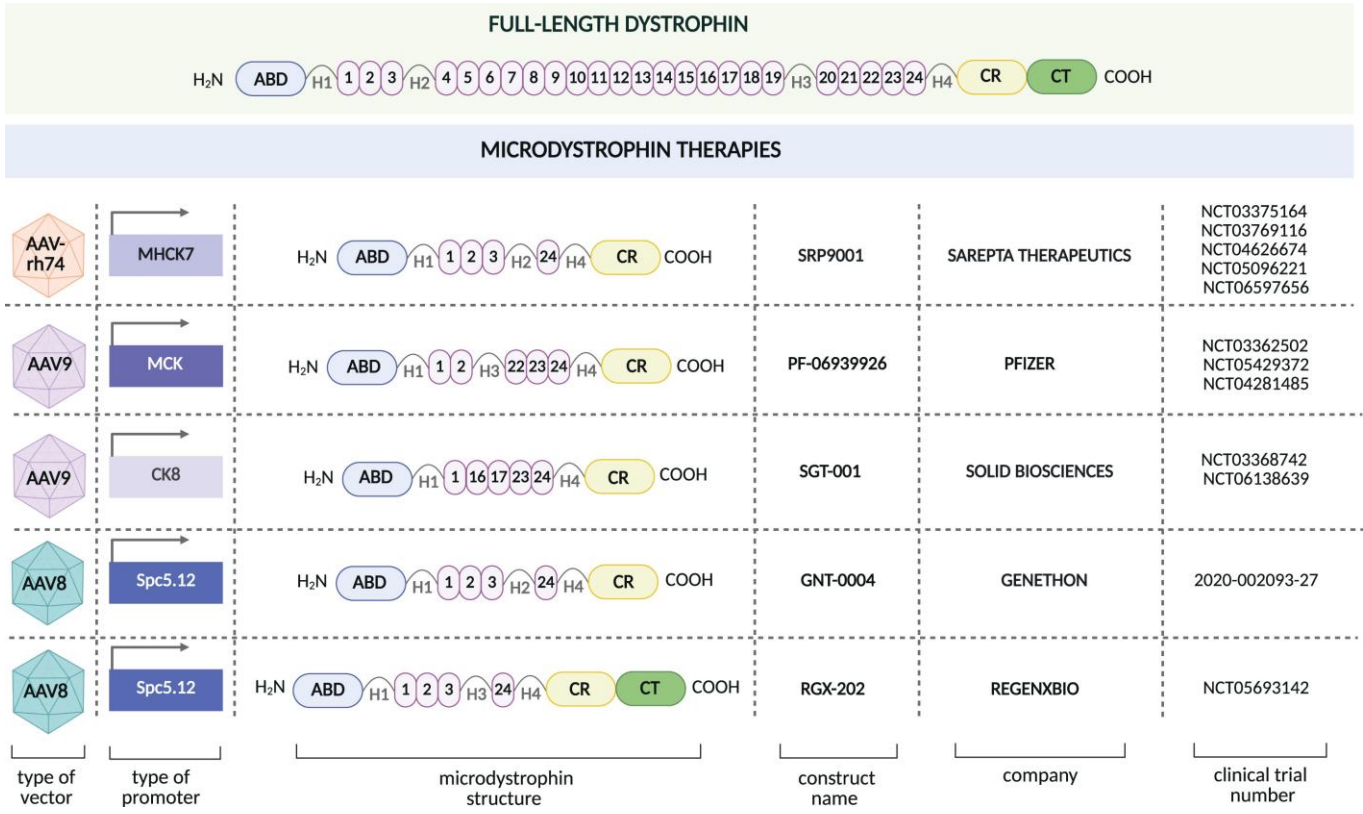
Structure of Elevidys and Micro-dystrophin

(Illustration)



Adapted from references 1) and 2)

1) Review data at the time of approval [Structure of delandistrogene moxeparvovec]
2) Review data at the time of approval [Overview of delandistrogene moxeparvovec]

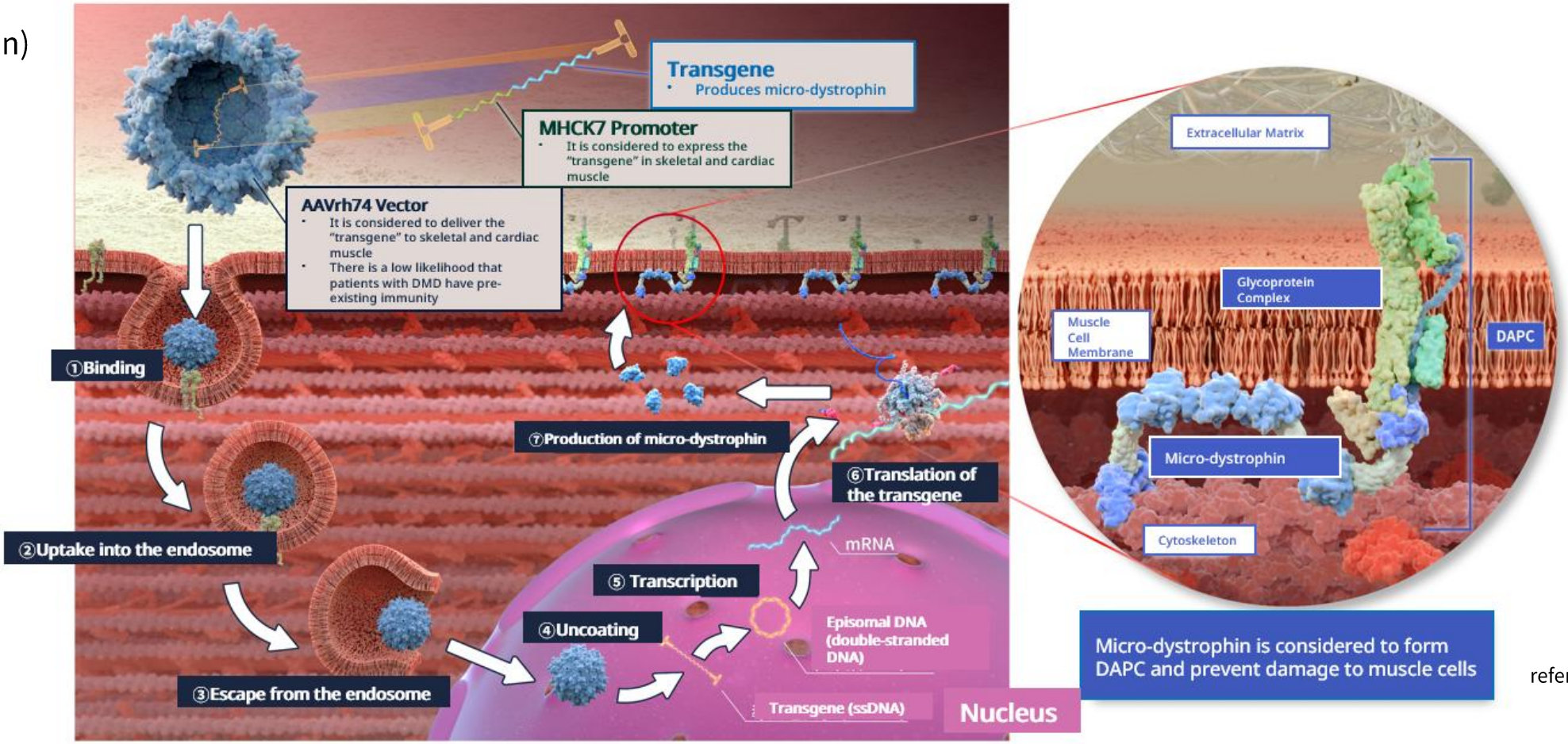


Loboda A, et al. Genetic strategies for therapy of Duchenne muscular dystrophy. Mol Ther Nucleic Acids. 2025;36(4):102759

