Shifting of Pharmaceutical Companies towards Orphan Drug Market: A Trend Analysis

Khushboo
Roll no. 0294

Guided by: Dr Sandesh Sharma
Associate Professor

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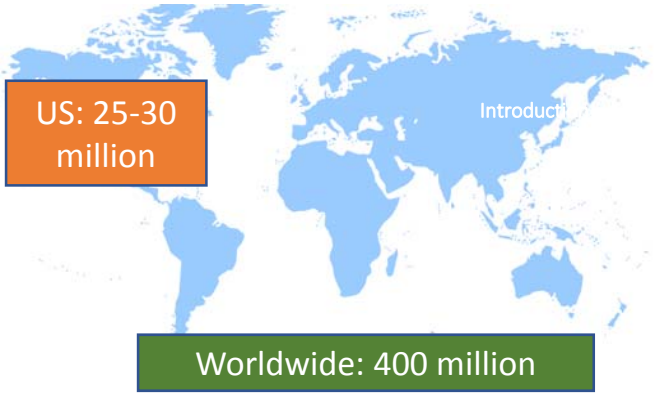
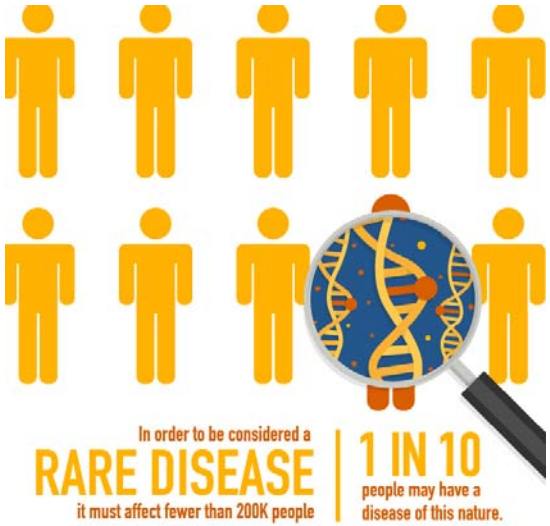
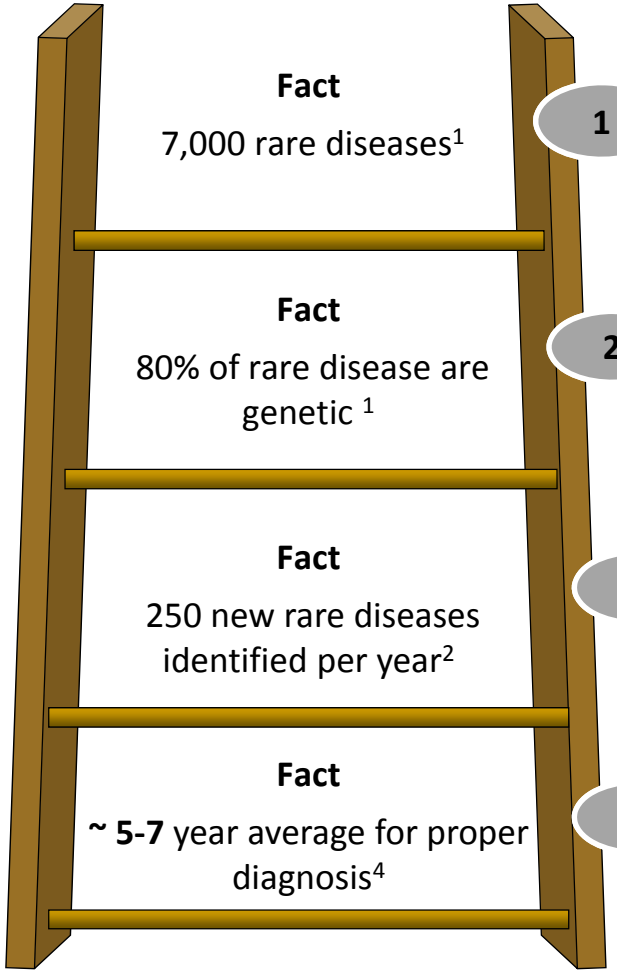
Rare/ Orphan Diseases in a nutshell …





- According to the FDA, rare diseases are defined as affecting **fewer than 200,000 people**
- Individually, **rare diseases are unique** but **collectively 25-30 million Americans** are anticipated to have one of 7,000 known rare diseases
  - **50% of these are children**
- Only **5%** of known rare diseases currently have an **approved therapy**

Orphan disease landscape



According to Global Genes, there are **7,000 rare disease** affecting around **400 million people** globally[1]

~50% of rare diseases impact **children**; 30% of children with a rare disease will live <5 years[1]

The number of orphan diseases with **no approved treatment** is estimated between **4,000 – 5,000**[3]

Patients often need **~ 8 MD** appointments before receiving the right diagnosis[1]

