

Therapeutic Cancer Vaccines Market to 2019

Pipeline Indicates Safer Treatments and Extended Patient Survival, though High Prices May Limit Uptake



GBI Research Report Guidance

- Chapter two gives an overview of cancer causes, symptoms, treatment options and its relation to the immune system. The types, strengths and weaknesses of therapeutic cancer vaccines is also discussed.
- Chapter three gives an overview of the only currently marketed therapeutic cancer vaccine Provenge – including sales and clinical trial data.
- Chapter four provides in depth pipeline drug analysis of the most researched cancer indications including breast, lung and prostate cancer. Including Phase breakdown and the most common molecular targets throughout the pipeline.
- Chapter five gives predicted market forecasts for the top cancer indications globally and for the major global pharmaceutical markets of the US, UK, France, Spain, Italy and Japan up to 2019.

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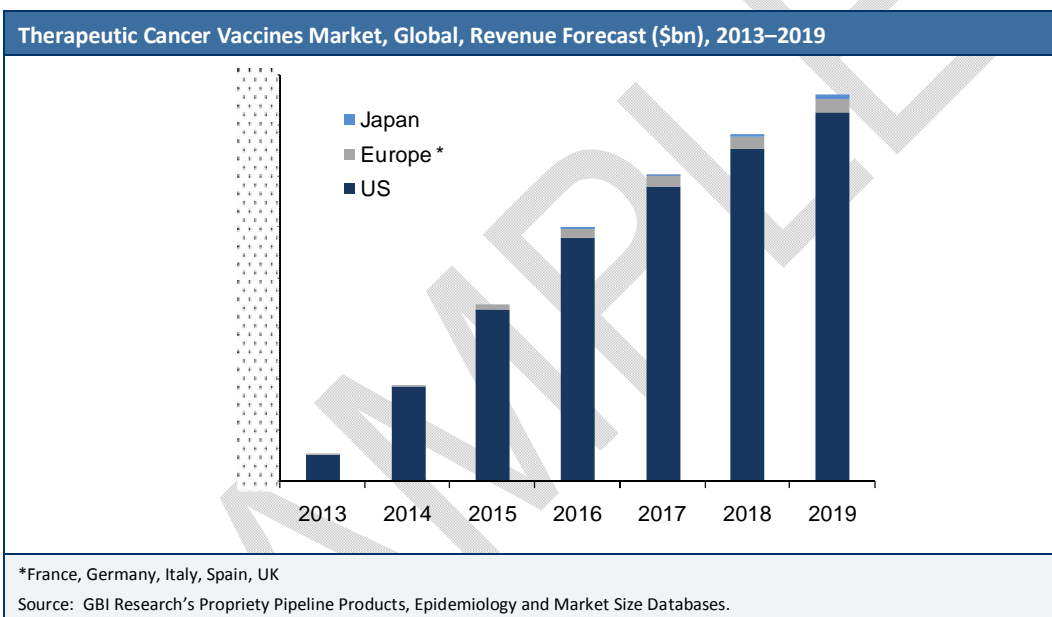
Executive Summary

Therapeutic Cancer Vaccines Market Predicted to See Large Growth over the Forecast Period as Numerous Novel Vaccines are approved.

The therapeutic cancer vaccines market is anticipated to grow rapidly throughout the forecast period from an estimated \$XX billion in 2013 to approximately \$XX billion by 2019, driven primarily by the approval of up to XX vaccines across seven indications, XX of which have no currently approved therapeutic vaccine.

The US is predicted to be the largest market due to the anticipated higher performance of these novel vaccines within this market where, unlike in the European markets, sales will not be severely restricted by their high cost-to-clinical-benefit ratio. The US market will also be driven by the high cost of the vaccines as specialty drugs, which is set to increase yearly at a rate substantially higher than that of the consumer price index.

As such, the US market is predicted to account for XX% of the total global therapeutic cancer vaccines market in 2013, decreasing slightly to XX% in 2019 with the approval of numerous vaccines in the EU and Japan, but remaining overwhelmingly dominant throughout the forecast period and into the foreseeable future.



