

**Market Analysis of Duchenne Muscular
Dystrophy-2022**

Dissertation Submitted to



The IIHMR University, Jaipur

for the partial fulfillment for the award of
the degree of Master of Business
Administration (MBA)

in

Hospital and Health Management/Pharmaceutical
Management

by

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Under the Supervision and Guidance of

Dr. Deepti Sharma

2022

DECLARATION BY STUDENT

I hereby declare that this dissertation titled “**Market Analysis of Duchenne Muscular Dystrophy-2022**” is the bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

Niyati Oli

20.06.2022

CERTIFICATE

This is to certify that dissertation titled “**Market Analysis of Duchenne Muscular Dystrophy-2022**” is a record of the research work undertaken by Niyati Oli in partial fulfillment of the requirements for the award of the degree of MBA (Hospital and Health Management) from the IIHMR University, Jaipur under my guidance and supervision and his/her approach to the research study has been sincere, scientific, and analytical.

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Abstract

Duchenne muscular dystrophy (DMD) is the most prevalent kind of muscular dystrophy in children, affecting around 1 in every 5000 live male births. Following the discovery of pathogenic mutations in the dystrophin gene in 1986, genotype/phenotype connections developed, and the role of the dystrophin protein in skeletal, smooth, and cardiac muscles, as well as the brain, was clarified. The muscle cannot withstand the stress of repetitive contractions if the dystrophin protein is missing or has been altered quantitatively or qualitatively. Dystrophin serves as a bridge and anchoring protein between the sarcomere and the sarcolemma, and its absence or diminution causes significant muscle damage that is ultimately irreversible, with connective tissue and fat eventually taking its place. This study aims to critically evaluate the economic landscape and key market trends concerning treatment of Duchenne muscular dystrophy. The study is exploratory in nature and is based on both qualitative and quantitative data. The data has been collected from various secondary sources. The study period includes the period from 2017 to 2022. Descriptive analysis has been carried out to understand the current treatment market for DMD. Understanding of the molecular pathways involved in DMD has led to the development of several treatment options that address various elements of disease etiopathogenesis, resulting in the approval of effective orphan medications for this illness. In this arena, treatment improvements have been exponential, with second-generation medications currently entering clinical trials as gene therapy, perhaps giving a more successful approach to the disease. The advent of mutation-specific medicines, increased prevalence of the disease, and enhanced diagnostics are all contributing to the rise. The market is likely to increase as a result of government initiatives encouraging target-specific therapies and attractive reimbursement rules. Furthermore, the increasing acceptability of targeted medicines like Exondys51, Translarna, and Emflaza is expected to expand the therapeutic area. Though, the high cost of therapies continues to be a barrier to the expansion of the DMD medication landscape. Early detection of genetic diseases might allow for the most effective use of novel gene treatments to change the course of the disease, perhaps extending life and function. To persuasively show safety and efficacy in delivering these medicines to patients, rational and rigorous use of relevant design principles is required.

Acknowledgement

I take this opportunity to express my heartfelt gratitude and deep regards to Dr. Deepti Sharma (Associate Professor, IIHMR University), for providing me with the wonderful mentorship.

I would like to express my sincere thanks to Dr. Ashish Joshi for giving me an opportunity for allowing me to do my dissertation with FHTS, Dr. Mansi Gupta for being the guiding light in the tunnel, Suhasini Lanka and Sofia Saggu for their constant encouragement and continuous support and providing guidance, suggestions, and expertise during training. I am grateful to all the professionals in FHTS for generously imparting their knowledge and valuable time that motivated me to do my best during the internship.

I would also like to take this opportunity to thank Dr. PR Sodani, President, IIHMR University, Jaipur. Finally, I express my very profound gratitude to my parents for providing me with unfailing support and constant encouragement throughout the years of my study and through the process of researching and writing thesis. The accomplishment would not have been possible without them.

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Abbreviations

DMD	Duchenne Muscular Dystrophy
CDC	Centers for Disease Control and Prevention
CK	Creatine Kinase
EU	European Union
EU5	France, Germany, Italy, Spain and the UK
EEA	European Economic Area
FDA	Food and Drug Administration
NDA	New Drug Application
EMA	European Medicines Agency
AONS	Antisense Oligonucleotides
AAV	Adeno-Associated Virus
BMD	Becker Muscular Dystrophy
DAPC	Dystrophin-Associated Protein Complex
TGF	Transforming Growth Factor
PMO	Phosphorodiamidate Morpholino Oligomer
nmDMD	Nonsense Mutation Duchenne Muscular Dystrophy
NSAA	North Star Ambulatory Assessment
HDAC	Histone Deacetylase
HPGDS	Hematopoietic Prostaglandin D Synthase
PDCO	Pediatric Development Committee
PIP	Pediatric Investigation Plan
NBS	Newborn Screening
ADHD	Attention-Deficit Hyperactivity Disorder
ASD	Autism Spectrum Disorders
CCWG	Care Considerations Working Group
PPMD	Parent Project Muscular Dystrophy
MDA	Muscular Dystrophy Association
WDO	World Duchenne Organization
QOL	Quality of Life
MHRA	Medicines and Healthcare products Regulatory Agency
HAS	Haute Autorité de santé (French National Authority for Health)

1 Introduction

DMD, a kind of muscular dystrophy that affects mostly boys and advances rapidly, is known as Duchenne muscular dystrophy (DMD). X-linked recessive heritage may transmit the DMD gene mutation on to future generations, however the illness usually strikes members of families with no prior history of the condition. Lower limb weakness and loss of function is the first sign of DMD, which progresses to the upper limbs. In terms of number of genes found, DMD, which encodes dystrophin, is the second-largest gene to date. Boys having Duchenne muscular dystrophy are unable to produce the dystrophin protein in the muscles because they lack the enzyme ⁽¹⁾.

When it comes to childhood-onset muscular dystrophy, DMD is by far the very common. One out of every 3,500 live male births will be harmed, according to the projections. As children become older, they are more likely to develop the condition. Muscular dystrophies impact an estimated 250,000 persons in the United States. ⁽¹⁾. Because DMD is a genetic disorder, having a member of the family with the condition increases your chance of developing it yourself ⁽²⁾.

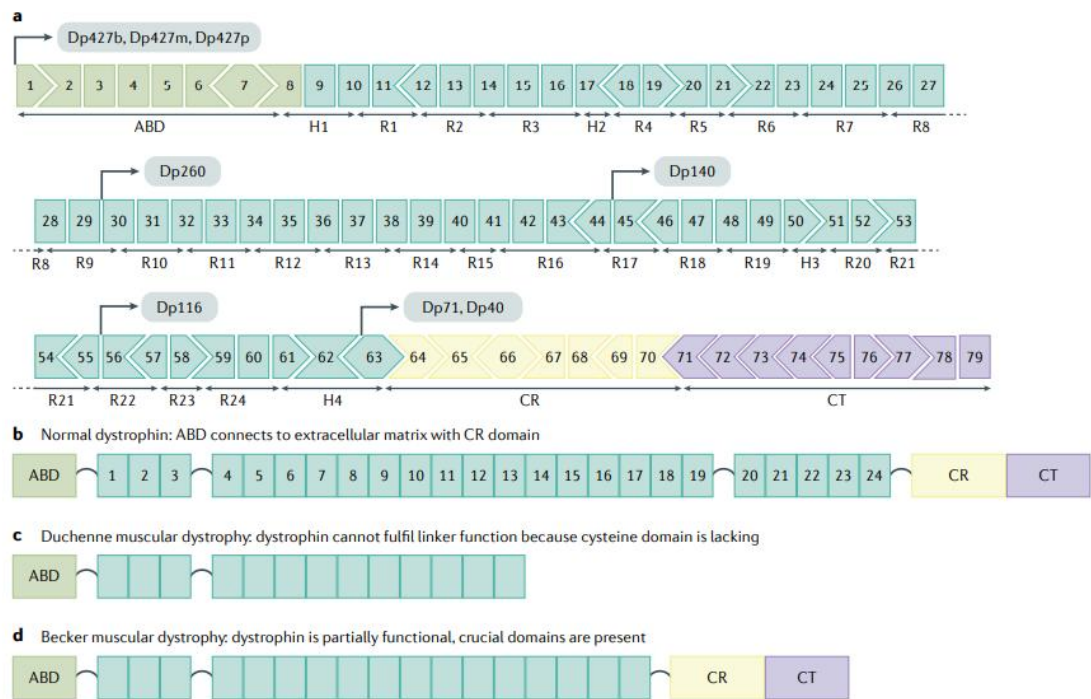


Figure 1.1 Diagrammatic depiction of DMD and dystrophin protein.

Source: Duchenne muscular dystrophy, Nature, 2021 ⁽³⁾

A collection of hereditary illnesses characterized by increasing muscle weakening and cell death of muscle, with the substitution of muscle cells by fat and fibrosis, are known as muscular dystrophies, corresponding to the “Centers for Disease Control and Prevention” (CDC). Between ages 7 and 13, DMD has traditionally culminated in the inability to walk and death in the teens or early twenties. Despite the early start of symptoms, the average age of diagnosis is five years. It was expected that one in 3,500 (2.9 per 10,000) male births are affected by DMD and one in 18,518 (0.5 per 10,000) male births are affected by Becker muscular dystrophy. On January 1st, 2007, the general frequency in the United States among men aged 5--24 years was 1.3-1.8 per 10,000 ⁽⁴⁾.

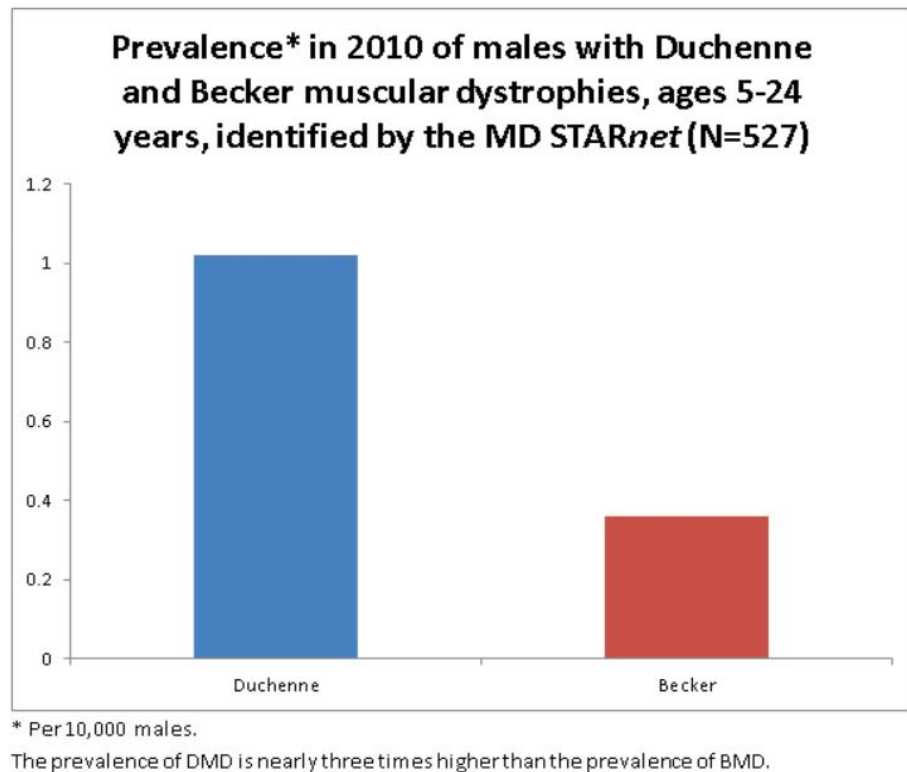


Figure 1.2 Prevalence of DMD in the US

Source: Centers for Disease Control and Prevention, 2020 ⁽⁵⁾

Symptoms commonly develop before the age of six and can even appear in infancy. Motor milestones, including as sitting and standing on one's own, are often the first signs of developmental delays. Boys with DMD often begin walking at the age of 18 months. Leg and pelvic muscular weakness develops over time and is connected to a decrease in muscle mass (wasting). Dyspnea and difficulty walking up stairs are signs of muscle weakness. The arms, neck, and other parts of the body may also experience muscle weakness, although not to the same degree or at such an early stage as the lower half.

Fat and connective tissue ultimately take the place of the extra muscle tissue in the calf muscles (pseudohypertrophy). Due to muscle fiber shortening and connective tissue fibrosis, leg muscles become ineffective. It's possible that your calves may hurt from time to time.

Males between the ages of one and six are more likely to have symptoms. Muscular strength declines rapidly between the ages of 6 and 11. The majority of boys are confined to a wheelchair by the time they are twelve if they need braces to walk. Skeletal abnormalities of the spine and other places result from aberrant bone development ⁽¹⁾.