Mechanism of Action of Elevidys

- The micro-dystrophin gene carried by Elevidys is considered to be expressed in skeletal and cardiac muscle.[1)]
- It is considered that expression of micro-dystrophin in muscle cells improves muscle function and prevents the loss of muscle strength.[2)]

(Illustration)



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1) Review data at the time of approval [Structure of delandistrogene moxeparvovec]
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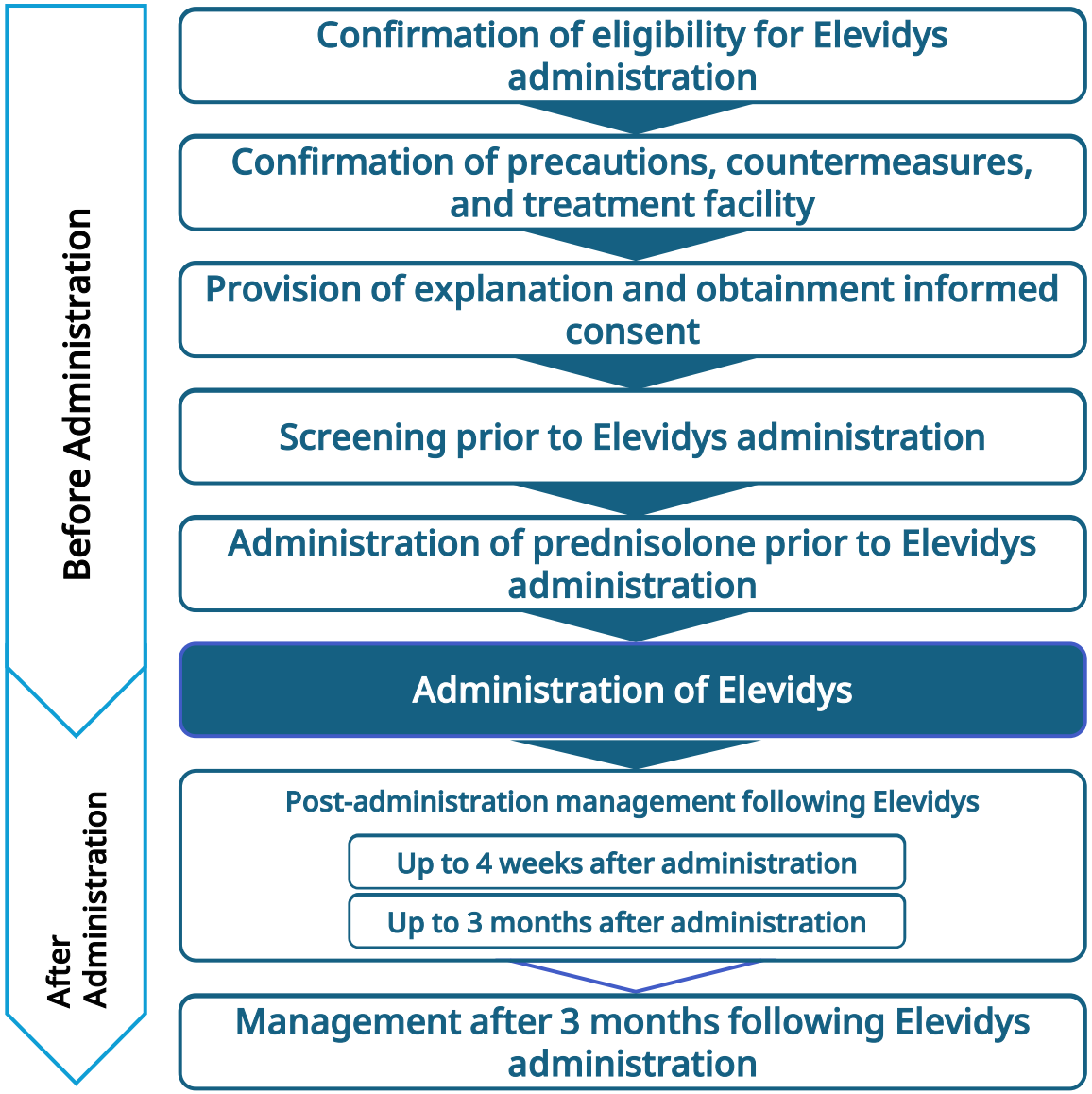
Treatment Flow with Elevidys



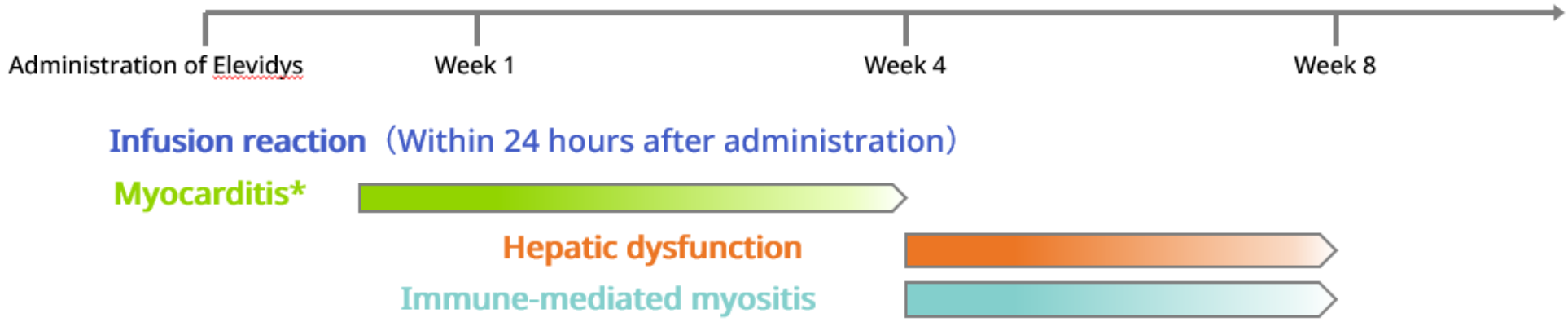
Elevidys Intravenous Infusion Appropriate Use Guide (Revised January 2026)

Adverse Reactions and Issues Requiring Attention and Their Countermeasures

Serious Adverse Reactions

- The general timing of onset is as follows.[1)–3)] Among early adverse reactions, myocarditis occurring within several days after administration is suggested to be associated with innate immune responses to the viral vector. On the other hand, immune-mediated myositis occurring 4 to 8 weeks after administration is considered to be the result of acquired immune responses to micro-dystrophin.[3)]

<Timing of onset of each adverse reaction (schematic)>



*In cases of delayed myocarditis, treatment as immune-mediated myositis may be required.[4)]

