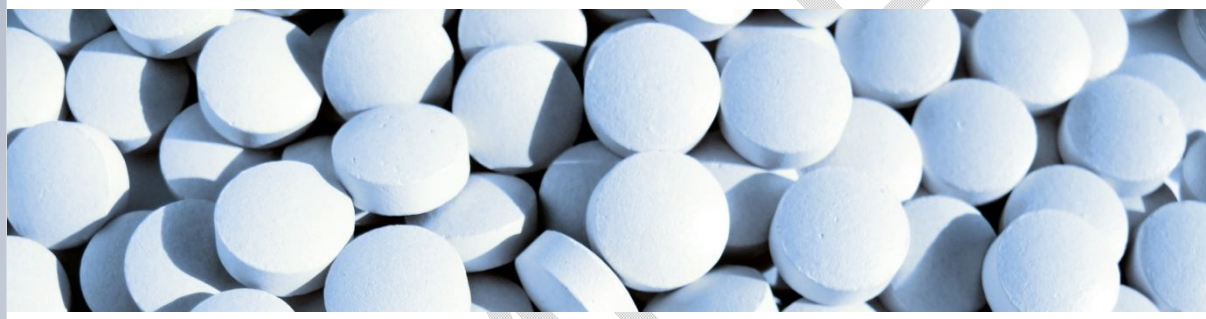
Glioblastoma Multiforme Therapeutics in Asia-Pacific Markets to 2020

Novel Therapeutic Approaches Target High Unmet Need in Newly Diagnosed and Recurrent GBM



GBI Research
Global Business Intelligence

GBI Research Report Guidance

- Chapter two provides an introduction to GBM, detailing the etiology, epidemiology, diagnostic tests, disease staging and typical prognoses for patients. An analysis of current treatment algorithms and options is also included.
- Chapter three offers detailed analysis of the four drugs currently marketed for this indication. Detailing the key characteristics of these drugs, including: safety and efficacy, clinical trial outcomes, tolerability, dosing, administration, historical sales, prices and overall competitive strength. These products are also compared in a comprehensive heat map.
- Chapter four provides detailed analysis of the pipeline for GBM, by stage of development, molecule type, program type and mechanism of action. It also analyses recent clinical trials in this indication by enrollment, duration and failure rate. Finally, promising late-stage pipeline molecules are analyzed and assessed in terms of their potential competitive strength.
- Chapter five supplies market forecasts for the GBM market, including: epidemiology, treatment usage patterns, pricing and market size for the 2012–2019 period. Four major Asia-Pacific markets (Australia, China, India and Japan) are covered and data are presented on a country-by-country level, with further analysis of key market drivers and barriers.
- Chapter six describes the major deals that have taken place in the global GBM market in recent years.

Glioblastoma Multiforme Therapeutics in Asia-Pacific Markets to 2020 – Executive Summary

Glioblastoma Multiforme Therapeutics Market in Asia-Pacific Region to Post High Growth to Reach $105.8m by 2020

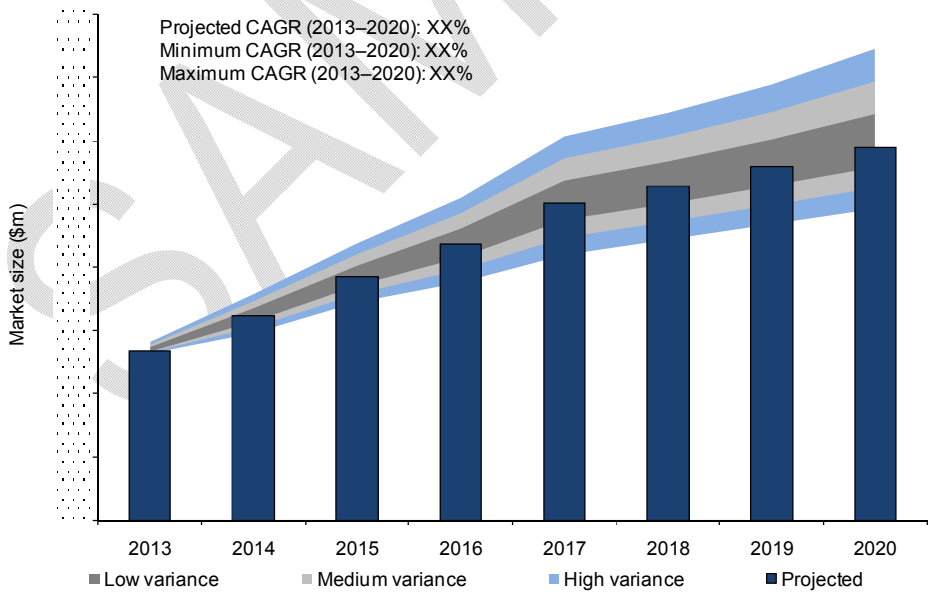
India and Australia have more promising candidates that could see approval in the forecast period compared with China and Japan.

The Glioblastoma Multiforme (GBM) therapeutics market in the four Asia-Pacific (APAC) markets of Australia, China, India and Japan was worth $XXm in 2013, and is expected to grow at a Compound Annual Growth Rate (CAGR) of XX% to $XXm by 2020. Japan was the largest of these markets in 2013, valued at $XXm, equivalent to a share of XX%, closely followed by China at $XXm or XX%. This significant expected growth is due to the probable approval and market entries of Rindopepimut (CDX-110), Cotara (TNT-1) and Avastin (bevacizumab) in some of the APAC regions during the forecast period.

India and Australia have more promising candidates for possible approval in the forecast period than China and Japan. The growth forecast for Japan, however, is still high, even though it has just one candidate in late-stage development that could be approved during the forecast period, due to recent approval of Avastin. Japan is expected to post a high CAGR of XX%, second only to India among the APAC countries. The GBM market in India is currently the smallest, estimated at $XXm in 2013, but is expected to post the highest growth, at a CAGR of XX% until 2020. There are four promising GBM drugs in the pipeline in India that could have a significant impact on market growth – Rindopepimut and BIOMAb (nimotuzumab) for newly diagnosed GBM; Avastin and Cotara for treatment in the recurrent setting.

