MARKET ASSESSMENT OF ORPHAN DRUGS

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in

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by

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Under the Supervision and Guidance of

Dr. Rahul Sharma

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I hereby declare that this dissertation titled “Market Assessment of Orphan Drugs” submitted by Dikshita Hatwar, Enrollment no.- 0237 is the bonafied 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 Information derived from the published or unpublished work of others has been duly acknowledged in the text.

X

Dikshita Hatwar

Name of the student- Dikshita Hatwar

Date- 24/06/2022

CERTIFICATE

This is to certify that dissertation titled "Market assessment of orphan drugs" is record of the research work undertaken by Dikshita Hatwar in partial fulfillment of the requirements for the award of the degree of MBA (Pharmaceutical 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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CONTENTS

ABBREVATIONS:

ODA - Orphan Drug Act

NORD - National Organization for Rare Disorders

CDER – Center for Drug Evaluation and Research

GDP – Gross Domestic Product

CAGR – Compound Annual Growth Rate

CNS – Central Nervous System

CAR-T – Chimeric antigen receptor T-cell

LAMEA – Latin America, Middle East and Africa

FDA – Food and Drug Administration

HTA – Health Technology Assessment

Project Report

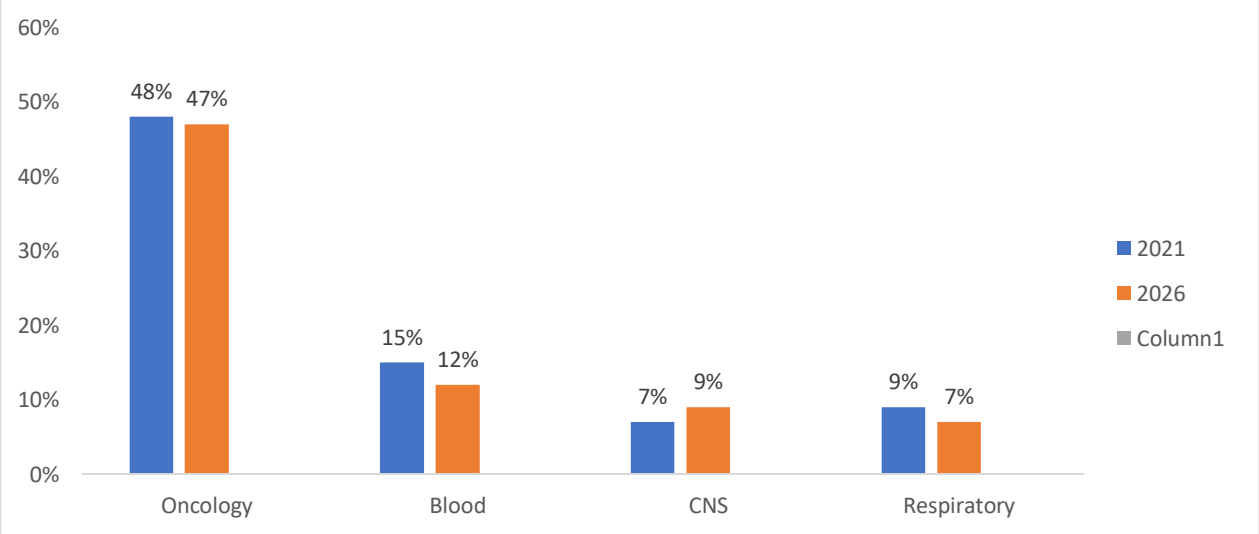
INTRODUCTION:

Rare Disease:

A rare disorder in the US is one that affects less than 200,000 persons overall. In the Orphan Drug Act, this description of a rare disease was provided (1983). Rare disorders became known as orphan diseases because pharmaceutical companies refused to create therapies for them due to the disease's low prevalence and unknown origin

Every country has its own definition or description of a rare disorder. A condition is considered to be rate in the European Union (EU) if it affects fewer than 1 in 2,000 people

There are roughly 7,000 rare diseases worldwide. While the number of people affected by a specific rare disorder is small, the total number of people impacted by a rare disease is huge. The majority of rare disorders are tough to track, making it difficult to estimate the actual number of uncommon disorders or the number of people affected by them