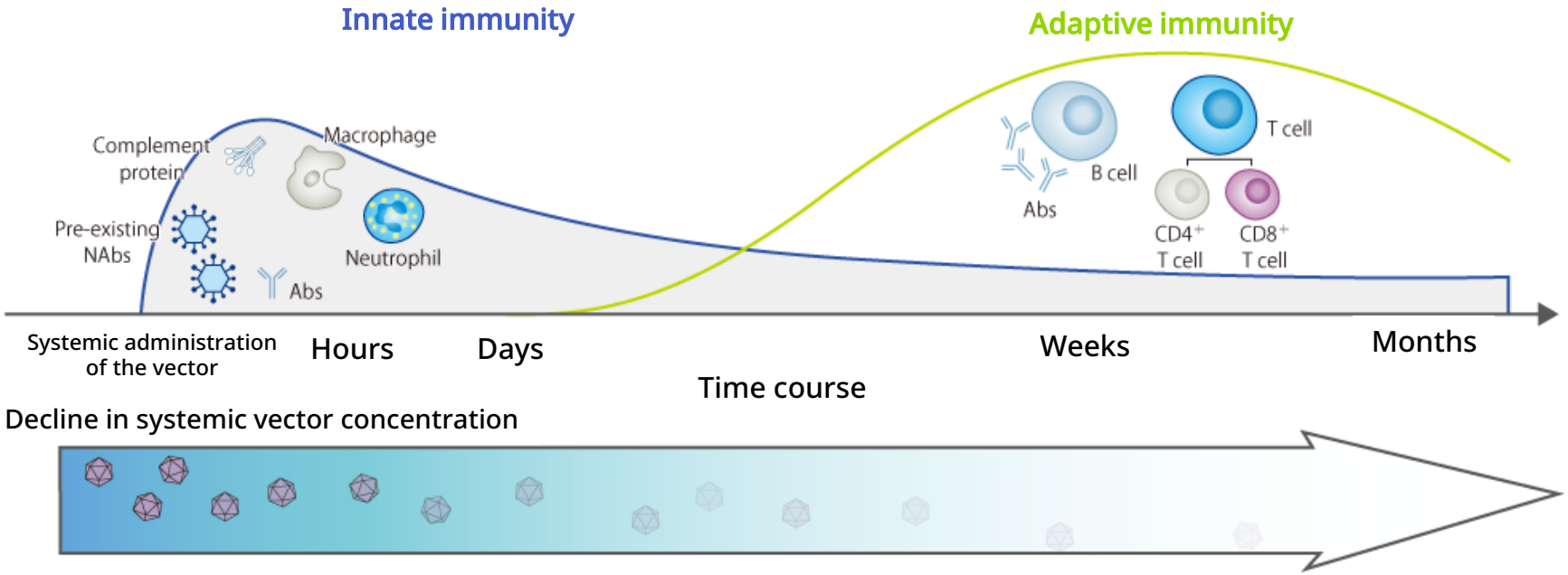
Adapted from references 1) - 4)

1）Review data at the time of approval [Multinational Phase III clinical study in patients with DMD (SRP-9001-301)]
2）Review data at the time of approval [Pooled analysis of safety studies]
3）Zaidman CM, et al. J Neuromuscul Dis. 2024; 11: 687-99.
Conflict of interest: This study was supported by Sarepta Therapeutics.
The authors include employees of Sarepta Therapeutics and individuals who have received research funding, consulting fees, and other compensation from Sarepta Therapeutics, F. Hoffmann-La Roche Ltd., and Genentech.
4）Kaufman BD, et al. J Neuromuscul Dis. 2024: 22143602241303357.
Conflict of interest: The authors include individuals who have received consulting fees from Sarepta Therapeutics.

Adverse Reactions and Issues Requiring Attention and Their Countermeasures
Serious Adverse Reactions

- Following AAV-mediated gene transfer, innate immune responses are activated within hours to several days, while acquired immune responses are observed after several weeks. Along with these immunological responses, the systemic vector concentration is considered to decrease.[1)]

<Course of immunological responses after AAV gene transfer (schematic)>



Adapted from 1)

Reprinted from Mol Ther Methods Clin Dev., 25, Mendell JR, et al., Testing preexisting antibodies prior to AAV gene transfer therapy: rationale, lessons and future considerations, 74-83, Copyright (2022), with permission from Elsevier.

1) Mendell JR, et al. Mol Ther Methods Clin Dev. 2022; 25: 74-83.

Conflict of interest: This study was supported by Sarepta Therapeutics. The authors include employees of Sarepta Therapeutics and individuals who have received research funding, consulting fees, and other compensation from Sarepta Therapeutics and Genentech.

Adverse Reactions and Issues Requiring Attention and Their Countermeasures

Implementation of Tests Before and After Administration of This Product

- Please perform the tests shown in the figure below both before initiation and after administration of this product.
- If the patient is followed up at another facility after the administration of this product, please ensure that the same tests are performed and confirm the patient's condition.
- For monitoring items and frequency beyond 3 months after administration of this product, please confirm the patient's condition and consult with the appropriate specialist. After 1 year, perform monitoring in conjunction with routine DMD examinations.

Test Schedule

		Baseline※1	After administration										
			Day 2–3	Week 1	Week 2	Week 3	Week 4	Weekly up to 3 months thereafter	Month 3	Month 4	Month 5	Month 6	Month 9	1 year
Liver (including partial TMA)	AST、ALT	●		●	●	●	●	●	●	○	○	●	○	●
	γ-GTP	●		●	●	●	●	●	●	○	○	●	○	●
	Albumin	●		●	●	●	●	●	●	○	○	●	○	●
	APTT	●		●	●	●	●	●	●	○	○	●	○	●
	PT%／PT-INR	●		●	●	●	●	●	●	○	○	●	○	●
	Total bilirubin / Direct bilirubin	●		●	●	●	●	●	●	○	○	●	○	●
	CK※2	●		●	●	●	●	●	●	○	○	●	○	●

● Required ○ Recommended

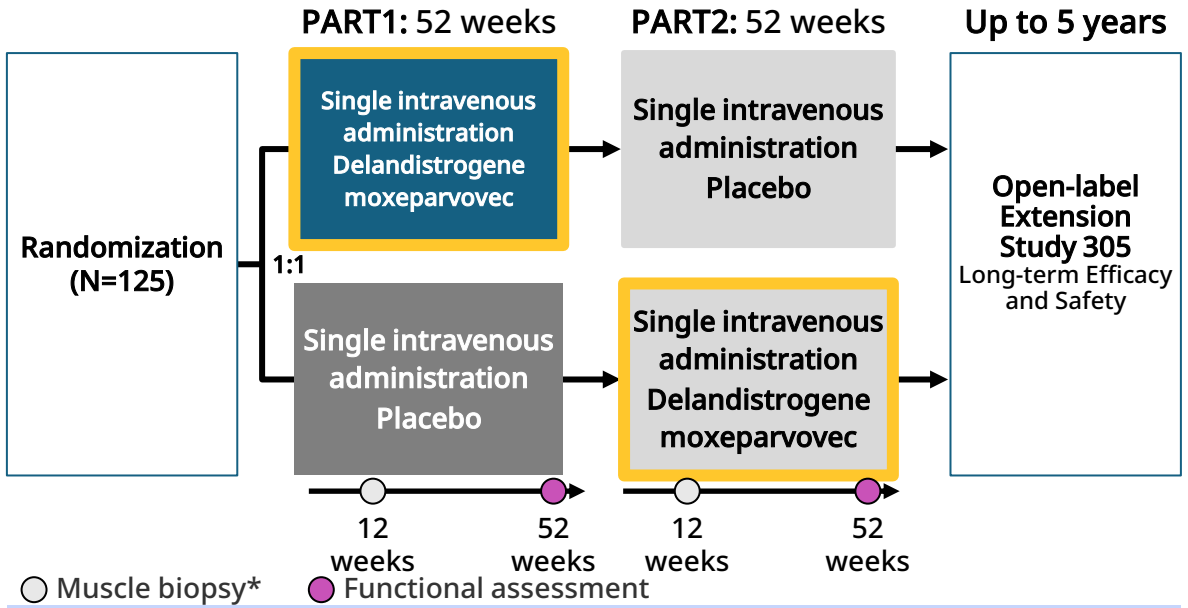
※1：For baseline cardiac examinations, use results obtained within 6 months prior to administration of this product.
※2：Although CK levels are not clinical laboratory values directly related to hepatic dysfunction, AST and ALT are often elevated in DMD patients due to muscle breakdown, making it difficult to assess hepatic dysfunction. In such cases, CK levels are useful in differentiating hepatic disease from muscle-derived enzyme elevation. Fluctuation patterns of CK levels and their divergence from AST and ALT levels suggest the complication of hepatic disease, leading to an appropriate evaluation.
TMA：Thrombotic Microangiopathy、APTT：Activated Partial Thromboplastin Time、PT：Prothrombin Time、PT-INR：Prothrombin Time–International Normalized Ratio