The pipeline presents two promising novel therapies – Rindopepimut and Cotara – that could have a significant bearing on the GBM market in the APAC region. Phase II studies of Rindopepimut demonstrated a relatively high median Overall Survival (OS), and a significant survival benefit when compared to historic controls treated with the standard of care. However, the vaccine is limited to the XX% of GBM patients who are Epidermal Growth Factor Receptor (EGFR) variant (v) III-positive. Phase II studies of Cotara showed similar OS to Avastin, with slightly better Progression Free Survival (PFS) improvement in recurrent GBM. As a single-infusion therapy, Cotara is likely to become a good alternative second-line treatment.

Glioblastoma Multiforme Therapeutics, Asia-Pacific, Market Size ($m), 2013–2020



Source: GBI Research Proprietary Pipeline Products Database; GBI Research Proprietary Marketed Products Database

GBI Research
Global Business Intelligence

1 Table of Contents

1.1 List of Tables

1.2 List of Figures

2 Glioblastoma Multiforme Therapeutics in Asia-Pacific Markets to 2020 – Introduction

Glioblastoma Multiforme (GBM), a World Health Organization (WHO) Grade IV tumor, is the most common and aggressive human brain tumor. It accounts for approximately XX% of all brain tumors and mainly affects adults aged 45–65. In the US and EU, the annual incidence was estimated to be two to three cases per 100,000 people. Owing to this low incidence and prevalence population, GBM fulfills the criteria for an orphan disease under US and EU legislation.

In comparison with the growing diversification of therapeutic options across many indications in oncology, the landscape of most brain cancer types has been stagnant, with very limited scientific, technological or pharmaceutical advancement. The current GBM market therefore offers very limited treatment options, and there remain huge areas of unmet need.

The use of standard care generally results in anOverall Survival (OS) duration of no longer than 15 months in GBM patients.

The standard of care consists of a combination of three treatment strategies: surgery, radiation therapy and chemotherapy. Temodar (temozolomide), a chemotherapeutic agent, is considered the first-line treatment. Despite these treatments, however, prognosis remains extremely poor, with a high rate of tumor recurrence. The use of standard care generally results in an Overall Survival (OS) duration of no longer than 15 months. Therefore, there is a clear and urgent need for more effective initial therapies, as well as treatments for recurrent tumors. One of the major challenges to the development of viable therapeutic options for GBM is the presence of the Blood–Brain Barrier (BBB). Many chemotherapy drugs used in systemic tumors are unsuitable candidates in the treatment of GBM, as the molecular size is too large to penetrate the BBB. It has been suggested that the presence of active efflux transporters and tight junctions in the intact BBB restrict the delivery of targeted therapies to glioma cells (Agarwal et al., 2013). This means that there is a specific need for therapeutic or technological advances in drug delivery. Additionally, the extensive heterogeneity in GBM makes the disease extremely difficult to treat, and results in low response to treatment.

Another unmet need relates to the management of recurrent GBM, with the therapeutic window becoming increasingly narrow for patients with tumor recurrence. The treatment options for recurrent GBM are the targeted therapy Avastin (bevacizumab), and off-label use of several chemotherapy agents. Recently, there have been major setbacks in the development of effective targeted therapies for recurrent GBM, due to low efficacy. Additionally, the search for a partnering agent for Avastin therapy is ongoing and proving challenging with regards to efficacy and safety.

One promising late-stage vaccine, Rindopepimut possesses the potential to fulfill one of these unmet needs. If its superiority in prolonging OS in newly diagnosed patients is established in future trials, it is expected to be used in combination with the first-line treatment and drive significant growth in the GBM market. Another candidate, Cotara, a targeted therapy with a novel delivery method, is expected to enter into competition as a second-line treatment with Avastin. However, the drug is unlikely to fulfill the unmet need in recurrent GBM, due to the lack of additional OS benefits over Avastin. This means that huge market opportunities for more effective treatments will remain in recurrent GBM.

2.1 Disease Introduction

GBM is characterized by the presence of necrosis and the development of an abnormally high concentration of blood vessels around the tumor (ABTA, 2013). GBM tumors are characterized by extensive heterogeneity. The tumor arises from astrocytes, which are the star-shaped glial cells that make up the supportive tissue of the brain. These tumors are highly invasive due to their ability to proliferate rapidly, which is accelerated by the large network of blood vessels (ABTA, 2012).

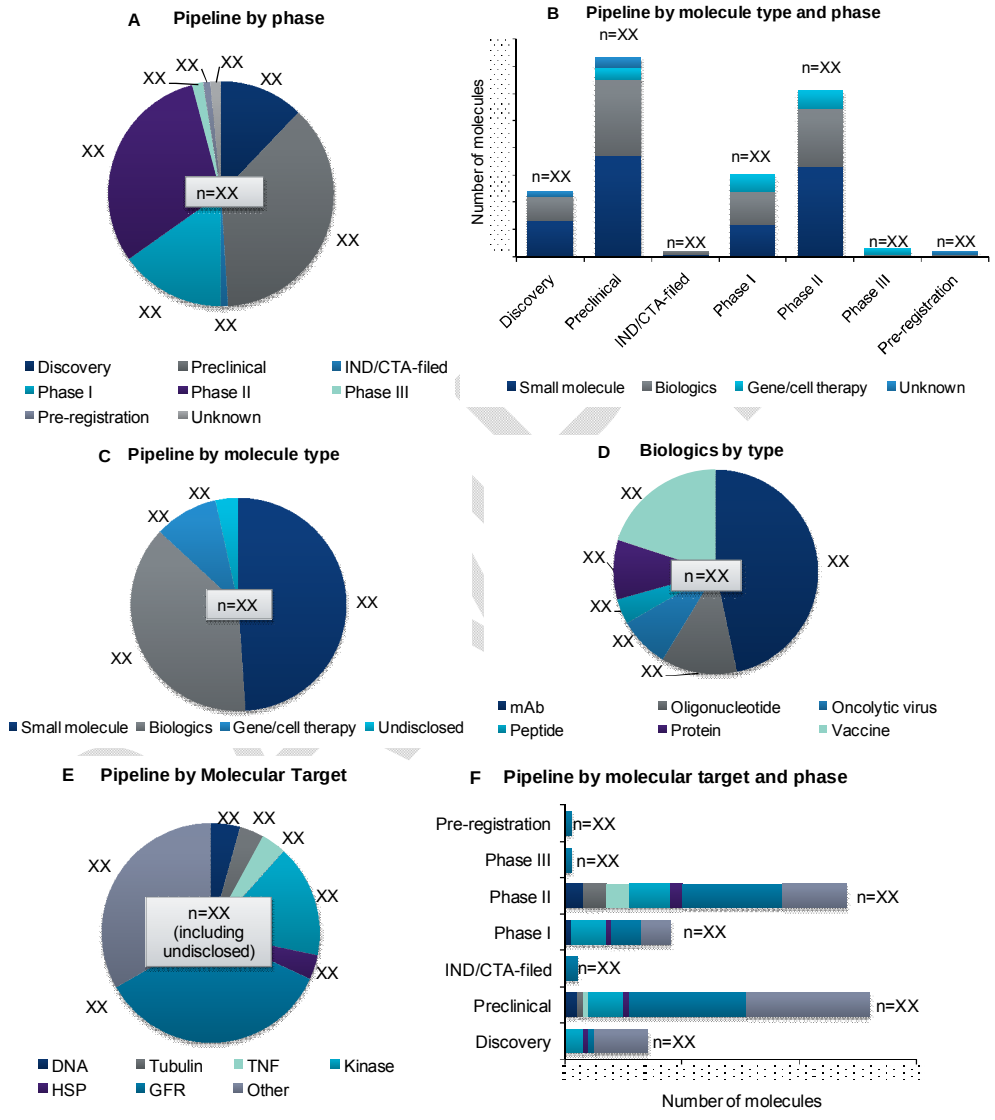
GBM either manifests from astrocytes without any clinical or histologic evidence of a less malignant precursor lesion, or arises from low-grade diffuse astrocytoma or anaplastic astrocytoma, and these lead to the classifications of primary and secondary GBM, respectively. There is increasing evidence suggesting that the subtype of GBM is determined by the patient's genetic profile. Like other neoplasms, the development of GBM is likely a result of multi-step transformation, resulting from the acquisition of multiple genetic alterations.