Sources: 1: sireninteractive , 2: healthline, 3: orpha.net. 4: cen.acs.org

Adversity faced by rare disease patients

Difficult to Diagnose

Patients and caregivers may go on a diagnostic odyssey since the general medical community often lacks awareness and understanding of the disease. The average length of time from symptom onset to accurate diagnosis is approx. 4.8 years

- This can lead to misdiagnosis or a lengthy period of uncertainty for patients and caregivers as they wait for a confirmed diagnosis

Relatively low number of specialists

Specific orphan diseases often have a small pool of KOL treaters, specializing in the disease, that heavily influence treatment of that disease

- There is usually a relatively larger referral base of non-KOLs that rely on these KOLs for second opinions on diagnosis and treatment options

Challenging disease management

Orphan diseases often place a heavy burden on key stakeholders

- Parents/caregivers become 24/7 caretakers and may face significant burden from cost of treatments and ancillary support
- Specialists often run overloaded practices as they oversee the treatment of multiple complex diseases

Influential advocacy group

Advocacy groups typically facilitate outreach to patients and caregivers – they may be the first resource for newly diagnosed patients

- They often provide a disease overview as well as patient referral tactics and systems for information gathering

KOL- Key opinion leaders

Orphan Drug Act in 1983 (21CFR Part 316)

Relevant excerpts from the Act include:

There are many diseases and conditions, such as Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy which affect such small numbers of individuals residing in the United States that the diseases and conditions are considered rare in the United States

Adequate drugs for many of such diseases and conditions have not been developed

Drugs for these diseases and conditions are commonly referred to as "orphan drugs"

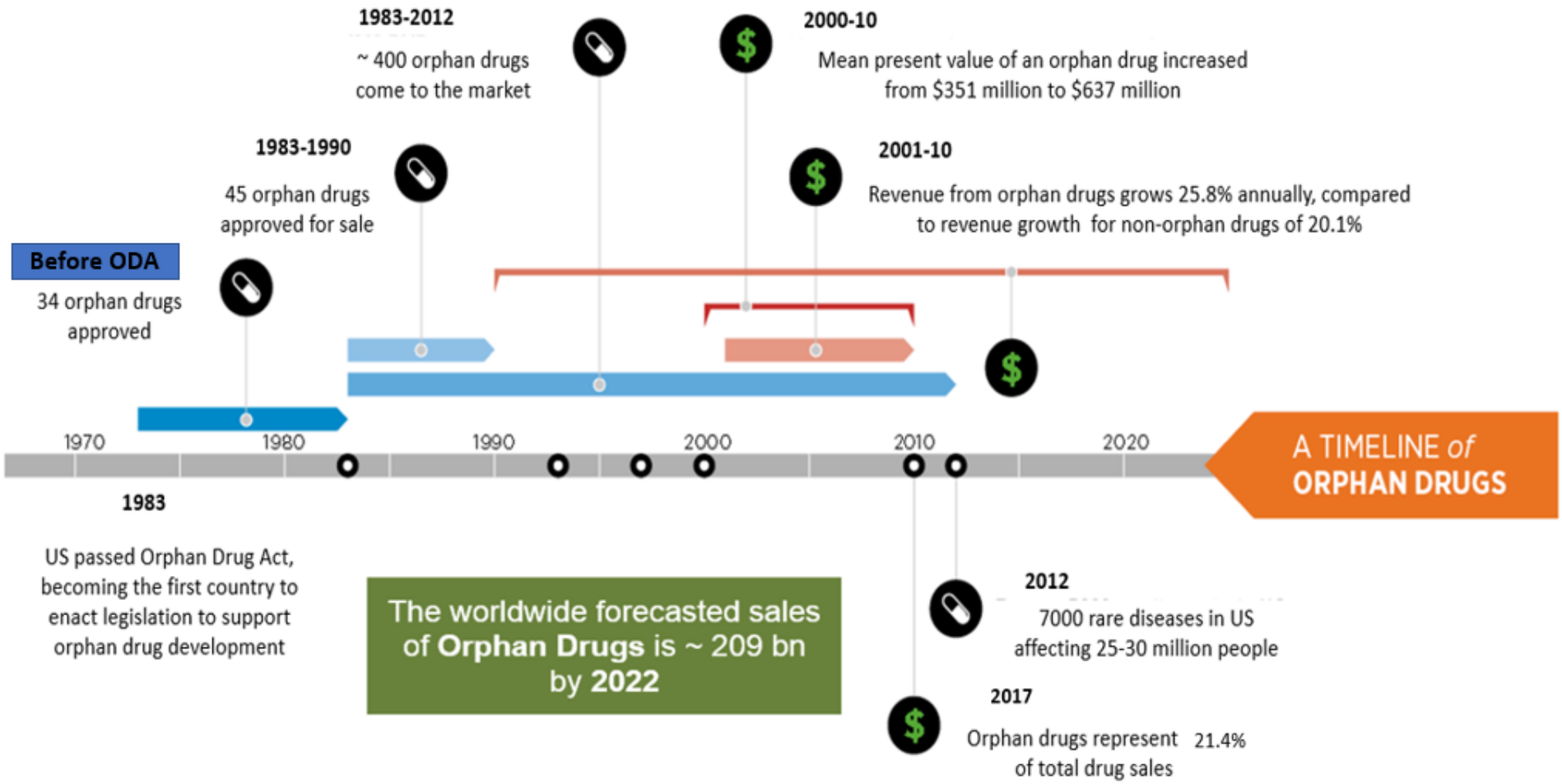
Because so few individuals are affected by any one rare disease or condition, a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss