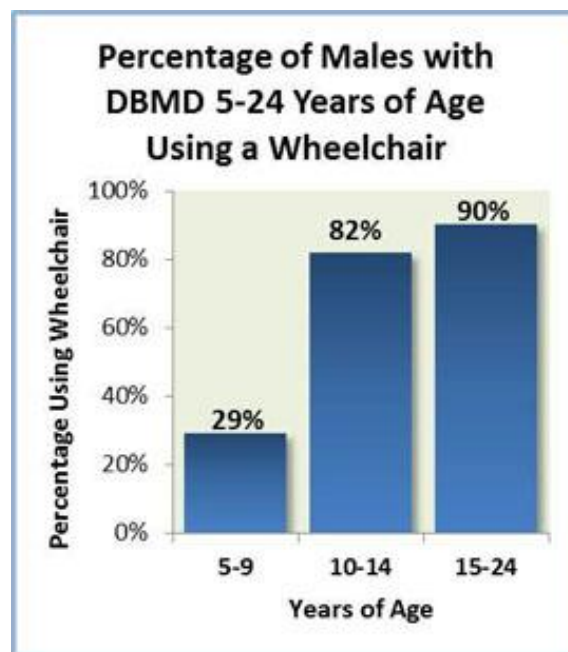


Figure 1.3 Percentage of males with DBMD using wheelchair

Source: MD STARnet Data and Statistics, CDC, 2020 ⁽⁶⁾

Breathing problems are typically caused by muscular weakness and structural abnormalities. Cardiomyopathy (an enlarged heart) affects practically everyone, starting in their early teens in some cases and lasting until they reach the age of 18. Although

intellectual impairment is possible, it is not unavoidable, and it does not worsen as the condition continues.

DMD patients seldom live into their 30s. Breathing problems and cardiomyopathy are two of the most prevalent causes of mortality.

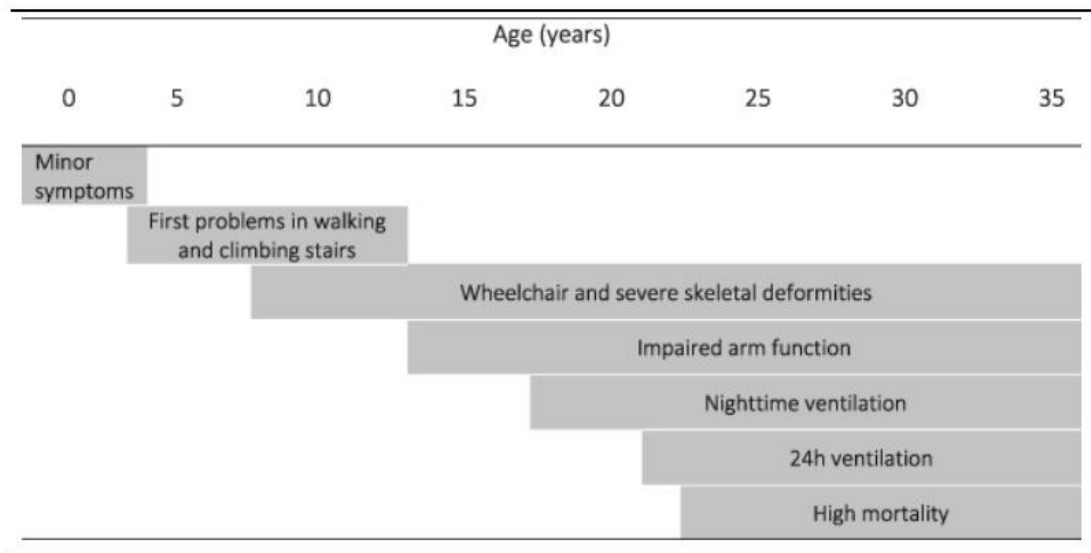


Figure 1.4 Typical course and transition in DMD

Source: Wiley Online Library, 2017 ⁽⁷⁾

Medical history, clinical examination, and molecular genetic testing are all necessary to confirm the diagnosis of Duchenne muscular dystrophy (DMD). Dissection and microscopic examination of damaged muscle tissue may show specific abnormalities to muscle fibers, if genetic testing is inconclusive. Muscle protein concentrations may be measured with the use of specialized blood tests (such as creatine kinase) (immunohistochemistry).

It's possible to identify certain genetic abnormalities, such as duplications, deletions, or single-point mutations by conducting a molecular genetic test. Samples of blood or muscle cells may be used for testing. Before a baby is born, several procedures may be used to detect DMD (prenatally).

Muscle biopsy samples may sometimes be used in a specialized test to assess the presence and concentrations of certain proteins in cells. ⁽¹⁾.

Muscle biopsy samples may sometimes be used in a specialized test to assess the presence and concentrations of certain proteins in cells. Immunofluorescence, immunostaining, and Western blot (immunoblot) are some of the methods that can be employed. Antibodies that respond to proteins like dystrophin are used in these assays. Antibodies are applied to tissue samples from muscle biopsies, and the results can be used to assess whether a certain disease is present. These antibodies may be used to determine whether or not a certain muscle protein is present in cells taken from muscle biopsies, as well as the amount and size of that protein ⁽²⁾.

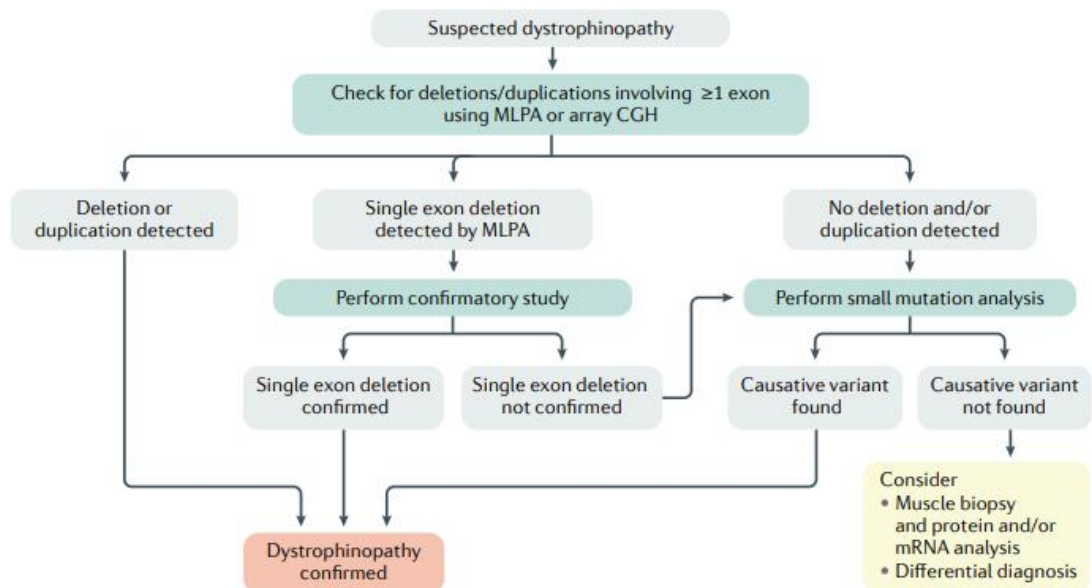


Figure 1.5 Diagnostic decision tree to confirm DMD

Source: Duchenne muscular dystrophy, Nature, 2021 ⁽³⁾

DMD is presently incurable. Each patient's symptoms are taken into consideration while developing a treatment plan. To prevent contractures, physical treatment and active and passive exercise should be employed. Scoliosis or contractures may need surgery for

certain persons. Braces may help to avoid contractures. In order to walk (ambulate), mechanical help (like canes and braces) may be necessary ⁽²⁾.

Corticosteroids are often prescribed to people with DMD. Patients who use these medications see a 2–3-year delay in the onset of muscular weakening and eventual loss of mobility. DMD patients often get one of two types of corticosteroid medication: deflazacort and Prednisone (that are not available in the United States) ⁽²⁾.

Sarepta now leads the DMD market with a robust pipeline that includes three approved antisense oligonucleotide products: and Vyondys 53 (golodirsen), Exondys 51 (eteplirsen), and the recently approved Amondys 45 (casimersen). These drugs are for people who have mutations. In combination, all of the drugs approved in the last several years can treat about 30% of all DMD patients ⁽²⁾.

In the United States, Vyondys 53 was certified in 2019 for affected role for exon 53 skipping. Its primary opponent is Viltepso (viltolarsen), which was licensed for use in the US and Japan in 2020. As far as I know, NS Pharma is the exclusive source of Viltepso. Obtaining EU clearance for the medicine, which is now being investigated in EU sites, may need further evidence. In their separate clinical trials, the first medicine increased dystrophin levels by 0.88%, while the second treatment increased levels by 1.98%. There were 58 DMD patients in the first study, and just eight DMD individuals were included in the second study, which was much smaller. Another country that has authorized Viltepso for DMD patients is Japan. As a result, the Japanese market is projected to be dominated by it ⁽⁸⁾.

One of the most major pharmaceutical companies, PTC Therapeutics, has two licensed drugs. Despite the European Economic Area's (EEA's) 2014 approval of Translarna (ataluren) for the therapy of Ambulatory DMD patients 2 years and older, the FDA's 2017 rejection of the drug's efficacy was surprising. Based on the Translarna dystrophin experiment, the business plans to resubmit an NDA to the FDA in 2021. In the United States, the FDA's decision on the approval is keenly anticipated. PTC also plans to expand the scope of its EMA label to include patients who are on the move. Another PTC drug, Emflaza (deflazacort), is intended for all DMD patients over the age of five. The medicine was approved in the United States in 2017 and is thought to be better than traditional corticosteroids like prednisone and prednisolone. Although medicine has had substantial hurdles in the United States due to its extraordinarily expensive cost of

therapy, emflaza has been accessible in Europe for more than a decade at a considerably reduced cost ⁽⁸⁾.

There is a growing need for treatments for Duchenne muscular dystrophy due to factors such as an increasing prevalence of the condition, greater investment in biopharmaceutical R&D to develop new disease medicines, and enhanced public awareness campaigns ⁽⁹⁾.

2 Rationale of the Study

Treatment for Duchenne muscular dystrophy (DMD) is growing as a result of increasing disease burden, expanded biopharmaceutical R&D to create novel disease therapies, and enhanced DMD awareness campaigns. The high expense of treatments, on the other hand, is a roadblock to the development of new DMD medications. With indigenous innovation and expert training, it is envisaged that cost would decline, enabling the potential to expand. The following topics are covered in the report:

- Current status of DMD therapeutic market-2022
- Competitive landscape linked with Duchenne muscular dystrophy treatment across US, EU5 and Japan
- Regulatory considerations for the care of DMD.
- Factors driving the growth of DMD treatment market

3 Research Question

What are the key market trends for Duchenne muscular dystrophy in the second quarter of 2022, and how will the competition environment shift?

4 Research Objectives

- To analyze the current market scenario through reports in the second quarter of 2022 of the Duchenne muscular dystrophy global market.
- To understand the competitive landscape associated with Duchenne muscular dystrophy treatment.
- To comprehend the developments and regulatory considerations for the treatment of DMD.
- To learn about market drivers and barriers.

5 Research Methodology

- **Search Strategy**

To critically evaluate the economic landscape concerning the treatment of DMD, a review of research methods using numerous techniques, as well as prominent mainstream media pieces, was accomplished. Desk/secondary research will be conducted, with the proposed technique being used to locate publications that are related to the research topics. On March 21, 2022, the preliminary exploration began. On June 18, 2022, the investigation came to a halt. Using a five-step methodological framework, which includes the following steps: (i) recognizing the exploration topic, (ii) recognizing relevant exploration articles, (iii) research selection, and (iv) recording the data and (v) reviewing the results. Details of the search strategy, eligibility criteria, and the selecting of research were provided in great detail.

- **Search Terms**

The author used the following search terms and database- appropriate syntax to review the literature on the overview and market of Duchenne muscular dystrophy: "Google Scholar, PubMed/MEDLINE, were searched using the following search terms and database-appropriate syntax to review the literature on the overview and market of Duchenne muscular dystrophy":

- ("DMD"[All Fields] OR "Duchenne muscular dystrophy"[All Fields] OR "Recent Duchenne muscular dystrophy treatment recent "[Supplementary Concept] OR "Duchenne muscular dystrophy"[All Fields] OR "DMD"[All Fields] OR "India"[All Fields] OR "US" [All Fields] OR "Europe" [All Fields] OR Japan [All Fields] OR "DMD"[All Fields] AND ("Market Analysis" [Title/Abstract]) AND DMD [Title/Abstract] OR market [Title/Abstract] [Supplementary Concept])
- Market research study as a research design (Descriptive study)
- Surveys, analyst reports, and company websites are all good sources of secondary data.
- MS Excel is a good tool for data analysis.

The above search terms were combined to execute a search with the below inclusion criteria:

1. Relevant articles published in the last 5 years where full-text articles available for public use.

2. A literature review published in the English language.
3. Duchenne muscular dystrophy as an inclusion criterion

Criteria for exclusion: Other muscular dystrophies

In order to select the research for this review, the authors conducted a two-step process. In the first stage, all of the retrieved papers' titles and abstracts were checked for relevance. Step two included reading all of the research from step one in their entirety.

The author pursued to explain with a non-systematic random, virtual, digital study for the estimated and evaluated market landscape of treatment options for Duchenne muscular dystrophy. Market analysis was also accomplished by evaluating the opportunities and obstacles in the Market of Duchenne muscular dystrophy treatment therapies/drugs.