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2 Introduction

2.1 Cancer Epidemiology

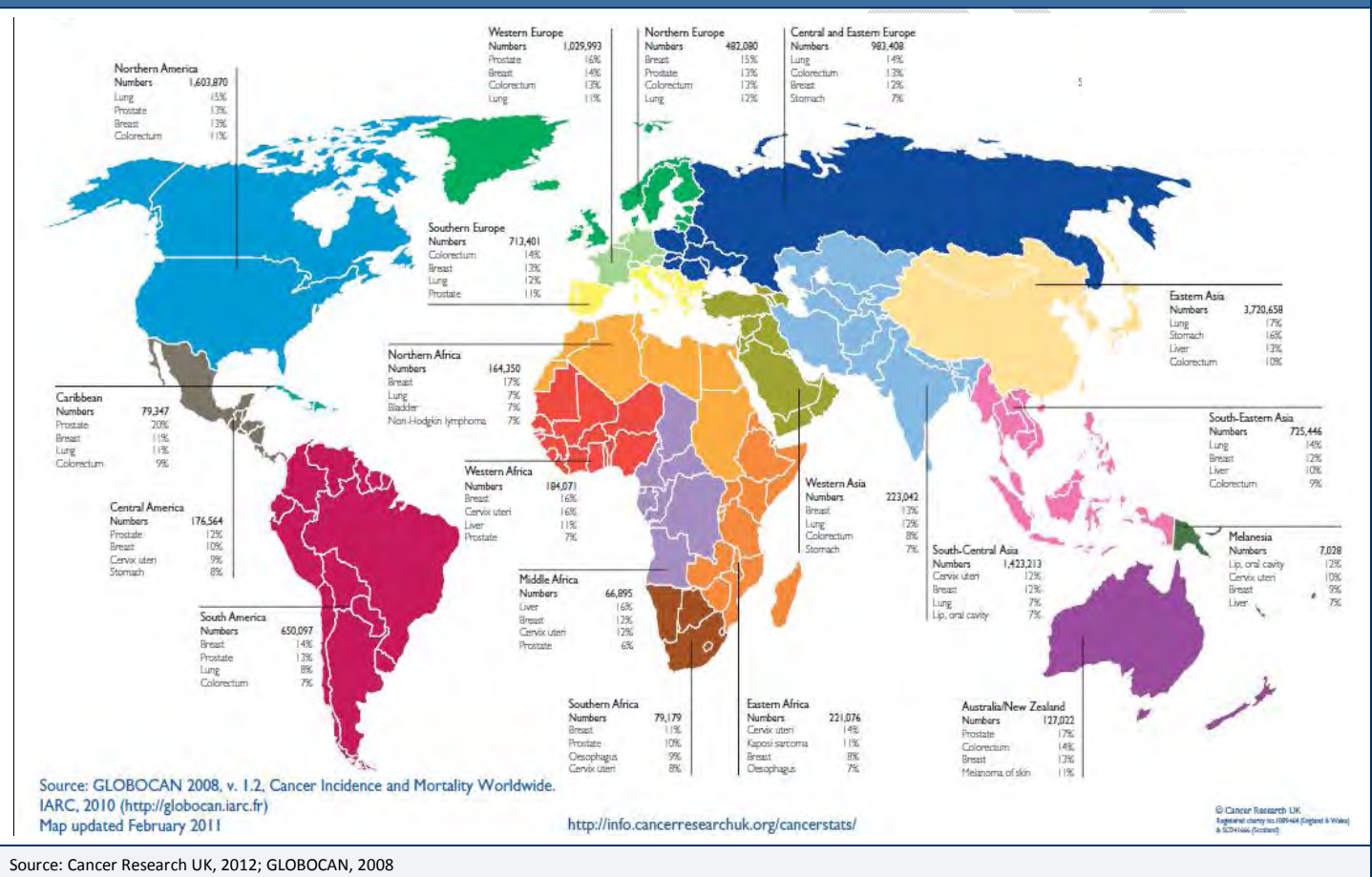
Approximately XX million new cases of cancer are diagnosed globally per year, making it the second leading cause of death behind heart disease. The global burden of cancer is expected to rise as a result of an aging population in most developed countries and the adoption of cancer-associated activities such as smoking and physical inactivity (Jemal et al., 2011). Globally, the most frequently diagnosed cancer in females is breast cancer, accounting for approximately XX% of all cancer cases, whereas in men lung cancer is the leading cancer site, accounting for XX%. However, the most common types of cancer vary according to country, race and age, as shown in Figure 1.

