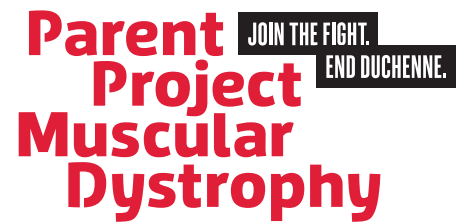


Duchenne Muscular Dystrophy

BACKGROUND



What is Duchenne Muscular Dystrophy?

Duchenne muscular dystrophy is a genetic disorder characterized by the progressive loss of muscle. It is a multi-systemic condition, affecting many parts of the body, which results in deterioration of the skeletal, heart, and lung muscles.

Duchenne is caused by a change in the [dystrophin gene](#). Without dystrophin, muscles are not able to function or repair themselves properly. Becker muscular dystrophy, which is less severe than Duchenne, occurs when dystrophin is manufactured, but not in the normal form or amount.

Because the dystrophin gene is found on the X-chromosome, it primarily affects males, while females are typically [carriers](#). However, some females can manifest varying ranges of physical symptoms of Duchenne and are therefore called "[manifesting carriers](#)".

Who is Parent Project Muscular Dystrophy?

Parent Project Muscular Dystrophy was founded in 1994 by president and CEO Pat Furlong and a group of parents and grandparents who were frustrated by the lack of investment in Duchenne research. When doctors diagnosed her two sons, Christopher and Patrick, with Duchenne in 1984, Pat didn't accept "there's no hope and little help" as an answer. Duchenne is the most common fatal, genetic childhood disorder, which affects approximately 1 out of every 3,500 boys each year worldwide. It currently has no cure.

With Pat at the helm, Parent Project Muscular Dystrophy began working to understand the pathology of the disorder, the extent of research investment, and the mechanisms for optimal care. Her sons lost their battle with Duchenne in their teenage years, but her fight continues, on behalf of all families affected by Duchenne muscular dystrophy. The name of the organization reflects PPMD's grassroots origins, parent-led focus, and passion, and is recognized around the world as the leader in the Duchenne community. Due to PPMD's efforts, families affected by Duchenne have better access to state-of-the-art care information, research is moving forward at an accelerated pace, legislation now exists to fund Duchenne research and outreach programs, and there are multiple approved therapies.

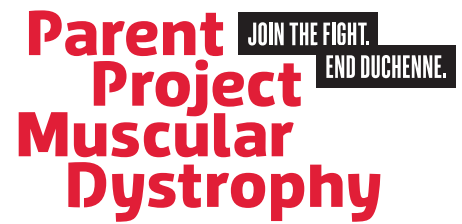
PPMD's MISSION & IMPACT

Parent Project Muscular Dystrophy (PPMD) fights to end Duchenne. We accelerate research, raise our voices to impact policy, demand optimal care for every single family, and strive to ensure access to approved therapies.

PPMD is proud to have played a vital role in every single victory against Duchenne since 1994 and our compassion, strength, and innovation continue to lead this community.

Gene Therapy

and its Application for Duchenne Muscular Dystrophy



What is Gene Therapy?

Gene therapy is a medical intervention that treats or prevents disease by correcting, modifying, or replacing genes, as opposed to traditional interventions like drugs or surgery.¹ A newer mechanism of gene therapy, called genome editing, uses molecular tools to permanently modify the existing DNA.² Gene therapy products are being studied to treat diseases including cancer, genetic diseases, and infectious diseases.³

How Does Gene Therapy Work?

There are many gene therapy modalities, but the common feature is the delivery of some genetic material into cells to correct, modify or replace disease causing genes. One strategy, known as gene replacement, works by delivering a functional gene to cells in order to begin producing a functional protein in faulty cells throughout the body that have been affected by disease. In Duchenne cases, the faulty gene affects a protein's need to protect the muscles, called dystrophin. In the absence of dystrophin, muscle is susceptible to damage and leads to the progressive loss of muscle replaced by fat and fibrosis. Current gene replacement strategies in Duchenne aim to deliver a shortened functional copy of the gene to muscle cells. Due to the difficulty of reaching many of the muscles in the body, scientists began using viruses to reach target cells because of their natural ability to navigate the human body. In nature, viruses are designed to enter the cell nucleus, essentially "infecting" it, and depositing their own genetic code to start producing more virus. In the case of gene therapies, the viruses have been modified to not be disease causing and instead carry the therapeutic genetic material to cells to help correct the disease.