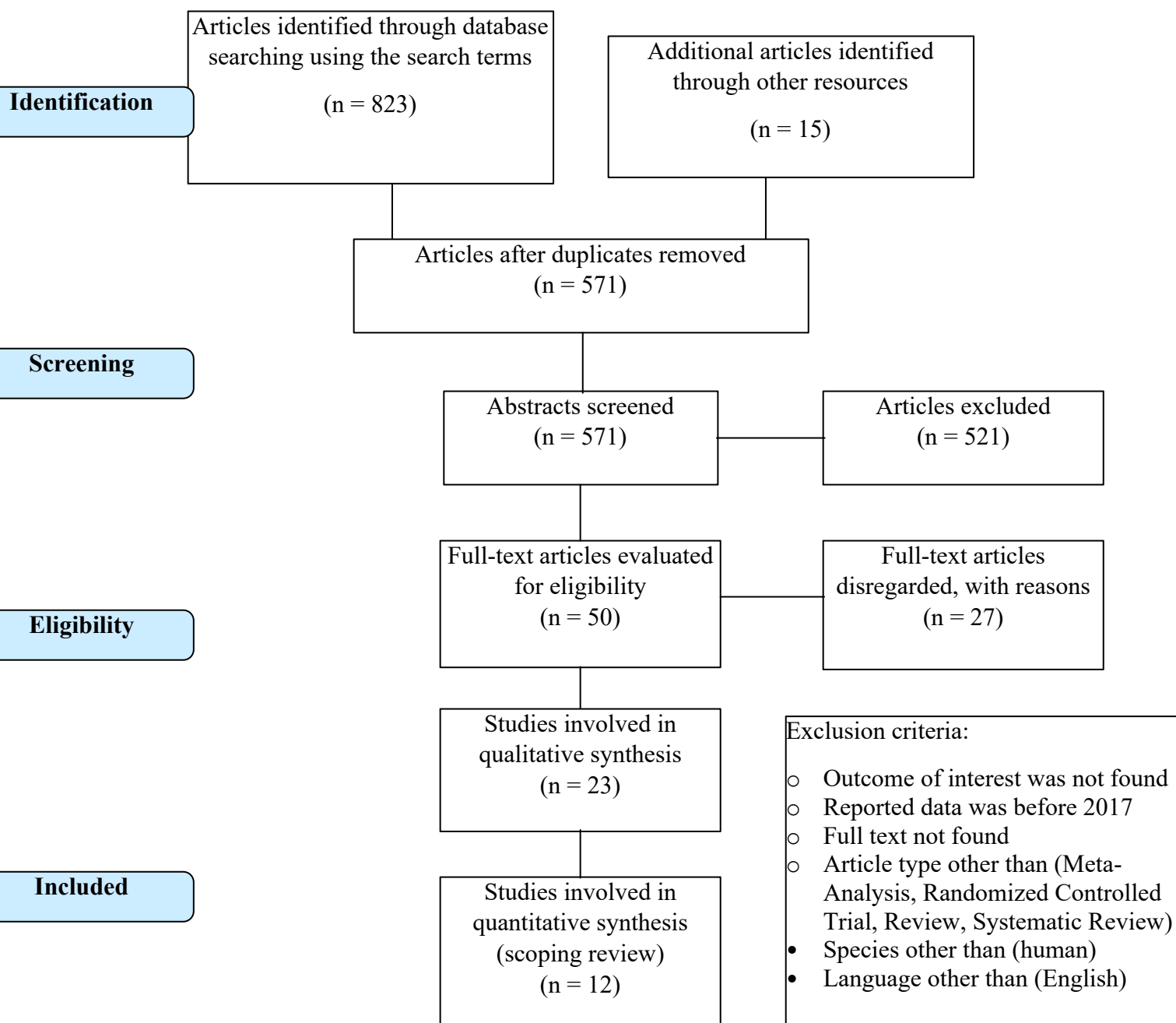


Figure 1 Flowchart of literature search process

• Data Collection Methods and Tools

Secondary research resources comprised journals, product brochures, company websites, documents, corporate biographies, twelve-monthly reports, as well as widespread internet searches. This was carried out to discover numerous topics of proficiency and publications that could take the US EU5 and Japan market evaluations and estimates. Secondary research and databases offered online were used to assemble information regarding significant clinical trials, mergers, deals, procurements, and

innovative Duchenne muscular dystrophy drugs introduces that will influence the industry.

- **Implications of the research**

- Raise awareness about Duchenne muscular dystrophy.
- Enlist the available as well as emerging treatment options in the market.
- Describe the protentional market drivers and barriers.

6 Literature Review

Figure 6.1 Table Review of literature

Author (year)	Study	Research Design	Salient Features
“Agnieszka Łoboda and Józef Dulak” (2020)	“Muscle and cardiac therapeutic strategies for Duchenne muscular dystrophy: past, present, and future”	Systematic review	The objective of this study was to outline potential therapy alternatives and present the current state of several, yet inadequate, techniques for slowing the course of DMD illness. The authors of this study point out that the majority of pharmacological agents simply address the disease's symptoms. Some medications that target the fundamental cause, such as golodirsen, eteplirsen, and ataluren, have recently received conditional approval; Only a small proportion of those with DMD may benefit from these treatments, since they can modify specific mutations in the DMD gene (10).

“Salvatore Crisafulli, Janet Sultana, Andrea Fontana, Francesco Salvo, Sonia Messina, and Gianluca Trifirò” (2020)	“Global epidemiology of Duchenne muscular dystrophy: an updated systematic review and meta-analysis”	Systematic review and Meta-analysis	This study's goal was to estimate the prevalence of DMD worldwide, as well as the prevalence of DMD in new-borns. The pooled epidemiological prevalence estimates were produced by doing a meta-analysis using random-effects logistic models for both overall and birth prevalence and in two independent core populations (i.e., all human being and in males only). There were 7.1 instances per 100,000 males and 2.8 cases per 100,000 people worldwide, but the frequency of DMD births was 19.8 cases per 100,000 live male births globally⁽¹¹⁾.
“Fernanda Fortunato, Rachele Rossi, Maria Sofia Falzarano, Alessandra Ferlini” (2021)	“Innovative Therapeutic Approaches for Duchenne Muscular Dystrophy”	Review	This review looks at the various novel techniques (cell-based, gene-based, and pharmacological) that was established to restore effective dystrophin in DMD muscles. As promising as these approaches are, and as many clinical investigations on DMD patients as possible have been done or have already been finished, fibrotic dystrophic muscle remains a challenge for gene and cell therapy. As a result, future

			treatment methods should involve a combination of medicines that consider the health of the muscle as well as the downstream consequences of dystrophin deficiency ⁽¹²⁾ .
“S. Ryder, R. M. Leadley, N. Armstrong, M. Westwood, S. de Kock, T. Butt, M. Jain, and J. Kleijnen” (2017)	“The burden, epidemiology, costs and treatment for Duchenne muscular dystrophy: an evidence review”	Systematic review	This systematic review focuses on DMD therapy, severity, progression, and quality of life. It also contains the most up-to-date information about DMD's burden, epidemiology, sickness expenses, and treatment trends. It was determined that indirect costs are a prominent component of this disease and should be considered when designing suitable care packages and coordinating health and social care financial planning. The cost burden per capita rises as the condition progresses ⁽¹³⁾ .
“Sarah R. Rivera et al.” (2020)	“Medical management of muscle weakness in Duchenne muscular dystrophy”	Survey study	The results of a comprehensive literature review and input from an expert panel were used to compile a list of statements on the usage of presently available pharmaceuticals in the United States to treat DMD. The responses of the panellists were gathered using a modified Delphi method.

			When payer restrictions do not influence decision, either deflazacort or prednisone weekend dose was preferable among corticosteroid regimens. A corticosteroid and eteplirsen should be administered to most individuals with exon 51 skip-amenable mutations ⁽¹⁴⁾ .
Megan A. Waldrop and Kevin M. Flanigan (2019)	“Update in Duchenne and Becker muscular dystrophy”	Review	The study's main objective was to outline current genetic treatment techniques and discoveries for DMD, as well as to highlight changes to existing DMD standard of care recommendations. ⁽¹⁵⁾ .
“Shelagh M. Szabo, Renna M. Salhany, Alison Deighton, Meagan Harwood, Jean Mah, and Katherine L. Gooch” (2021)	“The clinical course of Duchenne muscular dystrophy in the corticosteroid treatment era: a systematic literature review”	Systematic review	The objective of this study was to evaluate the age at major clinical milestones in the corticosteroid period (loss of ambulation, cardiomyopathy, ventilation, scoliosis, and death). This research also shed light on a variety of difficulties in interpreting and comparing outcome estimates to define the clinical course of DMD ⁽¹⁶⁾ .
“Damon R. Asher, Khampaseuth Thapa, Sachi D. Dharia, Navid Khan, Rachael A.	“Clinical development on the frontier: gene therapy for	Review	This review examines how gene healing for rare diseases defies established clinical development paradigms, and suggests a step-by-step

Potter, Louise R. Rodino-Klapac” (2020)	duchenne muscular dystrophy”		strategy to design and analysis to promote gene therapy's broader application. It also suggests that thorough preclinical research is necessary for developing an efficient gene delivery platform and selecting the most effective dosage ⁽¹⁷⁾ .
“Manisha Goyal, Ashok Gupta, Kamlesh Agarwal, Seema Kapoor, and Somesh Kumar” (2021)	“Duchenne Muscular Dystrophy: Genetic and Clinical Profile in the Population of Rajasthan, India”	Prospective study	Exon deletions, duplications, and point mutations were examined in 120 clinically diagnosed DMD patients in this prospective study. According to the findings, genetic testing must be the first line of defence in suspected DMD cases. It was suggested that creating exon-specific medications or continuing mutation-specific therapy may be beneficial ⁽¹⁸⁾ .
Harry Wilton-Clark and Toshifumi Yokota (2022)	“Antisense and Gene Therapy Options for Duchenne Muscular Dystrophy Arising from Mutations in the N-Terminal Hotspot”	Review	This review covers the present state of N-terminal antisense and gene treatments for DMD, with a particular emphasis on exon-skipping therapy for duplications and deletions, as well as micro dystrophin therapy ⁽¹⁹⁾ .

“Yuko Shimizu-Motohashi, Hirofumi Komaki, Norio Motohashi, Shin’ichi Takeda, Toshifumi Yokota, and Yoshitsugu Aoki” (2019)	“Restoring Dystrophin Expression in Duchenne Muscular Dystrophy: Current Status of Therapeutic Approaches”	Review	The aim of the article is to discuss the present state of DMD therapy options, with an emphasis on techniques that can restore dystrophin. It also suggests that research designs or drug structures be optimised in the future to aid in the evaluation of medication efficacy. After long-term use of the treatment, real-world data may indicate new drugs' genuine efficacy, such as an increase in survival rates⁽²⁰⁾.
“Nigama Chandra Sattenapalli, Anka Rao Areti S.N. Koteswara Rao G., Uma Sankar Kulandaivelu, Rajasekhar Reddy Alavala, Ravi Manne” (2022)	“Study of Clinical Features and Diagnosis Pattern of Duchene Muscular Dystrophy in Southern India”	Observational survey	The study's objective was to perform an observational survey in southern India on preliminary analysis, family history, related symptoms, and DMD diagnosis ratio. The main finding in this South Indian research group was milestone delay. Despite a small margin, the majority of the studied population had "no blood relation among parents" in their family history⁽²¹⁾.

7 Results/Findings

7.1 DMD Overview

A deadly X-linked recessive disease, DMD is marked by the absence of functioning dystrophin, a protein essential for muscle stability and strength. By the age of five, most

people with Duchenne muscular dystrophy (DMD) have significant lower limb weakness and mobility difficulties, progressing to the point that they need a wheelchair by the age of twelve. As of now, there is no cure for Duchenne muscular dystrophy (DMD), hence current treatment is directed at slowing the onset of the illness and then providing end-stage assistance if necessary. Although this therapy may prolong the lives of DMD patients into their late twenties, it is not a cure. Many side effects have been attributed to the use of corticosteroids ⁽¹⁹⁾.

Multiple studies have examined the applicability of gene and antisense therapy to treat DMD, and the FDA has authorized five pharmaceutical candidates for the treatment of a subset of DMD patients, and these medications are presently on the market. Exon 43–55 Hotspot Mutants are being treated with all authorized medications. Gene therapy may be defined in a variety of ways, but in general, it refers to treatments that use recombinant genetic components. Gene therapy offers the potential to give long-term treatment with just one treatment, successfully curing several illnesses at their source. However, immunogenicity, undesired mutations, and off-target effects might put patients at risk, restricting the use of various gene therapy procedures. The antisense treatment, on the other hand, employs synthetically manufactured DNA-like compounds known as antisense oligonucleotides (AONs) that are aimed for mRNA without supplying extra genes to express. If you have a long-term condition, you may find that AONs are more expensive and complicated to administer than other medications ⁽¹⁹⁾.

The DMD industry is projected to produce higher than USD 8 billion through earnings in the seven major markets by 2020, thanks to the recent introduction of exon-skipping drugs and the projected approval of additional treatments (the United States, Italy, Germany, Spain, France, the United Kingdom, and Japan) by 2030 ⁽⁸⁾.

Duchenne Muscular Dystrophy has long been an attractive candidate for gene therapy, but it has been difficult to overcome various technological hurdles. Patients with DMD confront a significant hurdle in overcoming the high cost of approved medicines. R&D, including increasing recognition and neonatal screening, are anticipated to enhance detection and therapy for this patient group ⁽⁸⁾.