Orphan drugs market by disease

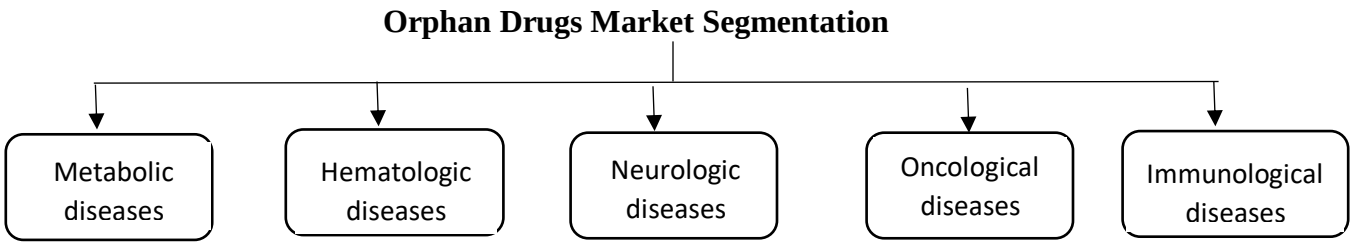
Causes of Rare Disease:

Rare diseases have many different causes. The vast majority of rare diseases are genetic in nature, meaning they are caused by alterations in genes or chromosomes. There are two causes of genetic disorders. In the first category, genetic alterations that cause illness development are inherited. This means that these genetic alterations are handed down via successive generations. Genetic disorders of the second type occur at random in the first patient in a family to be diagnosed with a hereditary disease

Many rare diseases are not passed down through families. Infections, uncommon malignancies, and autoimmune illnesses are among them. It means that they are not passed down from generation to generation. Many rare diseases still have unclear causes or etiologies. Examples of rare diseases include **Idiopathic Pulmonary Fibrosis, Lennox Gastaut Syndrome, Acute Hepatic Porphyria, Retinitis Pigmentosa etc**.

Orphan Drugs:

Orphan drugs are highly pharmacological agents with specialized functions used to treat rare (orphan) diseases. The orphan drug market is growing due to favorable government policies and a rise in the number of cases of rare diseases. The global orphan medicines market was worth $1,40,000.0 million in 2020 and is anticipated to arrive $4,35,686.3 million by 2030, 2021 to 2030 will see a CAGR of 11.8 percent (Suraj Sajeev, Monika Darandle, Onkar Sumant, 2022). To offer a complete overview of the market, the worldwide orphan medicines market is split by disease type and region. Furthermore, the availability of market exclusivity for orphan drug developers, as well as an increase in orphan drug indications to treat a variety of diseases such as lymphoma, leukemia, myeloma, and others, all contribute to the market's growth. A limited patient pool for clinical trials and product promotion, as well as expensive treatment expenses per patient, are impeding market expansion. However, rise in innovative indications for existing orphan medications, as well as unexplored emerging markets, are projected to present profitable prospects for the orphan drugs market during the projected timeframe.



Metabolic diseases:

- Hunter's Syndrome
- Gaucher Disease
- Fabry Disease
- Hypoparathyroidism
- Others

Hematologic diseases:

- Haemophilia
- Hereditary Angioedema (HAE)

Neurologic diseases:

- Huntington's Disease
- Alzheimer's Disease
- DMD
- Others

Oncological diseases:

- Multiple Myeloma
- Renal Cell Carcinoma
- Pancreatic Cancer
- Ovarian cancer

Market Segmentation By Region:

North America

- Mexico
- Canada
- United States

Europe

- France
- Italy
- Spain
- Germany
- UK
- Rest of Europe

Asia-Pacific

- Australia
- China
- Japan
- Rest of Asia-Pacific

LAMEA

- South Africa
- Turkey
- Brazil
- Rest of LAMEA

Orphan Drug Act:

On January 4, 1983, the Orphan Drug Act (commonly known as ODA) was approved. Since the change in ODA, there has been a significant shift in the development of orphan products.