Gene therapies are manufactured through the cultivation of virus and host cells grown in labs. The batches of cells are increased in scale until the cells are harvested for the extraction of the virus. The viruses are then purified to prevent contamination within the patient's body, then deployed with the necessary genes to begin the re-creation of key proteins.⁴ Many companies have specialized facilities dedicated to the research and development of gene therapies in order to advance the knowledge of the treatment. On the regulatory side of manufacturing, the FDA has issued numerous guidance documents focused on gene therapy product design, testing, safety, and clinical trial designs. FDA assesses developed gene therapies to ensure that they are safe and of the highest quality prior to reaching the target patient population. Following the manufacturing and purification processes, gene therapies are often administered intravenously to a patient for the gene to be delivered to the faulty cells and protein production to commence.

History of Gene Therapy

The first gene therapy trial began in 1990 at the National Institutes of Health (NIH) to treat a young girl with adenosine deaminase (ADA) deficiency. Following this first trial, the science and treatment methods behind gene therapy advanced. This advancement reached a significant point in 2002 when a gene therapy drug, Genidicine, was approved in China, but this product was not approved in Europe or the U.S. The first gene therapy drug, Glybera, was approved in Europe and the U.S. in 2012. By 2015, over 2,200 gene therapy clinical trials have been initiated and that number continues to grow today.⁵

PPMD's Gene Therapy Initiative

In early 2017, Parent Project Muscular Dystrophy (PPMD) launched our Gene Therapy Initiative, a long-term concept that seeks to accelerate the potential of gene therapy as a therapeutic for Duchenne. Our early strategy was to bring attention to and fund key questions that must be answered in order for the technology to progress towards approvals.⁶

Since the launch of the Initiative, PPMD has funded over \$7 million in a variety of gene therapy and related approaches to several institutions, including Dr. Jerry Mendell's work at Nationwide Children's Hospital's Research Institute, which led to the development of ELEVIDYS.

First-Ever Gene Therapy for Individuals with Duchenne

In June of 2023, the Sarepta drug ELEVIDYS was approved in the U.S. through an accelerated drug approval by the FDA, for use in children ages 4 to 5, to treat Duchenne muscular dystrophy. Accelerated drug approvals through the FDA are designed to allow for earlier approval of drugs to treat serious conditions.⁷ ELEVIDYS is a single-dose gene transfer therapy designed to target the production of micro-dystrophin in skeletal muscle. The first infusion of ELEVIDYS was administered on August 2, 2023, at Children's National Hospital in Washington, DC, to a 5-year-old boy.

PPMD is thrilled that FDA has granted an Accelerated Approval to ELEVIDYS, a gene therapy that provides systemic delivery of a microdystrophin construct that targets both skeletal and cardiac muscle achieved through one IV injection. Despite the incredible advances made with five prior drug approvals for Duchenne, our community continues to have significant unmet needs. The approval of a dystrophin replacement strategy further builds upon, and extends, the positive impact of Duchenne therapy development to date.

WHAT COMES NEXT

Gene therapy is a promising treatment option for Duchenne and other genetic conditions. There still remain challenges with safely delivering therapy, ensuring access to patients with pre-existing antibodies, enabling re-dosing of patients as the durability of the therapy wanes, and the continued development of novel gene therapy strategies. PPMD will keep fighting for federal and other sources of medical research funding to ensure we can build upon these successes and continue to expand our treatments and cures.

Last updated November 2023

¹ <https://medlineplus.gov/genetics/understanding/therapy/genetherapy/>

² Ibid

³ <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy>

⁴ https://www.gene-therapies.org/files/ugd/b11210_493197baa0f04ef885b872b5959217c8.pdf?index=true

⁵ https://globalgenes.org/wp-content/uploads/2018/11/Guide-to-Gene-Therapy_Toolkit_spread_DIGITAL-1.pdf

⁶ <https://www.parentprojectmd.org/research/current-research/our-strategy-impact/ppmds-gene-therapy-initiative/>

