MARKET OPPORTUNITY ASSESSMENT FOR ORPHAN INDICATIONS

Dissertation
At
ZS Associates, Gurgaon

By
Rishi Aneja

Under the guidance of
Dr. Neetu Purohit

MBA Hospital & Health Management
2013–15

Institute of Health Management Research
Jaipur
2015

INSTITUTE OF HEALTH
MANAGEMENT RESEARCH
(WHO Collaborating Centre for District Health System Based on Primary Health Care)

IIHMR UNIVERSITY

TO WHOMSOEVER MAY CONCERN

This is to certify, Rishi Aneja student of MBA Hospital and Health Management (2013-2015) from The IIHMR University, Jaipur has undergone internship training at ZS Associates,Gurgaon from 9th Feb 2015 to 8th May 2015. The Candidate has successfully carried out the study designated to him during internship training and his approach to the study has been sincere, scientific and analytical.

The Internship is in fulfillment of the course requirements.
I wish him all success in all her future endeavors.

Col, (Dr.) Ashok Kaushik
Dean, Academics and Student Affairs
The IIHMR University, Jaipur

Dr. Neetu Purohit
Associate Professor
The IIHMR University,
Jaipur

ZS Associates India Pvt. Ltd.
3rd to 8th floors, Block-A4
IT/ITEs SEZ of DLF Limited
Village - Silokhera, Sec-30
Gurgaon (Haryana) 122002 India
T | +91 124 679 7000
F | +91 124 679 7001

www.zsassociates.com

SALES+MARKETING

May 8, 2015

EXPERIENCE CERTIFICATE

This is to certify that Mr. Rishi Aneja (10599) has served in our organization from February 9, 2015 to May 8, 2015. At the time of leaving he was working in the capacity of Knowledge Management Associate - Intern based at New Delhi office.

He has successfully completed his Project on "Are orphan/ rare diseases the next big focus for traditional (Large/ Mid/ Small) size pharma Companies"

He comes across as a committed, sincere & diligent person who has a strong drive & zeal for learning.

We wish you all success in future endeavors.

For ZS Associates India Pvt Ltd

Esha Gulati
Manager - Human Resources

Nitin Aggarwal
KM Principal

INSTITUTE OF HEALTH
MANAGEMENT RESEARCH
(WHO Collaborating Centre for District Health System Based on Primary Health Care)

IIHMR UNIVERSITY

INSTITUTE OF HEALTH MANAGEMENT RESEARCH, JAIPUR

CERTIFICATE BY SCHOLAR

This is to certify that the dissertation titled .....Market Opportunity Assessment for Orphan / Rare diseases..... and submitted by (Name) .Rishi Aneja..... Enrollment No. .....1488..... under the supervision of .....Dr Neetu Purohit..... for award of MBA Hospital and Health Management/ MBA Pharmaceutical Management of the university carried out during the period from 9th Feb 2015 to 8th May 2015 embodies my original work and has not formed the basis for the award of any degree, diploma associate ship, fellowship, titles in this or any other Institute or other similar institution of higher learning.

Signature

Rishi Aneja

1, Prabhu Dayal Marg, Near Sanganer Airport, Jaipur- 302029, Rajasthan, India.
Ph.: 0141- 3924700, 2791431- 32, Fax: 0141- 3924738, E-mail: iihmr@iihmr.org, Web.: www.iihmr.org

Executive Summary

The pharmaceutical industry is experiencing change in ways it hasn't ever before. On the demand side, we are seeing an aging population, increased prevalence of "Western" diseases, and a dramatic growth in global access to pharmaceuticals. On the supply side, we are seeing increased competition from emerging market players, and a shift in the way drugs are being developed, manufactured, and delivered. Meanwhile, policy makers are struggling with an inherent conflict between desire to provide improved access to better medicines and the need to curb the growth of healthcare expenditures.

One topic at the centre of all of these changes is the Orphan drugs market. Orphan products will offer competition to some of the most expensive drugs on the market, but also require high investment.

Regulatory environment plays a very big role in determining the market for Orphan drugs in all geographies across the globe. Regulations have been set in place in order to prevent the launch of such inappropriate Orphan Product in market and thereby prevent associated adverse events (due to their complex molecular structure and consequent difference in immunological reaction offered by the body on their intake). So they need to undergo stringent regulatory approval process before they can be brought into the market for selling. This offers entry barrier for new players willing to enter this market space and also even the established pharmaceutical manufacturers first need to know the suitable markets in terms of market demand for Orphan products based on need analysis and also regulatory setting that exists there so that they can check the feasibility for themselves before investing in to Orphan market which requires a huge lot of

investment right from manufacturing till their approval for getting launched in the market. So the manufacturers would definitely wish to know by researching that which geographies or markets across the globe will offer maximum opportunity for Orphan product approval and consequently their sales that help them earn revenue in return of huge investment.

This study helps in finding out the opportunity for traditional sized pharma companies to venture into the Orphan Market which is considered to be more niche, precarious but of high value. Research Questions were developed like

What is the current scenario of the Orphan (Global and US) market ?

Which are the companies currently investing in the Orphan drug space ?

What is the amount of work done by the identified companies in the Orphan Market in different practice areas and types?

Accordingly, Research Objectives were formulated such as

- To Understand the Market scenario (Global and US Specific) of Orphan drugs by identifying the number of Orphan indications present worldwide, the number of Pharmaceutical companies investing into Orphan space by taking the number of drugs marketed / pipeline for Orphan indications into consideration.

The Specific objectives were :

- To evaluate the Orphan flagged Pharmaceutical companies and the amount of work done by ZS with these companies and priortize them

The Methodology was followed to fulfil and achieve all objectives that involved deciding upon study geographies followed by literature review of the market setting that exists in these geographies for Orphan products,followed by deciding upon the parameters that need to be assessed. The following parameters have been taken into consideration:Existence of Orphan indications, presence of small / mid /large pharmaceutical companies investing into the Orphan drugs , either marketing drugs or have orphan drugsin the pipeline.

As per the various variations of the definition of the parameters that came into knowledge on studying these parameters in the geographies under study and accordingly, **Segmentation** of the work done by each Pharmaceutical company was done to identify the amount of investment in which practice area (Sales / Marketing) thus, helps us in determining the most opportunistic or least restrictive markets for Orphans.

Finally findings were obtained where Novartis achieved the highest overall relative rank thereby suggesting that it offers least restrictive market for Orphan having 6 orphan projects in total and 15 Orphan drugs in their portfolio.

Conclusion

Shire,Novartis and Pfizer were observed to be investing the maximum for Orphan since they had maximum of number of drug products in development and in market for Orphan indications.

On creating the unique list of Orphan drugs for different indications, it was identified that the indication Pulmonary Arterial Hypertension had the maximum number of orphan drugs in Market and in pipeline.

Adalimumab (trade name : Humira) by Abbvie pharmaceuticals for rheumatoid arthiritis was found to be the most successful Orphan drug in Market on taking the overall sales for the particular drug in consideration.

Afamelanotide (trade name : Scenesse) by Clinuvel Pharmaceuticals for Actinic keratosis was found to be the least succesful Orphan drug in Market on considering the overall sales for that particular product.

Non- Hodgkin Lypmhoma was observed to have the maximum incidence and prevalance for any Orphan indication with incidence of 7,000 and prevalence of approx 40,000

Acknowledgement

I would like to express the deepest appreciation to my Project Lead Amit Pangasa (Manager ZS Associates, Knowledge Management) for the vision and foresight which inspired me to conceive this project.

I am particularly indebted to my Project Manager Sherin Alexwho has shown the attitude and the substance of a genius: she continually and persuasively conveyed a spirit of adventure in regard to research and scholarship, and an excitement in regard to teaching. Without hersupervision and constant help this dissertation would not have been possible.

My heartfelt thanks to my Guide at IIHMR Professor Dr.NeetuPurohit, who had a been a constant support and provided me guidance to steer my research and come out with conclusion.

I want to pay my gratitude towards the IIHMR, Jaipur for providing me with the opportunity to work with such a good organization.

By extension I'd like to offer my thanks to all the staff of the ZS Associates including a special thanks to my PD Manager Amudha Sharma (Knowledge Management Consultant) for their support throughout my tenure for internship at ZS Associates.