There is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs

It is in the public interest to provide such changes and incentives for the development of orphan drugs

Source: 1. FDA

Timeline of the Orphan drugs



Source: 1. magazine.pamplin

Orphan Drug Designation & Authorization Process

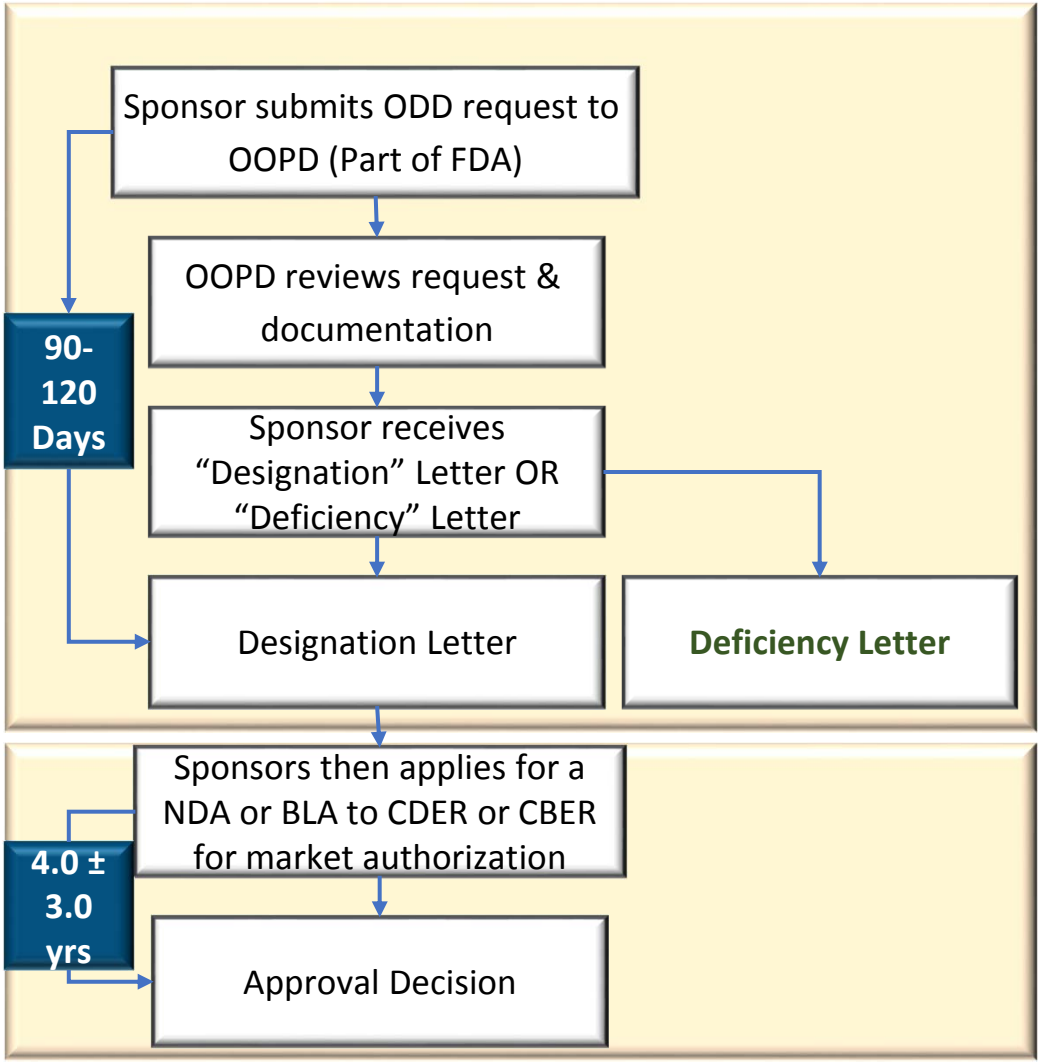
Step 1 **Orphan Drug Designation (ODD)**

Documentation requirements for ODD Application:

- *Sponsor & Drug Details (including statement of request)*
- *Description of the rare disease and why therapy is needed*
- *Scientific rationale for drug use*
- *Whether the drug applies for the orphan subset or even a broader common disease*

Step 2 **Orphan Drug Approval**

In certain cases, FDA may grant approval to a sponsor to market an orphan drug based on certain post marketing requirements