2.2 Disease Initiation and Propagation

Malignant tumors result from the abnormal proliferation of single cells of any type within the body, ultimately causing a failure in the regulation of tissue growth. Initiation is a multistep process, with cells gradually becoming malignant through a series of alterations in the functioning of oncogenes, which promote cell growth and regulation, angiogenesis, and tumor suppressor genes which inhibit cell division and survival.

There are multiple scenarios and substances that cause cancer initiation and so no single factor can be attributed to cancer initiation as it is a complex multistep process. However, many carcinogens have been identified, such as viruses, radiation and chemicals.

Figure 1: Therapeutic Cancer Vaccines Market, Global, Common Cancers and Incidence Rates, 2008



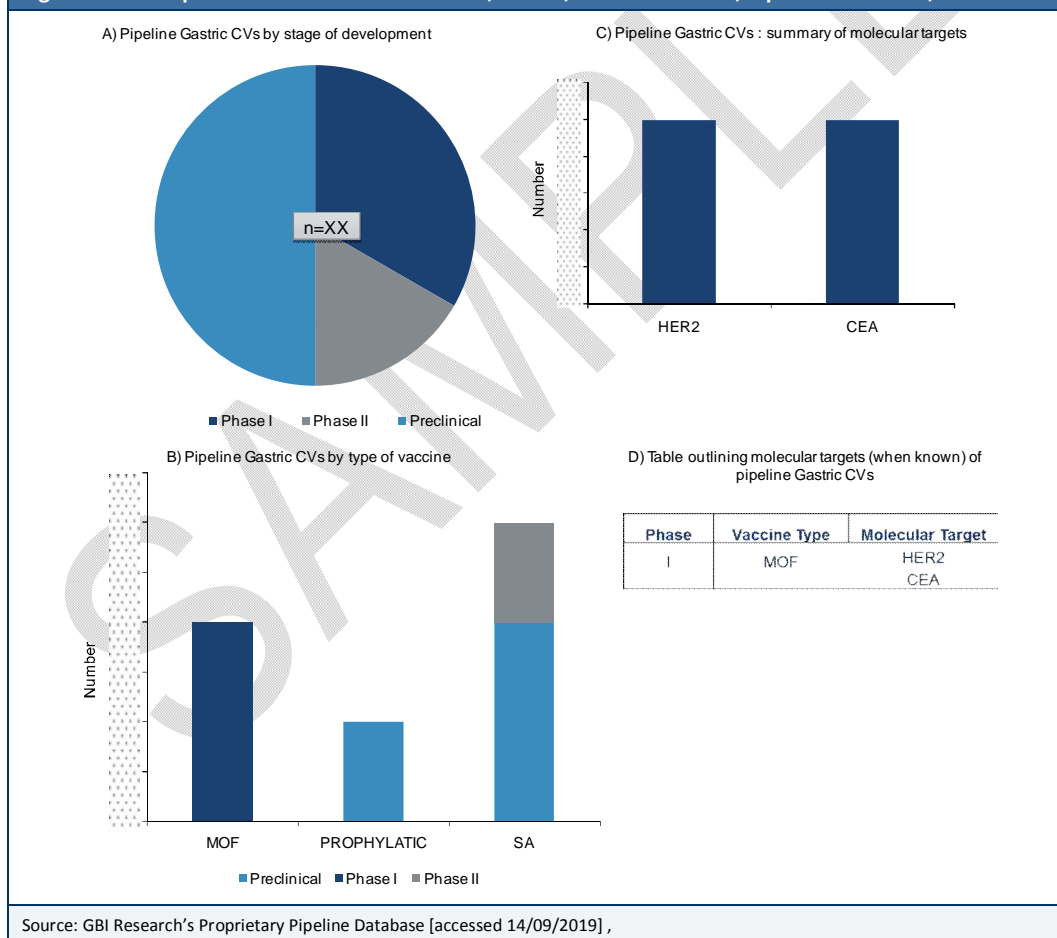
4.1.1.4 Stomach Cancer

Approximately XX cases of stomach (or gastric) cancer are diagnosed globally per year. The highest rate is seen in East Asian countries, where approximately XX in every XX new cases are diagnosed per year, substantially higher than the average annual global incidence rate of XX per 100,000 (Cancer Research UK, 2012). As the fourth most common cancer globally, any stomach cancer vaccine introduced to the market can be expected to generate high sales and revenues, providing it is more effective or safer than currently available forms of treatment. Even with a small market percentage share any therapeutic cancer vaccine can be expected to generate revenues in the millions as a result of the large target market, particularly if successfully introduced into any of the large East European countries where incidence and prevalence rates of gastric cancer are more than double elsewhere in the world.

Unlike the other most highly diagnosed cancers, the size of the developmental pipeline for stomach cancer vaccines does not correlate well with the incidence rate of stomach cancer. In comparison, the developmental pipeline of the remaining top four most common cancers (prostate, lung, breast and colorectal) have up to five times more vaccine candidates in the developmental pipeline (not taking into account vaccine candidates that target a range of cancer indications).

Of the XX cancer vaccines currently in development for stomach cancer, only one, a specific antigen-based vaccine, is in late-stage (Phase II) clinical development, the target of which is unknown.

Figure 7: Therapeutic Cancer Vaccines Market, Global, Stomach Cancer, Pipeline Overview, 2013



5.8 Prostate Cancer

5.8.1 Treatment Usage Patterns and the Impact of Emerging Vaccines

Provenge is currently the only approved therapeutic cancer vaccine and is indicated for the treatment of patients with asymptomatic or minimally symptomatic castrate-resistant prostate cancer. It therefore fills a clinical niche, as other treatments aim to treat prostate cancer before this stage (such as hormone therapy for hormone sensitive prostate cancer), or when the cancer has become symptomatic (chemotherapeutic treatment with docetaxel). Net revenue was approximately \$XXm in 2010 on its approval by the FDA, rising to \$XXm in 2011, but revenues have been consistently below expectations. Provenge is anticipated to be approved for the treatment of prostate cancer in Europe in 2013 and Japan in 2016, thus increasing its revenue. However, GBI Research believes sales will begin to decline from 2017 with the anticipated approval of DCVax-Prostate and Prostavac, both of which are indicated for the same target market.