With warm regards,

Rishi Aneja

Table of Contents:

List of Tables and figures

1. Background

More than 25 years of orphan drug regulations have yielded several new treatments for patients with rare diseases. Orphan diseases are typically those that are having no commercial incentives to research and develop actual therapies. To boost the pharmaceutical companies to invest in the development of orphan drug, various countries, beginning with the USA, they have announced their own regulations to provide suitable motivations. There is a significant degree of similarity in the incentives provided from one nation to another and this variety from market exclusivity for the product in its proposed indication (the most important incentive) to tax credits and reduction or waivers of fees.

The World Health Organization gives the idea about Orphan or Rare diseases as; it is the pathological conditions that affect 0.65-1 out of every 1000 population. The EU defines a rare disease that affecting 5 peoples out of 10,000 Europeans; The USA accept the condition as a Rare disease as it affecting less than 200,000 peoples or the condition that affects less than 1 out of 5,000 in the general population; Japan has the limit up to 50,000 Japanese patients and Australia accepts the disease as an Orphan disease, that affects less than 1 at 2000 Australian patients. There are approximately 6,000 Orphan diseases, out of which 80% are genetic.

As Pharmaceutical companies generally invest many millions of dollars to develop single new drug, the interest of companies were diverted towards the development of drugs that are used for the large patient population (Non-Orphan drugs). But due to enforcement of the own legislation regarding the incentives, tax credits and research funds, the companies are now attracted towards the development and marketing of the Orphan medicinal products.

3. Literature Review

Overview of Orphan drugs

Orphan drugs are medicinal products intended for diagnosis, prevention or treatment of life-threatening or debilitating rare diseases. They are "orphans" because the pharmaceutical industry has little interest under normal market conditions in developing and marketing drugs intended for only a small number of patients suffering from very rare conditions.

In the USA it is defined as one that affects fewer than 200 000 individuals, but in Japan the number is 50 000 and in Australia 2000 . These numbers clearly relate to the population sizes of these countries, but even adjusting for that, the definitions vary from about 1 to 8 in 10 000. The European Community definition is less than 5 in 10 000. The WHO has suggested a frequency of less than 6.5–10 in 10 000, although that seems rather high. There are also lists of diseases, mostly genetic disorders, that are regarded as being rare. As a group they have nothing in common apart from their rarity, but the lists vary strikingly in length; for example, that published by the US National Organization for Rare Disorders contains about 1200 items,while NIH's Office of Rare Diseases publishes a list of over 6000, ranging from Aagenaes syndrome (lymphoedema and intrahepatic cholestasis) to Zuska's disease (lactiferous fistulae of the breast)

An orphan drug can be defined as one that is used to treat an orphan disease. For example, haemarginate, used to treat acute intermittent porphyria, variegate porphyria, and hereditary coproporphyria , is an orphan drug. However, it comes as a surprise that ibuprofen can also be categorized as an orphan drug, because it

has been used to treat an orphan disease, namely patent ductusarteriosusineonates (whether orphans or not). This observation stresses that barriers to the development of orphan drugs do not occur only at the premarketing stage; in some cases it may not be commercially worth mounting an efficacy trial, even of a drug whose efficacy elsewhere is well established. Indeed, there may be little incentive to mount an efficacy trial of a well established drug in a rare condition, or even in a relatively common condition in a subgroup of individuals – consider the many drugs that are licensed for use in adults but not in children.

Ultra – Orphan diseases are currently defined as diseases with fewer than 6,000 patients in the U.S , includes 83 % of all rare diseases.

Some Ultra- Orphan chronic conditions :

Table 1

Condition	Product	Avg. Drug Cost / person / year
Haemophilia B	Nonacog Alfa	35,000
Mucopolysaccharidosis Type 1	Laronidase	360,360
Gaucher's Disease	Cerezyme , Miglustat	1,00,000 (average)
Fabry's Disease	Fabrazyme / Replagal	126,880

Ultra – Orphan diseases make up over 80% of the orphan disease universe , less than 15% of new orphan designations address these diseases.

The overall number of approved orphan products addressing ultra orphan diseases remains low (18 % of total orphan approvals).

3.1 Timeline of Orphan drugs :

1979

FDA/NIH Task Force Issues Report

Task force chaired by Marion Finkel, MD, of FDA issues report calling for measures to address the need for more resources to be directed toward drugs "of limited commercialvalue" (drugs for small patient populations).

1979 – 1980

Patient Advocates Form Ad Hoc Coalition

Leaders of rare disease patient organizations form a coalition to provide advocacy together on behalf of legislation to encourage the development of treatments for people with rare diseases.

1980

Pre Orphan Drug Act

Only 10 new drugs were developed by the pharmaceutical industry for rare diseases in the decade before 1983.

January 4, 1983

Orphan Drug Act Passed

After rare disease patient advocates mobilized support for the Orphan Drug Act, which had been sidelined in Congress, it was approved by the House and Senate in December 1982 and signed by President Ronald Reagan on January 4, 1983. Those same patient leaders then established NORD to continue their collaboration, realizing that "Alone we are rare. Together we are strong."

February 1983

First Orphan Drug Approved

The Food and Drug Administration (FDA) grants first marketing approval to an orphan drug - Panhematin® for acute intermittent porphyria and other acute porphyrias. Desiree Lyon Howe, co-founder and executive director of the American Porphyria Foundation and for many years a NORD board member, participated in research on this orphan drug.

May 4, 1983

NORD Founded

NORD is incorporated to represent the shared interests and goals of all Americans affected by rare diseases. Abbey Meyers, considered the primary consumer advocate responsible for the Orphan Drug Act, is named president

1984

Orphan Drug Act Amendment

The Orphan Drug Act is amended to define a rare disease as any disease affecting fewer than 200,000 Americans or a disease with a higher prevalence but for which there is no reasonable expectation that a therapy would recover the cost of development.

1985

Orphan Drug Act Amendment

The Orphan Drug Act is amended again to extend marketing exclusivity to both patentable and unpatentable products.

1999

European Union adopts Orphan Law

European Union adopts law similar to Orphan Drug Act (Regulation on Orphan Medicinal Products).

2000

Rare Diseases Act Introduced

Senators Ted Kennedy and Orrin Hatch introduce the Rare Diseases Act, advocated by NORD to enhance federal funding for rare disease research and accelerate the development of treatments. The House later splits this legislation into two separate bills – the Rare Diseases Act and the Orphan Products Development Act

2011

Affordable Care Act Signed

The Affordable Care Act signed by President Obama provides insurance reforms for which NORD lobbied, such as ending annual and lifetime insurance caps and eliminating discrimination based on pre-existing conditions.

The Orphan drug space represents a large and growing oppurtunity for Pharma& Biotech companies , due to favourable dynamics

11. Drivers and Challenges for Orphan drug Market

There are several challenges associated with orphan drug development. Two noteworthy obstacles include the difficulty in locating and recruiting patients and the logistical problems related to trial organization. These factors are thought to increase the costs incurred by orphan drug R&D. However the trials focused on orphan drugs are significantly shorter and have a quicker review time than trials involving non-orphan drugs.These positive factors, plus others shown in Figure 5, are likely to outweigh the aforementioned challenges.

Table 2

R & D Drivers	Commercial Drivers
Tax Credits	Favourable Reimbursement
R & D Grants	Longer Exclusivity
Waived FDA fees	Lower marketing costs
Shorter development timelines	Faster Uptake
Greater Regulatory Success	Premium pricing

A substantial number of orphan drugs in the sample set were oncology-related: 40 percent of the orphan drugs in the sample set dealt with oncology, compared to only 10 percent in the non-orphan drug sample set. This is consistent with orphan drugs across the FDA database. The orphan drug samples also had a larger share of biological versus small molecule drugs. One possible reason for the intense focus on this particular therapeutic area is that the underlying genetic aberration of oncology often provides the signature for disease identification. In the pharmaceutical industry, oncology has also taken the lead in the recent evolution to customized, or precision, medicine. The approach of utilizing biomarkers in targeting treatments and therapies further explains this therapeutic area's majority share of orphan drug approvals, in addition to the field's susceptibility to smaller, individualized

subsets of larger patient populations. It has long been speculated that the heyday of the blockbuster drug model has declined or died. But, researchers found that of the 86 orphan drugs included in the study, 25 were blockbusters; meaning, 29 percent of orphan drugs have annual sales greater than $1 billion. This is comparable to 83 out of the 291 non-orphan drugs that were considered to be blockbusters (which is also 29 percent). The number of blockbusters approved each year remained constant between 2000 and 2010, suggesting that the blockbuster model is not dead, but remains an important part of pharmaceutical R&D, supplemented by emerging areas such as rare disease research.