Risk factors for DMD include gender (predominantly men) and family history

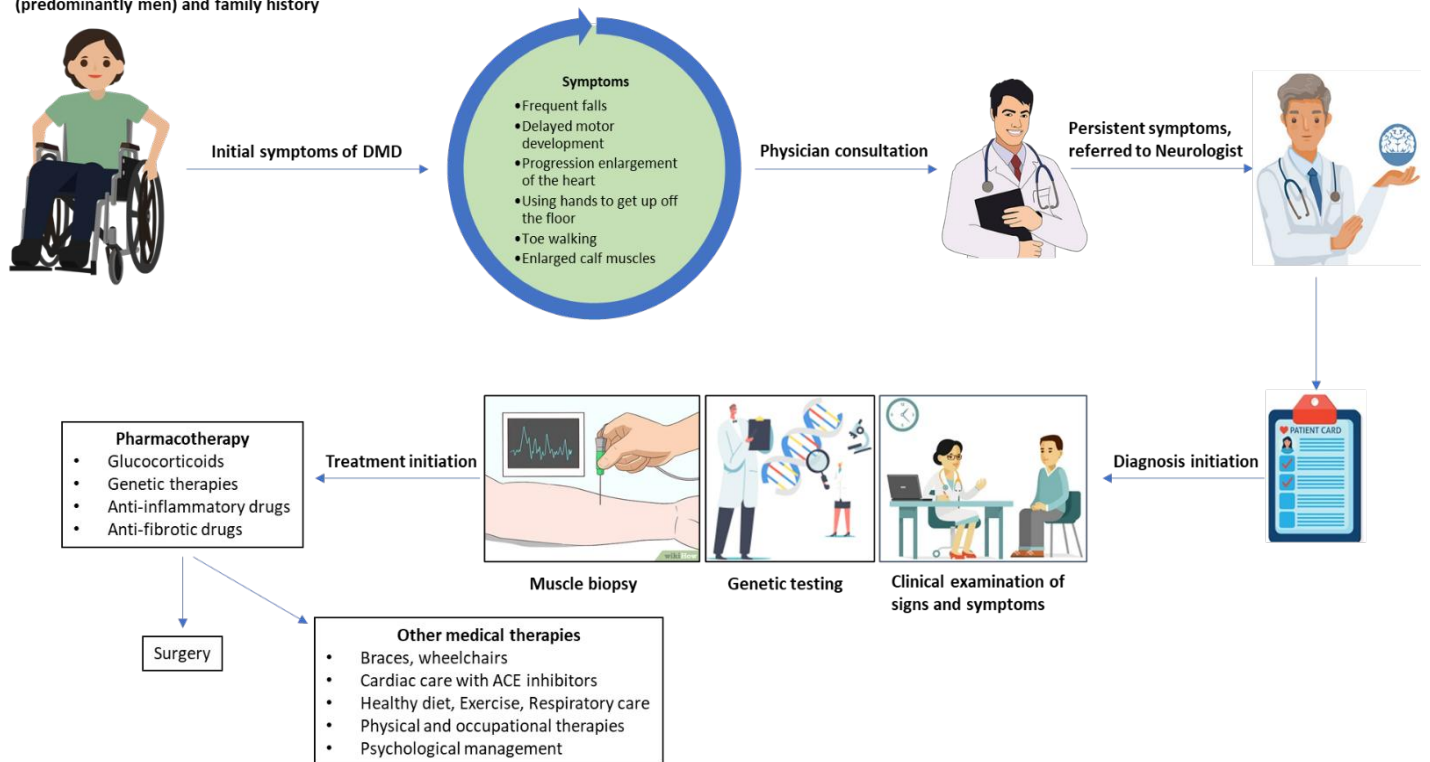


Figure 7.1 Patient journey of DMD

7.2 DMD Inheritance

In females, there are two copies of X-chromosome. Males have one X and one Y chromosome, respectively. There is a 50/50 split between mother and father when it comes to the chromosomes that each parent provides. The X and Y chromosomes are always passed down from father to son in males. A girl receives one X chromosome from each father. Understanding some basic genetics is crucial in understanding how Duchenne can develop one or more moments in a family. There are 46 chromosomes in human bodies, each of which has 23 pairs of chromosomes:

- 44 autosomes (pairs 1-22)
- 2 sex chromosomes (pair 23)

Because the Duchenne gene is placed on the X chromosome, it is critical to understand chromosomes. As a result, Duchenne is an X-linked disease that may be handed on to sons from mothers who are transporters of the inherited mutation ⁽²²⁾.

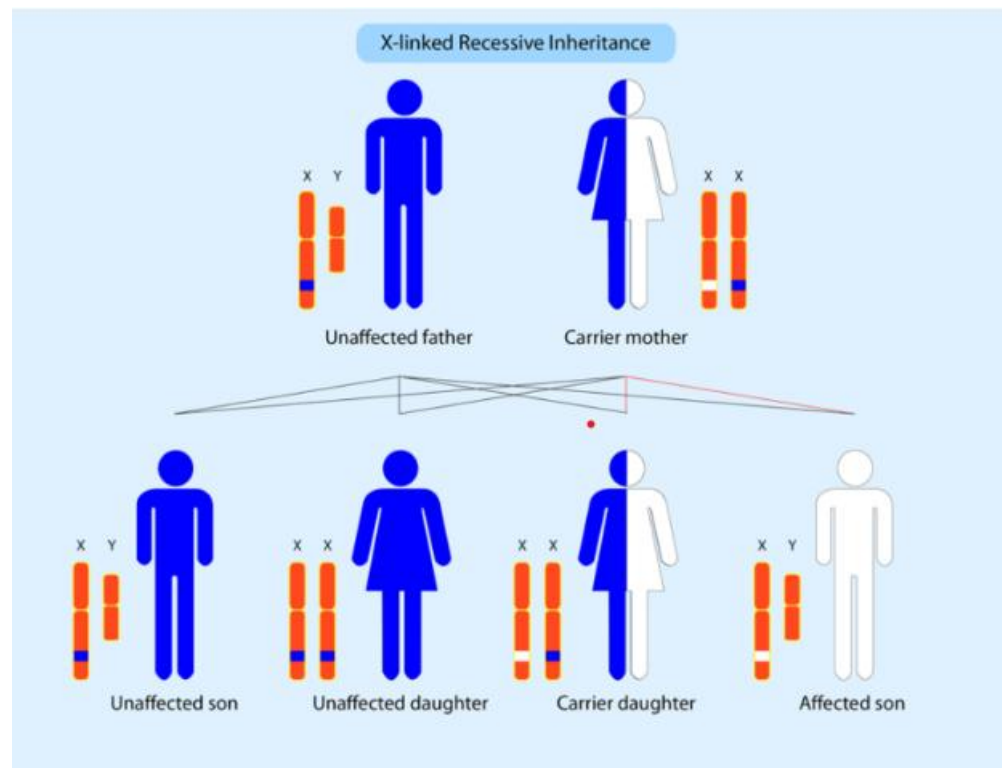


Figure 7.2 X-linked recessive inheritance of DMD

Source: Parent Project Muscular Dystrophy, 2022 ⁽⁷⁾

Dystrophin mutations are passed from mother to kid 50% of the time if the mother has the gene mutation.

- Duchenne muscular dystrophy affects about one in two children born to a carrier mother.
- Carrier women are 50% more likely than non-carrier women to have another child who will be a carrier or manifest a carrier.

There is no way for a mother to influence which X chromosome her child inherits.

Due to random genetic mutations that may occur at any point throughout the pregnancy, Duchenne may not be transferred from father to child. In almost one out of every three

instances, there is no previous history of Duchenne in the family. To put it another way, it may impact anyone of any ethnicity or culture.

Women are typically unaffected by dystrophin gene mutations due to their ability to have two copies of the X-chromosome (the "backup" copy of the gene). If the X chromosome is mutated, men are more likely to be affected by Duchenne or Becker than females since they have only one copy of the X chromosome. Because of the difference between the number of X chromosomes, Duchenne and Becker are more common in men than in women ⁽²²⁾.

Carriers are females that have one dystrophin gene mutation. Carriers have a higher likelihood of having Duchenne-positive males and Duchenne-positive girls. Female carriers of Duchenne are frequently unaffected by the disease because they produce adequate dystrophin protein. Females, on the other hand, might experience some of the symptoms of Duchenne, such as muscular weakness and cardiac difficulties. Some girls can show the characteristic signs of Duchenne, albeit it is uncommon. A manifesting carrier is what this is called. A healthcare provider who is experienced with Duchenne should examine all carriers ⁽²²⁾.

Type and Frequency of Mutations Held within the TREAT-NMD DMD Global Database

Total	7,149	Percentage of total mutations
Large mutations	5,682	79
Large deletions (≥ 1 exon)	4,894	68
Large duplications (≥ 1 exon)	784	11
Small mutations	1,445	20
Small deletions (<1 exon)	358	5
Small insertions (<1 exon)	132	2
Splice sites (<10 bp from exon)	199	3
Point mutations	756	11
Nonsense	726	10
Missense	30	0.4
Mid-intronic mutations	22	0.3

Figure 7.3 Type and frequency of mutations held within the DMD global database

Source: TREAT-NMD Global Database ⁽²³⁾

7.3 Therapeutic Developments for Duchenne Muscular Dystrophy

Dystrophin-restoration procedures and approaches that focus on the implications of dystrophin loss to retain muscular tissue for as long as possible are both under study as treatment possibilities for DMD. The treatment options for DMD do not reestablish muscle tissue and function, thus treating patients as soon as possible is imperative. Furthermore, because only muscle expresses dystrophin (transcript targeting) or benefits from dystrophin expression, the success of dystrophin-restoring treatments will be determined by muscle quality (genome editing and gene delivery) ⁽³⁾. Effective therapeutics for DMD is still being researched. In other cases, the goal is to enhance muscle quality and function by addressing the underlying molecular mechanisms that contribute to DMD. Gene addition, exon skipping, stop codon readthroughs, and genome editing are among the DMD treatments that may at least partially restore the

production of functional dystrophin protein. Treatments that target pathways involved in DMD's pathogenesis are also being considered. ⁽²⁴⁾. In the future, it's conceivable that a mix of treatments will be employed to restore dystrophin and preserve muscle quality while also slowing disease progression ⁽³⁾.

- Stem cell transplantation

Since the beginning, stem cell transplantation has been the most common method of restoring dystrophin function. Since the relocated cells will include a functional copy of DMD and help in muscle regeneration following the transplant, the rationale for DMD stem cell transplantation is rather interesting. However, stem cell therapy is challenging due to the enormous amount of muscle mass (>30 percent of body mass) and the great number of specific skeletal muscles (>700). Re-transplanting corrected patient-derived cells or using allogenic stem cell transplantation (that needs immunosuppression in the recipient) are two alternatives for stem cell transplantation. Myoblasts, pericytes, bone marrow-derived cells, and mesenchymal stem cells are few stem cells that may be applied for transplantation. Satellite cells ⁽³⁾.

- Gene therapy

Dystrophin deficiency (DMD) is a genetic disorder in which the body's ability to produce the protein is impaired. A viral vector is used to deliver a functional copy of the DMD cDNA to affected tissues. Adeno-associated viruses (AAVs) show a predilection for skeletal muscles and the heart, despite the fact that most viruses have no such preference. They're really good at infecting these tissues. Genome editing techniques like CRISPR/Cas9 have made it possible to make precise alterations to the genome ⁽³⁾.

- Exon skipping

Three ASOs have been authorized for DMD, however this was established on modest levels of dystrophin restoration rather than verified functional improvements. Exon 51-swapping ASO Drisapersen, with a 2'-O-methyl phosphonothioate modification, was tested in placebo-controlled experiments. Particular mutant dystrophin proteins may be created using ASOs, which skip exons in response to specific mutations. A single exon may be skipped to create a variety of different dystrophins, such as exons 47–50 and 48–50, as well as the missing exon 52. Chemical modifications, muscle-homing conjugates and arginine-rich peptide conjugates are among of the strategies being tested to improve ASO efficiency and absorption by heart and skeletal muscle. – As a therapy

option for larger groups of patients, multiexon skipping is being studied. As a result of this research, patients with BMD and exon 45–55 deletion are the focus of attention because of their moderate symptoms ⁽³⁾.

- Nonsense mutation readthrough

In addition to ataluren, that was accepted by the European Medicines Agency, gentamicin has been studied as a therapy for DMD due to its stop codon readthrough potential. Long-term therapy, however, is not an option due to its safety profile. Several additional chemical compounds have been tested in the hopes of finding a readthrough medication with a superior safety profile ⁽³⁾.

- Utrophin upregulation Utrophin

A ubiquitous protein found at neuromuscular junctions that is highly homologous to dystrophin and can attract the majority of the proteins involved in the DAPC. Utrophin is produced in the same areas of muscle fibers as dystrophin in growing muscles, however, when dystrophin expression begins, utrophin synthesis is downregulated in muscle. Utrophin is frequently increased in DMD patients and animal models lacking dystrophin, and additional elevation of utrophin in mice models improved DMD pathogenesis ⁽³⁾.