Note:1) OOPD - Office of Orphan Products Development; 2) CDER - Center for Drug Evaluation and Research; 3) CBER - Center for Biologics Evaluation and Research; * NDA – New Drug Application; BLA - Biological Licensing Application

Source for data: 1. NCBI, 2. Evaluate Pharma Orphan Drug Report 2015, 3. FDA Orphan Drug Designation

Rationale

- With only a limited number of the population affected by a rare disease, the justification for investing considerable funds for clinical studies by the pharmaceutical industry has always been a challenge and a real barrier to innovation. But as opportunities continue to diminish in disease areas addressing the mass market of patients, the pharma industry are encouraged to look at rare diseases as an opportunity to establish themselves in areas within healthcare with limited treatment options, and huge clinical unmet needs

Objectives

- To study and analyze the trends in orphan drugs approval

- To categorize the orphan drug manufacturer based on market capitalization and analyze the orphan market dynamics

- To analyze the trends of mergers and acquisitions amongst pharmaceutical companies

Methodology

Literature Review

A non-systematic literature review was undertaken to study the orphan drugs approval, included in articles in journals, industry publications, and articles in magazines and research papers

Study duration

The study was conducted for 3 months, based on orphan drugs approval in the time duration of **2010-2016**

Data collection

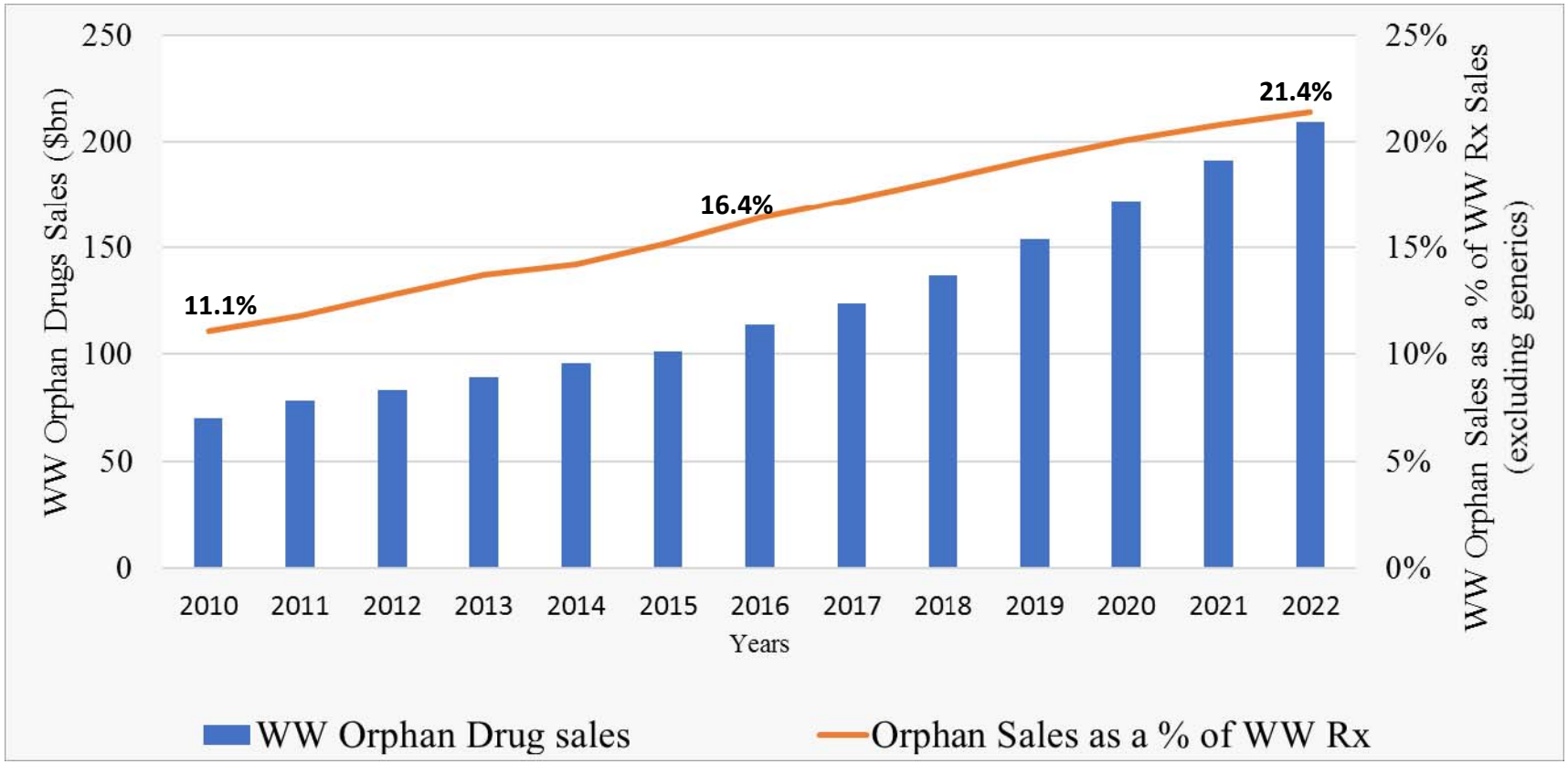
Publicly available secondary research data sources