ODA was enacted to provide a boost to pharmaceutical businesses and increase the production of medications for the management of rare diseases. In 1984, the Orphan Drug Act was modified. Rare diseases were defined by the new amendment as those in the US affecting fewer than 200,000 people. This orphan disease categorization also covered medications for conditions affecting more than 200,000 persons, with the caveat that there be no commercial motivation. This implies that the expense of producing and promoting the medication in the US ought to exceed the proceeds from US sales

Incentives provided by ODA:

ODA offers pharmaceutical companies a considerable reward in the shape of a 7-year marketing exclusivity. Additionally, ODA made available a number of funds that will be given annually to pharmaceutical companies or academic researcher, as well as a tax credit of 50% for expenses incurred when orphan drugs are assessed for their curative potential or ability to treat a condition (George J. Brewer, 2009). The number of orphan medication marketing approvals has dramatically increased since the ODA's enactment

AIM: To perform the market assessment of orphan drugs

OBJECTIVE: 1. To investigate competitive landscape of the orphan medicines market by analyzing leading market competitors and their tactics.

2.To an in-depth examination of the global orphan pharmaceuticals market, as well as current trends and forecasts for the future

LITERATURE REVIEW:

An article by U.S FDA (Orphan Products: Hope for people with rare disease, 2018) stated, "New rare diseases are discovered often, and these are the results of many causes like mutations or defects in gene. These are very difficult to diagnose but the symptomatic treatment could work efficiently. These diseases can also be misdiagnosed with other similar diseases. In 1983, Congress passed the Orphan drug Act, which resulted in development of more than 250 orphan drugs. Patients suffering from orphan diseases find life very traumatic and stressful. Support groups comes into play and their role is evolving."

An article by Divya Sardana, Cheng Zu, Minlu Zhang, Ranga C Gudivada, Lun Yang and Anil G. Jegga (Drug repositioning for orphan diseases) stated, "There is an enormous need for an opportunity to discover therapeutics for rare or orphan diseases. The fact that drug development is complicated, time-consuming, and expensive, with extremely low success rates, contributes to the scarcity of therapeutics for orphan diseases. An effective alternative strategy for increasing the discovery of orphan diseases therapeutics is the discovery of links between an existing drug product and an orphan disease"

An article by Laura Joszt (5 things about the Orphan drug Act, 2019) stated, " The 5 things about the law and its impact the purpose of the act showed the shift in orphan drug development than before, the key incentive in ODA is that pharmaceutical manufacturers receive 7 years of marketing exclusivity, the impact has been an increase in orphan drugs coming to market, the controversy was

manufacturers viewing ODA as a way to maximize profits by turning products that treat a small number of patients into multibillion-dollar sellers and there were pertinent issues with ODA"

An article by George J. Brower (Drug development for orphan disease in the context of personalized medicine, 2009) stated, "Orphan diseases are frequently so rare that a physician may only see one case per year or less. As a result, proper treatment is a one-on-one encounter between doctor and patient. Positive developments include formation of the National Organization for Rare Diseases, the Orphan Drug Act, the development of a grant program to fund orphan drug development, the formation of the National Institutes of Health Office of Rare Diseases, and the passage of orphan drug legislation by other countries. Progress has increased, but the 300 orphan drugs and devices approved in the last 25 years are still only a drop in the bucket compared with the many thousands of orphan diseases".

An article by Lieven Annemans, Eline Picavet, David Cassiman, Irina Cleemput (Market uptake of orphan drugs- A European Analysis) stated, "Variations in the market acceptance of an orphan drug have significant implications for access to care and treatment inequality. Orphan drugs were used differently in different European countries. The highest volumes and contributions of orphan drugs occurred in countries with a high GDP (and implicitly, a higher healthcare budget), regardless of the existence of an HTA-organization. Orphan drugs were less available in countries with low GDP when there was a formal HTA-organization. Budgetary constraints may result in the exclusion of less cost-effective orphan drugs".

METHODOLOGY:

Study Design: Descriptive study review through qualitative and quantitative secondary research

Setting of the study: Global market is being considered under study of orphan drugs. The study is conducted from India

Duration of study: The study duration is 3 months from March – June 2022

Data collection procedure: Secondary research based on internet-available literature. The data gathered from different research articles. Using search engines like Google, Google Scholar, SlideShare, Bing. Keywords selected to search relevant articles and reports

Source of data: Secondary research

Implications of research: The research will provide a clear market scenario of orphan drugs and diseases. Pharmaceuticals and biotech companies functioning in rare disease space. The market trends and the growth of orphan drugs, its regulations in US and Europe by FDA

OPERATIONAL DEFINITIONS:

- Orphan disease- An orphan disease may be a rare disease (according to US criteria, a disease that affects fewer than 200,000 people). In 1983, the U.S. government passed a law, called the Orphan Drug Act, to give drug companies certain financial benefits for developing orphan drugs that are safe and effective
- Orphan drugs- A medication that is used to treat, prevent, or diagnose an orphan disease
- Market assessment- A market analysis is a thorough examination of a company's competitors, customers, and other industry stakeholders
- Internal Stakeholders- Internal stakeholder are those who have a direct interest in a firm, such as employment, ownership, or investment
- External Stakeholders- External stakeholder are individuals who do not directly work for a firm but are influenced in some way by its activities and consequences

EXTENT OF THE STUDY:

- Importance of Orphan drugs
- New and upcoming drugs
- Market size of orphan drugs
- International organizations supporting orphan diseases
- FDA & EMA regulations- Policy reforms

RESULTS & DISCUSSIONS:

The orphan drug industry is not likely slow down. However quick expansion, a large number of the 7,000 or so rare diseases continue to be underserved (Melanie Senior and Andreas Hadjivasiliou, 2022). And, as other diseases become better understood and subdivided, they are more likely to get into the rare condition category. For valid scientific and medical reasons, most novel treatment approaches, including gene and cell treatments and gene-edited medications, first gain popularity in the treatment of rare disorders. Genetic diseases are relatively uncommon, as are some advanced, resistant tumours

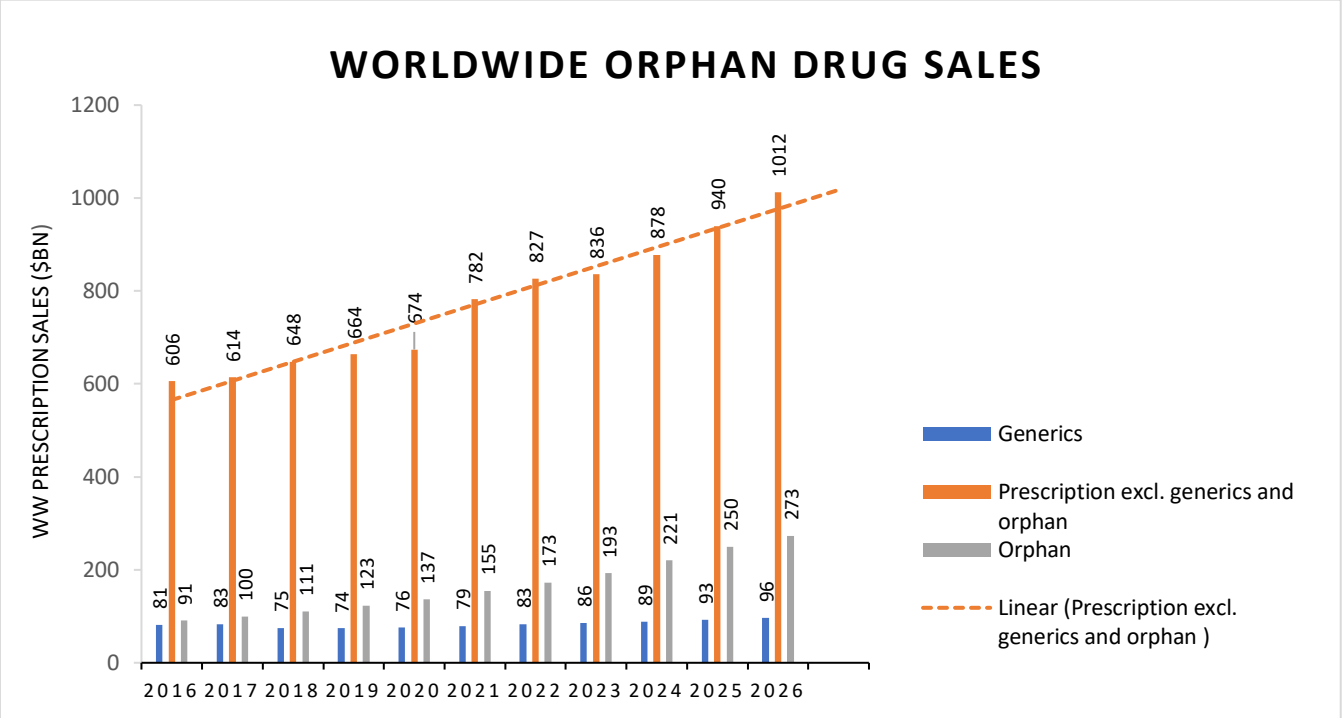
The pharmaceutical R&D pipeline is brimming with CAR-T cell therapies of the future, gene therapies, targeted cancer medications, and other therapies, novel therapies, many of which have orphan designations. The top ten pipeline orphan medicines' net present value forecasted 2026 sales is more than $42 billion (Melanie Senior and Andreas Hadjivasiliou, 2022)