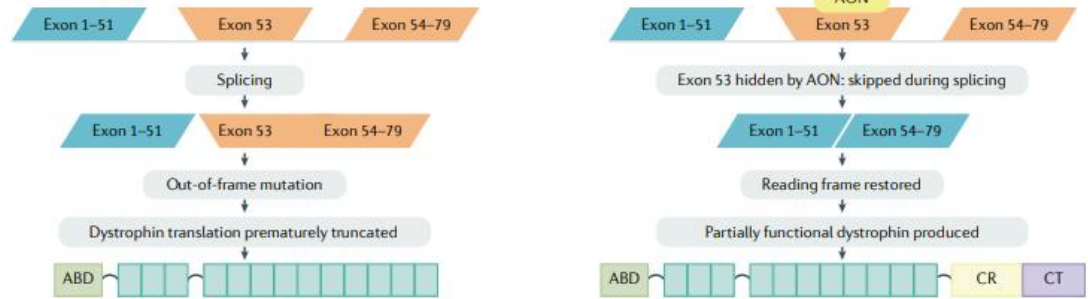
- Approaches to preserving muscle

Therapeutic methods for DMD are being developed that aim for the secondary effects of dystrophin depletion. Alternative steroids with a better protection profile are being investigated, for example, because continuous usage of glucocorticosteroids is associated with a slew of side effects. Compounds that increase muscle mass have also been studied as a potential therapy for DMD. Myostatin (a TGF family growth factor that suppresses muscle development) is one such example. There has also been researching on ways to increase mitochondrial function in people with DMD. Oxidative stress and fibrosis are predicted to be reduced by these substances. Individuals with Duchenne muscular dystrophy (DMD) who were not receiving corticosteroids had an improvement in respiratory function after using idebenone, a medication that targets mitochondrial function. It has also been shown that decreasing histone deacetylase may aid regeneration and reduce inflammation in people with DMD. As shown by muscle samples taken before and after the trial, a small open-label study of Givinostat found that it reduced fibrosis in all patients ⁽³⁾.

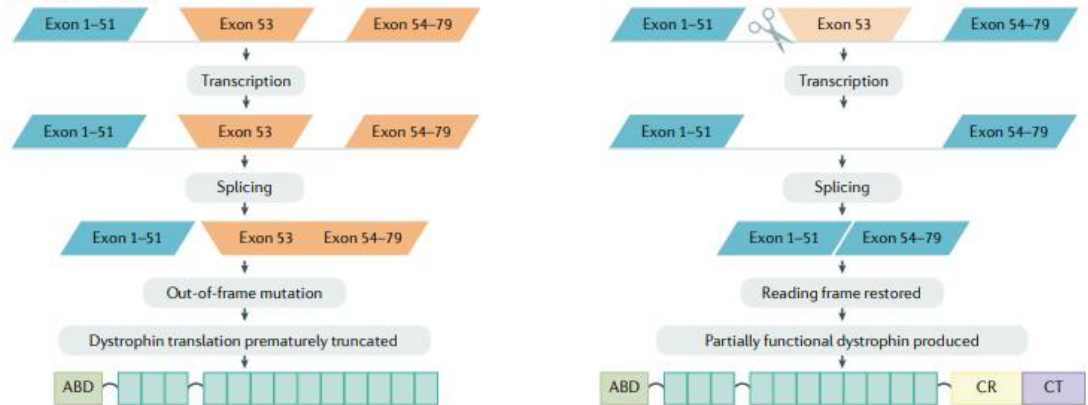
a Micro-dystrophin: minimalistic dystrophin proteins containing the most crucial domains are delivered by adeno-associated vectors



b Exon skipping



c Genome editing



d Stop codon readthrough

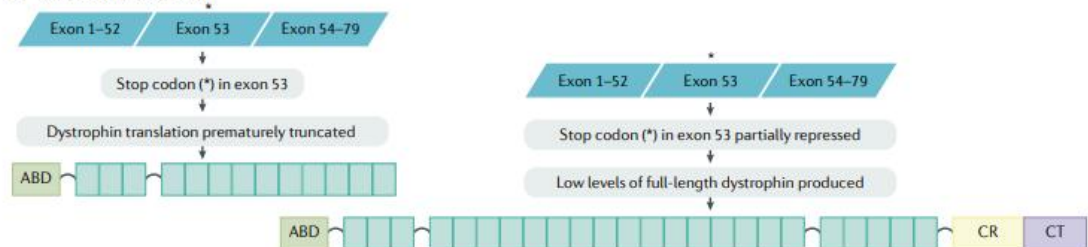


Figure 7.4 Dystrophin-restoring approaches

Source: Duchenne muscular dystrophy, Nature, 2021 ⁽³⁾

7.4 Approved Drugs

1. Those with DMD who have a gene mutation that can be treated with exon 45 skipping may utilize Sarepta Therapeutics' Amondys 45 (casimersen) as an antisense oligonucleotide. For those individuals with genetic defects that allow for exon 45 skipping, Sarepta's proprietary PMO and exon-skipping technology binds to exon 45 of dystrophin pre-mRNA utilizing Sarepta's phosphorodiamidate morpholino oligomer (PMO) chemistry. A dystrophin protein with an internal truncation is produced by skipping exons. The US FDA approved Amondys 45 under fast review in 2021 because it increased dystrophin synthesis in skeletal muscle of those who would benefit from exon 45 skipping ⁽²⁵⁾.
2. Sarepta Therapeutics' Vyondys 53 is an antisense oligonucleotide that is used to treat DMD in those who have a DMD gene mutation that is susceptible to exon 53 skipping. Vyondys 53 binds to exon 53 of dystrophin pre-mRNA utilizing Sarepta's patented phosphorodiamidate morpholino oligomer (PMO) chemistry and exon-skipping technology, causing exon 53 to be excluded or "skipped" during mRNA processing in patients with exon 53 skipping genetic variants. To make a dystrophin protein that is internally shortened, exon skipping is employed. Because it boosted dystrophin production in the skeletal muscle of those who potentially benefit from exon 53 skipping, Vyondys 53 was approved under accelerated review ⁽²⁶⁾.
3. The US FDA has given Viltepso, a drug developed by Nippon Shinyaku, fast permission to treat a hereditary illness linked to gradual muscle degradation. The FDA approved Viltepso (viltolarsen) injectable in 2019 for the treatment of people with DMD who have a confirmed dystrophin gene mutation that is responsive to exon 53 skipping. Viltepso is also approved for the treatment of DMD in Japan ⁽²⁷⁾.
4. PTC Therapeutics' (PTC) Emflaza is a kind of corticosteroid that acts as an anti-inflammatory and immunosuppressive agent. The US FDA approved Emflaza for the treatment of DMD in people aged 5 and above in February 2017, making it the first drug to be approved for the treatment of DMD regardless of genetic mutation. The medicine may now be used to treat DMD patients aged 2 and above, thanks to the updated labeling. The medicine is also approved and available in Europe to treat DMD ⁽²⁸⁾.

5. It is the first FDA-approved Duchenne muscular dystrophy medicine for patients with a confirmed dystrophin gene mutation that can be treated by skipping exon 51, Sarepta Therapeutics' Exondys 51, developed by Sarepta Therapeutics. In certain people, it encourages the body to produce a shorter form of dystrophin protein. This application was approved under accelerated approval because of a rise in dystrophin in skeletal muscle found in certain individuals treated with Exondys 51 ⁽²⁹⁾.
6. For the treatment of genetic illnesses caused by nonsense mutations, Ataluren is a new orally delivered small-molecule drug. To treat Duchenne muscular dystrophy, ataluren has been tried in clinical trials (nmDMD). nmDMD therapy with Ataluren is authorized in the European Union (EU), Iceland, Norway, Liechtenstein, Israel, and South Korea under the brand name Translarna ⁽³⁰⁾.

Table 7.1 Approved therapies for DMD

Product	Company	Approval	Designation	Population and Age-group	RoA	MOA	Molecule Type
AMONDYS 45	Sarepta Therapeutics	US: 2021	US: Orphan Drug Designation	Child: 7 years to 13 Years	Intravenous	Exon 45 skipping	Antisense oligonucleotide
Viltepso	Nippon Shinyaku	US: 2020 Japan: 2020	Japan: Sakigake Designation EC: Orphan Drug Designation	Child: 4 years to 9 years	Intravenous	Exon 53 skipping	Antisense oligonucleotide
VYONDYS 53	Sarepta Therapeutics	US: 2019	US: Orphan Drug Designation	Child: 6 years to 11 years	Intravenous	Exon 53 skipping	Antisense oligonucleotide
Emflaza	PTC Therapeutics	US: 2017	US: Fast Track Designation, Orphan Drug Designation		Oral	Steroid receptor agonists	Small molecule
EXONDYS 51	Sarepta Therapeutics	US: 2016	US: Fast Track	Child: 2 years to 5	Intravenous	Exon 51 skipping	Antisense oligonucleotide

			Designation, Orphan Drug Designation	years			
Translarna	PTC Therapeutics	EU: 2014	US: Orphan Drug Designation EU: Orphan Medicinal Product Designation	Child, Adult Older Adult: 5 years and older	Oral	Protein synthesis stimulants	Small molecule

7.5 Key Challenges Encountered by the Approved Therapies

All of the approved pharmaceuticals were approved quickly, and further proof is required to keep all of the therapies on the market. Furthermore, based on DMD's historical history, the chances of entering the market vary between 7MM to 7MM. Surprisingly, in regard to regulatory approval (i.e., EMA vs. FDA), In the DMD market, some drugs have been licensed by one jurisdiction but rejected by another based on the same clinical evidence. As a consequence, obtaining clearance for current treatments outside of the countries in which they have been pre-approved is very difficult. Translarna, for example, which is certified in the European Economic Area, met the key requirements for approval in the United States, but none of Sarepta's exon-skipping drugs have been approved outside of the United States ⁽⁸⁾.

7.6 Scope of Upcoming Therapies

Clinical Trials in Duchenne

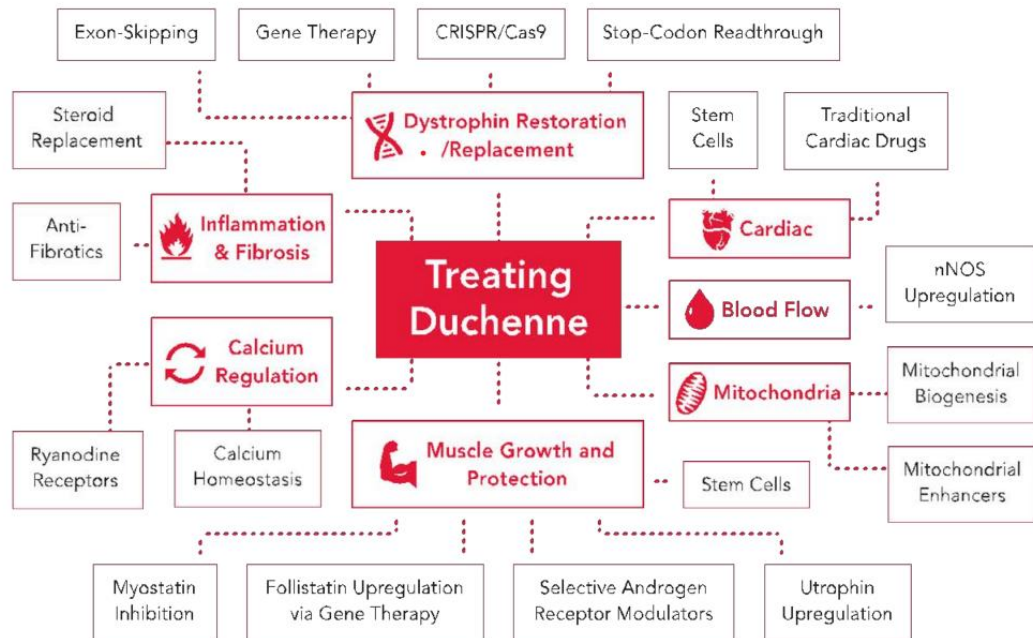


Figure 7.5 Clinical trials in DMD

Source: Parent Project Muscular Dystrophy, 2022 ⁽⁷⁾

The drugs that have been approved face substantial challenges. Ongoing medicines should be expected to proceed with fair competition between licensed and new treatments, since some innovative therapies target the patient population currently occupied by established medications. These are the important players and rivals that you should be aware of ⁽⁸⁾.