Excerpt from Elevidys Intravenous Infusion Appropriate Use Guide (Revised January 2026)

Multinational Phase III Clinical Study (EMBARK Study Part 1)

Study Overview: Design and Methods

A multinational Phase III randomized, double-blind, crossover, placebo-controlled study evaluating the safety and efficacy of delandistrogene moxeparvovec in ambulatory boys aged 4 to 7 years with confirmed DMD gene mutations



Key Inclusion Criteria:

- Ambulatory male patients aged ≥4 to <8 years at the time of randomization
- Patients with a confirmed diagnosis of DMD (whose DMD gene mutations are entirely within exons 18–79)
- Patients who are able to comply with assessments for motor function evaluation
- Patients with an NSAA score >16 and <29 at the screening visit
- Patients with a time to rise from the floor of <5 seconds at the screening visit
- Patients who have received oral corticosteroids for at least 12 weeks prior to screening under a stable daily dose regimen
- Patients with rAAVrh74 antibody titers <1:400 (not elevated) as measured by ELISA

Stratified by age group at randomization (≥ 4 to < 6 years vs. ≥ 6 to < 8 years) and NSAA total score at screening (≤ 22 vs. > 22)

Primary Endpoint

- Change from baseline to Week 52 (Part 1) in total NSAA score

Key Secondary Motor Function Endpoints

- Change from baseline to Week 52 in the following:
  - TTR (time to rise from floor)
  - 10 meter walk/run (10MWR)

Other Secondary Motor Function Endpoints

- Change from baseline to Week 52 in the following:
  - SV95C measured using a wearable device (Syde)
  - 100meter walk/run (100MWR)
  - Time to ascend 4 steps

Safety Endpoints

- TEAEs, serious adverse events, and adverse events of special interest
- Clinically significant changes in laboratory values

Primary and secondary endpoints were tested using a statistical hierarchy to control the overall type I error at a two-sided significance level of 0.05

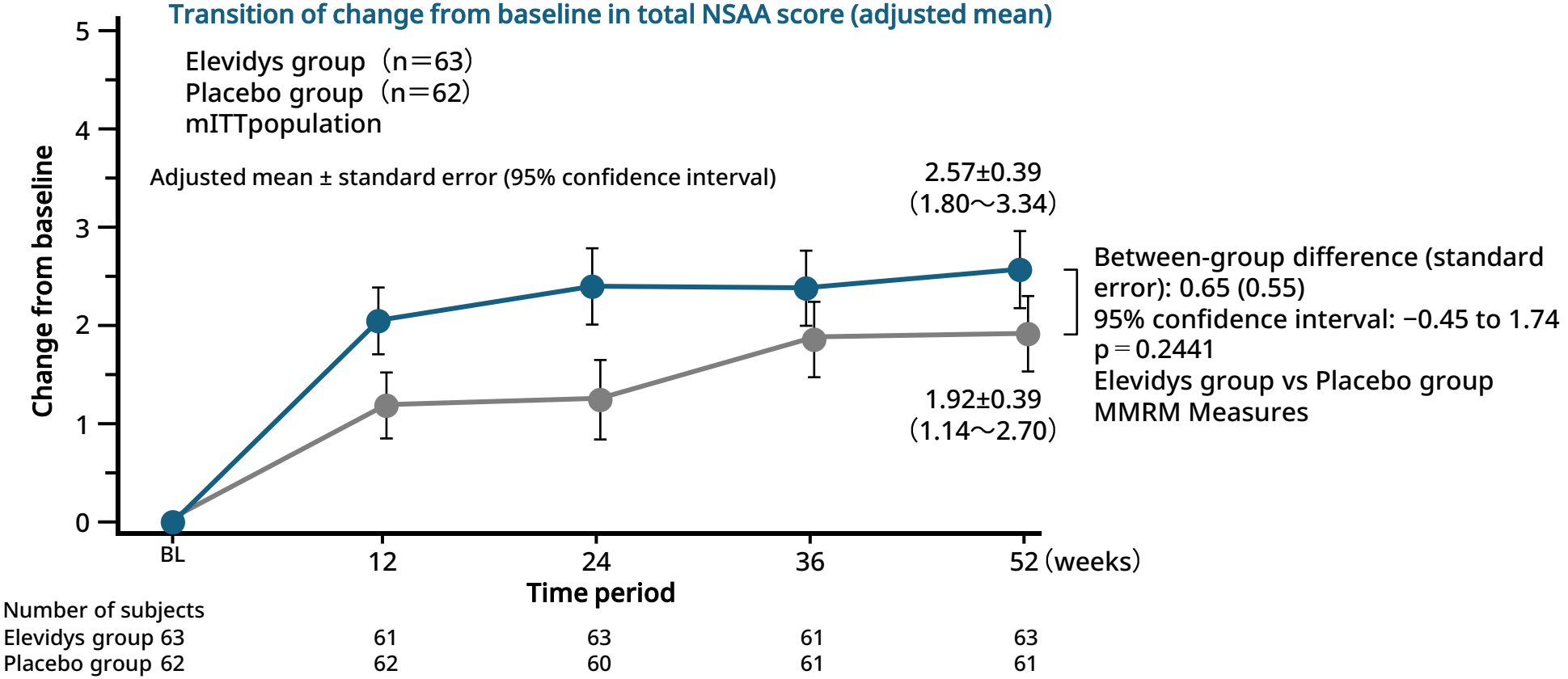
*Based on the experience and feasibility of the study sites, only a subset of participants will undergo muscle biopsy for expression evaluation. †Not reported in this presentation; however, additional endpoints were included in the sequential testing. 10MWR:10-meter walk/run、 100MWR: 100-meter walk/run、 AE:Adverse event、 DMD:Duchenne muscular dystrophy、 IV:Intravenous administration、 NSAA:North Star Ambulatory Assessment、 rAAVrh74:Recombinant adeno-associated virus serotype rh74 (rhesus macaque isolate)、 SAE:Serious adverse event、 SV95C:95th percentile stride velocity、 TEAE:Treatment-emergent adverse event、 TTR:Time to rise from the floor

Adapted from review data at the time of approval [Multinational Phase III clinical study in patients with DMD (SRP-9001-301)]

Primary Endpoint: Change from baseline to Week 52 in total NSAA score (confirmatory analysis endpoint)

- The adjusted mean change from baseline to Week 52 in total NSAA score was 2.57 in the Elevidys group and 1.92 in the placebo group.
- The between-group difference was 0.65, and no statistically significant difference was observed; superiority of the Elevidys group over the placebo group was not demonstrated. The gatekeeping procedure for this endpoint was therefore concluded (p = 0.2441; Elevidys vs placebo; MMRM analysis).