Orphan drug sales continue to outperform the overall market

With a CAGR of 12% between 2021 and 2026, the orphan medicine market is growing more than faster than the non-orphan market by two times. By 2026, orphan medication sales will contribute for 20% of overall prescription drug sales. (Melanie Senior and Andreas Hadjivasiliou, 2022)

Over half of the FDA's Center for Drug Evaluation and Research (CDER) approvals have received orphan status

Over 50% of FDA's CDER approvals in 2021 were orphan drugs



After almost 40 years of comparatively constant development, orphan medicine currently comprises a pillar of the pharmaceutical industry with this class foreseen to shovel in $217bn in 2024. That is over 18% of typical prescription income in 2024. Remarkably, the marketplace is so sturdy that rare sicknesses now take domestic a huge part of FDA drug approvals. Orphan medications received just under half (44%) of the most recent FDA approvals in 2019

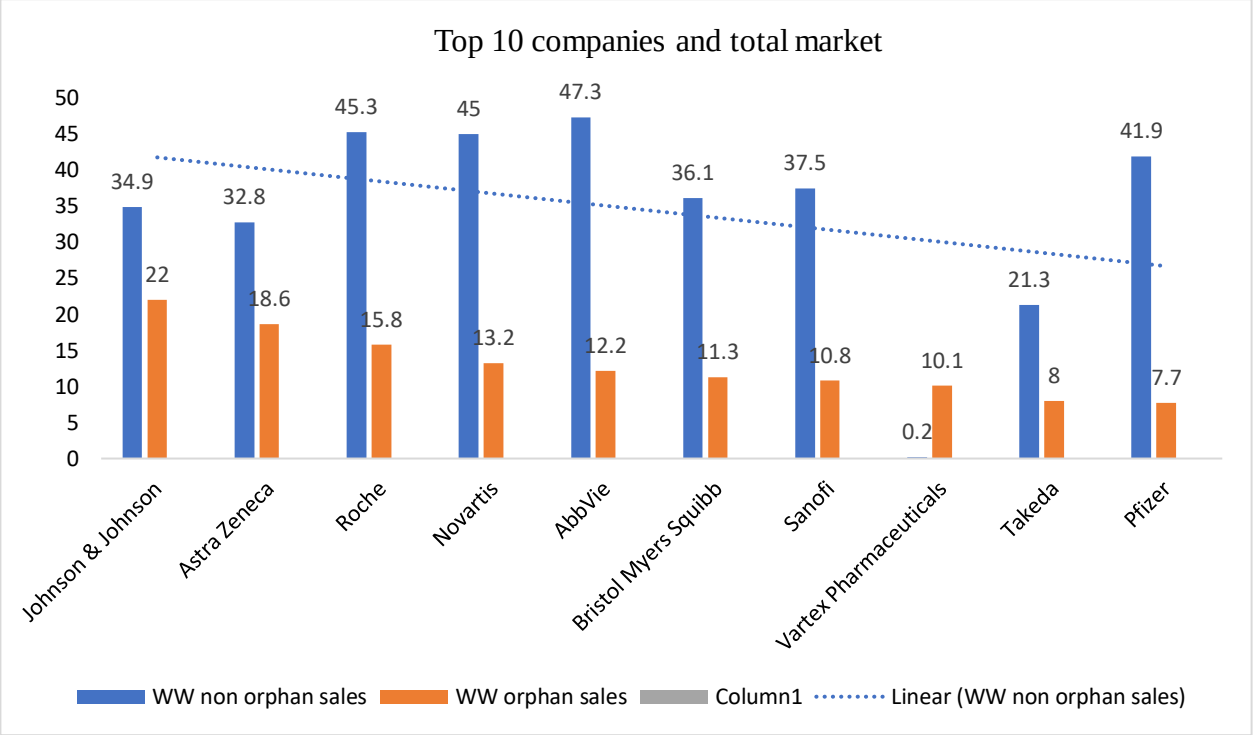
Top 10 companies & top markets: orphan drug sales