Data Collection tools

To identify Orphan drugs approval, searches of FDA databases, Pharma companies databases using keywords such as “Orphan drugs”, “Novel drugs approval”, “Orphan drug market”, “Mergers and acquisitions” were undertaken

FDA- Food and Drug Administration

Worldwide Orphan Drug sales and share of prescription drug market (2010-16)

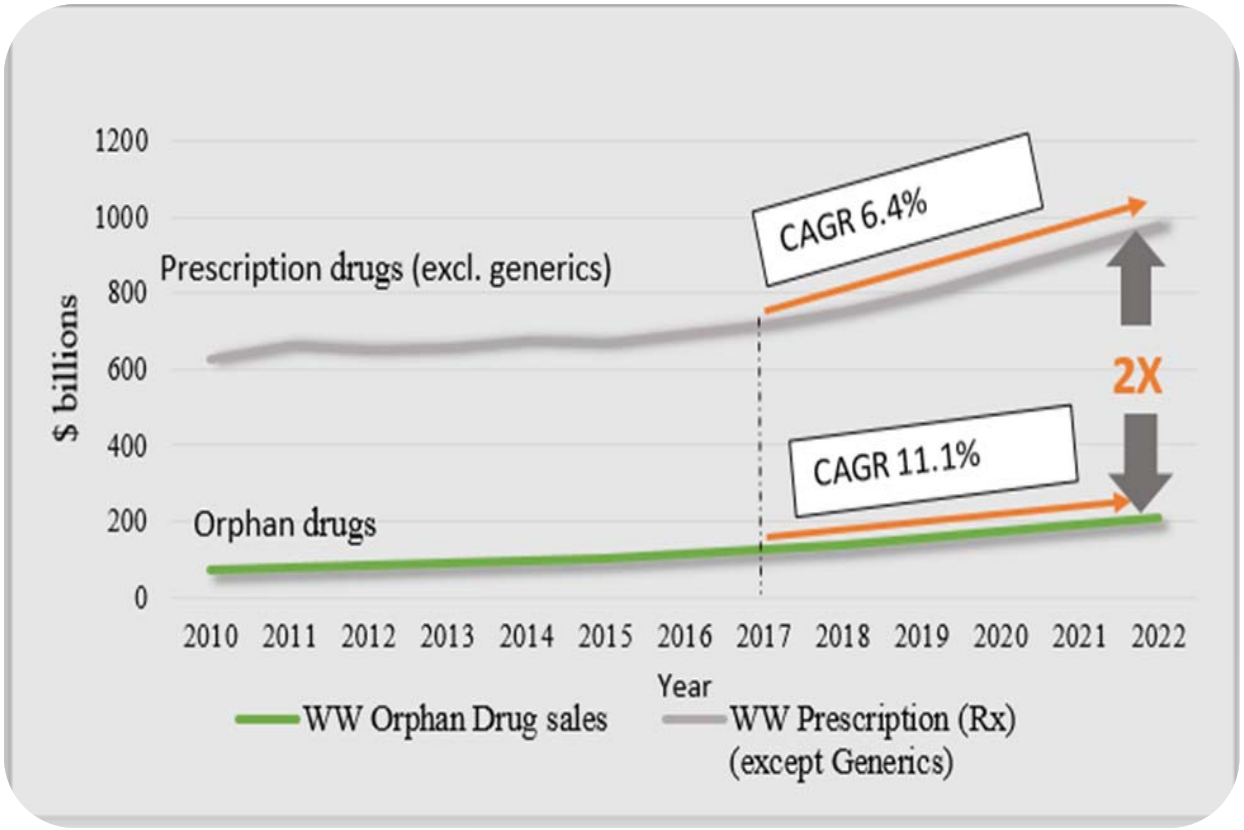


Worldwide Orphan Drugs sales in 2010 was $70bn and in 2016 was $114bn

The forecasted sales in 2022 is $209bn

OD are expected to account for 21.4% of total prescription sales in 2022