4.1 Overall Pipeline

Unusally, discovery phase represents a very small proportion of the pipeline (XX%).

Overall, there are currently XX drugs in the GBM pipeline. Analyses of pipeline products by stage of development have shown that the XX are in the early preclinical stage, which represents XX% of the entire pipeline. This is followed by Phase II and Phase I with XX and XX drugs each, constituting XX% and XX% of the pipeline respectively, as shown in Figure 8A. The pre-registration Phase, as expected, constitutes a small proportion of the pipeline, at XX%. What is unusual is that the discovery Phase represents a very small proportion of the pipeline. There are only XX drugs in this Phase, accounting for XX%, although disclosure of R&D activity at this stage is at the company's discretion, meaning the number of programs is likely to be underestimated.

Figure 8: Glioblastoma Multiforme, Global, Overall Pipeline, 2013

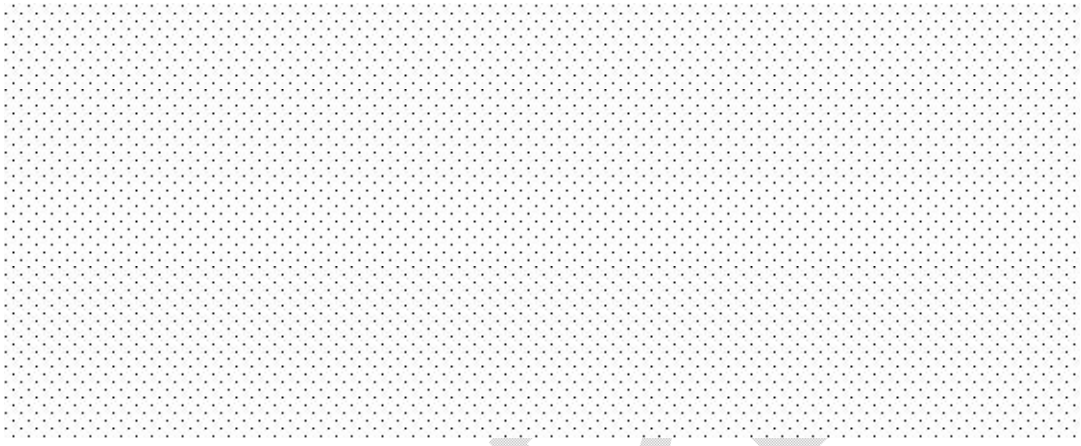


Source: GBI Research Proprietary Database, Pipeline Products

In panel E, 'Kinase' includes tyrosine kinase, PI3K and other protein kinase. 'Other' includes drugs targeting calcium channel, topoisomerase, toll-like receptor, and chemokine receptor.

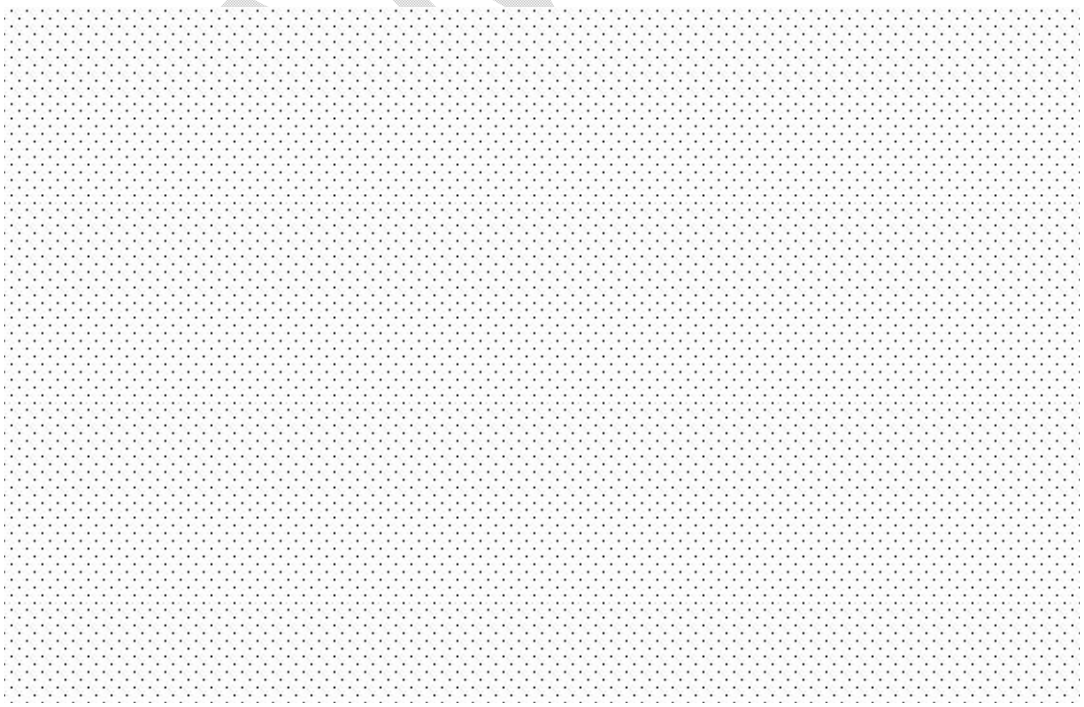
CTA: Clinical Trial Approval; GFR: Growth Factor Receptor; HSP: Heat Shock Protein; IND: Investigational New Drug; mAb: monoclonal Antibody; n: number; TNF: Tumor Necrosis Factor