		Worldwide orphan sales ($bn)			Worldwide non orphan sales		Percentage of sales from orphan drugs	
Rank	**Company**	**2021**	**2026**	**CAGR**	**2021**	**2026**	**2021**	**2026**
1	Johnson & Johnson	13	22	+11,1%	39.3	34.8	25%	39%
2	Astra Zeneca	6.6	18.6	+22,5%	28.6	32.9	19%	36%
3	Roche	10.0	15.8	+9,2%	39	45.2	21%	26%
4	Novartis	13.6	13.2	-0,8%	37.3	45	27%	23%
5	AbbVie	7.6	12.2	+9,3%	46.5	47.2	14%	20%
6	Bristol Myers Squibb	22.0	11.3	-12,4%	23.5	36	48%	24%
7	Sanofi	7.1	10.9	+7,9%	31.6	37.4	18%	22%
8	Vertex Pharmaceuticals	6.1	10.1	+7,2	0.0	0.2	100%	98%
9	Takeda	5.6	8	+3,3	23.1	21.2	23%	27%
10	Pfizer	6.2	7.7	+8,6	65.2	41.8	7%	16%

Source: Evaluate Pharma

Nearly 40% of Johnson and Johnson's drugs sales by 2026 will be produced by orphan drugs. They will represent more than a fifth of the sales of seven other significant pharma companies. J&J will possess displaced BMS from the orphaned top-seller slot of 2024 by 2026 when patents on BMS' bestselling, orphaned Revlimid, developed by Celgene, expire this year

Alexion will help AstraZeneca, while oncology-focused Roche & Swiss neighbor Novartis are third and fourth respectively. AstraZeneca's projected CAGR of 22.6% between 2021 and 2026, driven by Alexion, is more than double the next-best 11% from Johnson and Johnson. Expected -12.5 CAGR for BMS during the period is due to the sales decline of Revlimid, it pulled in $12.8 billion in 2021



FOREMOST FIRM BY THERAPEUTIC AREA

Therapeutic category	WW annual sales ($bn) (2021)	Lead company
Oncology	75.1	Bristol Myers Squibb
Blood	23.0	Roche
Immunomodulators	1.9	Sanofi
CNS	13.3	Biogen
Endocrine	4.0	Novartis
Gastro-Intestinal	1.0	Takeda
Systemic Anti-infectives	1.8	Merck & Co
Musculoskeletal	4.1	Sarepta Therapeutics
Various	10.2	Sanofi
Respiratory	13.5	Vertex Pharmaceuticals
Cardiovascular	6.7	Johnson & Johnson
Dermatology	0.1	Torii Pharmaceutical

Source: Evaluate Pharma

Continued domination of cancer

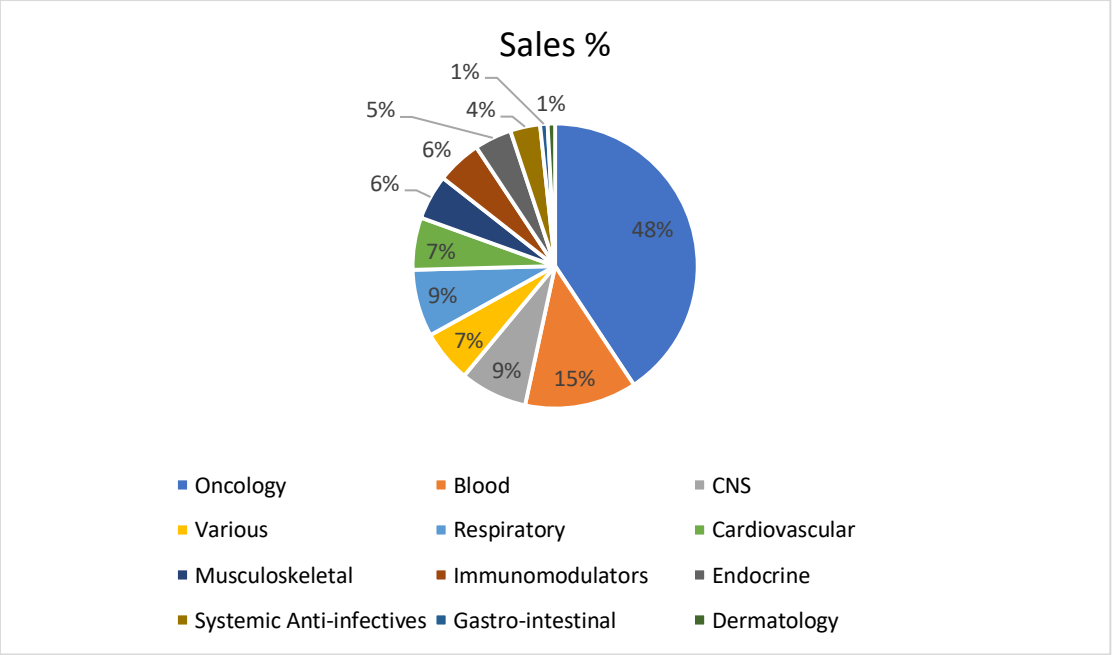
Six out of ten pipeline items for orphan pharmaceuticals are still being developed for the treatment of cancer. Looking at the larger orphan R&D pipeline, CNS disorders are in second place behind blood diseases, which include haemophilia and beta thalassemia