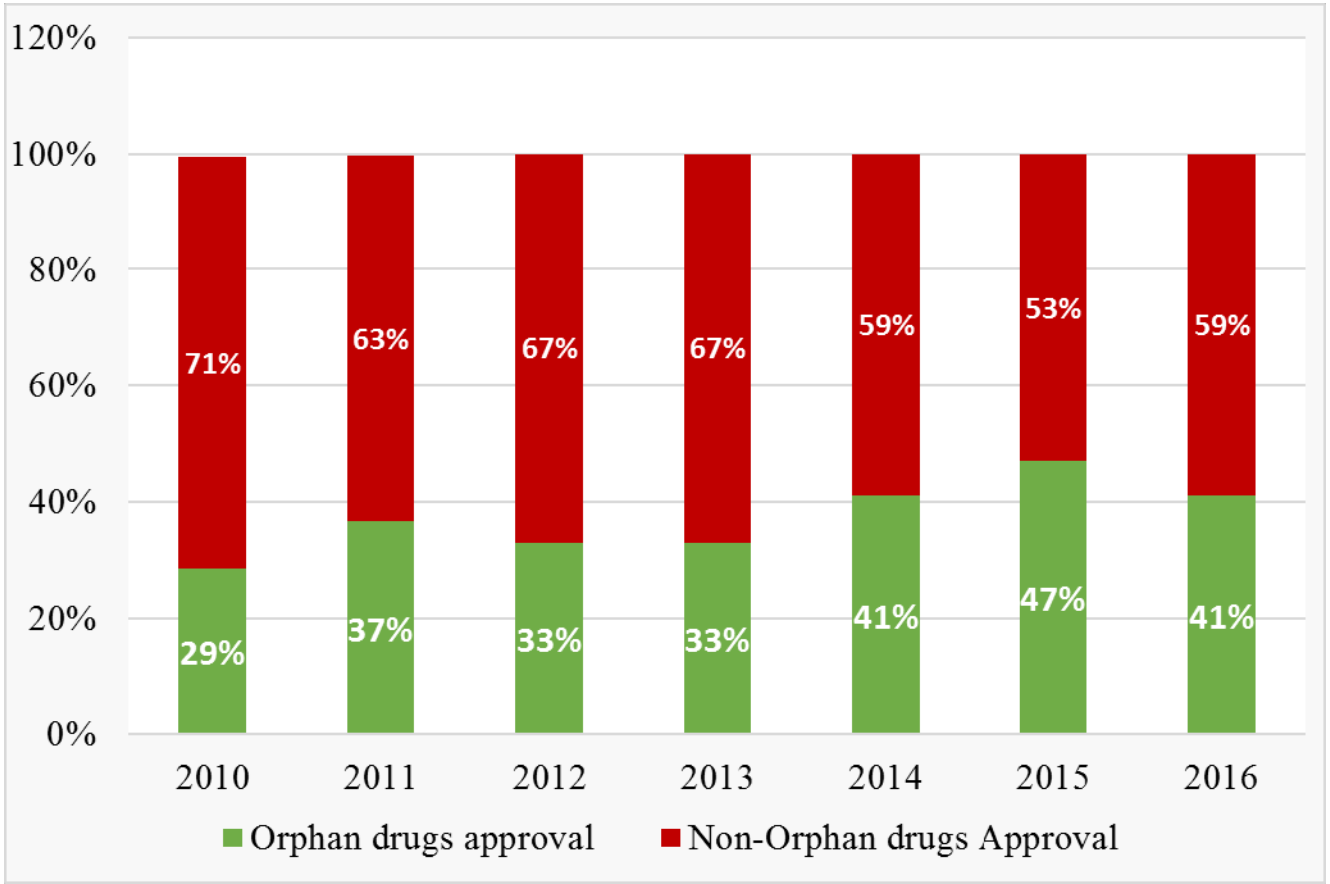
Forecasted worldwide change in CAGR



Worldwide orphan drug sales expected to grow 2x the overall prescription drug market

Both big pharma and small startups are working heavily on developing therapies for rare diseases

Percentage of Orphan drugs approval



Increase in the orphan drugs approval with the increasing years

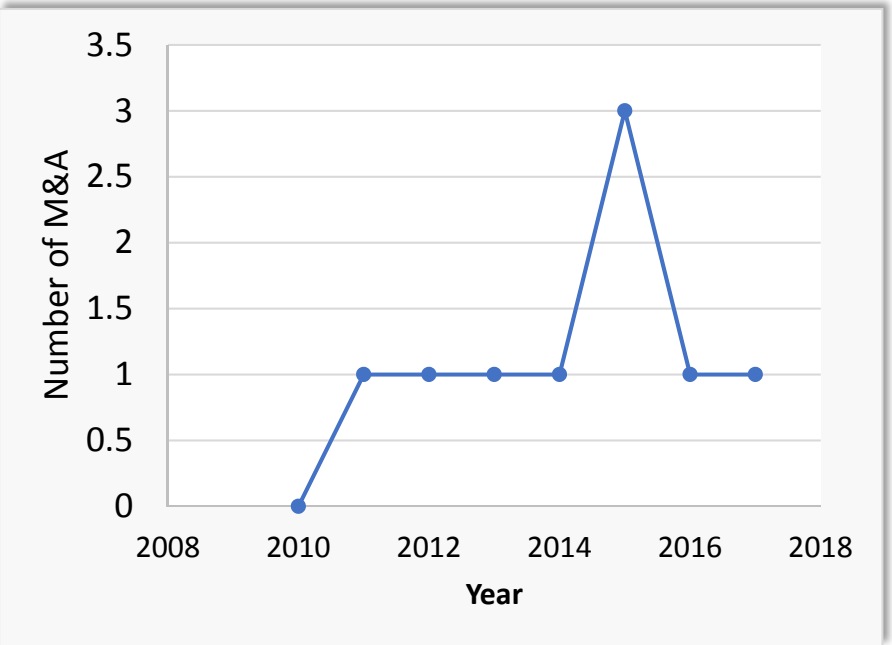
Segregation of large, mid, and small cap pharmaceutical companies with Orphan Drug approval during 2010-2016