3.2 CHALLENGES FOR DEVELOPMENT OF ORPHAN DRUGS

The population affected is growing

With over 7,000 rare diseases registered and 452 compounds presently in progress. Approximately 350 million people worldwide suffer from a rare disease. 50% of these patients are children. Growth in R&D for rare disease is growing at twice the rate of common diseases. The mainstream of unusual diseases are in the areas of cancers and genetic disorders.

The diseases are complex

A major factor in orphan drug development is the complexity of the disease profile itself. Understanding the epidemiology of the disease and translating that to clinical trial design is daunting. Personalized medicine and genomic mapping have lent new insights in the origin of these diseases. These new tools allow researchers to identify narrow patient populations

through genetic mapping, a critical step to overcoming the challenge of patient recruitment in these rare diseases.

Challenging feasibilities and study design

Rare diseases in the US are classified as 1 patient from 200,000. This number fluctuates worldwide, but most of the countries defining rare disease as one with a low prevalence in an existing sample size. However one issue is constant. Rare diseases make patient employment challenging. These insignificant sample proportions challenge outdated clinical development feasibilities geographically, affecting site selection and patient enrolment.

Challenging regulatory climate

Regulatory practice is by nature, inflexible. Before legislation was enacted to address rare disease, researchers and patients were left with few options. Traditional approaches to clinical studies for drug development were not well suited for the accelerated development and adaptive methods needed to address the issue of rare disease and the challenges imposed. Many of the regulatory barriers to this research have been addressed. In the US, the FDA has addressed the need for accelerated review timelines; fast track and accelerated approval processes to facilitate development and review; priority review; and expanded access of patients to investigational products.

Strides are being made with regard to evaluation of new methods for clinical trial scheme, emerging educational agendas for investigators, and increasing communication with stakeholder groups – both in academia and advocacy. This outreach provides new hope for these patients.

Stakeholder groups hold the keys

The combination of patient shortage for a disease, combined with an elevated paediatric focus makes enrolment of a significant hurdle to overcome the possibility of the study. The requirement to improve the solutions have given rise to a new era of collaboration.

Patient Advocacy Groups

At the centre of any disease is the patient. Before regulatory authorities recognized the importance of drug development for rare illness, only 10 compounds were approved by US.

3.3 CURRENT STATUS OF REGULATION IN DIFFERENT COUNTRIES

USA

FDA's orphan drug regulations are intended to create market-based incentives for manufacturers of products for populations with rare diseases. As Per the Orphan Drug Act of 1983, a rare disease is termed as the disease condition affecting lesser than 200,000 population across United States.

This act consents FDA to provide the products approved to treat the orphan conditions special marketing protections (7 years of market exclusivity), tax credits to offset some of the costs of development, faster regulatory reviews and additional assistance from FDA reviewers during the development and review process.

EUROPE

A disease or disorder that affects fewer than 5 out of 10,000 citizens is termed as rare condition in Europe (Orphan Drug Regulation 141/2000). Superficially, this may give the impression of scarcity, but by means of this account, rare diseases may affect as many as 30 million European Union citizens.

According to EURORDIS (European Organization for Rare Diseases), the number of rare diseases are about 6,000 to 8,000, many of them having genetic basis, with medical proposal describing approximately five new rare disease every week. From which it has been concluded that 25 to 30 million people are reported to be affected by these diseases in Europe.

JAPAN

A drug must meet the following three conditions in order to be considered for orphan drug designation in Japan. Condition which affects less than 50,000 population is termed as rare disease in Japan. The drug having capability to treat a disease condition for which there are no other treatments available in Japan or the proposed drug is clinically superior to drugs which is already available on the Japanese market is specified as Orphan drugs under the legislation in Japan.

The applicant should have a clear product development plan and scientific rationale to support the necessity of the drug in Japan. New Drug Application (NDA) can be submitted after clinical trials are completed. There should be anticipated that while Japan has orphan drug legislation which has opportunity for interpretation with other countries.

3. Rationale of study:

In response to this requirement and need raised by pharma clients, the study involves the identification of Orphan indication present currently taking specific parameters into consideration. Thereafter,listing down all the Orphan designated products currently in the market and in pipelineThis study helps finding out the most opportunistic markets from around the globe depending upon available forecasted secondary data. Opportunity assessment will help pharma MNC'S to decide upon wether they should go to for investment into Orphan space.

4. Research Questions:

1. What is the current scenario of the Orphan (Global and US) market ?
2. Which are the companies currently investing in the Orphan drug space ?
3. What is the amount of work done by the identified companies in the Orphan Market in different practice areas and types?

5. Objectives

To Understand the Market scenario (Global and US Specific) of Orphan drugs by identifying the number of Orphan indications present worldwide, the number of Pharmaceutical companies investing into Orphan space by taking the number of drugs marketed / pipeline for Orphan indications into consideration.

5.1 Specific Objectives

To evaluate the Orphan flagged Pharmaceutical companies and the amount of work done by ZS with these companies and priortize them.

6. Study design and methods:

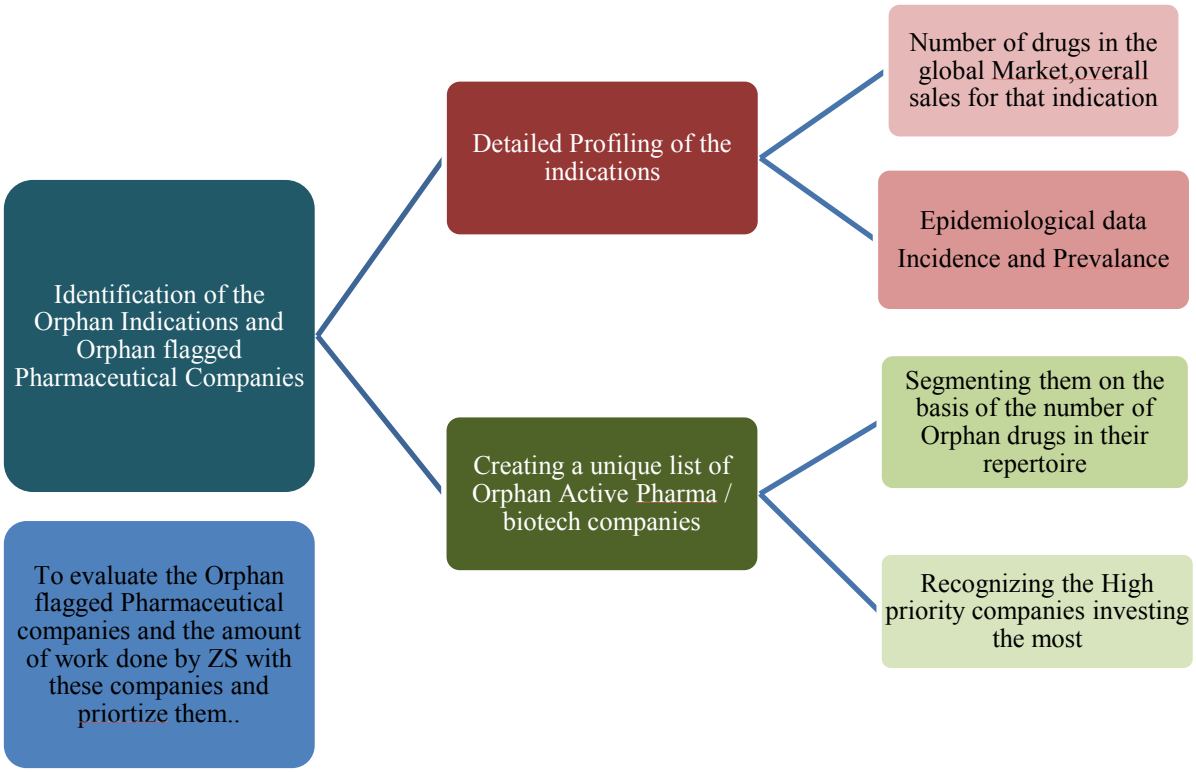
a) Type of study: Exploratory Secondary Research

b) Geographies under study:- United States

c) Study subjects: Orphan/Ultra-orphan indications and products

d) Data (information) to be collected: Recording of Market scenario in study geographies under consideration.

e) Data collection tools: ZS Specific data sources and publically available secondary research data sources depl



- ZS specific Data sources*are search for English language reviews and reports on Orphan marketspace
- Popular websites specific to Europe (European Medicines Agency), United States (Food and Drug Administration), were visited and studied thoroughly. The links for them are: http://www.ema.europa.eu/ema/ , http://www.fda.gov/
- Apart from these websites next most visited website was Orphanet this is a dedicated source of information on Orphan products.
- Grey literature was referred to e.g. various articles found on Google search using various strings and keywords related to Orphan drugs.