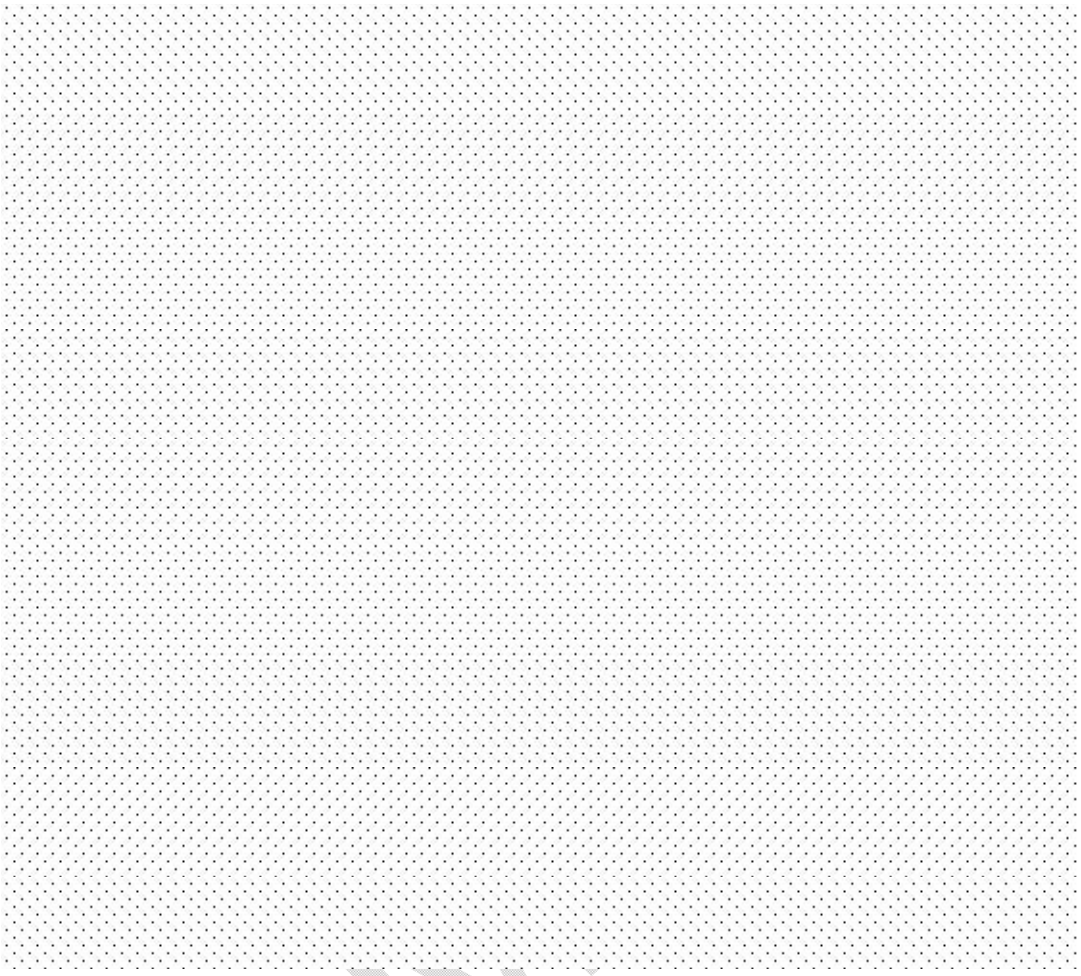
Nearly half of the GBM pipeline is made up of small molecules, with XX pipeline candidates. This is followed by biologics and gene/cell therapies, constituting XX% and XX% of the pipeline respectively, as shown in Figure 8C. XX drugs did not have a disclosed molecule type. With a significant presence in the overall GBM pipeline, small molecules are found at all developmental stages, and their presence is particularly apparent in the discovery Phase and Phase II. They are equally distributed throughout the other Phases, representing XX% in each, except Phase III where no small molecules are found, as shown in Figure 8B. Biologics in the GBM pipeline mainly consist of a mixture of mAbs, vaccines and oncolytic viruses. As shown in Figure 8D, XX% of the biologics are mAbs. This is followed by vaccines and oncolytic viruses, constituting XX% and XX% respectively. The remaining biologics, which have comparatively lower presence in the pipeline, are oligonucleotides, proteins and peptides.