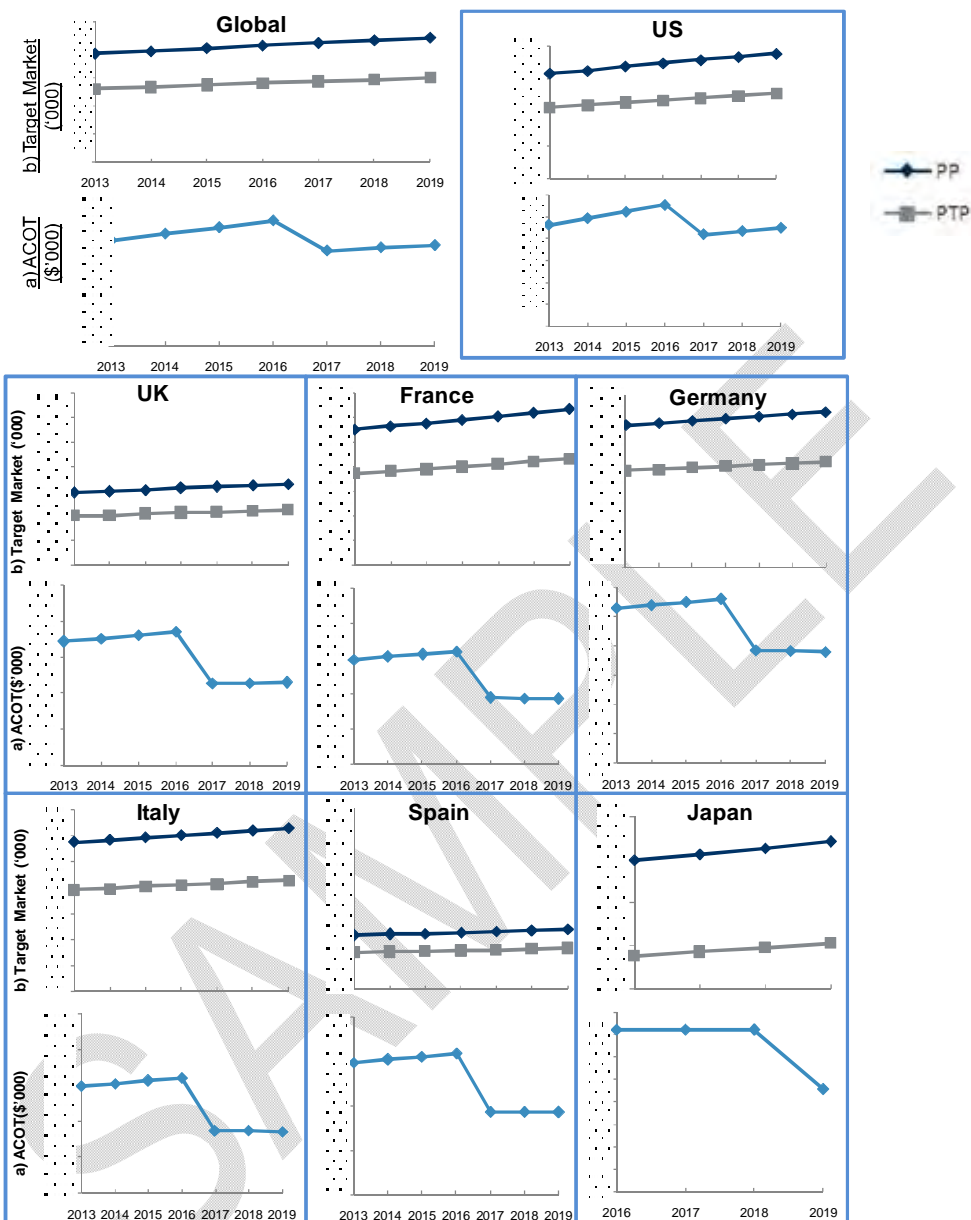
Prostavac is a microorganism-facilitated vaccine currently under development by Bavarian Nordic, and is indicated for patients with asymptomatic or minimally symptomatic castrate-resistant metastatic prostate cancer. It is therefore expected to be a direct competitor for Provenge. In Phase II clinical trials patients treated with Prostavac had an increase in overall survival of XX months (XX months versus XX months for controls) (Kantoff et al., 2010b). This is significantly higher than the additional XX months in overall survival in patients treated with Provenge (Small et al., 2006). Furthermore, as microorganism-facilitated vaccines are deemed cheaper to manufacture and distribute, Prostavac is anticipated to be significantly less expensive than Provenge, with an initial cost of approximately \$XX.

DCVax-Prostate is an autologous cellular immunotherapy (DC) vaccine currently under development by Northwest Biotherapeutics and is indicated for the treatment of patients with hormone-refractory prostate cancer. In clinical trials the response rate was XX%, with overall survival being increased by an average of XX months to XX months (Northwest Biotherapeutics (2011b)). Unlike Prostavac and Provenge which target only metastatic late-stage prostate cancer patients, DCVax-Prostate is also indicated for the treatment of patients without metastasis, which account for approximately XX% of late-stage prostate cancer patients. Furthermore, DCVax-Prostate is anticipated to cost significantly less than Provenge and other targeted cancer therapies at approximately \$XX for up to three years of treatment (Northwest Biotherapeutics, 2011b).

It is therefore anticipated that following the approval of Prostavac and DCVax-Prostate in the US and Europe in 2017 and Japan in 2019, sales of Provenge will decrease yearly as these products are considered more effective and less expensive. DCVax-Prostate is likely to account for a significant market share due to its larger target market and superior clinical benefit in terms of overall survival. Prostavac can be expected to experience limited sales, potentially being offered to patients who do not have a response to treatment with DCVax-Prostate.

5.8.2 Annual Cost of Treatment

The annual cost of treatment with each individual prostate cancer is anticipated to increase yearly with inflation. This is anticipated to be close to the consumer price index in Japan and the European countries, but is forecast to be significantly higher in the US market where specialty drugs have historically increased in price at a rate high above that of general inflation. In all countries the annual cost of therapy is expected to reflect the cost of treatment with Provenge until 2017 when with the anticipated approval of Prostavac and DCVax-Prostate are expected to substantially drive down the annual cost of treatment with therapeutic prostate cancer vaccines.