Note* (names of data sources are confidential and cannot be revealed here)

7. Data Collection

7.1 Identification of the Orphan indications :

Identification of the currently known orphan disease states was done through secondary research and through publicly available information primarily through Orphan web page www.orpha.net.

An Excel sheet was prepared listing down all the 7,000 identified Orphan indications..

Similarly after identifying the Orphan indications , the next step was to explore the pharmaceutical market in the Orphan Space i.e exploring the market space for rare diseases by :

1) Identifying the number of pharmaceutical companies investing in Orphan drug space by listing down the number of drug products they have in market and number of drugs in pipeline for Orphan indications for global market and US specific separately.

After Identification , segmentation was into different categories for broad profiling of the respective disease state.

It was done in a manner

Orphan designated products on Market was profiled by taking their drug name , disease state , Brands by which it was marketed globally and its route of administration into consideration.

Pipeline products with orphan designation were profiled on similar lines as the marketed drugs were.

On gathering the above required information , an excel spreadsheet was prepared incorporating the collected data in the format mentioned below :

For Marketed drugs (Global and US) Fig. 2

Drug Name	Brands	Marketed by	Originator	Licensee	Other Organisation	Mechanism of action	Route of Administration	Indication	Annual Sales

For Pipeline drugs (US) Fig. 3

Drug Name	Brands	Brand names in US	Developed by	Licensee	Other Organisation	Mechanism of action	Route of Administration	Indication	Therapeutic Area

For tracking down the Orphan market landscape more comprehensively , Epidemiological factors were also taken into consideration on similar lines.

Epidemiology (US) Fig. 4

Indication name	Population	Country	Gender	Source	Statistic	Name of report	Incidence and Prevalance

A Total of 453 pharmaceutical companies were identified which had a minimum of atleast 1 Orphan/Ultra Orphan product in their portfolio.

For each product/company combination, identification of the work done that is orphan specific to estimate the amount of orphan specific work performed in ZS.It was basically done to determine the gaps in the current work associated with orphan to target companies and practice areas more effectively.

A summary Grid was prepared in which the following actions were taken :

Categorization of the Active companies based on the number of drugs they have in Market and in pipeline.

The classification is as follows-

- High Pipeline/High Marketed
- High Pipeline/Low Marketed
- Low Pipeline/High Marketed
- Low Pipeline/Low Marketed

For further bucketing the companies more comprehensively, a set of scenarios were developed to segregate the list into the 4 categories listed above.

- **Control 1ipe**

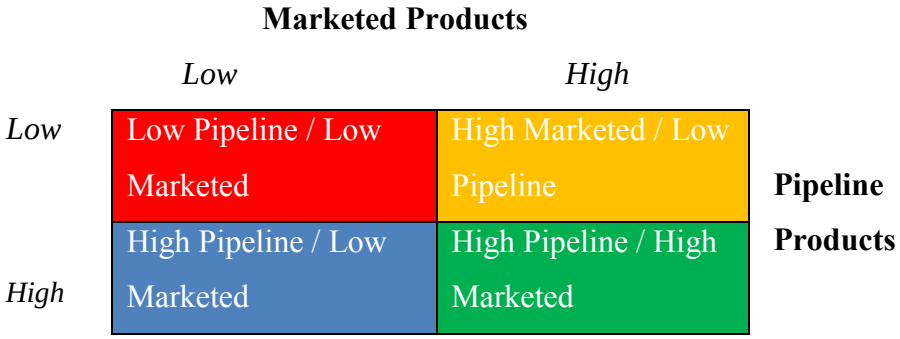
High Pipeline - greater than or equal to 3 Orphan drugs in pipeline

Low Pipeline - less than 3 Orphan drugs in pipeline

High Marketed - greater than or equal to 5 Orphan drugs in Market

Low Marketed - less than 5 Orphan drugs in Market

The Grid : Fig. 5



Out of 453 Companies identified

3 were placed in High Pipeline / High Marketed Segment

16 were recognized as High Pipeline / Low Marketed

5 were placed in Low Pipeline / High Marketed

429 were found to be in Low Pipeline / Low Marketed

Detailed study of the companies which fell into the High Marketed / High pipeline segment , High Maketed / Low Pipeline segment and Low Marketed / High Pipeline Segment was done to assess the market opportunity for these companies so that the less explored business / Practice area could be tapped.

8. Data Analysis

Table 3. High Pipeline / High Marketed Segment

Company Names	Total Pipeline (Global)	Marketed (Global)	Categories (Control 1)
Novartis	6	9	High Pipeline/High Marketed
Pfizer	5	8	High Pipeline/High Marketed
Shire	4	5	High Pipeline/High Marketed

Companies falling under the segment High Pipeline / High Marketed :

1. Pfizer
2. Shire

3. Novartis

Company Overview :

1. Novartis

As a science-based and patient-oriented healthcare, Novartis strives to be a global leader in growing areas of healthcare. Novartis focuses its business on three leading divisions with strong innovation power and global scale: pharmaceuticals, eye care and generics. These three leading divisions are supported by our research organization, the Novartis Institutes for BioMedical Research (NIBR), and a centralized services group, Novartis Business Services, to facilitate collaboration across our divisions, and drive efficiency and productivity gains. Novartis aims to develop innovative products in growing areas of healthcare. At the same time, Novartis are expanding our presence in the emerging markets of Asia, Africa and Latin America, where there is fast-growing demand for access to high-quality medicines and healthcare.

Novartis strategies for Orphan drug market :

- Markets 13 orphan drugs and has an additional 23 orphan designations within its portfolio
- Explicit strategy to get products to market quickly has led to multiple orphan approvals while the firm continues to pursue indications with larger patient populations.

With 6 drugs in Pipeline and 9 marketed drugs , Novartis was ranked 1st in the High Pipeline / High Marketed segment

2. Pfizer

Pfizer Inc. (Pfizer), incorporated on June 2, 1942, is a bio pharmaceutical company. The company applies science and resources to discover, develop and manufacture healthcare products. The Company provides medicines, vaccines and consumer healthcare products. The Company operates its business through three operating segments, which include Global Innovative Pharmaceutical segment (GIP); the Global Vaccines, Oncology and Consumer Healthcare segment (VOC), and the Global Established Pharmaceutical segment (GEP).

The Company provides medical information to healthcare providers, patients and other parties, transparency and disclosure activities, clinical trial results publication, grants for healthcare quality improvement and medical education, partnerships with global public health and medical associations, regulatory inspection readiness reviews, internal audits of Pfizer-sponsored clinical trials and internal regulatory compliance processes. The Company's products include Lyrica, the Prevnar family of products, Enbrel, Celebrex, Lipitor, Viagra, Zyvox, Norvasc, Sutent, BeneFIX, Vfend, Pristiq, Genotropin, Refacto AF/Xyntha, Chantix/Champix, Xalatan/Xalacom, Medrol, Zoloft, Xalkori, Inlyta, Relpax, Rapamune and the Premarin family of products, among others. Global Innovative Pharmaceutical segment Global Innovative Pharmaceutical segment (GIP) consists of medicines in a range of therapeutic areas. These therapeutic areas include immunology and inflammation, cardiovascular or metabolic, neuroscience and pain, rare diseases and women's or men's health. Global

Vaccines, Oncology and Consumer Healthcare segment Global Vaccines, Oncology and Consumer Healthcare segment (VOC) focuses on the development and commercialization of vaccines and products for oncology and consumer healthcare. The VOC segment also includes its global Consumer Healthcare business, which manufactures and markets a range of over-the-counter (OTC) products. Global Established Pharmaceutical segment Global Established Pharmaceutical segment (GEP) includes the brands that have patent-protected products and generic pharmaceuticals. GEP includes the Company's sterile injectable products and biosimilar development portfolio

Pfizer's orphan and genetic disease unit focuses its research on protein challenges that underlie many rare, genetic diseases. It pays particular attention to hematology and neuromuscular diseases. Pfizer and Protalix received approval by the FDA in May for taliglucerase alfa (Elelyso™) as a long-term enzyme-replacement therapy for type 1 Gaucher disease, but were denied EMA approval in favor of Shire's earlier EMA-approved therapeutic. Other global filings are under way.