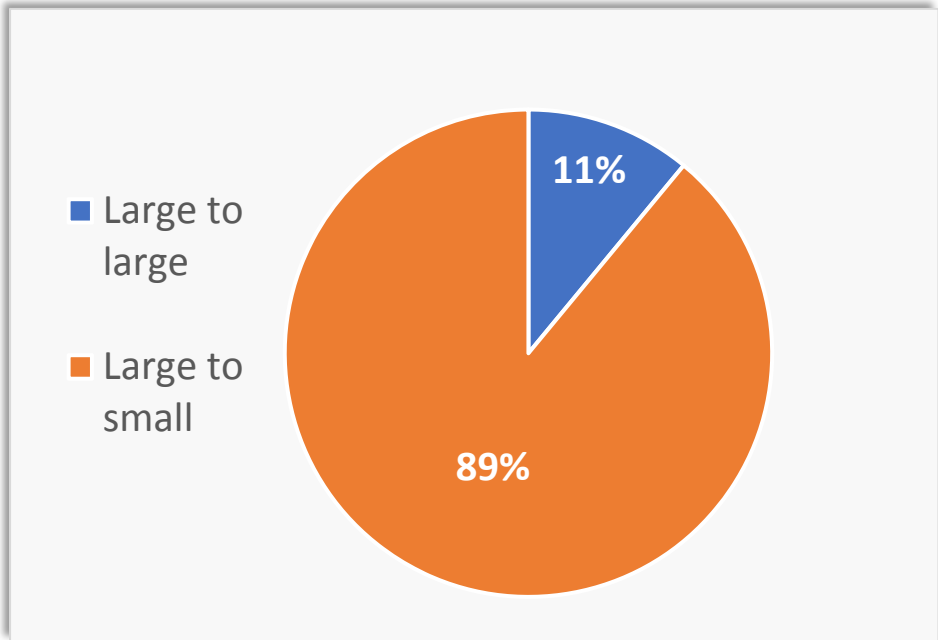
Increase has been seen in the number of large, mid & small cap pharma companies

Large cap pharma company	> $ 10 bn
Mid-cap pharma company	$ 2-10 bn
Small cap pharma company	< $ 2 bn

bn- Billion

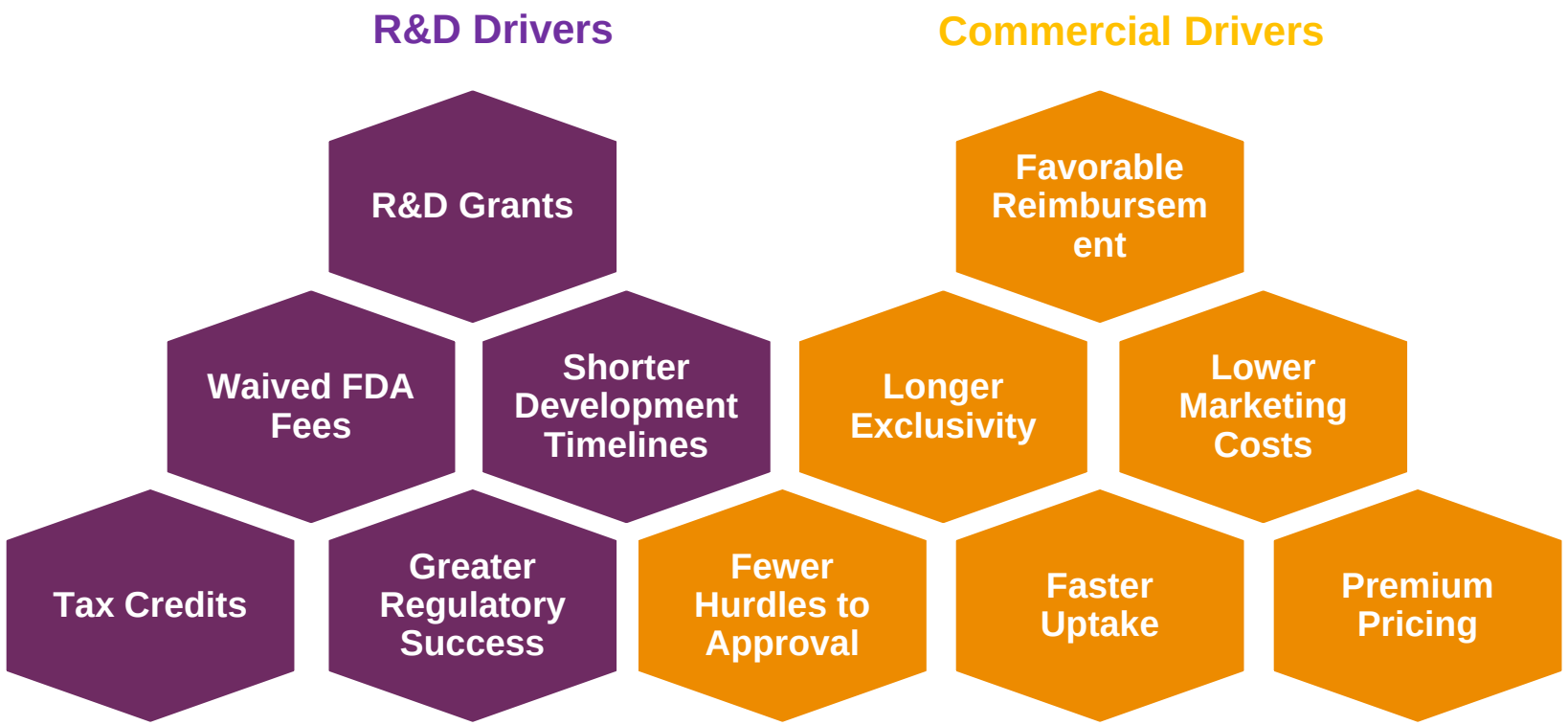
Mergers and Acquisitions in the Orphan Drug market