Figure 29: Therapeutic Cancer Vaccines Market, Global, Prostate Cancer, Annual Cost of Treatment (\$'000) and Target Market ('000), 2013–2019


Source: GLOBOCAN, 2008

6 Appendix

6.1 *Provenge Clinical Trial Titles (Table 3)*

Sipuleucel-T as Neoadjuvant Treatment in Prostate Cancer

Immunotherapy with APC8015 (Sipuleucel-T, Provenge) for Asymptomatic, Metastatic, Hormone-Refractory Prostate Cancer

Provenge (TM) for the Treatment of Hormone-Sensitive Prostate Cancer

Provenge (Sipuleucel-T) Active Cellular Immunotherapy Treatment of Metastatic Prostate Cancer after Failing Hormone Therapy

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6.5 Market Definitions

The global therapeutic cancer vaccines market comprises the top seven global pharmaceutical markets of the US, the UK, Germany, France, Spain, Italy and Japan.

The top five European countries comprise the UK, Germany, France, Spain and Italy.

The prevalence population is the estimated number of people at any given point of time who are affected by the type of cancer being discussed.

The treatment population is the percentage of the prevalence population being treated for cancer in any given year.

6.6 Abbreviations

ACI:	Active Cellular Immunotherapy
AI:	Anti-Idiotypic
ALWC:	Allogeneic Whole-Cell Derived
APC:	Antigen-Presenting Cells
ASCI:	Antigen-Specific Cancer Immunotherapeutic
AUWC:	Autologous Whole-Cell
BCG:	Bacillus Calmette-Guérin
BSC:	Best Supportive Care
CAGR:	Compound Annual Growth Rate
CEA:	Carcinoembryonic Antigen
CI:	Cellular Immunotherapy
DC:	Dendritic Cell
DNA:	Deoxyribonucleic Acid
FDA:	Food and Drug Administration
GBM:	Glioblastoma Multiforme
GM-CSF:	Granulocyte Macrophage Colony Stimulating Factor
GSK:	GlaxoSmithKline
HPI:	Hyperacute Pancreatic Immunotherapy
HPV:	Human Papilloma Virus
KLH:	Key Limpet Hemocyanin
mAb:	monoclonal Antibody
MAGE:	Melanoma-Associated Antigen
MOF:	Microorganism Facilitated
OV:	Oncolytic Virus
PAP:	Prostatic Acid Phosphatase
PSA:	Prostate-Specific Antigen
PSMA:	Prostate-Specific Membrane Antigen
SA:	Specific Antigen
TAA:	Tumor-Associated Antigen
PP:	Prevalence Population

PTP: Potential Treatment Population

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6.8 Research Methodology

GBI Research's dedicated research and analysis teams consist of experienced professionals with marketing, market research and consulting backgrounds in the medical devices industry as well as advanced statistical expertise.

GBI Research adheres to the codes of practice of the Market Research Society (www.mrs.org.uk) and the Strategic and Competitive Intelligence Professionals (www.scip.org).

All GBI Research databases are continuously updated and revised.

6.8.1 Coverage

The objective of updating GBI Research coverage is to ensure that it represents the most up-to-date vision of the industry possible.

Changes to the industry taxonomy are built on the basis of extensive research of company, association and competitor sources.

Company coverage is based on three key factors: market capitalization, revenues, and media attention/innovation/market potential.

An exhaustive search of 56 member exchanges is conducted and companies are prioritized on the basis of their market capitalization,

The estimated revenues of all major companies, including private and governmental, are gathered and used to prioritize coverage.

Companies which are making the news, or which are of particular interest due to their innovative approach, are prioritized.

GBI Research aims to cover all major news events and deals in the medical industry, updated on a daily basis.

The coverage is further streamlined and strengthened with additional inputs from GBI Research's expert panel (see below).

6.8.2 Secondary Research

The research process begins with exhaustive secondary research on internal and external sources being carried out to source qualitative and quantitative information relating to each market.