Pfizer strategies for Orphan drug market :

- Acquired FoldRx and created orphan disease unit in 2010
- Assets under development in CF, Gaucher, Huntington and others
- Launched Xalkori in 2011, targeting <7% of non-small cell lung cancer patients.

With 5 drugs in pipeline and 8 drugs marketed Pfizer was Ranked 2nd in the High marketed / High pipeline segment.

3. Shire

Shire Plc is a Jersey-registered, Irish-headquartered global specialty biopharmaceutical company.[3] Originating in the United Kingdom with a large operational base in the United States, its brands and products include Vyvanse, Adderall XR, Intuniv, Lialda,Pentasa, Fosrenol, Replagal, Elaprase, VPRIV, Firazyr and Dermagraft.

Shire develops and provides healthcare in the areas of behavioural health, gastrointestinal conditions, rare diseases, and regenerative medicine.

Shire is a leader in the development and marketing of orphan drugs for genetic diseases, with four marketed products, a global footprint and an unrivalled focus on patients. Partnerships and acquisitions have been central to our success to date, and remain core to its future growth. The business grew out of Shire's 2005 acquisition of Transkaryotic Therapies and has since engaged in multiple further partnerships and acquisitions, including the Jan. 2013 purchase of Lotus Tissue Repair, Inc.

Shire strategies for Orphan drug market ;

Has been competing in the orphan space since acquiring TKT in 2006

- 4 marketed products (Elaprase, Firazyr, Replagal, Vpriv)
- 3 products in clinical trials
- 5 products in preclinical development

With 4 drugs in Pipeline and 5 drugs in Market ,Shire was placed 3rd in the High Pipeline / High Marketed division.

Table 4 Low Pipeline / High Marketed Segment

Company Names	Total Pipeline (US)	Marketed (Global)	Categories (Control 1)
Bayer HealthCare	2	5	Low Pipeline/High Marketed
Celgene Corporation	2	5	Low Pipeline/High Marketed
Genzyme Corporation	0	5	Low Pipeline/High Marketed
Glaxosmithkline	1	9	Low Pipeline/High Marketed
Spectrum Pharmaceuticals	1	5	Low Pipeline/High Marketed

1) Glaxosmithkline ;

GlaxoSmithKline plc (**GSK**) is a British multinational pharmaceutical company headquartered in Brentford, London. It was the world's sixth-largest pharmaceutical company in 2014, after Pfizer, Novartis, Sanofi, Hoffmann-La Roche and Merck. The company was established in 2000 by the merger of Glaxo Wellcome (formed from Glaxo's 1995 acquisition of Burroughs Wellcome) and SmithKline Beecham (from the 1989 merger of Beecham Group and SmithKline Beckman Corporation).

The company has a primary listing on the London Stock Exchange and is a constituent of the FTSE 100 Index. As of 6 May 2015 it had a market capitalisation of £73 billion, the fourth-largest of any company listed on the London Stock Exchange. It has a secondary listing on the New York Stock Exchange. Andrew Witty has been the chief executive officer since May 2008.

GSK has a portfolio of products for major disease areas such as asthma, cancer, infections, mental health, diabetes and digestive conditions. Its drugs and vaccines

earned £21.3 billion in 2013; its top-selling products that year were Advair, Avodart, Flovent,Augmentin, Lovaza and Lamictal. The company applied for regulatory approval in 2014 for the first malaria vaccine, RTS,S, which it plans to make available for five percent above cost. GSK's consumer healthcare products, which earned £5.2 billion in 2013, include Sensodyne and Aquafresh toothpaste, the malted-milk drink Horlicks, Abreva for cold sores, Breathe Right nasal strips,Nicoderm and Nicorette nicotine replacements, and Night Nurse, a cold remedy

GSK manufactures products for major disease areas such as asthma, cancer, infections, diabetes and mental health. Its biggest-selling in 2013 were Advair, Avodart, Flovent,Augmentin, Lovaza, and Lamictal; its drugs and vaccines earned £21.3 billion that year. Other top-selling products include its asthma/COPD inhalers Advair, Ventolin, and Flovent; its diphtheria/tetanus/pertussis vaccine Infanrix and its hepatitis B vaccine; the epilepsy drug Lamicatal; the antihyperlipemia drug Lovaza; and the antibacterial Augmentin.

Medicines historically discovered or developed at GSK and its legacy companies and now sold as generics include amoxicillin and amoxicillin-clavulanate,[31] ticarcillin-clavulanate mupirocin and ceftazidime for bacterial infections, zidovudine for HIV infection, valacyclovir for herpes virus infections, albendazole for parasitic infections,sumatriptan for migraine, lamotrigine for epilepsy, bupropion and paroxetine for major depressive disorder, and cimetidine and ranitidine for gastroesophageal reflux disorder. Among these, amoxicillin, amoxicillin-clavulanate, mupriocin, zidovudine, albendazole, and ranitidine are listed on the World Health Organization's list of essential medications.

GSK's consumer healthcare division, which earned £5.2 billion in 2013, sells oral healthcare, including Aquafresh, Maclean's and Sensodyne toothpastes; and drinks such asHorlicks, Boost, a chocolate-flavoured malt drink sold in India, and formerly Lucozade and Ribena, sold in 2013 to Suntory for £1.35bn. Other products include Abreva to treat cold sores; Night Nurse, a cold remedy; Breathe Right nasal strips; and Nicoderm and Nicorette nicotine replacements

Announced rare disease unit in 2010, building off of their Promacta business in the US, alliances with Prosensia and JCR pharma, and including Duchenne, Hunter, Fabry, Gaucher.

With 1 drug in pipeline and 9 marketed drugs , Glaxosmithkline was placed in the Low Pipeline / High Marketed segment.

2. Bayer Healthcare

Bayer HealthCare Pharmaceuticals is the pharmaceutical division of Bayer HealthCare AG. Bayer market our products in more than 100 countries, and in 2014 generated sales of more than 12 billion. More than 39.000 members of staff currently work for Bayer HealthCare Pharmaceuticals worldwide.

Bayer aim to improve people's quality of life with our products. To achieve this, Bayer concentrate on the research and development of innovative drugs and novel therapeutic approaches. At the same time, they are constantly improving established products. In this context, Bayer HealthCare Pharmaceuticals uses the experience it has gained from over a century in the business.

Bayer concentrates on the following major therapeutic groups in which Bayer make fundamental contributions to medical progress:

- Cardiology
- Oncology
- Ophthalmology
- Hematology
- Gynecological Therapy

With 2 drugs in pipeline and 5 marketed , Bayer Healthcare was placed in the Low Pipeline / High Marketed segment.

3. Celgene Corporation

Celgene Corporation is an American biotechnology company that manufactures drug therapies for cancer and inflammatory disorders. It is incorporated in Delaware and headquartered in Summit, New Jersey. The company's major products are Thalomid (thalidomide), which is approved for the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum ("ENL"), as well as in combination with dexamethasone for patients with newly diagnosed multiple myeloma, and Revlimid (lenalidomide), for which the company has received FDA and EMA approval in combination with dexamethasone for the treatment of multiple myeloma patients who have received at least one prior therapy. Revlimid is also approved in the United States for the treatment of patients with transfusion-dependent anemia due to Low- or Intermediate-1-risk Myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities. Both Thalomid and Revlimid are sold through proprietary risk-management distribution programs to ensure safe and appropriate use of these pharmaceuticals. Vidaza is approved for the treatment of patients with MDS. Celgene also receives royalties from Novartis Pharma AG on sales of the entire

Ritalin family of drugs, which are widely used to treat Attention Deficit Hyperactivity Disorder(ADHD).