⁷ <https://www.fda.gov/drugs/nda-and-bla-approvals/accelerated-approval-program>

Help End Duchenne Muscular Dystrophy

By Supporting Research, Care Considerations, and Therapy Development

Sign the FY25 Duchenne MD Appropriations Letter on Quill

Dear Colleague –

Duchenne muscular dystrophy and the milder form, Becker muscular dystrophy, are rare X-linked recessive diseases belonging to a group of conditions known as dystrophinopathies. Duchenne and Becker are caused by mutations in the dystrophin gene leading to the absence or reduced production of the dystrophin protein, a protein that is key to stabilization of the muscle cell membranes. This lack of dystrophin in muscle leads to progressive muscle weakness and loss over time causing premature death. Affecting 1 of every 5,000 boys, Duchenne is typically diagnosed during the first few years of life. A muscle wasting disorder, Duchenne gradually robs children of their ability to walk by their teenage years. Over time, their muscles weaken further to the point of paralysis, with most patients living only into their late 20s.

Although there are now seven FDA-approved therapies that may help slow its progression, there is currently no cure for Duchenne or Becker. However, there is reason for hope, due in large part to the support and research funding Congress has provided:

- More than 35 potential therapies are in various stages of clinical testing.
- The life expectancy of the average Duchenne patient has increased by about 10 years over the past 10 years, driven in large part by development and dissemination of Care Standards.

Now is the time to continue building upon these successes and move closer to achieving the goal of ending Duchenne and Becker by supporting research, public health, and therapy development initiatives. We invite you to help keep this momentum going by signing the FY25 Duchenne Muscular Dystrophy appropriations sign-on letter. This year, we are requesting language to:

- Increase CDC's Muscular Dystrophy Program funding from \$7.5 million to \$10 million.
- Fund the Duchenne Muscular Dystrophy Research Program (DMDRP) within the Department of Defense (DOD) Congressionally Directed Medical Research Programs (CDMRP) at \$15 million.
- Urge NIH's NHLBI to support research that characterizes cardiomyopathy in Duchenne and Becker Muscular Dystrophy.
- Encourage NHLBI to convene a workshop with key leaders to establish viable cardiac measures to combat cardiomyopathy.
- Enhance CDC Muscular Dystrophy research and disease surveillance initiatives to better understand care and outcomes.
- Encourage FDA to make every effort to incorporate all relevant patient experience data across its regulatory obligations.

The full request is below. We urge you to co-sign this letter to advance these priorities and bring us closer to the day of ending Duchenne.

Please sign this letter on Quill. If you have any questions, please contact Jackie Weinrich (jackie.weinrich@mail.house.gov) with Rep. Matsui or Megan Porter (megan.porter@mail.house.gov) with Rep. Balderson.

Sincerely,

DORIS MATSUI
Member of Congress

TROY BALDERSON
Member of Congress

The Honorable Robert Aderholt
Chair
Labor, HHS, Education,
& Related Agencies Subcommittee
Committee on Appropriations
Washington, DC 20515

The Honorable Rosa DeLauro
Ranking Member
Labor, HHS, Education,
& Related Agencies Subcommittee
Committee on Appropriations
Washington, DC 20515

The Honorable Andy Harris
Chair
Agriculture, Rural Development, FDA,
& Related Agencies Subcommittee
Committee on Appropriations
Washington, DC 20515

The Honorable Sanford Bishop, Jr.
Ranking Member
Agriculture, Rural Development, FDA,
& Related Agencies Subcommittee
Committee on Appropriations
Washington, DC 20515

The Honorable Ken Calvert
Chair
Defense Subcommittee
Committee on Appropriations
Washington, DC 20515

The Honorable Betty McCollum
Ranking Member
Defense Subcommittee
Committee on Appropriations
Washington, DC 20515

Dear Chairmen Aderholt, Harris, and Calvert and Ranking Members DeLauro, Bishop, and McCollum:

Thanks in large part to the leadership of Congress starting with the passage of the Muscular Dystrophy Community Assistance, Research and Education (MD CARE) Act in 2001, significant progress has been made over the past 20+ years in the fight to end Duchenne and Becker Muscular Dystrophy (DBMD), the most common lethal genetic disorder diagnosed during childhood. We are writing to urge that, as you prepare your Fiscal Year 2025 Appropriations bill, you include provisions to help further these pursuits, particularly to advance scientific breakthroughs, to accelerate therapy development, to ensure consistent high-quality care across the country, and to help improve life for patients and caregivers affected by this disease.

As a result of the MD CARE Act and subsequent amendments, federal commitments to research have expanded, helping spur scientific breakthroughs to develop potential therapies. These commitments have also leveraged significant non-federal funding from academic institutions, industry, and venture investors in a true public-private partnership model. In addition to research breakthroughs, the MD CARE Act has helped capture important epidemiological data, information that has helped standardize and improve patient care and inform payer decision making.