Transition of change from baseline in total NSAA score (adjusted mean)



Number of subjects				
Elevidys group 63	61	63	61	63
Placebo group 62	62	60	61	61

Covariates in the MMRM model: treatment group (categorical variable), visit (categorical variable), interaction between treatment group and visit, age group at randomization (categorical variable), baseline total NSAA score, interaction between age group at randomization and visit, and interaction between baseline total NSAA score and visit
In the evaluation of NSAA, when three or fewer items out of 17 were missing, the total NSAA score was calculated by multiplying the mean score of the completed items by 17; when four or more items were missing, the score was treated as missing.
Unless otherwise specified, missing values for individual items were not imputed. Missing data were assumed to be missing at random.
Data cutoff date: September 13, 2023

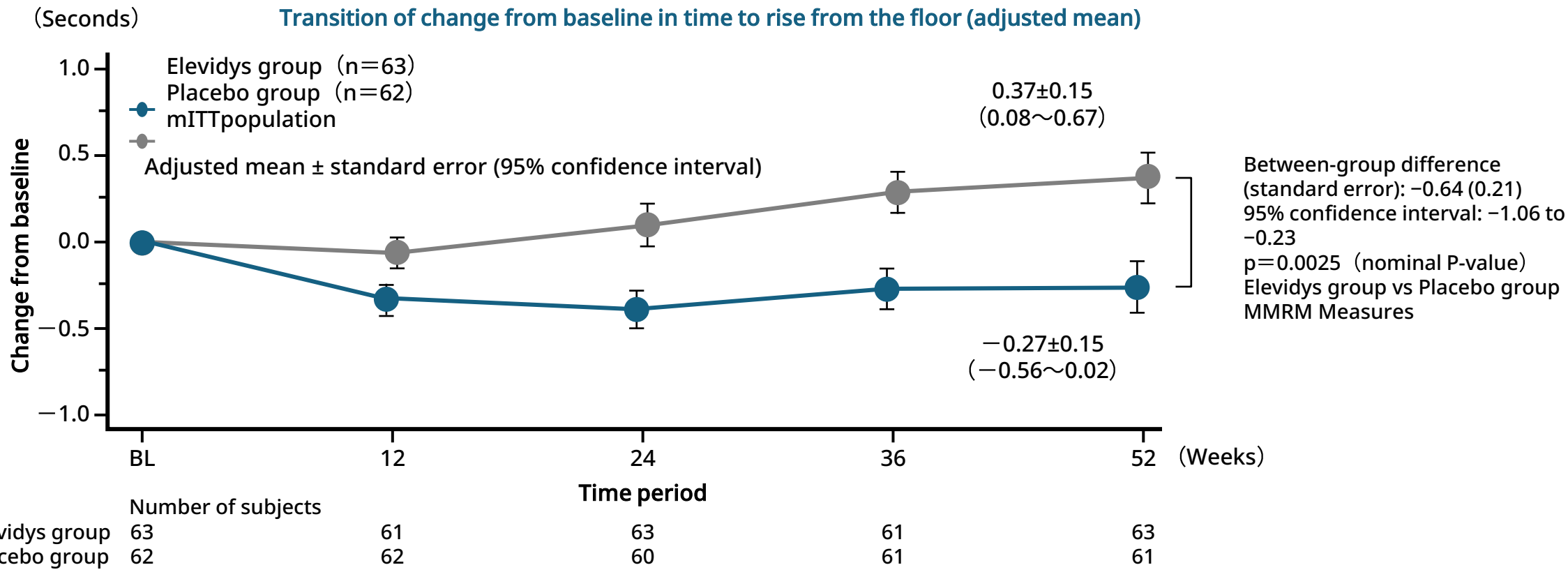
Mendell JR, et al. Nature Medicine 2025 (1):332-341.

Adapted from review data at the time of approval [Multinational Phase III clinical study in patients with DMD (SRP-9001-301)]

Key Secondary Endpoint

Change from baseline to Week 52 in time to rise from the floor

- The adjusted mean change from baseline to Week 52 in time to rise from the floor was −0.27 seconds in the Elevidys group and 0.37 seconds in the placebo group, with a between-group difference of −0.64 seconds [p = 0.0025 (nominal p-value); Elevidys vs placebo; MMRM Measures]



Number of subjects	BL	12	24	36	52
Elevidys group	63	61	63	61	63
Placebo group	62	62	60	61	61

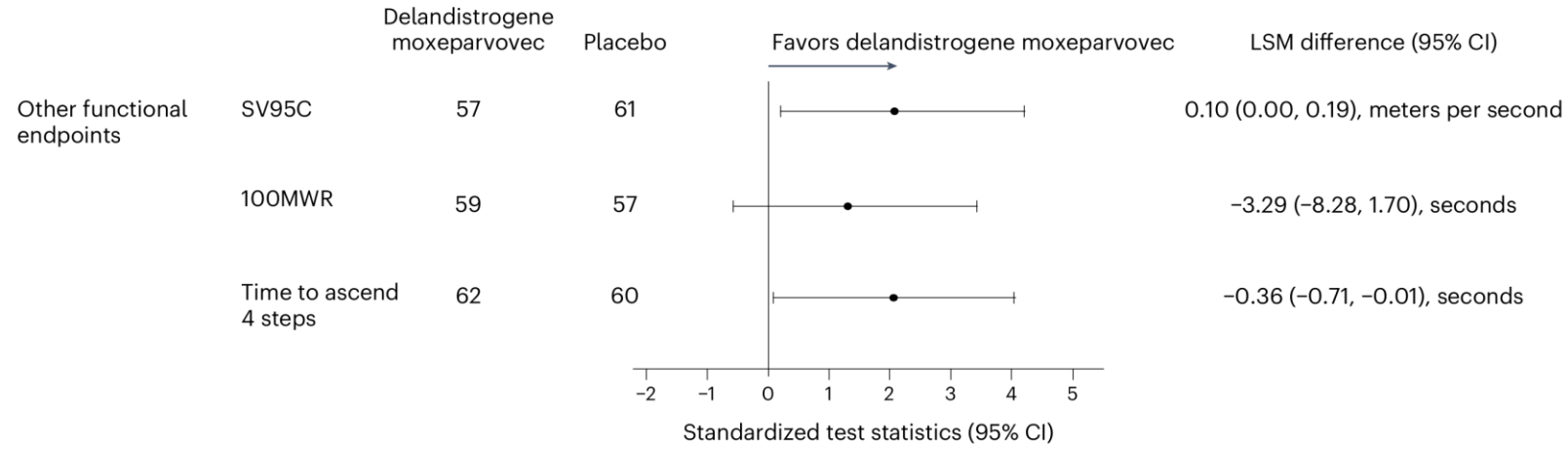
Covariates in the MMRM model: treatment group (categorical variable), visit (categorical variable), interaction between treatment group and visit, age group at randomization (categorical variable), baseline time to rise from the floor, NSAA total score at screening (≤22, >22), interaction between age group at randomization and visit, and interaction between baseline time to rise from the floor and visit
If data were missing and the score for Item 12 of the NSAA was 0 (i.e., requiring the use of external support such as a chair or wall, or unable to perform), the time to rise from the floor was imputed as 30 seconds, which was considered the maximum plausible value.
Data cutoff date: September 13, 2023

Mendell JR, et al. Nature Medicine 2025 (1):332-341.

Adapted from review data at the time of approval [Multinational Phase III clinical study in patients with DMD (SRP-9001-301)]

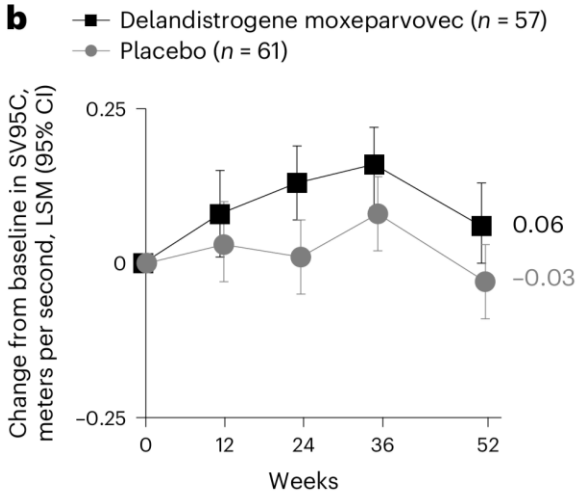
Secondary Endpoints for Motor Function Assessment

a **All motor function assessment results at Week 52 using a forest plot**

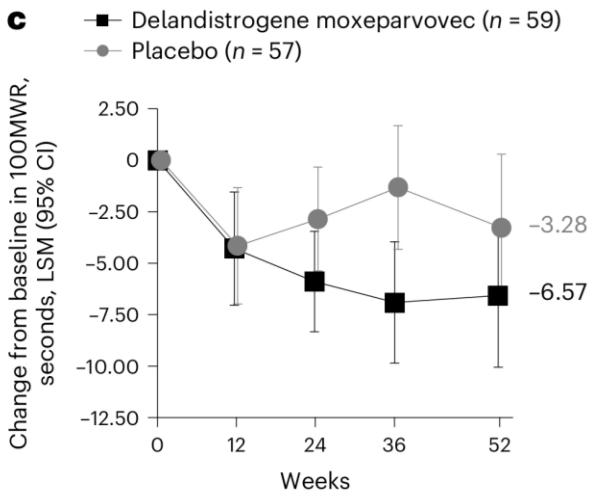


SV95C:
95th percentile of stride velocity measured using a wearable device attached to the ankle
100MWR:
Time to walk/run 100 meters
Time to ascend 4 steps:

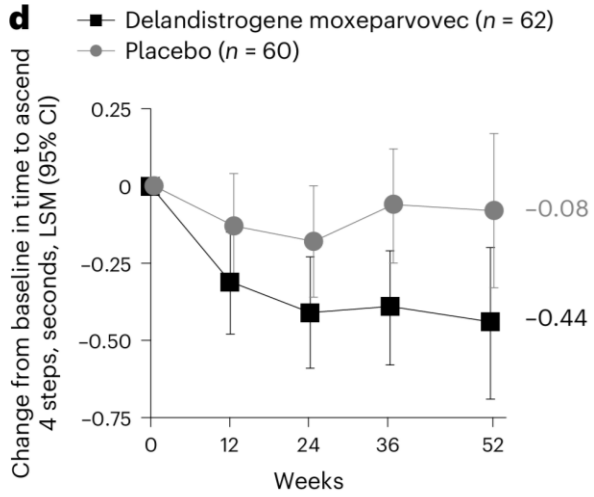
Change from baseline to Week 52 in SV95C



Change from baseline to Week 52 in 100-meter walk/run time



Change from baseline to Week 52 in time to ascend 4 steps



Mendell JR, et al. Nature Medicine 2025 (1):332-341.

Continuous Management: Process from Pre-Administration to Long-Term Follow-Up

Strict eligibility confirmation and monitoring are required

Phase 1: Pre-administration

Baseline tests conducted from one month to several days prior (detailed evaluation of complement, liver function, troponin I, etc.), and initiation of the pre-treatment steroid protocol.

Phase 2: Administration / peri-administration period

Single intravenous administration. Several hours of in-hospital monitoring for acute hypersensitivity.

Phase 3: Intensive monitoring period

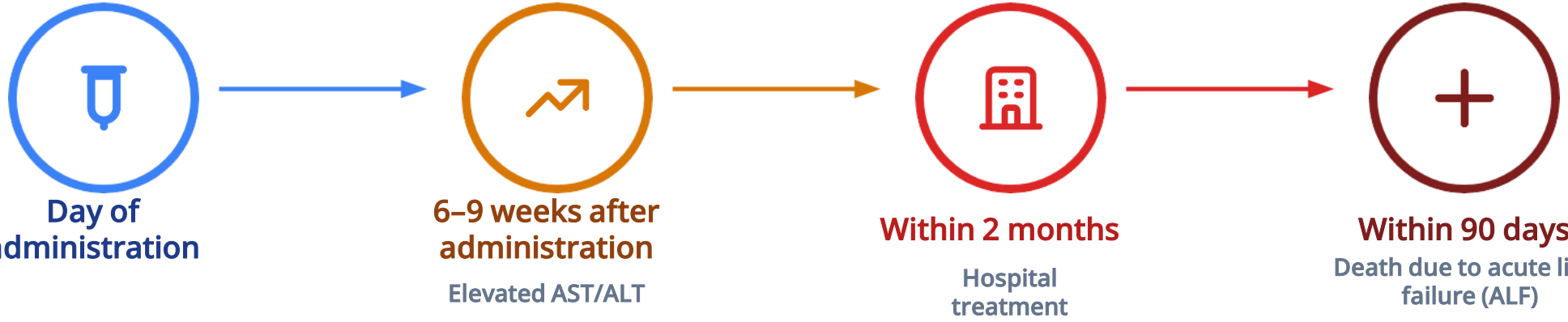
Approximately 90 days after administration, when risk is considered particularly high. Frequent weekly measurement of liver enzymes, cardiac enzymes, platelets, etc. Immediate coordination with BRIDGE-NMD upon detection of abnormalities.

Phase 4: Long-term follow-up

Continuous evaluation of efficacy and monitoring for late-onset adverse events.

Prepared by the presenter

Serious Case Reports in Non-Ambulatory Patients (United States)



Critical Case Details

Patient Profile:

Two non-ambulatory DMD patients aged 15 and 16

Outcome:

Both cases resulted in death due to acute liver failure (ALF) within 90 days after administration

Clinical Implications

Administration has been discontinued in non-ambulatory patients (United States)

Acute liver failure added as a serious adverse reaction in the electronic package insert

A high-risk signal in advanced non-ambulatory patients.

Careful monitoring of liver function and reassessment of immunosuppressive management are essential

Approval of Gene Therapy Products for DMD and Strengthening of Safety Measures

Regulatory Approval

Approval of gene therapy products for DMD in Japan.

Discussion at the Central Social Insurance Medical Council

In discussions toward NHI price listing, concerns regarding safety and the need for countermeasures were raised.

Director's Notification Strengthening of Safety Measures

Based on these discussions, a notification was issued by the Ministry of Health, Labour and Welfare. Specific safety measures were mandated, including stricter patient selection criteria and enhancement of monitoring systems.

Involvement of the Japanese Society of Child Neurology

Played a leading role in establishing appropriate use guidelines, certifying administration sites, building collaboration systems, and establishing adverse event management systems, thereby developing the foundation for safety measures.

Identification of Serious Adverse Reaction Risks

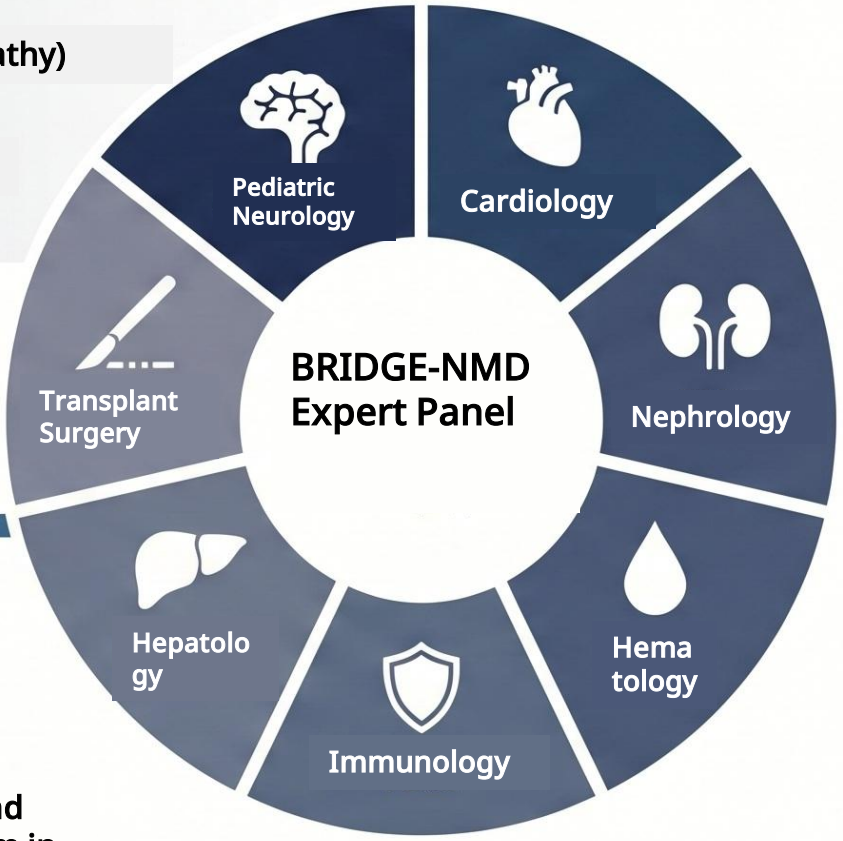
Hepatic Disorders (Acute Liver Failure)