- It leads to better financial planning and control
- Diversification of scope of operation
- Reduced competition

Growing opportunity for pharma companies, due to a variety of favorable dynamics



Source: 1. books.google, 2. Hathaway C et. 2009 May

R&D- Research and Development

R&D and Commercial Incentives for obtaining Orphan Drug Designations (ODDs)

Financial Incentives	
R&D Grants	▪ The FDA's grant program is to support clinical development of products used for rare diseases ▪ **Phase 1 studies are eligible for up to $250,000 per year for up to 3 years. Phase 2 and 3 studies are eligible for up to $500,000 per year up to 4 years**
Waived FDA fees	▪ Orphan drugs are exempt from PDUFA fees - FDA PDUFA filing or user fees are waived for companies with less than $ 50 million worldwide revenues. PDUFA fees for application requiring clinical data are currently ~ **$ 2 million**
Tax credits	▪ Tax credits can apply to as much as **50%** of qualified clinical development costs

Regulatory Incentives	
Greater Regulatory Success	The approval process for orphan drugs is also often fast, lessening the risks of lengthy, expensive and failed developments. Measures available: ▪ Fast-track approval ▪ Breakthrough designation ▪ Accelerated approval pathway ▪ Priority review designation
Shorter development timelines	▪ The time taken from Phase 2 to market is shorter due to smaller clinical trials and FDA' s Priority Review & Fast Track designations ▪ On average, **the timeline for Orphan drugs is 3.9 years while traditional drugs take 5.4 years to reach market**
Longer exclusivity	▪ **7 years** of market exclusivity

Source for data: 1. FDA.gov, 2. Rarediseease.nhs, 3. Nature.Com

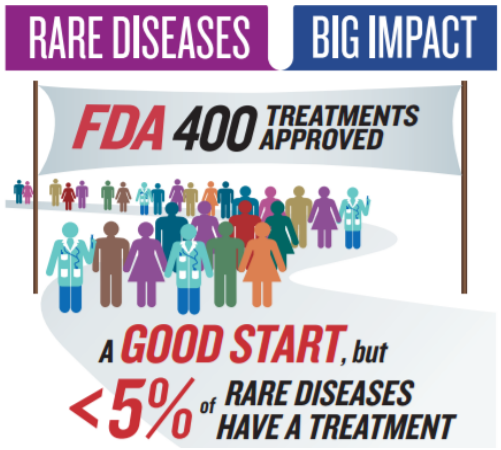
PDUFA- Prescription drug user fee act

Conclusion

- The percentage of molecules granted orphan drug status, by FDA, suggests that pharmaceutical companies are diversifying into new therapy area, which was overlooked earlier
- Economic and commercial drivers, further fuel the economic power of orphan drug development
- Though, pharmaceutical industry has a history of generating high value and will continue to surpass challenges by utilization of technologies, but, still for many rare diseases medications are unavailable, which shows that there is need of right planning as well as understanding for their risk and benefits

Business Impact for ZS

- This project will serve as an internal reference document for teams that will work with clients or on-shore teams in orphan vertical
- This document will help in encouraging ZS clients to shift in this domain keeping in view the following key market drivers:



"Just because what you're experiencing doesn't fit into an easily diagnosable box doesn't mean you should be easily dismissed and overlooked." – Megan Wirts

Thank you