4.2 Molecular Targets

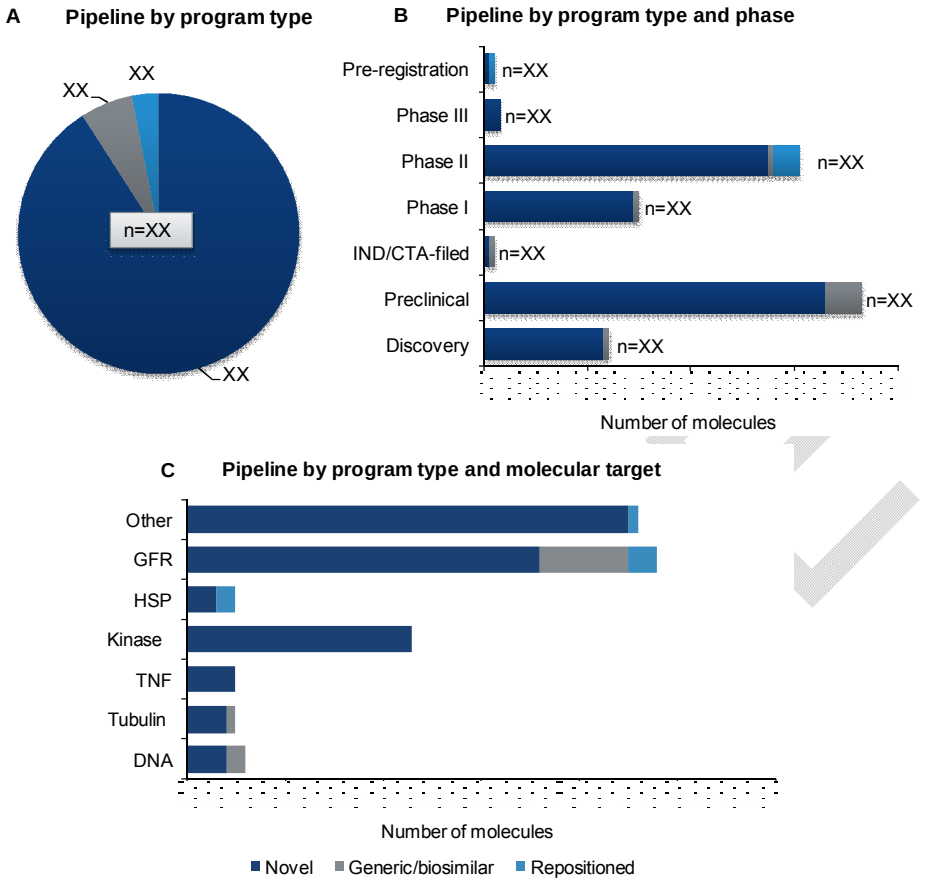
The GBM pipeline products are categorized into seven groups in terms of their molecular targets, as shown in Figure 8D. Molecular targets are not disclosed for XX% of the pipeline products. The analysis shows that the majority of drugs, XX% of the XX disclosed products, target a GFR. These are mainly antagonists acting on multiple GFRs, with the majority targeting EGFR and Vascular Endothelial Growth Factor Receptor (VEGFR). Kinase inhibitors also have a significant presence, and constitute XX% of the pipeline. The rest of the pipeline consists of products targeting DNA, TNF, HSP and tubulin.





The distribution of programs types by molecular target is shown in Figure 9C. XX of the generic drugs target DNA, and the other targets tubulin, while the nine biosimilars target GFRs. The XX drugs that have been repositioned are targeting GFRs and HSP. It is not unusual to see inhibitors targeting GFRs being repositioned from other types of cancers to GBM, due to their involvement in many signaling pathways in the pathogenesis of multiple types of cancer.

Figure 9: Glioblastoma Multiforme, Global, Program Type by Phase and Molecular Targets, 2013



Source: GBI Research Proprietary Database, Pipeline Products

CTA: Clinical Trial Approval; GFR: Growth Factor Receptor; HSP: Heat Shock Protein; IND: Investigational New Drug; n: number; TNF: Tumor Necrosis Factor.

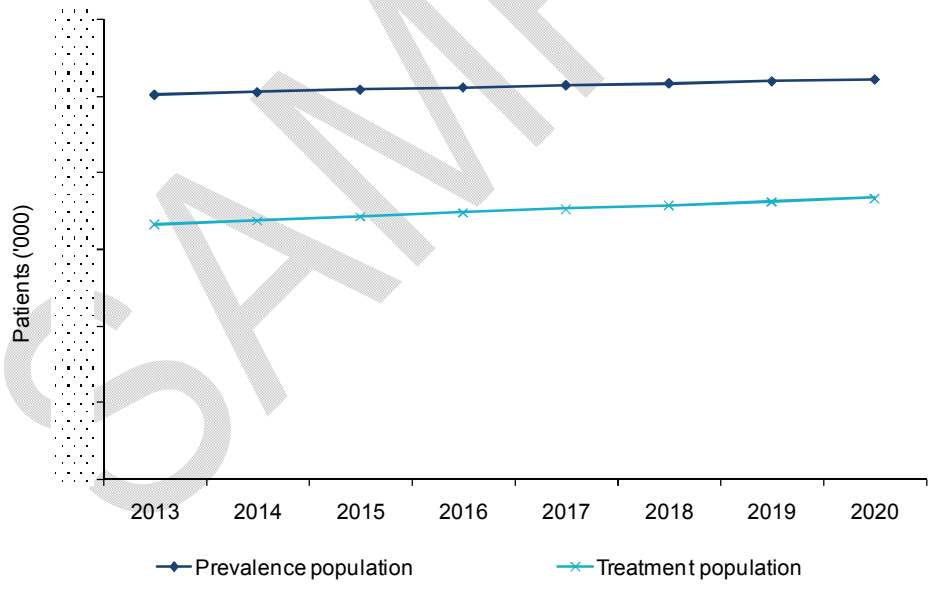
5 Glioblastoma Multiforme Therapeutics in Asia-Pacific Markets to 2020 – Market Forecast to 2020

5.1 Asia-Pacific Market

5.1.1 Treatment Use Patterns

The total prevalence population of GBM in these four Asia-Pacific countries was estimated at XX in 2013, and is expected to grow at a Compound Annual Growth Rate (CAGR) of XX% to reach XX by 2020. Prevalence rate is highest is Australia at XX per 100,000, although China had the largest number of total cases for GBM in 2013. Prevalence population was estimated at XX cases in China in 2013, closely followed by India at XX cases, owing to the large population size in these two countries. In a retrospective study across multiple medical centers covering New South Wales (NSW) and Australian Capital Territory (ACT), incidence of GBM is reported to have increased significantly from XX to XX cases per XX from 2000 to 2008 (Dobes et al., 2011a).