Table 7.2 Scope of upcoming therapies

Source: DelveInsight Business Research, 2021 ⁽⁸⁾

Potential treatments	New key players, significant competition
SRP-5051 (Sarepta)	Sarepta is developing SRP-5051, a drug for those with Duchenne

	muscular dystrophy (DMD) who can benefit from exon 51 skipping. After three months, dystrophin synthesis was eight times higher with the 30 mg/kg monthly dose of Exondys 51 than with Exondys 51 administered weekly for six months. Exon skipping was increased by 18 times when this dosage was used. Once lower dosages of Sarepta's SRP-5051 are available, it may eventually replace Exondys 51 as a more effective drug ⁽⁸⁾.
DS-5141b (Daiichi Sankyo)	Exon-skipping drug DS-5141b, administered by subcutaneous method in a Japanese Phase I/II clinical study, is another Daiichi product in development. With the same target patient population, Daiichi's medication is likely to be a formidable rival to Sarepta's Amondys 45. However, the release of Sarepta's treatment in Japan has our skepticism. There is a good chance that Daiichi's medication will face competition in the US market. Due to the fact that research on the medicine is still in its early stages, further high-phase trial results must be analyzed ⁽⁸⁾.
PF-06939926 (Pfizer), SRP-9001 (Sarepta), SGT-001 (Solid Biosciences)	The prospect of a DMD gene therapy may become a reality after nearly 15 years after the first gene treatment trial for DMD began, although with numerous difficulties along the road. In the United States, Sarepta Therapeutics, Solid Biosciences, and Pfizer are the three companies currently conducting competitive trials. Pfizer's PF-06939926 is in Phase III for 4–7-year-old patients, providing it possible market novel treatment, given the recent failure of Sarepta's Phase III gene therapy research. Sarepta is developing the SRP-9001 gene therapy for children and adolescents aged 4 to 17 who are on stable corticosteroids. Despite the favorable results of the SRP-9001 Phase II (Trial 102) trial, the primary functional aim of improving the NSAA total score was not encountered. The promising Phase II findings and reasonable tolerability outcomes are now expected to lead to an improved Phase III design. The company is creating SGT-001 for ambulatory, non-ambulatory individuals aged 4 years and older in Phase I/II study. The US FDA put the IGNITE-DMD trial on hold; however, it was eventually withdrawn in October

	2020. According to the company's first findings, creatine kinase levels have decreased, while NSAA and PODCI have improved. Gene therapy's market share in DMD is not promising, given recent disappointing outcomes from gene treatments like SRP-9001 and very harmful side effects from Pfizer's gene therapy ⁽⁸⁾.
Vamorolone (Reveragen + Santhera)	As a result of the huge patient base it is targeting, vamorolone, which is being developed in Phase II research for 4–7-year-old ambulatory children, is likely to gain a significant share of the market throughout the projection period. The medicine is a dissociative steroid, which means it activates certain cells while suppressing others in the body, much like other corticosteroids. In the United States and Europe, it was categorized as an orphan medication, as well as a Fast Track and RPD in United States. It has also been classified as Promising Innovative Medicine in the United Kingdom. In the ongoing study, the drug has proven to be highly effective and safe. The medicine is projected to be approved by early 2023 if priority review is granted ⁽⁸⁾.
Givinostat (Italfarmaco), TAS-205 (Taiho Pharma)	Givinostat, an orally accessible HDAC constrain, is now being researched for the care of DMD. The medication was labeled as a Rare Pediatric Disease by the US FDA in October 2020. The FDA has previously awarded the company Orphan Drug status as well as Fast Track status. Phase II proof-of-concept study on Givinostat was released by Italfarmaco in June 2021, and the company is now beginning a Phase III trial in the aim of receiving FDA clearance by 2023. Taiho Pharmaceutical has developed TAS-205, a HPGDS inhibitor. We predict approval since the medicine is now being tested in Japan for the treatment of individuals with DMD. Patients with ambulatory DMD are being examined for both Givinostat and TAS-205 ⁽⁸⁾.
Pamrevlumab (Fibrogen)	The capacity of Pamrevlumab to increase cardiac function, grip strength, and muscle function preservation is the drug's key selling feature. As a result, the drug is predicted to be a viable market participant for the foreseeable future, with the added

	benefit of alleviating the fundamental problems that DMD patients face. The drug is aimed at both non-ambulatory and ambulatory patients ⁽⁸⁾ .
CAP-1002 (Capricor),ATL1102 (Antisense)	CAP-1002 attempts to improve cardiac function, upper limb function, and pulmonary function, among other things. Antisense aims to increase upper limb function as well, therefore it will likely compete with ATL1102 to some extent. In light of the low level of competition, ATL1102 is expected to do well in the non-ambulatory patient market. ATL1102's Phase II trial also showed good results. Since non-ambulatory patients can't get out of bed, long-term corticosteroid therapy is presently the mainstay of care. Thus, the medicine has a good possibility of winning the non-ambulant DMD market with a significant number of patients. EU5 countries are expected to get access to the medicine before the United States does, according to the EMA's Paediatric Committee's (PDCO) involvement in its Paediatric Investigation Plan (PIP).It is also hoped that the drug would reduce the need for corticosteroids ⁽⁸⁾ .

7.7 Organizations Contributing Towards DMD

Table 7.3 Organization working for DMD

Organizations contributing to the fight against DMD		
S. No.	Organization Name	Description
United States		
1	DMD Care Considerations Working Group (CCWG)	The DMD Care Considerations Working Group establishes standards for DMD patients' care. Based on clinical viewpoint and knowledge, the company published a guideline in 2010, which was revised in 2014 (31).
2	Muscular Dystrophy Association (MDA)	An international non-profit health association, the Muscular Dystrophy Association (MDA), was created in 1950 and is concentrating on finding a cure for muscular dystrophy, as well as other

		related conditions. Since its inception, MDA has committed over \$1 billion in funding towards neuromuscular disease research, making it the largest non-federal source of funding. MDA provides a variety of educational programs for clinicians and experts who work with people who have a neuromuscular illnesses ⁽³²⁾ .
3	Parent Project Muscular Dystrophy (PPMD)	PPMD has been investing in every possible therapy option for Duchenne since 1994. PPMD takes a cutting-edge strategy to identify solutions for Duchenne that will benefit every individual affected by the condition. Over USD 50 million has been invested in Duchenne research by PPMD. It creates clinical trial procedures and technologies to solve present hurdles in the development of Duchenne drugs. This includes novel clinical trial designs that simultaneously evaluate several medications, multiple arms, and various firms, allowing participation from newborns to adults, reducing placebo exposure, and permitting faster success or failure results ⁽³³⁾ .
EU-5		
4	Muscular Dystrophy UK	In order to combat muscle-wasting disorders, Muscular Dystrophy UK (previously the Muscular Dystrophy Campaign) brings together people, families, and healthcare providers. Founded in 1959, the organization's dedication to finding treatments and, eventually, cures via research, as well as driving improvements in care and quality of life, is as strong now as it has ever been ⁽³⁴⁾ .
5	TREAT-NMD	TREAT-NMD, a neuromuscular network, offers a foundation for the rapid dissemination of the most promising novel therapies to patients. This organization's mission has always been to provide

		the tools needed by industry, physicians, and scientists alike to advance new treatment approaches from preclinical research into the clinic, as well as establish best practices for neuromuscular patients around the world, since its inception in January 2007. To transform the scientific landscape in the area of neuromuscular illness, TREAT-NMD started as an EU-funded "network of excellence." Since its inception in Europe, the network has expanded to include notable specialists, patient groups, and industry leaders from across the world, all working together to ensure that future trials and solutions are ready ⁽³⁵⁾.
6	World Duchenne Organization (WDO)	The World Duchenne Group is a worldwide umbrella organization that brings together national patient organizations from all over the world. Its mission is to develop a cure and effective therapies for DMD, promote high standards of care, and educate parents and individuals living with the disease all across the world. WDO reaches out to nations where there is a scarcity of information about Duchenne and enables the exchange of information concerning fundraising and lobbying efforts among member organizations ⁽³⁶⁾.
7	Action Duchenne	When Action Duchenne was established in 2001, it was the first national organization devoted to aiding persons with Duchenne muscular dystrophy. Building a community by uniting and assisting families and spreading awareness about Duchenne, as well as working toward a more inclusive society by promoting the value of human equality, daily acceptance of disability, and accessibility, as well as working toward a more inclusive society by

		spreading awareness about Duchenne ⁽³⁷⁾ .
Japan		
8	Japan Muscular Dystrophy Association	The Japan Muscular Dystrophy Association (Corporation) tasks are to support research into the pathophysiology of muscular dystrophy and identify appropriate treatments for it, as well as to offer medical care to patients and their families so that they may retain a decent quality of life (QOL). There are currently around 2,000 members in the association ⁽³⁸⁾ .

7.8 Recent Developmental Activities from the Pharmaceutical Sector in DMD

❖ Phase III trial of CAP-1002 therapy launching in the US

Capricor Therapeutics announced in January 2022 that they would begin a Phase III study of their novel cell treatment, CAP-1002. The medication is supposed to help rebuild muscle cells by regulating immune system activity. The drug enhanced muscle and cardiac role in persons with DMD, according to results from a previous experiment called HOPE-Duchenne. One of the few treatments for patients who are in the final stages of the illness, the medicine is predicted to be effective. Regardless of the mutation that causes the disease, it is supposed to operate equally effectively in all people with DMD⁽³⁹⁾.

❖ Sarepta's therapy study demonstrates enhanced motor functions

Children's motor abilities improved significantly after being treated with Sarepta's gene therapy medication, SRP-9001, according to the latest findings from Sarepta's study in January 2022. The NSAA - test of practical motor skills – found that these individuals scored higher compared to a group of individuals who were receiving placebo⁽⁴⁰⁾.

❖ SOLID gene therapy pipeline community update

The DMD community received an update from SOLID Biosciences in January 2022 that contained information from their pre-clinical research projects as well as the most current findings from their gene therapy clinical trial.⁽⁴¹⁾

❖ Dystrogen Therapeutics announces the first patient to get Chimeric Cell Therapy for DMD and reports on the results after six weeks.

DMD chimeric cell treatment has been administered to a trial participant for the first time in January 2022, Dystrogen Therapeutics said at the beginning of the year. Cells from people with Duchenne muscular dystrophy (DMD) and healthy muscle cells are combined to form "chimeric" cells. This strategy is believed to increase muscular function without triggering an immunological reaction ⁽⁴²⁾.

❖ Antisense Therapeutics obtained a positive PIP assessment from UK MHRA

As of December 2021, Antisense Therapeutics reported that the MHRA has awarded pediatric trial design for the antisense inhibitor medicine ATL1102, which they are creating for Duchenne muscular dystrophy (DMD), a positive conclusion. The company will now be permitted to perform a Phase III study medication in United Kingdom. The drug has been shown to be powerful dzxzecreased inflammation in both animals and people by inhibiting critical cells that cause inflammation in DMD ⁽⁴³⁾.

❖ RegenXBio receives FDA consent for a gene therapy testing

The FDA has authorised a clinical trial of RegenXBio's gene therapy treatment for DMD, the company said in January 2022. In the H1 of 2022, they want to begin their studies in the United States. ⁽⁴⁴⁾.

❖ Myogene Bio award to accelerate novel gene-editing therapy in the clinic

In December of last year, Myogene Bio revealed that the United States had received a USD 3.4 million grant from CIRM to help bring a revolutionary gene-editing medicine to the clinic. Since the UK Duchenne has decided joining forces with Myogene, the National Institutes of Health, and Parent Project Muscular Dystrophy to help support Myogene's funding request, this critical pre-clinical research may now proceed ahead. ⁽⁴⁵⁾.

❖ Phase III Trial of Pfizer's Gene Therapy Expected to Open in the US in June

Pfizer received approval from the US FDA in May 2022 to launch US sites for the Phase III CFFREO clinical study, which will evaluate the investigational gene treatment PF-06939926 in boys with DMD. The FDA placed a hold on Pfizer's application to begin the research in the US last year after requesting additional information about several of the tests which would be used to gauge the treatment's potency. Pfizer may now begin its research in the United States after the FDA removed its ban ⁽⁴⁶⁾.

❖ Vamorolone Filing for FDA Approval for DMD Expected by June

Santhera Pharmaceuticals and ReveraGen BioPharma stated in April 2022 that they will file for FDA approval of vamorolone as a DMD medication in the United States this year, with a filing likely by the end of June. Second-quarter completion of FDA filing of rolling new drug applications (NDAs) is anticipated. An announcement on an NDA's fate is expected to be made by the FDA in August. Meanwhile, the FDA will determine whether vamorolone qualifies for priority review, which would speed up the process and allow for an approval date as soon as 2023 ⁽⁴⁷⁾.

❖ FibroGen Completes Enrollment for Second Phase III Trial of Pamrevlumab

Pamrevlumab and corticosteroids are being tested in FibroGen Phase III research to see whether they may treat children with Duchenne muscular dystrophy. The trial will be completed in June 2022. (DMD). The LELANTOS-2 research has included 73 boys with DMD, ranging in age from 6 to 12, who are still able to walk ⁽⁴⁸⁾.

❖ Three DMD Gene Therapy Programs Terminated by Astellas, Citing Data

Astellas Gene Therapies stated in April 2022 that its gene therapy projects for DMD, AT702, AT751, and AT753, have reached the end of their research and development. The decision was made based on recent preclinical findings, according to a press statement from the company. As a treatment for Duchenne muscular dystrophy (DMD), AT751, AT702, and AT753 are exon-skipping medicines that target the dystrophin gene, which encodes the protein dystrophin. Muscular cells cannot create enough dystrophin due to abnormalities in this gene, resulting in increased muscle weakening ⁽⁴⁹⁾.

❖ An overview from the Italian Parent Project Conference

Dr. Alessandra Gaeta, Director of Research, attended meeting in February 2022. The 4-day event was jam-packed with academic and industrial speakers, covering the most recent advances in fundamental and translational research as well as clinical practice. The entire schedule, as well as audio recordings of the presentations, will be available soon. The following are some further conference updates:

- Pfizer is continuing to enroll patients in the Phase 3 study, with new safety measures in place.