TMA (Thrombotic Microangiopathy)

Immune-mediated myositis

Spoke
(Regional Facilities)

E-consultation



Seamless coordination between Hub and Spoke: Establishment of a system to ensure coordination from pre-administration and enable early detection of signs of adverse reactions

Registration of all cases for e-consultation and provision of advice: Establishment of a system in which all administered cases receive medical advice from an expert panel via BRIDGE-NMD

Medical guidance by specialists

Japanese Society of Child Neurology website https://www.childneuro.jp/general/8664/ (accessed June 2026)

Practical Implementation of E-consultation

Patients nationwide

Physicians nationwide

Medii

一般社団法人 日本小児神経学会
The Japanese Society of Child Neurology

Patients with DMD

Provision of appropriate treatment

Other in-hospital specialists (e.g., hepatology, cardiology)

Prescribing physician (primary physician)

Regional follow-up physicians

Consultation and information sharing

Platform: Medii E-consultation

Specialized medical advice

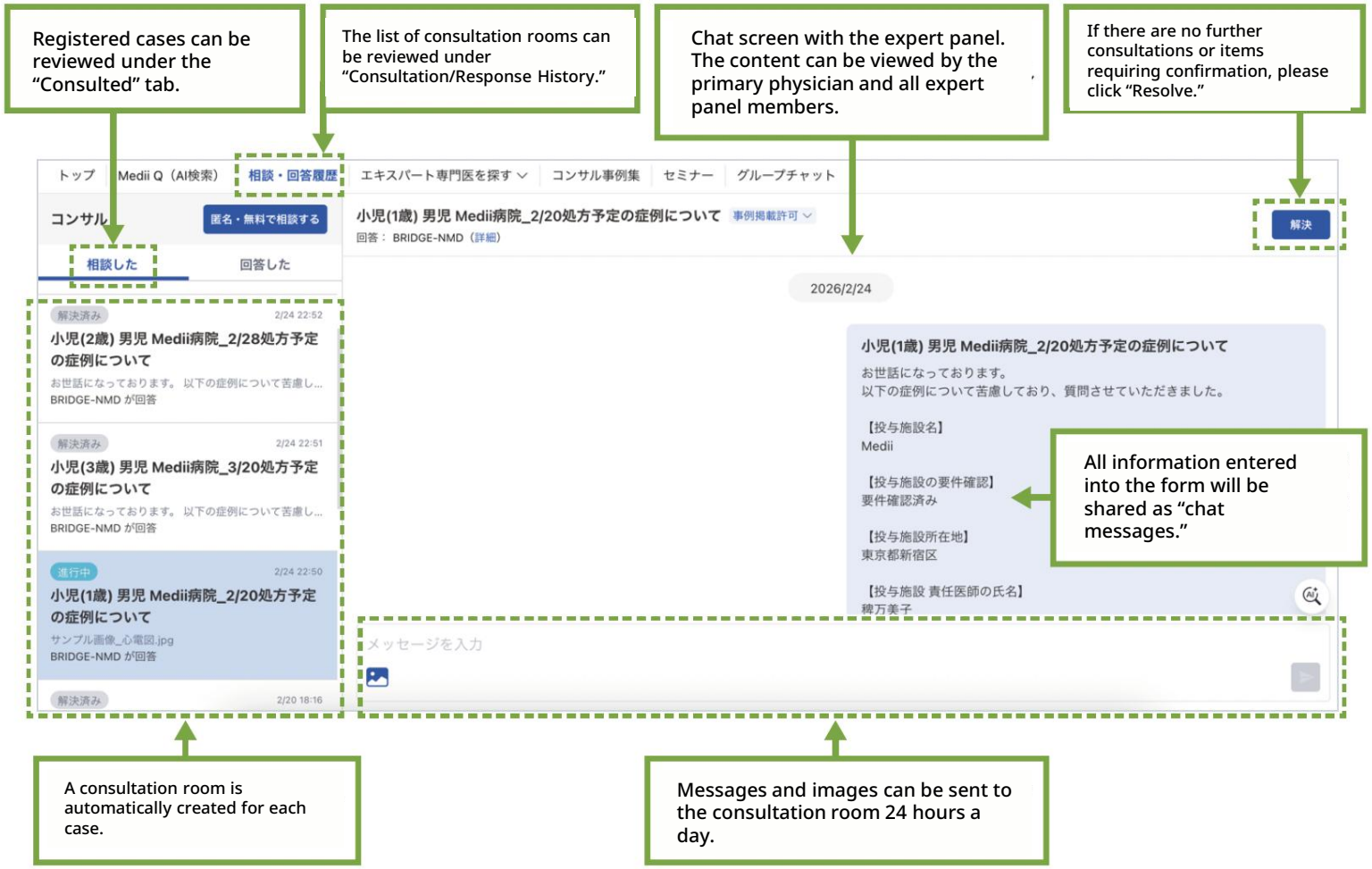
Expert Panel "BRIDGE-NMD"

Pediatric neurology, pediatric hepatology, pediatric hepatobiliary surgery, pediatric cardiology, pediatric immunology, pediatric nephrology, and pediatric hematology

Overview of the Adverse Event Management System in DMD Gene Therapy

Workflow of Adverse Event Management in DMD Therapeutics

Through a consultation platform established via case registration, it is possible to seek advice at any time, 24 hours a day, when there is uncertainty in clinical decision-making, including in the management of adverse events.



Overview of the Adverse Event Management System in DMD Gene Therapy

Workflow of Adverse Event Management in DMD Therapeutics

Through a consultation platform established via case registration, it is possible to seek advice at any time, 24 hours a day, when there is uncertainty in clinical decision-making, including in the management of adverse events.

<Prescribing Facility Information>		
投与施設名	＊	
投与施設所在地	＊	
投与施設 責任医師の氏名	＊	
フォローアップ施設名		
フォローアップ施設の所在地	＊	
フォローアップ施設の窓口医師 氏名	＊	
<Case Information>		
患者生年月	＊	
性別	＊	
家族歴	＊	
既往歴	＊	
治療歴	＊	
服薬歴	＊	
プレドニゾロン使用歴	＊	
プレドニゾロンの投与開始年齢	＊	
プレドニゾロンの投与量（mg/日）	＊	
直近（1ヶ月）の感染症罹患の有無と詳細	＊	
直近（1ヶ月）の予防接種歴	＊	
インフルエンザワクチンの接種状況と接種日	＊	
定期予防接種の接種状況	＊	
診断年齢（歳・ヶ月）	＊	
遺伝学的検査内容	＊	
遺伝学的検査結果（画像）	＊	＊＊