Figure 15: Glioblastoma Multiforme Therapeutics, Asia-Pacific, Treatment Use Patterns ('000), 2013–2020

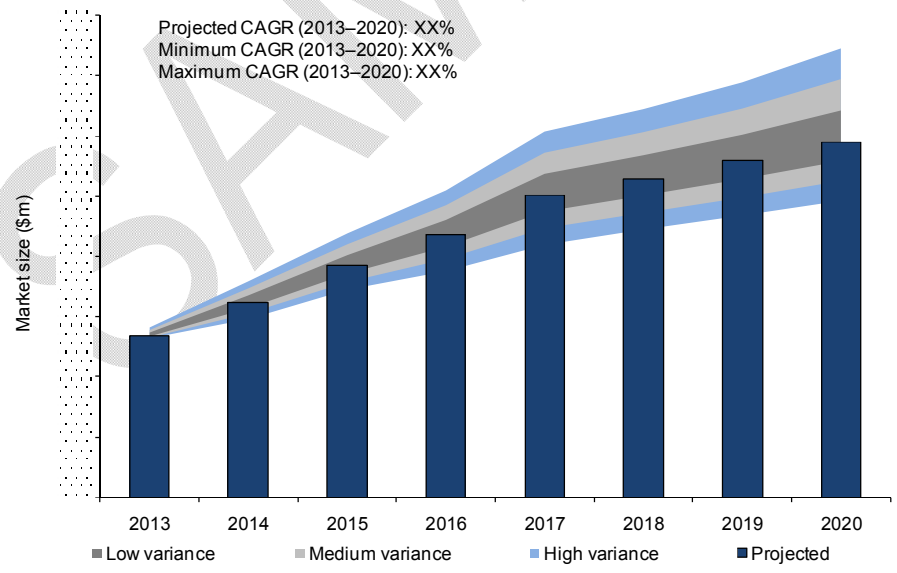


Source: GBI Research Proprietary Pipeline Products Database; GBI Research Proprietary Marketed Products Database

5.1.2 Market Size

Although the size of the GBM market is lowest in India among the APAC countries, the potential launches are expected to contribute towards a healthy growth, at a CAGR of XX%, more than doubling the market size during the forecast period. In India, although generic versions of temozolomide are already available in the market, even a modest uptake of the new drugs will boost growth, due to the much higher cost. The GBM market size in Australia has considerably reduced following the recent patent expiry of the key drug Temodar, and was estimated at $XXm in 2013. However, the premium revenues from the new launches are expected to offset the impact of this in the coming years, leading to solid growth at a CAGR of XX%. In addition, the overall growth in the APAC market will also be boosted by the 2013 approval of Avastin in Japan for the treatment of newly diagnosed and recurrent GBM.

Figure 16: Glioblastoma Multiforme Therapeutics, Asia-Pacific, Market Size ($m), 2013–2020



Source: GBI Research Proprietary Pipeline Products Database; GBI Research Proprietary Marketed Products Database

7 Glioblastoma Multiforme Therapeutics in Asia-Pacific Markets to 2020 – Appendix

7.1 Market Definitions

- The Glioblastoma Multiforme market includes the four major Asia-Pacific markets: Australia, China, India and Japan.
- The prevalence population is the estimated number of people at any given point of time that are affected by Glioblastoma Multiforme.
- The treatment population refers to the number of people taking pharmacological treatment for Glioblastoma Multiforme.

7.2 Abbreviations

2-HG: 2-Hydroxyglutarate

ACoT: Annual Cost of Treatment

ACT: Australian Capital Territory

AE: Adverse Event

APAC: Asia-Pacific

API: Active Pharmaceutical Ingredient

ATRX: Alpha Thalassemia/mental Retardation X linked

BBB: Blood Brain Barrier

bFGF: basic Fibroblast Growth Factor

CAGR: Compound Annual Growth Rate

CCHMC: Cincinnati Children's Hospital Medical Center

CDK: Cyclin-Dependent Kinase

CDKN: Cyclin-Dependent Kinase inhibitor

CED: Convection-Enhanced Delivery

cm: centimeter

CNS: Central Nervous System

CSF: Cerebrospinal Fluid

CT: Computed Tomography

CTA: Clinical Trial Approval

DNT: Dysembryoplastic Neuroepithelial Tumor

E2F: Early gene 2 Factor

EBRT: External Beam Radiation Therapy

EGFR: Epithelial Growth Factor Receptor

EIAED: Enzyme-Inducing Anti-Epileptic Drugs

EMA: European Medicines Agency

FDA: Food and Drug Administration

FDG-PET: [18F] Fluorodeoxyglucose Positron Emission Tomography

Flt3L: FMS-like tyrosine kinase-3 Ligand

G1/S: Gap 1 to Synthesis

GBM: Glioblastoma Multiforme
GFR: Growth Factor Receptor
Gy: Gray
HGG: High-Grade Gliomas
HIF: Hypoxia-Inducible Factor
HSP: Heat Shock Protein
IDH: Isocitrate Dehydrogenase
IND: Investigational New Drug
IgG: Immunoglobulin G
IL: Interleukin
KDR: Kinase insert Domain Receptor
KLH: Keyhole Limpet Hemocyanin
KPS: Karnofsky Performance Status
LGG: Low-Grade Glioma
LoH: Loss of Heterozygosity
mAb: monoclonal Antibody
MAH: Marketing Authorization Holder
mCi/cc: millicurie per cubic centimeter
MDM: Mouse Double Minute
mg/kg: milligram per kilogram
mg/m^2: milligram per square meter
MGMT: O6-Methylguanine-DNA Methyltransferase
MRI: Magnetic Resonance Imaging
MRS: Magnetic Resonance Spectroscopy
MTIC: Methyl-(Triazen-1-yl)Imidazole-4-Carboxamide
mTOR: mammalian Target Of Rapamycin
n: number
NICE: National Institute for Health and Care Excellence
NSCLC: Non-Small Cell Lung Cancer
NSW: New South Wales
OR: Objective Response
OS: Overall Survival
PBAC: Pharmaceutical Benefits Advisory Committee
PBS: Pharmaceutical Benefits Scheme
PCNSL: Primary Central Nervous System Lymphoma
PCT: Perfusion Computed Tomography
PCV: Procarbazine, lomustine, Vincristine
PFS: Progression-Free Survival