With 2 drugs in pipeline and 5 marketed , Celgene was placed in the Low Pipeline / High Marketed segment.

4. **Genzyme Corporation**

Genzyme Corporation is an American biotechnology company based in Cambridge, Massachusetts. Since its acquisition in 2011, Genzyme has been a fully owned subsidiary of Sanofi. In 2010 Genzyme was the world's third-largest biotechnology company, employing more than 11,000 people around the world. As a subsidiary of Sanofi, Genzyme has a presence in approximately 65 countries, including 17 manufacturing facilities and 9 genetic-testing laboratories, its products are sold in 90 countries. In 2007, Genzyme generated $3.8 billion in revenues with more than 25 products in the market. In 2006 and 2007 Genzyme was named one of Fortune Magazine's "100 Best Companies to Work for". The company donated $83 million worth of products worldwide; in 2006, it made $11 million in cash donations. In 2005, Genzyme was awarded the National Medal of Technology, the highest level of honor awarded by the president of the United States to America's leading innovators.
Sanofi Acquired Genzyme in 2011, with 6 commercial products in orphan and rare diseases, including Gaucher, Fabry and Pompe

With no drugs in pipeline and 5 marketed drugs , Genzyme was placed in Low Pipeline / High Marketed segment

5. Spectrum pharmaceuticals

Spectrum Pharmaceuticals is an American biopharmaceutical company. The company is located in Irvine, California.

Spectrum's drugs are for treatments in oncology and urology.

Approved drugs

In the US, Spectrum markets Fusilev, Folotyn, Marqibo, and Zevalin.

Fusilev (Levoleucovorin) for injection is a drug that was approved by the U.S. Food and Drug Administration in 2008 for the US; the drug had been on the market in a number of European countries.

Folotyn (pralatrexate) is marketed for relapsed or refractory Peripheral T-cell lymphoma.

Zevalin (Ibritumomab, Tiuxetan), as part of the Zevalin therapeutic regimen, is indicated for the treatment of patients with relapsed or refractory, low-grade or follicular B-cell non-Hodgkin's lymphoma (NHL), including patients with rituximab refractory follicular NHL. It has been approved by the FDA in 2002.

Marqibo (Vincristine sulfate liposomes injection) is a novel, sphingomyelin/cholesterol liposome-encapsulated formulation of the FDA-approved anticancer drug vincristine. Marqibo's approved indication is for the treatment of adult patients with Philadelphia chromosome-negative acute lymphoblastic leukemia (Ph-ALL) in second or greater relapse or whose disease has progressed following two or more lines of anti-leukemia therapy. It had been approved by the FDA in 2012.

In development

A number of drugs are currently investigated in clinical trials

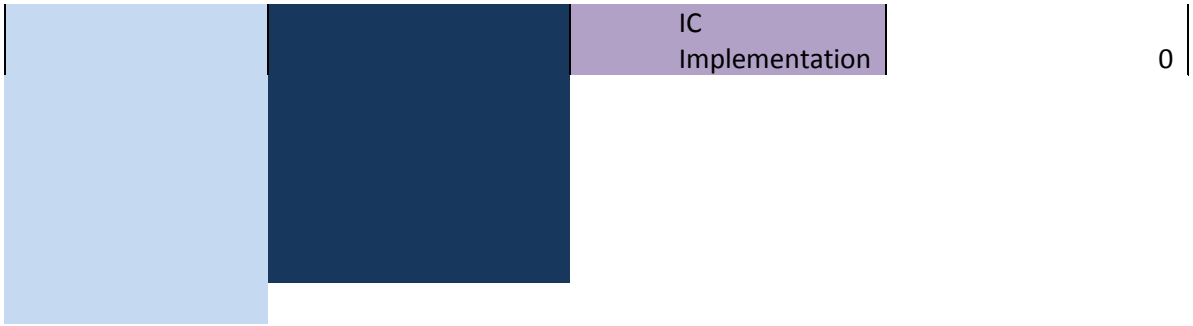
EOquin (Apaziquone) is a synthetic bio-reductive prodrug intended for the treatment of non-invasive bladder cancer that is currently in Phase 3 studies. Allergan hasINVESTEd money in 2008 to help develop this medication further and bring it to the market.[3] In Phase 2 studies are Ozarelix, for the treatment of prostate cancer and benign prostatic hypertrophy, Ortataxel, for the treatment of taxane-refractory tumors, and Satraplatin,for non-small cell lung cancer(NSCLC).

Other medications are in development or Phase 1 studies.

With 1 drug in pipeline and 5 marketed drugs , Spectrum Pharmaceuticals was placed in the Low Pipeline/ High Marketed segment.

Fig. 6 Pfizer Break up

Company			Pfizer
Total Projects			3
Business Area Split		Sales	0
		Marketing	3
Practice Area Split	Sales	Product perception	0
		BUSINESS INTELLIGENCE & INFORMATION MANAGEMENT	0
		Sales force Design	0
		Alignment Management	0
		Sales Force effectiveness	0
		Segmentation	0
		IC Implementation	0
		Forecasting	0
	Marketing	Product perception	2
		BUSINESS INTELLIGENCE & INFORMATION MANAGEMENT	0
		Sales force Design	0
		Alignment Management	0
		Sales Force effectiveness	0
		Segmentation	1



Pfizer with 3 orphan projects in total with ZS the and 0 in sales signifies that the business area of sales is yet to be tapped by Pfizer as far as Orphan marketspace is concerned.

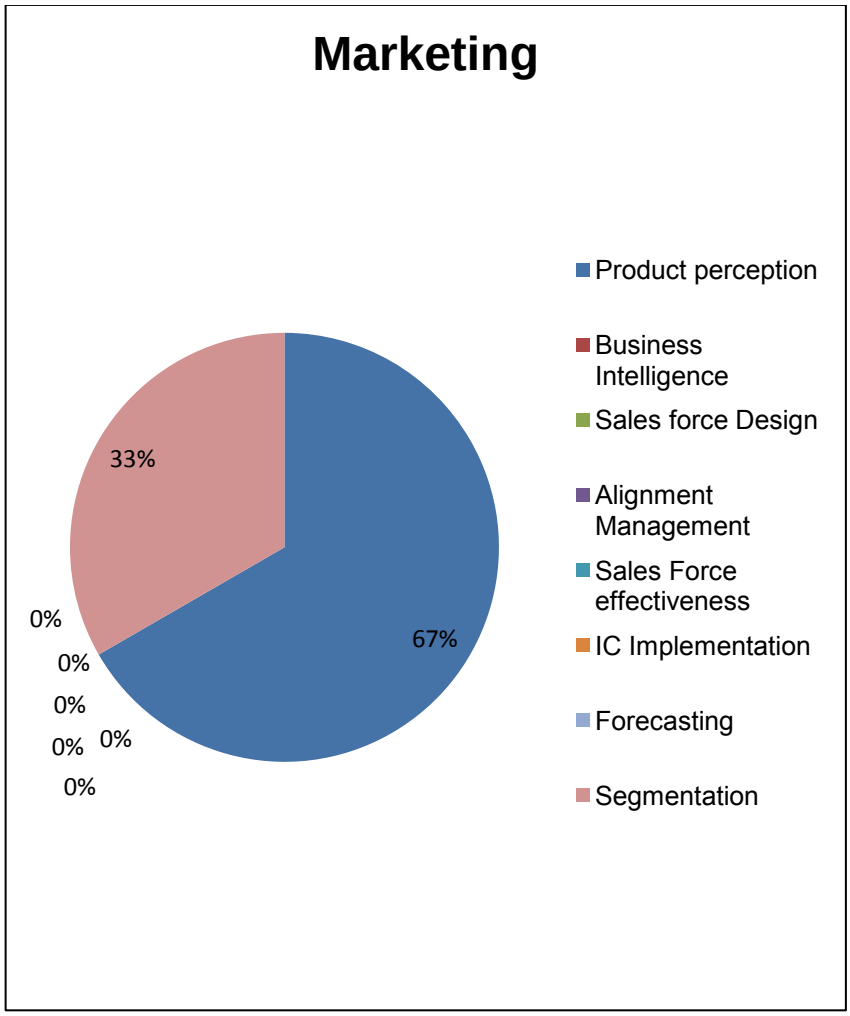
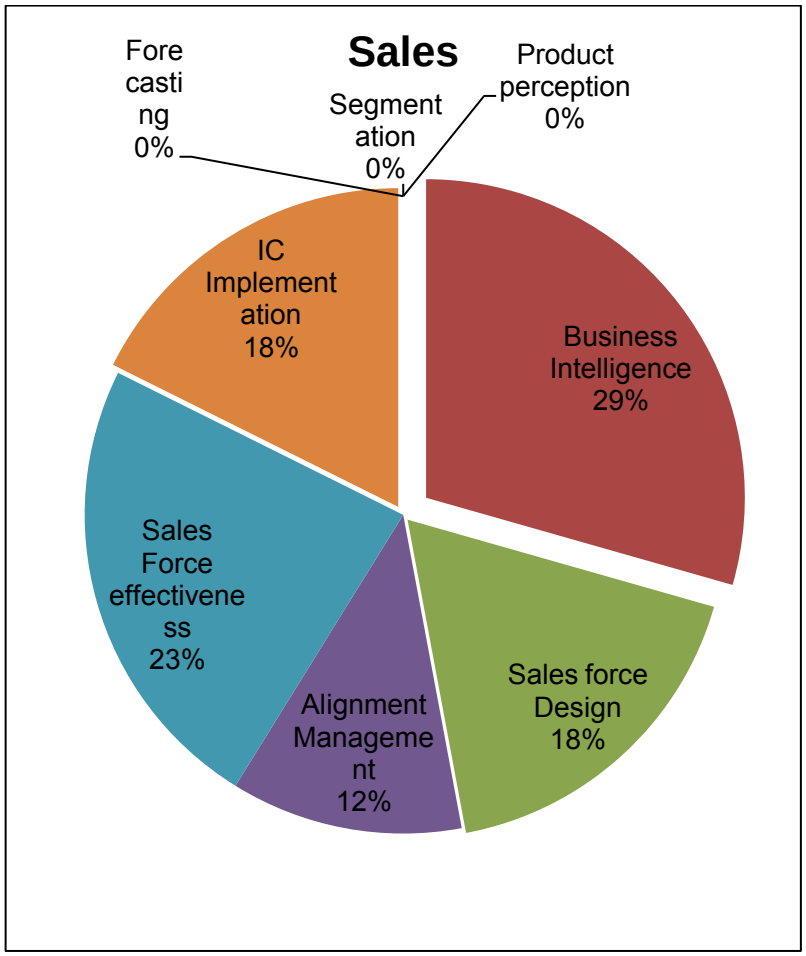