Our Fiscal Year 2025 Duchenne and Becker appropriations request contains language and provisions to help continue and strengthen these and other ongoing initiatives. Specifically, the request would:

- Increase funding for CDC's Muscular Dystrophy Program from \$7.5 million to \$10 million.
- Fund the Duchenne Muscular Dystrophy Research Program (DMDRP) within the Department of Defense (DOD) Congressionally Directed Medical Research Programs (CDMRP) at \$15 million.
- Direct the CDC to:
 - Enhance Muscular Dystrophy research and tracking initiatives including specific focus on better understanding care and outcomes for:
 - Patients treated in and out of Certified Duchenne Care Centers;

- Adults with Duchenne and Becker;
 - Those receiving multiple therapies including gene therapy;
 - various subpopulations.
- Update tracking to better understand disease impact on bone health, cardiovascular, and cognitive function.
 - Provide a report to Congress within 6 months of implementation of creation of a new plan.
- Directs the National Institutes of Health (NIH) to:
 - Urge the National Heart, Lung, and Blood Institute (NHLBI) to support research that characterizes cardiomyopathy in Duchenne and Becker Muscular Dystrophy (DBMD).
 - Encourages NHLBI to convene a workshop with key leaders to establish viable cardiac measures to combat cardiomyopathy.
 - Support research that examines the evidence of individuals with DBMD benefitting from a ventricular assist device (VAD) placement or heart transplant.
 - Encourage the Food and Drug Administration (FDA) to:
 - Build on its patient-focused drug development (PFDD) work by accepting relevant patient experience data as a part of new drug applications and incorporating it into product labeling to better inform patients, caregivers, and providers.

Much progress has been achieved in recent years, but much more work remains to be done. The FY 2025 Duchenne and Becker request will focus federal energies toward the highest priority needs to accelerate the development of therapies and treatments and to improve life for all patients impacted by this disease.

Below is the specific language we are requesting:

Centers for Disease Control and Prevention

\$10M for Muscular Dystrophy (increase from FY24 House drafted funding of \$7.5M)

Duchenne and Becker Muscular Dystrophy.— The Committee includes \$10,000,000 to enhance Muscular Dystrophy research and tracking initiatives. The Committee strongly encourages CDC to update research and tracking to better understand the outcomes for Duchenne and Becker muscular dystrophy treated both in and out of Certified Duchenne Care Centers; examine impacts of the condition on bone health, cardiovascular, and cognitive function; and investigate care and outcomes for adults with Duchenne and Becker, those receiving multiple therapies including gene therapy, and various demographic subpopulations. The Committee requests a plan for updating muscular dystrophy efforts along these parameters and a report back to Congress within 6 months.

National Institutes of Health

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Duchenne and Becker Muscular Dystrophy.— In light of improvements in care leading to patients living into their third decade, the leading cause of death in Duchenne and Becker Muscular Dystrophy (DBMD) patients is heart failure. The Committee urges NHLBI to support research that characterizes fibro-fatty replacement of cardiomyocytes in DBMD. There is a gap in the ability to develop novel cardiac therapeutics for DBMD due to a lack of accepted cardiac outcome measures. The Committee encourages NHLBI to convene a workshop with research, clinical, and patient organization leaders to work towards establishing viable cardiac outcome measures for the development of therapeutic agents to delay or treat heart disease in individuals diagnosed with Duchenne. There is growing evidence to support that select individuals with DBMD would benefit from ventricular assist device (VAD) placement or heart transplant. The Committee encourages NHLBI to support research to further

develop criteria for identifying patients who may benefit from such strategies.

Food and Drug Administration

Patient Experience Data.— The Committee supports the FDA’s efforts to identify patient experience data standards to inform clinical research design and regulatory review under the patient-focused drug development process and to accept such data as a part of new drug applications. The Committee also encourages FDA to make every effort to incorporate relevant patient experience and preference data into product labeling to better inform patients, caregivers and providers.