The secondary research sources that are typically referred to include, but are not limited to:

- Company websites, annual reports, financial reports, broker reports, investor presentations and SEC Filings.
- Industry trade journals, scientific journals and other technical literature.
- Internal and external proprietary databases.
- Relevant patent and regulatory databases.
- National government documents, statistical databases and market reports.
- Procedure registries.
- News articles, press releases and web-casts specific to the companies operating in the market.

6.8.3 Primary Research

GBI Research conducts hundreds of primary interviews a year with industry participants and commentators in order to validate its data and analysis. A typical research interview fulfills the following functions:

It provides first-hand information on the market size, market trends, growth trends, competitive landscape and future outlook.

- It helps in validating and strengthening the secondary research findings.
- It further develops the analysis team's expertise and market understanding.
- Primary research involves email and telephone interviews as well as face-to-face interviews for each market, category, segment and sub-segment across geographies.

The participants who typically take part in such a process include, but are not limited to:

- Industry participants: CEOs, VPs, marketing/product managers, market intelligence managers and national sales managers.
- Hospital stores, laboratories, pharmacies, distributors and paramedics.
- Outside experts: Investment bankers, valuation experts, and research analysts specializing in specific medical equipment markets.
- Key Opinion Leaders: Physicians and surgeons specializing in different therapeutic areas corresponding to different kinds of medical equipment..

6.8.4 Therapeutic Landscape

Revenues for each indication, geography-wise, are arrived at by utilizing the GBI Research market forecasting model. The global revenue for each indication is the sum value of revenues in all seven regions.

The annual cost of therapy for each indication is arrived at by considering the cost of the drugs, the dosage of the drugs and the duration of the therapy.

The generic share of the market for each indication is obtained by calculating the prescription share for generic drugs and the respective cost of treatment.

The treatment usage pattern which includes quantitative data on the diseased population, treatment-seeking population, diagnosed population and treated population for an indication, is arrived at by referring to various sources as mentioned below.

GBI Research uses the epidemiology-based treatment flow model to forecast market size for therapeutic indications.

6.8.5 Epidemiology-Based Forecasting

The forecasting model used at GBI Research makes use of epidemiology data gathered from research publications and primary interviews with physicians to represent the treatment flow patterns for individual diseases and therapies. The market for any disease segment is directly proportional to the volume of units sold and the price per unit.

$$\text{Sales} = \text{Volume of units sold} \times \text{Price per unit}$$

The volume of units sold is calculated on the average dosage regimen for that disease, duration of treatment and number of patients who are prescribed drug treatment (prescription population). Prescription population is calculated as the percentage of population diagnosed with a disease (diagnosis population). Diagnosis population is the population diagnosed with a disease expressed as a percentage of the population that is seeking treatment (treatment-seeking population). Prevalence of a disease (diseased population) is the percentage of the total population who suffer from a disease/condition.

Data on treatment-seeking rate, diagnosis rate and prescription rate, if unavailable from research publications, are gathered from interviews with physicians and are used to estimate the patient volumes for the disease under consideration. Therapy uptake and compliance data are fitted in the forecasting model to account for patient switching and compliance behavior.

To account for differences in patient affordability of drugs across various geographies, macroeconomic data such as inflation and GDP; and healthcare indicators such as healthcare spending, insurance coverage and average income per individual are used.

Annual cost of treatment is calculated using product purchase frequency and the average price of the therapy. Product purchase frequency is calculated from the dosage data available for the therapies and drug prices are gathered from public sources. The sources for the price of drugs are RxUSA, ZenRx, the UK Prescription Cost Analysis, the British National Formulary and data from the Japan Pharmaceutical Information Center (JAPIC).

The epidemiology-based forecasting model uses a bottom-up methodology and it makes use of estimations in the absence of data from research publications. Such estimations may result in a final market value which is different from the actual value. To correct this 'gap' the forecasting model uses 'triangulation' with the help of base year sales data (from company annual reports, internal and external databases) and sales estimations.

6.8.6 Analogous Forecasting Methodology

Analogous forecasting methodology is used to account for the introduction of new products, patent expiries of branded products and subsequent introduction of generics. Historic data for new product launches and generics penetration are used to arrive at robust forecasts. Increase or decrease of prevalence rates, treatment seeking rate, diagnosis rate and prescription rate are fitted into the forecasting model to estimate market growth rate.