Top 3 therapeutic category for orphan (rare) drugs

1. Cancer

2. Blood disorders

3. CNS



REFORM ORPHAN DRUG LAWS:

The epidemic and politics in the US prevented the implementation of multiple regulatory and medicine price change initiatives in 2021. However, proposals to change the expedited approval by the FDA process—which is crucial for orphan drugs—are on the table. These include stricter regulation of the post-marketing analysis necessary to determine whether or not complete clearance is necessary for "accelerated" goods.

Over the beyond numerous years, a cloud of legislative reform has accrued over the orphan drug sector. Sky-excessive pricing of authorized gene treatments has fueled bi-partisan consensus towards fee gouging (Karen Pomeranz, Karen Siriwardana, Freya Davies, 2020). Meanwhile, unparalleled jockeying for orphan drug designation has caused requires reform of the Orphan Drug Act (Karen Pomeranz, Karen Siriwardana, Freya Davies, 2020).

NEW MODALITIES:

A lot of novel techniques, including CAR-T cell therapy and gene-editing treatments, started in orphan symptoms. These maladies frequently have a bad prognosis, are genetically determined, and are neglected. They provide an expedited opportunity to show new technologies' proof of concepts. Orphans are predicted to continue to rise due to the discovery of new tools and medication research techniques, such as gene-modifying, AI-powered screening, and drug design. includes stem cell therapy, several cell- and gene treatments, a gene-editing treatment using CRISPR Cas9, Targeted and bispecific antibodies, RNAi therapy, and even Clene's CNM-Au8 for ALS, an oral suspension of gold nanocrystals

APPENDIX

A medical product that treats a rare disease or condition is called an orphan drug. The Orphan Drug Act of 1983, a component of US legislation, provides financial rewards for the creation of orphan drugs. According to the NORD, which played a key role in the creation of the Act, there are presently up to 7,000 rare diseases that may affect up to 30 million Americans. 38 orphan medications were approved in the US prior to the 1983 Act. The initial Orphan Drug Act was successful in US, which led to its adoption in other important markets, most notably those in the European Union in 2000 and Japan in 1993

CONCLUSION:

The estimated market value of the top 10 orphans in 2026 ranges from $3 billion to $13 billion. In terms of disease category, the oncology segment dominated the global market for orphan products in 2020. The global orphan medicines market was worth $1,40,000.0 million in 2020 and is anticipated to arrive $4,35,686.3 million by 2030. The growth of orphans is anticipated to continue being fueled by the development of new tools and methods for finding drugs, from gene editing to AI-assisted drug discovery and development. Furthermore, developers are beginning to group together in similar areas, thus there are currently numerous medicines available for certain ailments. Five of the top 10 orphans of 2026, accounting for more than half (56%) of total $65 billion in sales, deal with blood cancers. This is anticipated that a number of CAR-T cell therapy treatment alternatives will become blockbusters in coming years with CDER granting FDA approval for more than half of those orphan drugs in 2021. In terms of countries, North America is anticipated to develop at the fastest rate, registering a CAGR of 11.0 percent over the projected period for the orphan medicines market. North America represented the highest percentage of the worldwide orphan drugs market in 2020, and is predicted to stay dominant during the forecast period. This was attributed to presence of large patient pool and early adoption of advance drugs, strong presence of key players, availability of drugs, early diagnosis, and favorable compensation policies

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