PI3K: Phosphoinositide 3-Kinase

PIP2: Phosphatidylinositol 4,5-biphosphate

PIP3: Phosphatidylinositol (3,4,5)-triphosphate

PKB: Protein Kinase B

PR: Partial Response

PTEN: Phosphatase and Tensin homolog

RB: Retinoblastoma

RoA: Route of Administration

RT: Radiation therapy

S: Synthesis

SRS: Stereotactic Radiosurgery

TGF: Transforming Growth Factor

TIMP: Tissue Inhibitor of Metalloproteinases

TNF: Tumor Necrosis Factor

TNT: Tumor Necrosis Therapy

TRP: Tyrosinase-Related Protein

TTF: Tumor Treating Fields

TTP: Time-To-Progression

v: variant

VEGF: Vascular Endothelial Growth Factor

VEGFR: Vascular Endothelial Growth Factor Receptor

WHO: World Health Organization

7.3 Bibliography

- AANS/CNS (2014). Classification of Brain Tumors. American Association of Neurological Surgeons. Available from: http://www.aans.org/Media/Fact%20Sheets/Classification%20of%20Brain%20Tumors.aspx [Accessed August 15, 2013]
- ABTA (2012). Glioblastoma and Malignant Astrocytoma. American Brain Tumor Association. Available at: http://www.abta.org/secure/glioblastoma-brochure.pdf.
- ABTA (2013). Glioblastoma. American Brain Tumor Association. Available at: http://www.abta.org/understanding-brain-tumors/types-of-tumors/glioblastoma.html. [Accessed August 15, 2013].
- ABTA (2014a). Brain Tumor Statistics. American Brain Tumor Association. Available from: http://www.abta.org/about-us/news/brain-tumor-statistics/. [Accessed April 28, 2014].
- ABTA (2014b). Metastatic Brain Tumors. American Brain Tumor Association. Available from: http://www.abta.org/secure/metastatic-brain-tumor.pdf.
- ABTA (2014c). Neurological Exam. American Brain Tumor Association. Available from: http://www.abta.org/brain-tumor-information/diagnosis/neurological-exam.html. [Accessed March 13, 2014].
- Adamson C, et al. (2009). Glioblastoma multiforme: A review of where we have been and where we are going. *Expert Opinion on Investigational Drugs;* 18(8): 1061–1083.

7.4 All Pipeline Products by Phase

7.4.1 Discovery

Table 4: Discovery

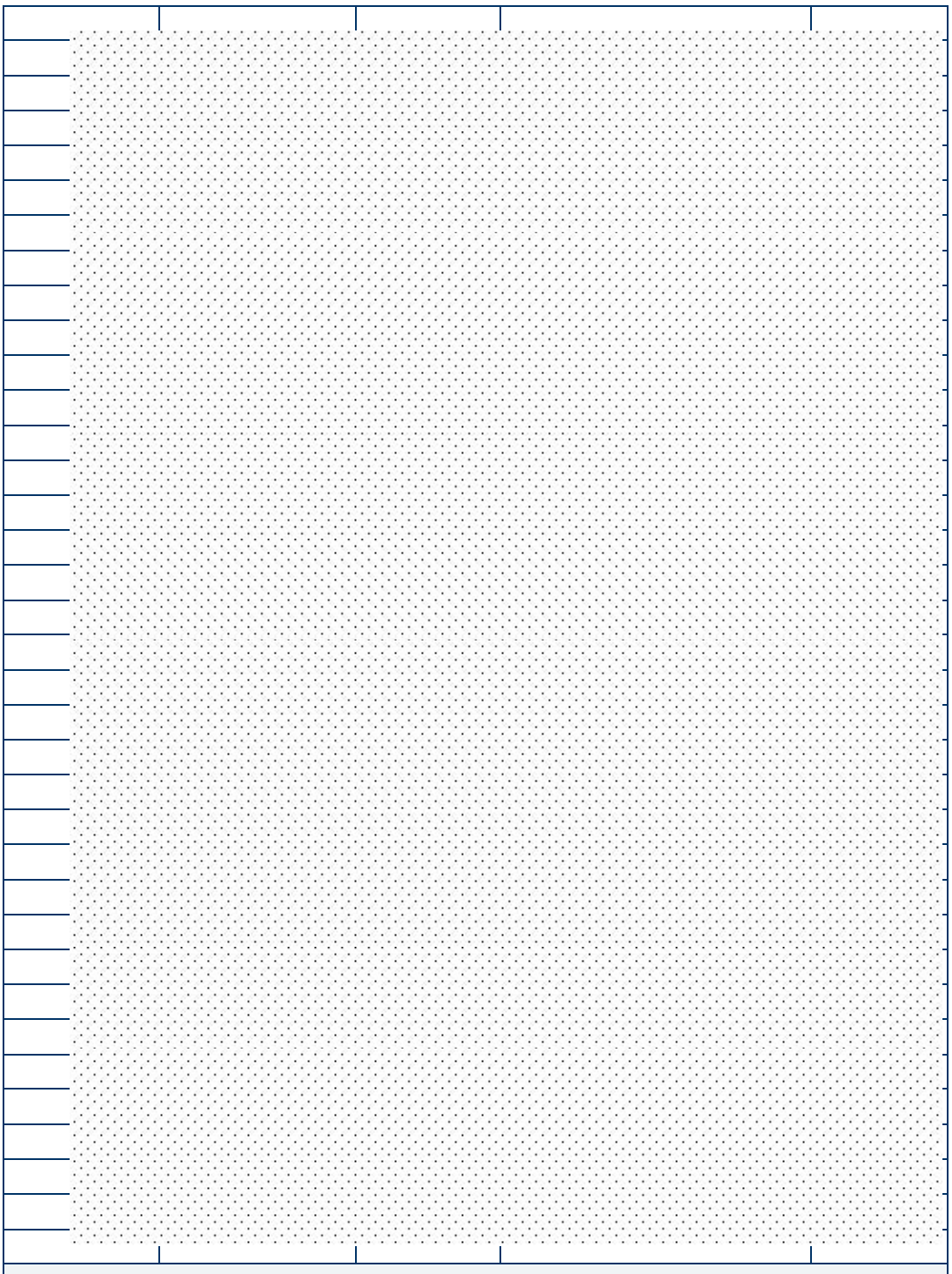
Product name	Company	Molecule type	Mechanism of action