- An exon 51 candidate from Dyne Therapeutics has gotten an IND from the FDA. By the second half of 2022, they want to be at the clinic, where they can begin their work.
- An antifibrotic medicine that has heart-specific effects was considered as part of Cumberland Pharmaceuticals' FIGHT DMD research using Ifetroban, an anti-fibrotic medication. They got an orphan program funding from the FDA and will begin a 12-month trial in the United States, using cardiac MRI to analyze the drug's effects ⁽⁵⁰⁾.

7.9 Reimbursement and Market Access

The present DMD market has six approved medications, four of which are approved in the United States, one in the EU, and one in Japan. Because DMD therapy is costly, the government, commercial or non-profit organizations, as well as the pharmaceutical company, offer reimbursement and market access for these medications. This aids in lowering the cost of therapy for DMD patients and making it more accessible to them.

Sarepta Therapeutics markets three of the six approved medications for DMD, including Exondys 51, Vyondys 53, and Amondys 45, which are used to treat DMD gene mutations susceptible to exon 51, 53, and 45 skippings, respectively. SareptAssist, the company's patient assistance service, is meant to help patients receive these prescriptions and stay on these medications once they get them. This program may cover some of the expenses involved with treatment, including co-payments, co-insurance, and deductibles. In addition, the company's Co-Pay Assistance Program was formed for qualifying individuals in the United States who have prescribed Exondys 51 treatment and have commercial health insurance. Patients who are uninsured or have been declared uninsured and fulfill certain qualifying standards may be eligible for the Patient Assistance Program. They may be liable for any additional expenditures incurred as a result of the drug's administration. A SareptAssist Case Manager can give eligibility information and assist with program enrolment. The company's patient aid foundation connects patients with charity groups that may be able to help them financially ⁽⁸⁾.

Nippon Shinyaku's Viltepso, which is sold in the United States by NS Pharma, is currently the only DMD medicine approved in Japan. The NS Support Patient Assistance Program ("PAP") is dedicated to providing free prescription medicines to uninsured persons in financial need. To confirm income levels, patients must submit

correct and comprehensive paperwork as specified below. Patients who are approved will be entitled to support for one year from the date of application. Each qualifying patient is entitled to a maximum program benefit of USD 20,000 per calendar year ⁽⁵¹⁾.

PTC offers financial support to DMD patients who are prescribed Emflaza through the PTC Care Assistance Program. Patients who do not have insurance or whose insurer rejects coverage are eligible to apply for this supplemental medicine program. Patients have out-of-pocket expenses are also eligible ⁽⁵²⁾.

The French Haute Autorité de Santé (HAS) has proposed a 15% reimbursement rate for Translarna, and the medicine has also been included in the Italian National Health System's prescription list for payment ⁽⁵³⁾.

7.10 Market Overview

Duchenne muscular dystrophy (DMD) occurs when a vital structural protein called Dystrophin is lacking from muscle, leaving it more vulnerable to damage. The body is unable to keep up with repair and regeneration, resulting in muscle loss and weakening. As a result, scientists are working feverishly to create alternative medicines that can replace Dystrophin, preserve muscle from damage, and stimulate muscle repair and renewal. Various research groups and organizations are also working on the creation of a smaller form of Dystrophin known as micro-Dystrophin. Micro-Dystrophin includes the bare minimum of the Dystrophin gene code required to produce a functional protein. As a result, the industry's extensive research and development is fuelling market expansion. The increasing incidence of DMD across the globe, expanding healthcare spending potential in the population of industrialized nations, and the availability of medical reimbursement are further reasons driving Dystrophin's market development. For various market competitors, the key development potential is the long-unmet need for the treatment of muscular dystrophy illnesses. Several companies are conducting clinical studies for the development of innovative therapies for the treatment of DMD. On the contrary, some severe laws and regulations governing medicine licensing throughout the world are a major impediment to market expansion ⁽⁵⁴⁾.

- **Country Insights**

The principal medicine used to treat DMD is glucocorticoids, specifically prednisone and deflazacort. Deflazacort, presently known as Emflaza in the United States, is a prednisone oxazoline derivative. Deflazacort has better bone-sparing and carbohydrate-

sparing qualities, as well as improved strength and function, with less weight gain. As a result, deflazacort has become the medication of choice. The expensive cost of this medicine, however, is a disadvantage. The medicine cost USD 89,000 per patient per year at the time of approval. However, in response to public outcry over the price, PTC Therapeutics, who acquired the medicine from Marathon Pharmaceuticals, reduced the price to roughly USD 35k/year for a kid of 25 kg, however then expanded the product's list price by around 9%, to more than USD 6k/year. Because of its exorbitant cost, this old-turned-new medicine is a substantial financial hardship for DMD sufferers. Families in the US have been paying USD 1,200 or less per year to buy Emflaza from Europe for years. To treat people with DMD, the US market now has five approved products: Emflaza, Vyondy 53, Exondys 51, Amondys 45, and Viltepso ⁽⁸⁾.

Steroid treatments, as well as an approved drug for DMD patients with nonsense mutation, now dominate the market in the EU5 nations. The European Union has given Translarna conditional approval to treat individuals with a nonsense mutation. Unlike the US market, which has five approved medicines, the European market only has one approved medication for DMD ⁽⁵⁵⁾.

The therapy for DMD in Japan is comparable to that in the United States and the European Union⁵. In the 1990s, steroid therapy for DMD was established in Japan. Prednisone was widely used around the world, but it was unavailable in Japan. Instead, in 2013, the focus was on the approval of prednisone for medicinal usage in DMD patients. While deflazacort was the most regularly prescribed glucocorticoid in Germany, Italy, and the United States, prednisone was the most commonly prescribed glucocorticoid in the United Kingdom. Because deflazacort and prednisone were not accessible in Japan until 2015, this was also true ⁽⁵⁶⁾.

Because of new product breakthroughs, high healthcare expenditures, and government awareness efforts, North America dominates the worldwide Duchenne muscular dystrophy market. Because of increased illness prevalence and the anticipated introduction of potential pipeline candidates, the US has dominated the regional market and is expected to retain its dominance. Furthermore, the market is likely to expand as more clinical studies are conducted throughout the world, particularly in the United States and Europe ⁽⁹⁾.

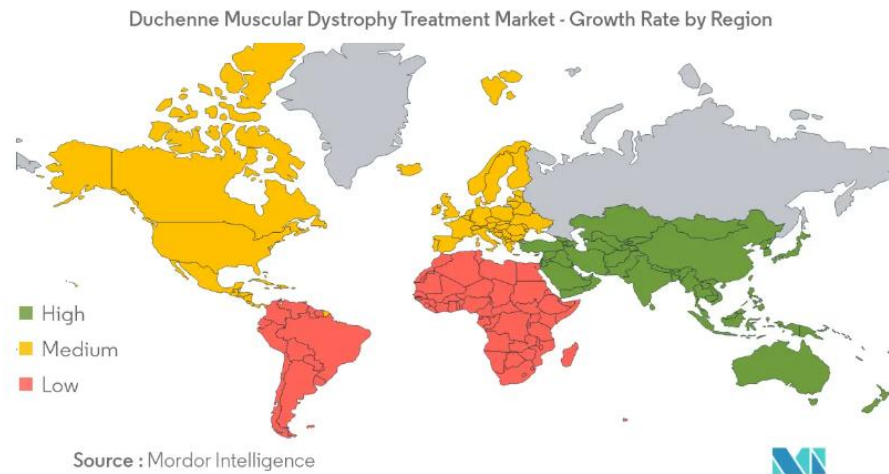


Figure 7.6 DMD treatment market – region wise growth

Source: Mordor Intelligence ⁽⁵⁷⁾

- **Therapeutic Approach Insights**

Mutation suppression, exon skipping, and steroid therapy are the three main therapeutic options on the market. More than one-fifth (14%) of DMD cases are caused by nonsense mutations, which shorten the protein. Drugs such as ataluren are able to circumvent nonsense mutations (Translarna). Mutation-suppressive drugs offer fewer negative effects and a longer half-life than steroids. It is predicted that exon-skipping therapy will grow the most rapidly of all therapeutic options. Approximately 50.0 percent and 90.0 percent of individuals with DMD mutations may benefit from single-exon and multi-exon skipping, respectively. Increased use of this therapeutic class and the release of new drugs in the pipeline are expected to improve growth prospects. Only corticosteroids have been found to increase muscle strength in patients with DMD when used in combination with other DMD medications. Corticosteroids, such as deflazacort (Emflaza), have been shown to postpone non-ambulation; however, steroid therapy's side effects make it difficult to use ⁽⁵⁸⁾.

DMD is a field with a lot of untapped potentials, as seen by the small number of medicines on the market and the wide range of candidates under development. There are multiple potential candidates in the pipeline in the United States, the EU5, and Japan,

with the bulk of them in Phase II and III clinical trials. Current late-stage pipeline therapies have the potential to meet unmet needs and significantly enhance DMD therapy. If these candidates make it to market, they have the potential to drastically alter the competitive landscape in the DMD arena, perhaps replacing current medicines in the treatment algorithm. These treatments are predicted to have a substantial commercial adoption, either as monotherapies or as add-on medications, given the existing unmet requirements of DMD patients ⁽⁵⁹⁾.

- **Covid-19 Analysis**

The COVID-19 epidemic has had an impact on a variety of businesses throughout the world. To slow the spread of the epidemic, governments throughout the world enacted tight lockdown measures and social distance standards. During the early phases of the pandemic, manufacturing facilities all around the world were shut down. Furthermore, the economic crisis that followed the epidemic might cause a major delay in the healthcare industry's commercialization. Small and medium-sized companies, which are the backbone of the technological industry, have seen a sharp reduction in income since the epidemic began in 2020. As a result, market participants faced several hurdles as supply chain interruptions were noticed. However, when additional supplies become available in the second half of 2022, things will improve ⁽⁵⁴⁾.

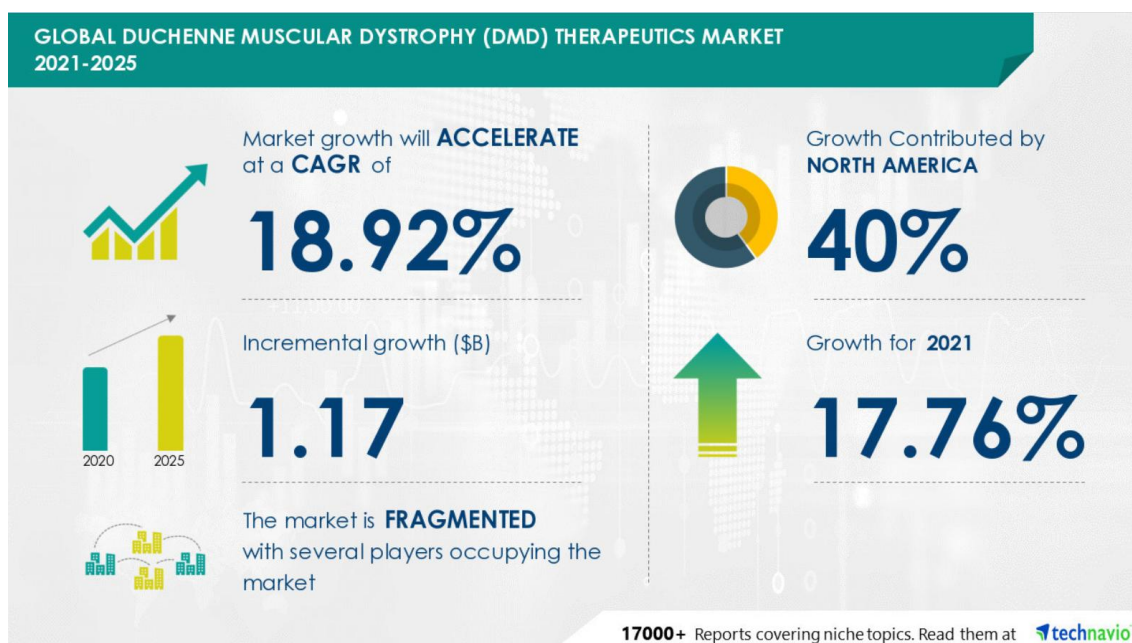


Figure 7.7 Global DMD therapeutic market

Source: Infiniti Research, 2022 ⁽⁶⁰⁾

7.11 Market Drivers

- **Robust Pipeline Activity**

Several firms are currently focusing on the development of DMD therapeutic options. Many companies, including Santhera Pharmaceuticals, Pfizer, Italfarmaco, Sarepta Therapeutics, Antisense Therapeutics, Solid Biosciences, and others, are developing and testing medications in late and mid-stage clinical trials. Gene treatments, cell therapies, exon skipping potential medications, Hematopoietic Prostaglandin D Synthase (HPGDS) inhibitors, HDAC inhibitors monoclonal antibodies, and others are all in the DMD ⁽⁶¹⁾.

- **Upcoming Launches and Approval**

Market expansion is likely to be fueled by the launch of new medications and increased access to treatments. The planned gene treatments from Sarepta, Solid Biosciences, and

Pfizer, as well as exon-skipping therapies from Daiichi Sankyo and Sarepta, and HPGDS inhibitors and HDAC inhibitors from Taiho Pharmaceuticals and Italfarmaco, are likely to be approved in the coming years. Santhera Pharmaceuticals and ReveraGen BioPharma plan to file for FDA approval of vamorolone as a DMD medication in the United States this year, with a decision expected by the end of June. Priority review of vamorolone, which would speed the process & allow for an early 2023 approval date, will be decided by the FDA at the same time. Gene therapies and exon-skipping treatments for other pipeline products will have significant yearly costs, resulting in large sales and market growth ⁽⁸⁾.