Figure 7 Shire Break up

Company			Shire
Total Projects			18
Business Area Split		Sales	17
		Marketing	1
Area Split	Sales	Product perception	0
		BUSINESS INTELLIGENCE & INFORMATION MANAGEMENT	5
		Sales force Design	3
		Alignment Management	2
		Sales Force effectiveness	4
		Segmentation	0
		IC Implementation	3
		Forecasting	0
	.Marketing	Product perception	0
		BUSINESS INTELLIGENCE & INFORMATION MANAGEMENT	0
		Sales force Design	0
		Alignment Management	0
		Sales Force effectiveness	0
		Segmentation	0
		IC Implementation	0
		Forecasting	1
		Pipeline Strategy	0
		Other	0

Shire being the highest priority company with 18 total projects , 17 being in sales and only 1 being in Marketing signifies that the Business area of Marketing could be tapped more efficiently for Shire as far as the orphan drug products are concerned.



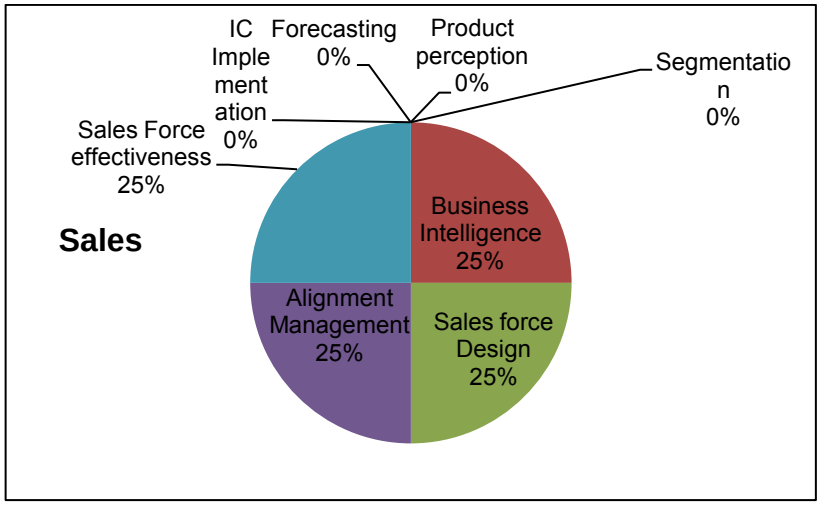
The pie chart shown here signifies the distribution of work done in Business Area sales with activities distributed evenly in IC Implementation , Business Intelligence , Sales force effectiveness , Sales force design and Alignment management.

No work was performed in Forecasting , segmentation and Product perception.

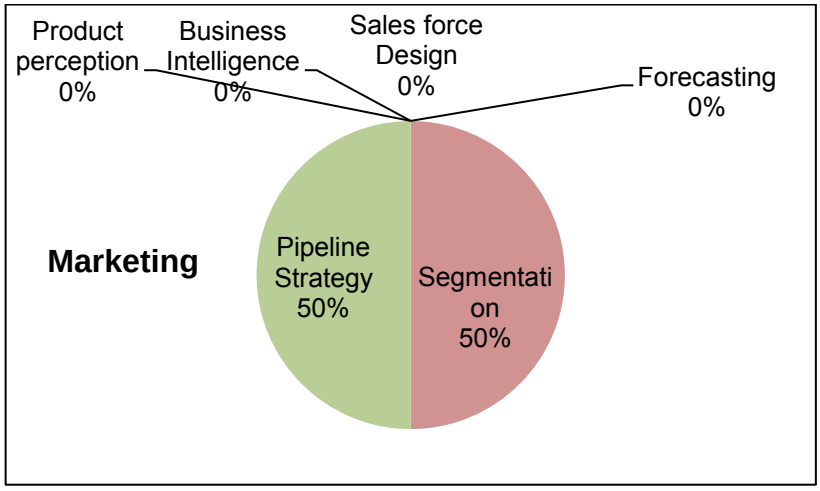
Figure 8. Novartis break up

Company			Novartis
Total Projects			6
Business Area Split		Sales	4
		Marketing	2
Practice Area Split	Sales	Product perception	0
		BUSINESS INTELLIGENCE & INFORMATION MANAGEMENT	1
		Sales force Design	1
		Alignment Management	1
		Sales Force effectiveness	1
		Segmentation	0
		IC Implementation	0
		Forecasting	0
	Marketing	Product perception	0
		BUSINESS INTELLIGENCE & INFORMATION MANAGEMENT	0
		Sales force Design	0
		Alignment Management	0
		Sales Force effectiveness	0
		Segmentation	1
		IC Implementation	0
		Forecasting	0
		Pipeline Strategy	1
		Other	0

Novartis with 6 Orphan projects in total having 4 in sales and 2 in marketing signifies the importance of investing more into the orphan drug space as far as business area of marketing is concerned.



Sales Activities were mainly focussed on Business Intelligence , Alignment management and sales force design



While Marketing Activities relied heavily on pipeline strategy and Segmentation.

10. Conclusion

- Shire,Novartis and Pfizer were observed to be investing the maximum for Orphan since they had maximum of number of drug products in development and in market for Orphan indications.

- On creating the unique list of Orphan drugs for different indications, it was identified that the indication Pulmonary Arterial Hypertension had the maximum number of orphan drugs in Market and in pipeline.

- Adalimumab (trade name : Humira) by Abbvie pharmaceuticals for rheumatoid arthiritis was found to be the most successful Orphan drug in Market on taking the overall sales for the particular drug in consideration.

- Afamelanotide (trade name : Scenesse) by Clinuvel Pharmaceuticals for Actinic keratosis was found to be the least succesful Orphan drug in Market on considering the overall sales for that particular product.