Department of Defense

Congressionally Directed Medical Research Program (CDMRP) Duchenne Muscular Dystrophy Research Funding: \$15M (increase from FY24 House drafted funding of \$10M)

Sincerely,

DORIS MATSUI
Member of Congress

TROY BALDERSON
Member of Congress

The Honorable Roger Wicker
U.S. Senate
555 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Doris Matsui
House of Representatives
2311 Rayburn House Office Building
Washington, DC 20515

The Honorable Amy Klobuchar
U.S. Senate
425 Dirksen Senate Building
Washington, DC 20510

The Honorable Brad Wenstrup
House of Representatives
2419 Rayburn House Office Building
Washington, DC 20515

RE: Support for the BENEFIT Act of 2023

Dear Senators Wicker and Klobuchar and Representatives Matsui and Wenstrup:

Thank you for your tireless efforts to encourage development of and expand access to treatments and cures for patients, including those with rare diseases. On behalf of the undersigned patient advocacy organizations, we write in strong support of your legislation, the Better Empowerment Now to Enhance Framework and Improve Treatments (BENEFIT) Act of 2023.

As you know, the 21st Century Cures Act (P.L. 114-255) includes sections 3001 and 3002, the Patient-Focused Impact Assessment (PFIA), which has accelerated the field of patient-focused drug development (PFDD). FDA now has a number of programs and policies in place to gather and assess patient perspectives within the regulatory review process, and patient advocacy organizations have been deeply engaged with the FDA over the past several years to develop PFDD tools that produce scientifically valid patient experience information. Tremendous progress has been made over the past decade since the fifth Prescription Drug User Fee Act (PDUFA) was authorized, including with PFIA and other provisions of 21st Century Cures. Now is the time to take the next step in moving patient perspectives and experience forward by enacting the BENEFIT Act.

The BENEFIT Act would require FDA to include in the benefit-risk assessment framework of a new drug application how patient experience data was considered in the review process. Currently, FDA includes patient experience data in reviews, but does not indicate how such data impacted the drug approval. Providing this information to the public, and patient communities making significant investments in developing PFDD, builds on transparency from PFIA and will accelerate PFDD strategies more broadly.

The field of patient engagement in drug development continues to flourish thanks to the continued interest and focus by Congress. The BENEFIT Act will build upon this foundation and fill a gap by appropriately disclosing how this data is considered as part of FDA review of new therapies. The BENEFIT Act initially passed the Senate in 2017 but further action was deferred as the 21st Century Cures was being implemented.

Now is the time to take this critical step in building the PFDD environment by passing the BENEFIT Act. The Cures 2.0 Act recognizes this as well by including a parallel provision to the BENEFIT Act. Thank you again for your leadership and we look forward to working with you to enact this legislation this Congress.

Sincerely,

AliveAndKickn
Alpha-1 Foundation
Alport Syndrome Foundation
ALS Association
American Brain Coalition
American Kidney Fund
Ara Parseghian Medical Research Fund
Barth Syndrome Foundation
Beyond Celiac
Coalition Duchenne
Congenital Hyperinsulinism International
CSNK2A1 Foundation
Cure CMD
Cure HHT
Cure Sanfilippo Foundation
Cure SMA
CureDuchenne
CureSHANK
Dravet Syndrome Foundation
EveryLife Foundation for Rare Diseases
FND Hope
FORCE: Facing Our Risk of Cancer Empowered
Foundation for Angelman Syndrome Therapeutics (FAST)
Foundation for Prader-Willi Research
Genetic Alliance
Hermansky-Pudlak Syndrome Network
Hope For Marian
International Pemphigus Pemphigoid Foundation
International WAGR Syndrome Association, IWSA
Jett Foundation
Kindness Over Muscular Dystrophy
Klippel-Trenaunay (K-T) Support Group
Little Hercules Foundation
Lupus Foundation of America
MLD Foundation
Mucopolysaccharidosis Type IV
National Ataxia Foundation
National Health Council

National Kidney Foundation
National MPS Society
National MS Society
NBIA Disorders Association
Organic Acidemia Association
Parent Project Muscular Dystrophy
Phelan-McDermid Syndrome Foundation
PXE International
RASopathies Network
RUNX1 Research Program
Ryan's Quest
Sophie's Neighborhood
Stickler Involved People
Sudden Arrhythmia Death Syndromes (SADS) Foundation
Susan G. Komen
SYNGAP1 Foundation
The Global Foundation for Peroxisomal Disorders
TSC Alliance
United Mitochondrial Disease Foundation
Usher 1F Collaborative
WISKOTT ALDRICH FOUNDATION
Zack Heger Foundation