- **Newborn Screening of DMD**

Given recent advancements in DMD therapy, newborn screening (NBS) programs for DMD are becoming more popular. Indeed, there is growing recognition that exon-skipping kids with DMD should be treated as soon as feasible (i.e., from birth) to optimize the therapeutic impact. CureDuchenne partnered with a hospital in Boston, Massachusetts, to start newborn screening campaign in the United States in July 2021. The collaboration made Brigham and Women's Institution the first and only hospital in the United States to provide parents the option of screening their newborn for DMD. The growing DMD patient pool is expected to be fueled by increased neonatal screening and disease awareness ⁽⁸⁾.

- **Increasing Awareness Program**

Market drivers include increased public awareness, greater access to health services, and increased disease understanding to assist in effective screening and diagnosis. Several non-profit groups are launching efforts to raise DMD awareness. The 7th of September, for example, is designated as World Duchenne Awareness Day. PPMD, which advocates for people with DMD, also runs a Duchenne Action Month awareness campaign in September. Such activities will aid in raising awareness about this uncommon condition, as well as assisting patients and caregivers in better understanding the disease and connecting with others who are living with DMD ⁽⁸⁾.

7.12 Market Barriers

- **High Treatment Cost**

The cost of treatment for DMD patients is significant since newer medicines such as gene therapies for the entire DMD population and exon-skipping tailored therapies are

both pricey. Although national health systems in some countries cover the cost of DMD, out-of-pocket payments may account for a significant portion of overall costs, particularly in countries where public health care administration is inadequate or non-existent. The expense of pharmaceuticals and medical treatment, as well as difficulties in obtaining medical care and social support services, were identified as major concerns that needed to be addressed ⁽⁶²⁾.

- **Multidisciplinary Care**

A variety of clinical symptoms linked with DMD need multidisciplinary care and attention to determine the proper etiology, diagnosis, and consensus on which a suitable medicine may be recommended. However, clinical care coordination is a time-consuming process that necessitates many attempts, resulting in an unmet need. This creates a roadblock in the proper prescription of available medicines, limiting market expansion ⁽⁶³⁾.

- **Lack of treatment options for non-ambulant DMD patients**

There are currently no therapy options available for non-ambulant DMD patients. Only Sarepta Therapeutics' SRP-9001 gene therapy ⁽⁶³⁾ and Capricor's CAP-1002 cell treatment are being studied for both ambulant and non-ambulant DMD patients ⁽⁶⁴⁾. Non-ambulatory DMD patients are targeted by FibroGen's FG-3019 and Antisense Therapeutics' ATL1102. This part of the DMD industry has been largely untouched in the past because all DMD patients eventually become non-ambulant. This is a disadvantage for the DMD market, and more major firms must step forward to find medicines for this devastating condition.

7.13 Unmet Needs

- **Challenges in the management of DMD**

DMD is caused by a mutation in the muscle dystrophin gene, which leads to rapid and irreversible muscular atrophy and death. For people with DMD, inflammation is a severe issue. Because the standard of therapy for DMD is dominated by corticosteroids, there is an unmet medical need. Furthermore, corticosteroids are ineffective owing to several side effects that must be handled. Due to the negative side effects of glucocorticoids, fewer people can take them as they get older, making disease treatment even more difficult. Furthermore, except for Emflaza, which is approved for kids aged two years and above, the approved treatments are geared toward younger DMD patients

rather than the older adult demographic pool of DMD patients. It's also worth noting that Emflaza was only evaluated on young adults and children, not on older persons and that the clinical trial that led to its approval only included patients aged 5 to 15.

- **Lack of approved therapies in Europe**

Corticosteroids were once the only therapeutic option for DMD in Japan. Muscle inflammation is treated with corticosteroids such as prednisone, deflazacort, and prednisolone. The impact is only partial, and clinical application is limited due to well-known steroid side effects. Corticosteroids have been used for more than two decades and are the only medicine shown to boost muscle strength ⁽⁶⁵⁾. Viltepso is currently the sole approved therapy for the treatment of DMD in Japan. However, it is only for DMD patients who have a mutation in exon 53, which occurs in just 8-10% of all DMD patients, and the approval is conditional ⁽⁶⁶⁾. In Europe, where Translarna is now the only approved therapy for DMD, a similar predicament exists ⁽⁶⁷⁾. Furthermore, the medications that are now accessible in the United States have gained fast approval, and ongoing approval is contingent on clinical benefit evidence from confirmatory trials. This suggests that there is an unmet need for effective medicines to address the rising desire for better and more treatment alternatives among DMD patients.

- **High requirement for parallel interventions**

Patients with DMD have gradual muscle degeneration and weakening, which leads to a loss of muscular strength in all of the body's organs. This increases the risk of cardiac, pulmonary, and some bone-related problems. As a result, DMD patients require many procedures for full care and management of bone therapy, pulmonary difficulties, and cardiology-related disorders, all of which are not well-established ⁽¹⁰⁾.

- **Coordination of clinical care**

DMD is linked to a slew of additional symptoms, including attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), cardiomyopathy, depression, dysphagia, and a variety of other conditions ⁽⁶⁸⁾. This necessitates treating these symptoms alongside the major indications, which are sometimes overlooked during DMD treatment and care.

7.14 SWOT Analysis

	Strengths	Weaknesses
Internal	• DMD's pipeline is strong, with several novel treatments in late-stage and early-stage clinical trials. • Several exons skipping therapies have been granted in the United States for the treatment of DMD, and Viltepso has just been launched in Japan. • Several organizations, including Muscular Dystrophy UK, Muscular Dystrophy Association, World Duchenne Organization, Parent Project Muscular Dystrophy, and others, are trying to address the issues that DMD sufferers' encounter. • Increased neonatal screening in the United States will aid in early therapy, preventing ambulation loss shortly.	• Glucocorticoids have a variety of side effects in the major therapy choices, although newer glucocorticoids, such as Emflaza, are not cost-effective in the United States. • There is no cure or reversible therapy for non-ambulant DMD patients. • Exon-skipping therapies have been denied approval in Europe for a variety of reasons. • According to the most recent findings, none of the gene treatments are producing adequate outcomes to go to the next stage. It seems unlikely that a gene treatment for DMD will be approved anytime soon.
	Opportunities	Threats
External	• Over the last several years, the diagnosed prevalence of DMD patients has increased significantly, creating a big window of opportunity for innovative therapies. • Possibility for Pfizer's gene therapy, which has a competitive advantage over Sarepta's gene therapy. • Greater commercial potential for therapies like Capricor's CAP-1002 and Antisense's ATL1102, which target a considerably bigger patient segment than Exon-Skipping	• Existing treatments are expensive. • Insufficient participant availability for trial execution. This is because DMD is a rare childhood condition, and the number of people who volunteer for clinical trials of new medications for DMD is quite low compared to other indications. • Rapid illness progression. • High pricing creates reimbursement and insurance issues. • To gain regulatory approval, increased effectiveness must be

7.15 DMD Scenario in India

The Ministry of Health notified the Delhi High Court in February 2021 that there are over five lakh individuals in the country suffering from the uncommon ailment Duchenne Muscular Dystrophy, and that genetic treatment is essential for them. The present cost of such therapy per child is around Rs 6 crore per year. Officials also indicated that the government does not have the financial resources to treat all DMD sufferers ⁽⁶⁹⁾.

Antisense oligonucleotide (AON), created by US and European pharmaceutical firms, is one of the available medicines on the global market. Exondys 51 employs exon-skipping technology to assist a DMD patient in producing a shortened version of the dystrophin gene. This medicine, however, is dependent on the patient's genetic sequence. This simply indicates that the medication will not be effective for all youngsters. The medicine costs between Rs 2-3 crore per year to treat a single youngster. Viltepso employs the same exon-skipping method as previously discussed. The medication must be imported and given for a year. In India, it costs roughly Rs 4 crore. As a result, the present treatment choices for treating DMD are limited and costly (over Rs. 2-3 crores per child a year). Drugs are generally imported from other countries, which drives up the cost of dosage and puts them beyond reach for most families ⁽⁷⁰⁾.

Treatments costing millions of rupees are out of reach for most Indian households. Many people in India have been able to obtain cash for medical treatments thanks to the introduction of internet crowdfunding sites. On crowdfunding services like Impact Guru, families have collected millions of dollars for rare illnesses and disorders like SMA and DMD. This was made possible thanks to the generosity of kind and generous contributors from all around the world who wished to aid these families in their time of need ⁽⁷⁰⁾.

In partnership with the Dystrophy Annihilation Research Trust (DART) in Bangalore and the All-India Institute of Medical Sciences (AIIMS) in Jodhpur, the Indian Institute of Technology (IIT) Jodhpur launched a Duchenne Muscular Dystrophy (DMD) research center in March 2022. The research center's key goals include developing an inexpensive and effective therapy for DMD patients using a bioengineered approach as

part of the Make in India drive, as well as performing social outreach programs for DMD patients and their parents ⁽⁷¹⁾.

In India, increased awareness is needed about DMD so that these young children can receive early diagnosis and, as a result, early treatment. This not only increases their prospects but also assures that they do not spend any more years suffering. While there is a discussion about DMD in India, this discussion must be translated into action, with initiatives done to make the therapy readily available and accessible throughout the country ⁽⁷⁰⁾.

8 Discussion

Symptoms of Duchenne muscular dystrophy intensify with time as the disease progresses. Dystrophin synthesis in adult muscle fibers and muscle stem cells is prevented by mutations in the DMD gene, which causes muscle atrophy and satellite cell malfunction. Efforts to enhance diagnosis and investigate treatment ways to treat this lethal condition have been ongoing ⁽⁵⁶⁾. There are a number of exon skipping drugs now being investigated in the clinic, and AON-mediated exon skipping is the most advanced treatment. Genome editing and cell-based therapies are two cutting-edge techniques that are presently being investigated and improved ⁽¹⁹⁾.

It's worth noting that all of the approved pharmaceuticals were given expedited approval and that further evidence is needed to keep all of the treatments on the market. A market entry probability of 7MM or above is reasonable considering the recent history of DMD. As it turns out, regulatory clearance in the DMD market varies by location (EMA vs FDA), with several instances of medications that have been licensed in one jurisdiction but refused in the other. Outcome is a considerable challenge for current drugs to acquire approval in areas outside of their pre-approved countries. Despite Translarna's success in the European Economic Area, none of Sarepta's exon-skipping drugs have been licensed for sale outside of the United States ⁽⁸⁾.

Many people with DMD who are not genetically sensitive to mutation-targeted treatments nonetheless have a considerable unmet need for disease-modifying therapy. Patients with DMD also confront a significant difficulty in overcoming the high cost of approved medicines. Innovation and lower development costs can secure a long-term future ⁽⁷²⁾.

Advances in gene therapy for DMD aim to cure genetically determined disease subgroups and establish an example for other inherited diseases. Despite the rapid growth of the DMD treatment business over the last decade, there is still a long way to go until these therapeutic procedures can totally cure—rather than merely modify—the pathology and phenotype of DMD patients ⁽⁷⁾.

9 Conclusion

In the coming years, the market is expected to develop at a rapid pace. The advent of mutation-specific medicines, increased prevalence of the disease, and enhanced diagnostics are all contributing to the rise. The market is likely to increase as a result of government initiatives encouraging target-specific therapies and attractive reimbursement rules. Furthermore, the increasing acceptability of targeted medicines like Translarna, Exondys51, and Emflaza is expected to expand the therapeutic area ⁽⁵⁸⁾.

Dystrophin function has been restored using a variety of different approaches, including cell-based, gene-based, and pharmacological. Patients with dystrophin deficiency may benefit from gene transfer using a safe, non-pathogenic viral vector known as AAV (adeno-associated virus) ⁽⁷³⁾. Although these tactics are promising, and multiple clinical studies on DMD patients are now underway or have previously been completed, poor targeting and low efficacy in fibrotic dystrophic muscle continue to stymie gene and cell-based treatments. As a result, it is becoming increasingly clear that upcoming therapeutic methods should comprise a combination of therapies, taking into account the health of the muscle as well as the downstream consequences of dystrophin deficiency ⁽¹²⁾.

The high cost of therapies continues to be a barrier to the expansion of the DMD medication landscape. Governments in all major areas, however, are adopting inexpensive healthcare policies, which influence company pricing strategies as well as reimbursement scenarios. Premium price potential for emerging DMD treatments is likely to be hampered by rising cost consciousness ⁽⁷⁴⁾.

Emerging medicines for uncommon diseases are changing the way clinical trials are conducted in difficult settings including unpredictable disease courses, historical control assessment, and the danger of underdosing. To effectively capitalize on the promise of this new therapy method, advancements in novel treatment alternatives will demand development in other elements of health care. This might necessitate the development of

new payment methods for one-time gene therapy. The most effective application of innovative gene therapy to alter the course of illness and maybe prolong life and function can be made possible by early diagnosis of genetic disorders. To persuasively show efficacy and safety in delivering these medicines to patients, rational and rigorous use of relevant design principles is required ⁽¹⁷⁾.

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