＊Required selection item
＊＊Attach image

<Physical Findings>		
身長（cm）	＊	
体重（kg）	＊	
肥満度（%）	＊	
歩行/ジャンプ（跳躍）動作	＊	
知的障害の有無	＊	
神経発達症の有無と診断名	＊	
<Blood Test Results>		
赤血球数（万/μL）	＊	
白血球数（/μ）	＊	
血小板数（万/μL）	＊	
ヘモグロビン数（g/dL）	＊	
AST（IU/L）	＊	
ALT（IU/L）	＊	
γ-GTP（IU/L）	＊	
アルブミン（g/dL）	＊	
APTT（秒）	＊	
PT%	＊	
PT-INR	＊	
総ビリルビン（mg/dL）	＊	
直接ビリルビン（mg/dL）	＊	
CK（IU/L）		
アンモニア（μg/dL）		
Dダイマー（μg/mL）		
ALP（U/L）		
C3（mg/dL）		
C4（mg/dL）		
CH_{50}（CH_{50}/mL）		
LDH（U/L）		
K（mEq/L）		
血液検査における破砕赤血球の所見	＊	
実施したウイルス検査値	＊	
BNP（pg/mL）		
NT-proBNP（pg/mL）		
心筋トロポニンI（cTnI）（ng/mL）	＊	
抗AAVrh74抗体値	＊	

<Liver Function / Imaging Findings>		
腹部エコー画像	＊	＊＊
腹部CT画像		
腹部MRI画像		
脂肪肝の有無	＊	
肝腫大の有無	＊	
脾腫の有無	＊	
肝性脳症の有無	＊	
<Cardiac Function / Imaging Findings>		
12誘導心電図画像	＊	＊＊
心エコーでの左室駆出率（LVEF）（%）	＊	
壁運動異常の有無	＊	
心嚢液貯留の有無	＊	
心臓MRIでの左室駆出率（LVEF）（%）		
心臓MRIでのLVEFの数値（%）		
遅延造影MRI		
<Elevidys Administration Information>		
エレビジス投与予定日	＊	
体重に基づくエレビジス投与量（mg/kg）	＊	
プレドニゾロン投与開始日	＊	
プレドニゾロン投与量（mg/kg/日）	＊	

Prevention of Viral Spread (Cartagena Act)

Manual for Compliance with Type 1 Use Regulations under the Cartagena Act for in vivo Gene Therapy Using Adeno-Associated Virus Vectors, 2nd Edition (Version dated March 1, 2024)

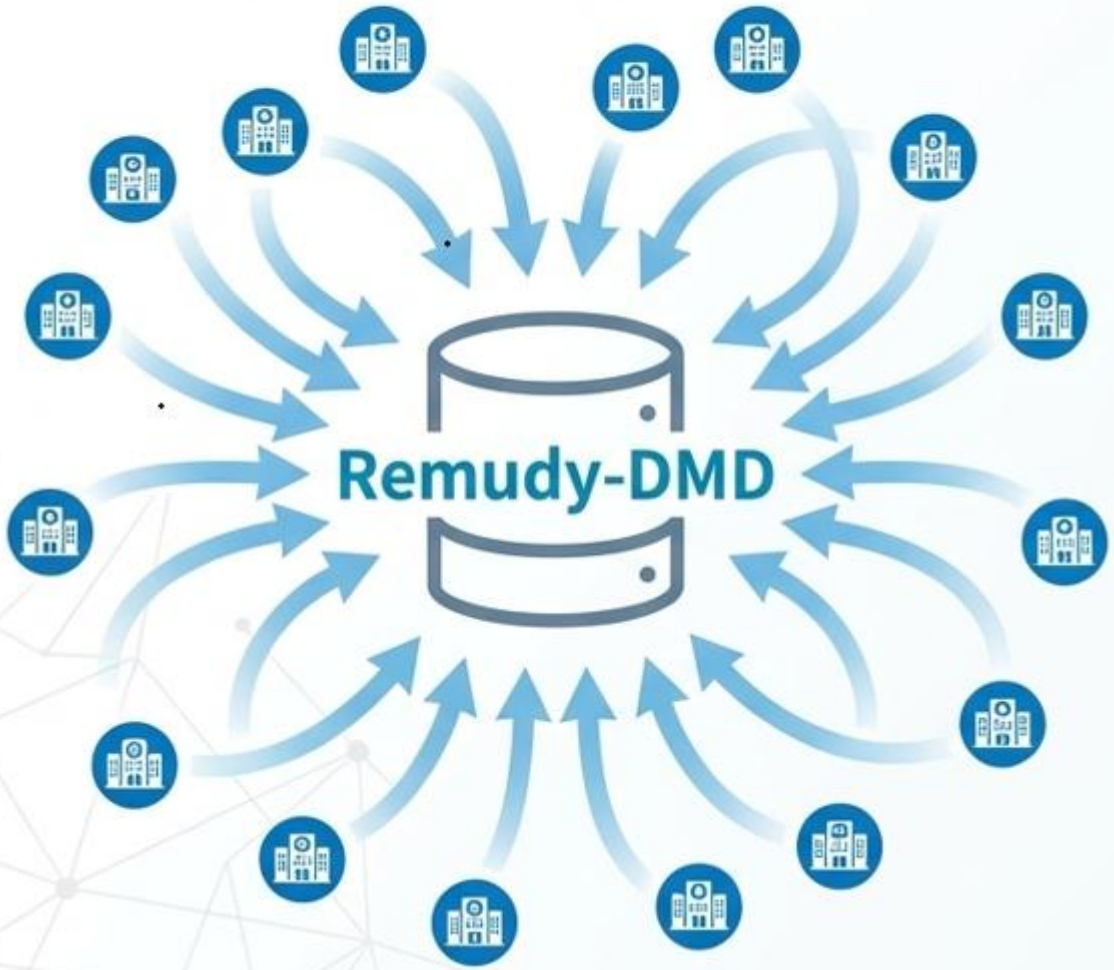
Japanese Society of Child Neurology website（https://www.childneuro.jp/about/6415/）(accessed June 2026)

「アデノ随伴ウイルスベクターを用いた*in vivo*遺伝子治療のカルタヘナ法第一種使用規程対応マニュアル 第2版」を公開いたします。本マニュアルは国立成育医療研究センターと国立精神・神経医療研究センターの共同研究のもと2020年に作成された第１版をもとに作成しており、神経・筋疾患を対象に急速に*in vivo*遺伝子治療の臨床開発が進む中でカルタヘナ法に準拠したうえで安全かつ円滑に遺伝子治療を進めていくための実践的なマニュアルとなっています。

アデノ随伴ウイルスベクターを用いた*in vivo*遺伝子治療のカルタヘナ法第一種使用規程対応マニュアル 第2版（2024年3月1日版）

Data Infrastructure: Building Long-term Evidence Using Registries

A data collection system that converts individual experience into “collective intelligence”



Mandatory registration of all cases

Certified medical institutions are required to continuously register treatment outcomes and follow-up data of all patients who have received the therapy into a database.

Standardized assessments

Standard operating procedures for objective motor function assessments (e.g., 10-meter walk, time to rise from the floor) that can be performed by anyone are distributed to ensure data quality.

Generation of evidence

Overcoming the limitations of individual institutional experience in rare diseases, long-term safety profiles and efficacy are objectively evaluated using aggregated real-world evidence (RWE).

Prepared by the presenter

Summary: A structured safety framework for managing risks

Inherent Risks

- Immune-mediated responses to AAV vectors and the introduced gene
- Reported serious adverse events overseas (e.g., acute liver failure)

Structural Solutions in Japan

- [Regulatory] Strict facility requirements and limitation of indication to ambulatory patients
- [Clinical] Pre-treatment evaluation of all cases by a multidisciplinary expert panel (BRIDGE-NMD)
- [Data] Intensive monitoring during the 90 days post-administration and creation of collective knowledge through full case registry registration

A system is in operation to objectively evaluate the inherent risks associated with medical innovation and to manage safety not based on individual experience but through a national-level structural infrastructure (systems, multidisciplinary teams, and data platforms).

Prepared by the presenter

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Person in charge：	Takayuki Sakurai, Tomoyuki Shimamura, Yayoi Yamada, Yuri Ikegaya, Mari Otsuka

INNOVATION BEYOND IMAGINATION

CHUGAI PHARMACEUTICAL

Roche A member of the Roche group