The proprietary model enables GBI Research to account for the impact of individual drivers and restraints in the growth of the market. The year of impact and the extent of impact are quantified in the forecasting model to provide close-to-accurate data sets.

6.8.7 Diseased Population

The diseased population for any indication is the prevalence. The prevalence population for this report is taken from numerous independent websites including GLOBOCAN 2008, Cancer Research UK and seer.cancer.gov.

6.8.8 Prescription Population

Cancer has multiple treatment options depending upon the stage of the disease and –previous effectiveness of other similar treatments. Options for treatment of cancer include surgery, radiotherapy, chemotherapy, hormonal therapy and immunology. The prescription population is defined as the number of patients who are prescribed biologic drug therapy. This is calculated as a percentage of the diagnosis population.

6.9 Market Size by Geography

The treatment usage pattern and annual cost of treatment in each country has been factored in while deriving the individual country market size.

6.9.1 Forecasting Model for Therapeutic Areas

Figure 31: GBI Research Market Forecasting Model

GBI Research Market Sizing Model			
Disease Population			
	General Population		743,535,048
	Qualifying condition 1 (Age/Sex/Occupation etc)		
	Qualifying condition 2 (Age/Sex/Occupation etc)		
	Prevalence tissue valve disease	0.2%	1,784,484
	Qualifying condition (complication, severity)		
	DISEASED POPULATION		1,784,484
Treatment Flow Patterns			
	Treatment Seeking Rate (Symptoms/Dis Awareness)	89%	1,588,191
	Diagnosis Rate (Clinical and Diagnostic Tests)	75%	1,191,143
	Prescription Rate (Physician Perception, Treatment Effectiveness)		
	Tissue Valve	70%	833,800
	Other Treatments for Valve (Surg/Med/None)		-
Fulfillment			
	Availability	NA	
	Willingness to Use (Patient Perceptions)	NA	
	Ready to Use (Surgery eligibility, Reuse etc)	NA	
Affordability at Price			
	HE as % of GDP spend		
	Average Income (per individual)		
	Patient Out-of-pocket Budget (Annual)		
	Budget allocation to one-time surgery		
	Budget allocation to other health needs		
	Average Payor Coverage		
	Patient Liability		
	Target Price (@ 20% pat lab)		
	ASP for Cost of Therapy		
	TOTAL PATIENT VOLUMES		
	Product Purchase Frequency	1	
	TOTAL UNIT VOLUMES		
	Pricing per Unit	\$ 18,000	
	Inflation		
	Price Decrease due to competition		
	Market Value		

Source: GBI Research

The above figure represents a typical forecasting model followed in GBI Research. As discussed previously, the model is built on the treatment flow patterns. The model starts with the general population, then diseased population as a percentage of the general population and then follows the treatment seeking population as a percentage of the diseased population and diagnosed population as a percentage of the treatment seeking population. Finally, the total volume of units sold is calculated by multiplying the treated population by the average dosage per year per patient.

6.10 Geographical Landscape

GBI Research analyzes seven major geographies: the US, the top five countries in Europe (the UK, Germany, France, Spain and Italy) and Japan. The total market size for each country is provided, which is the sum value of the market sizes of all the indications for that particular country.

6.11 Pipeline Analysis

This section provides a list of molecules at various stages in the pipeline for various indications. The list is sourced from internal database and validated for the accuracy of phase and mechanism of action at ClinicalTrials.gov and company websites. The section also includes a list of promising molecules which is narrowed down based on the results of the clinical trials at various stages and the novelty of mechanism of action. The latest press releases issued by the company and news reports are also the source of information for the status of the molecule in the pipeline.

6.12 Expert Panel Validation

GBI Research uses a panel of experts to cross verify its databases and forecasts.

GBI Research expert panel comprises marketing managers, product specialists, international sales managers from medical device companies; academics from research universities and key opinion leaders from hospitals.

Historic data and forecasts are relayed to GBI Research's expert panel for feedback and are adjusted in accordance with their feedback.

6.14 Disclaimer

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