  Non- Hodgkin Lypmhoma was observed to have the maximum incidence and prevalance for any Orphan indication

11. Disclaimer

Findings of this study is subject to change in case of change in status of any of the regulatory parameter under consideration in any of the geographies under study since the study is based on the publically available secondary data

12. Ethical considerations:

The following study being based on secondary/desk research will derive data from publically available data sources so there are no associated ethical considerations for the study.

13. Data Sources

1 http://thomsonreuters.com/products/ip-science/04_013/anoutlookonusbiosimilarcompetition-cwp-en.pdf
2 http://www.ema.europa.eu/ema/ , http://www.fda.gov/ , http://www.mhlw.go.jp/english/
3 http://www.gabionline.net/
4 ipapharma.org, ema.europa.eu1, ema.europa.eu2,ema.europa.eu/ema/index
5 thomsonreuters.com
6 http://www.china-pharm.net/download/ispe2013web/pdf-download/1030-2e.pdf
7 ema.europa.eu/ema/index, gabionline/Italian-Medicines-Agency, gabionline/biosimilars-policies-in-Spaingabionline.net.Germany, pmlive.french, pharmalinkconsulting

8 Source for data: bio-trends.com, www.gabionline,www.pmda.go, ec.europa.eu/enterprise,
9 Instructions_Biosimilars,
10 http://www.egagenerics.com/images/EGA%20Survey%20to%20MS%20on%20Biosimilars.pdf)
11 http://www.amgen.com/science/substitution_interchangeability.html
12 Source for data: safebiologics.org, www.amgen, www.biosimilarsnews.com, uspharmacist.com
13 source: Rovira, J., et. al. The impact of biosimilars' entry in the EU market. Granada (Spain) : Andalusian School of Public Health, 2011.
14 U.S. Food and Drug Administration. Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book). 2012.
15 http://www.shearman.com/~/media/Files/NewsInsights/Publications/2014/02/FTCWorkshopSeekstoSparkBiosimilarsCompetitionAntitrust020614.pdf
16 http://www.ashp.org/menu/News/PharmacyNews/NewsArticle.aspx?id=4019
17 See more at: http://www.ashp.org/menu/News/PharmacyNews/NewsArticle.aspx?id=4019#sthash.ZRg2lTHx.dpuf
18 http://www.china-pharm.net/download/ispe2013web/pdf-download/1030-2e.pdf
19 http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/12/WC500016817.pdf
20 **Parameter specific references**

1) Sources for parameter 1

1http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000408.jsp&mid=WC0b01ac058002958c

1http://www.pharmalinkconsulting.com/wp-content/uploads/2013/05/TOPRA-MAbs-Article-FINAL.pdf

http://www.gabionline.net/Reports/Biosimilar-policies-in-Spain

http://gabionline.net/Guidelines/Italian-Medicines-Agency-publishes-concept-paper-on-biosimilars

http://www.pmlive.com/pharma_news/new_french_regulatory_agency_ansm_afssaps_402076

http://gabionline.net/Biosimilars/General/Biosimilars-approved-and-marketed-in-Germany

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/%20HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/ucm113522.htm

http://www.raps.org/

http://www.hospira.com/

DR-Global Pipelines, Regulatory Pathways, and Key Stakeholder Perspectives of Biosimilars; March 2013

http://www.gabionline.net/Biosimilars/News/Russia-to-harmonize-biologicals-regulations

http://www.pmlive.com/pharma_intelligence/biosimilars_in_china_460090

http://www.pmlive.com/pharma_intelligence/biosimilars_in_china_460090

extra references

http://www.pharmachinaseminar.com/files/Biosimilars_in_China.pdf

file:///C:/Users/as8432/Downloads/Bettering_China%2527s_Biosimilars.pdf

http://www.raps.org/focus-online/news/news-article-view/article/4511/regulatory-approval-of-biosimilars-a-global-perspective.aspx

2) **sources for parameter 2**

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2013/05/WC500142978.pdf

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/09/news_detail_001615.jsp&mid=WC0b01ac058004d5c1

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/landing/human_medicines_regulatory.jsp&mid=WC0b01ac058001ff89

http://thomsonreuters.com/products/ip-science/04_013/anoutlookonusbiosimilarcompetition-cwp-en.pdf

http://www.lifescienceleader.com/magazine/current-issue-3/item/4545-biosimilars-in-emerging-markets

https://www.google.co.in/url?sa=t&rct=j&q=&esrc=s&source=web&cd=3&cad=rja&ved=0CDkQFjAC&url=http%3A%2F%2Fwww.chinabiotoday.com%2Fdownloads%2F20130322%2Fdownload&ei=pXG5Us3BIo3JrQfcsoHgAw&usg=AFQjCNFLPQeRQ-8DoCI-AKFXm5zax-EGMQ&sig2=tCN5R8-YWZNedUL24A8CAA&bvm=bv.58187178,d.bmk

3) **sources for parameter 3**

http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_report_en.pdf

C:\Users\as8432\Downloads\ZL101_00_002e_VV_Instructions_Biosimilars (1).pdf

bio-trends.com\News-and-Events\Press-Releases\Biologics-in-Immune-Infectious-Disease-092612

http://www.gabionline/

3.http://www.pmda.go/

3.http://www.healthtrustpg.com/biosimilars/pdf/ppd.pdf

3.http://www.pharmaphorum.com/articles/in-apac-the-biosimilar-market-is-set-to-grow

4) **sources of parameter 4**

4.http://www.egagenerics.com/images/EGA%20Survey%20to%20MS%20on%20Biosimilars.pdf)

4.http://www.firstwordpharma.com/node/1114074#axzz2ypWgn8Uz

4.http://www.healthtrustpg.com/biosimilars/pdf/ppd.pdf

5) **sources for parameter 5**

http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_market_012011_en.pdf

http://www.quintiles.com/library/experts/the-us-approval-pathway-for-biosimilar-products.pdf

269EEB673D&ei=OXr7UuiyDIK8rAeD6IG4BQ&usg=AFQjCNHLmGkHnwvqiExgriGrRFENzkRKtA&sig2=Hlc-TuA_JyXOS5z2tm5_jA&bvm=bv.61190604,d.bmk

http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_market_012011_en.pdf

http://www.amgen.com/pdfs/misc/Biologics_and_Biosimilars_Overview.pdf

http://www.gabionline.net/Reports/Biosimilar-policies-in-Spain

http://safebiologics.org/info-center.php

http://www.amgen/

http://www.biosimilarsnews.com/

http://www.uspharmacist.com/content/s/253/c/41438/

http://www.amgen.com/science/substitution_interchangeability.html

http://www.firstwordpharma.com/node/1114074?tsid=33#axzz2ypWgn8uZ.http://www.patentdocs.org/2014/03/china-pharmaceutical-regulatory-law-boot-camp.html

http://www.ibef.org/download/Biosimilars-in-India-30312.pdf

http://www.ipapharma.org/pt/Jan2013/11-14.pdf

6) **sources for parameter 6**

.http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_market_012011_en.pdf

http://www.quintiles.com/library/experts/the-us-approval-pathway-for-biosimilar-products.pdf

269EEB673D&ei=OXr7UuiyDIK8rAeD6IG4BQ&usg=AFQjCNHLmGkHnwvqiExgriGrRFENzkRKtA&sig2=Hlc-TuA_JyXOS5z2tm5_jA&bvm=bv.61190604,d.bmk

http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_market_012011_en.pdf

http://www.amgen.com/pdfs/misc/Biologics_and_Biosimilars_Overview.pdf

http://www.gabionline.net/Reports/Biosimilar-policies-in-Spain

http://gabionline.net/Reports/Biosimilars-policies-in-Italy

http://www.china-pharm.net/download/ispe2013web/pdf-download/1030-2e.pdf

http://www.ashp.org/menu/News/PharmacyNews/NewsArticle.aspx?id=4019#sthash.ZRg2lTHx.dpuf

http://www.china-pharm.net/download/ispe2013web/pdf-download/1030-2e.pdf

http://www.china-pharm.net/download/ispe2013web/pdf-download/1030-2e.pdf

7) **sources for parameter 7**

All the info has been derived from ZS Subscribed datasources the name of which cannot be shared.

ANNEXURE