Source: GBI Research

7.4.2 Preclinical

Table 5: Preclinical and IND/CTA-filed

Product name	Company	Molecule type	Mechanism of action	Stage of development



Source: GBI Research

7.4.3 Phase I

Table 6: Phase I

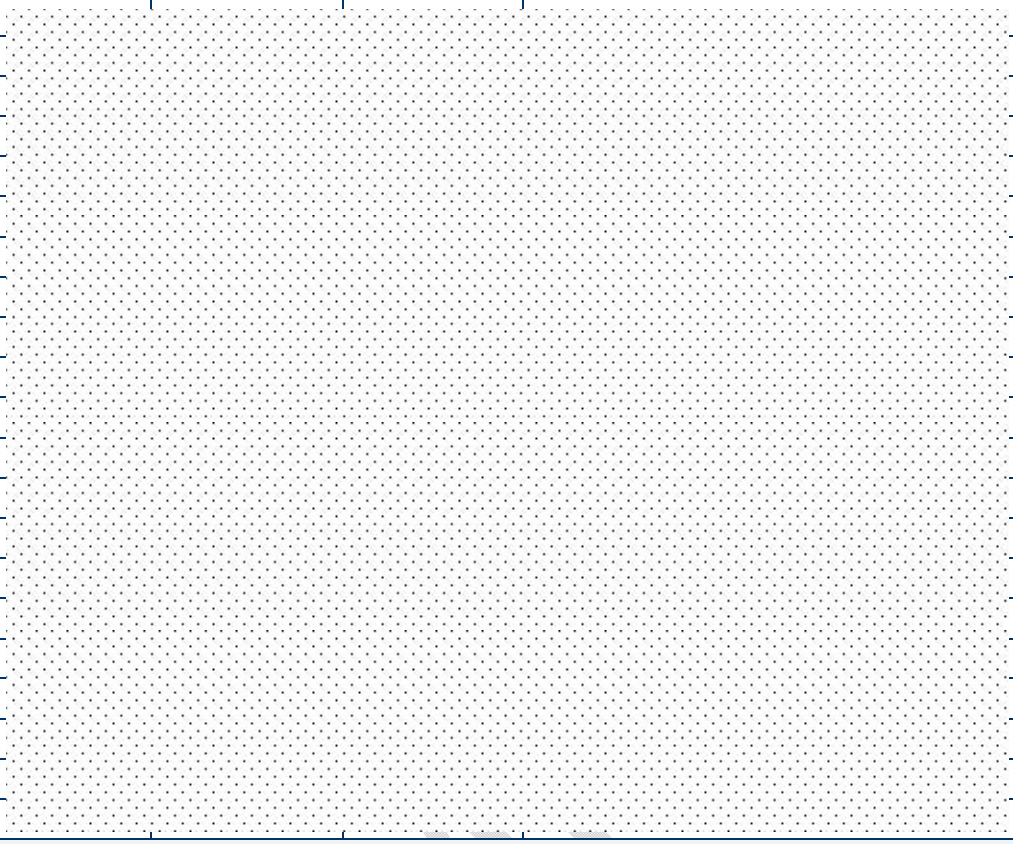
Product Name	Company	Molecule Type	Mechanism of Action

Source: GBI Research

7.4.4 Phase II

Table 7: Phase II

Product name	Company	Molecule type	Mechanism of action



Source: GBI Research

7.4.5 Phase III and Pre-Registration

Table 8: Phase III and pre-registration

Product name	Company	Molecule type	Mechanism of action	Stage of development

Source: GBI Research

7.4.6 Undisclosed stage of development

Table 9: Undisclosed stage of development			
Product name	Company	Molecule type	Mechanism of action
Source: GBI Research			

7.5 Market Forecasts to 2020

7.5.1 Asia-Pacific

Table 10: Glioblastoma Multiforme Therapeutics, Asia-Pacific, Forecast Data, 2013–2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR (%)
Prevalence population									
Treatment population									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									
Source: GBI Research Proprietary Pipeline Products Database; GBI Research Proprietary Marketed Products Database									

7.5.2 Australia

Table 11: Glioblastoma Multiforme Therapeutics, Australia, Forecast Data, 2013–2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR (%)
Prevalence population									
Treatment population									
ACoT ($)									
Maximum revenue ($m)									
Projected revenue($m)									
Minimum revenue ($m)									
Source: GBI Research Proprietary Pipeline Products Database; GBI Research Proprietary Marketed Products Database									

7.5.3 China

Table 12: Glioblastoma Multiforme Therapeutics, China, Forecast Data, 2013–2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR (%)
Prevalence population									
Treatment population									
ACoT ($)									
Maximum revenue ($m)									
Projected revenue($m)									
Minimum revenue ($m)									
Source: GBI Research Proprietary Pipeline Products Database; GBI Research Proprietary Marketed Products Database									

7.5.4 India

Table 13: Glioblastoma Multiforme Therapeutics, India, Forecast Data, 2013–2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR (%)
Prevalence population									
Treatment population									
ACoT ($)									
Maximum revenue ($m)									
Projected revenue($m)									
Minimum revenue ($m)									
Source: GBI Research Proprietary Pipeline Products Database; GBI Research Proprietary Marketed Products Database									

7.5.5 Japan

Table 14: Glioblastoma Multiforme Therapeutics, Japan, Forecast Data, 2013–2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR (%)
Prevalence population									
Treatment population									
ACoT ($)									
Maximum revenue ($m)									
Projected revenue($m)									
Minimum revenue ($m)									
Source: GBI Research Proprietary Pipeline Products Database; GBI Research Proprietary Marketed Products Database									

7.6 Research Methodology

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

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

All GBI Research databases are continuously updated and revised. The following research methodology is followed for all databases and reports.

7.6.1 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 that 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 pharmaceutical industry, updated on a daily basis.

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

7.6.2 Secondary Research

The research process begins with extensive 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 US Securities and Exchanges Commission (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

7.6.3 Therapeutic Landscape

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

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

7.6.4 Forecasting

GBI Research's forecasting model uses an epidemiology-based approach, in which sales for each product are calculated, based on the cost of that drug, and the number of patients using it.

Initially, based on peer-reviewed literature, the disease prevalence is calculated and extrapolated with historic trends and any other relevant inputs that have been gathered from the literature. In the same way, the fraction of prevalent patients that are diagnosed, and the fraction of diagnosed patients who are ultimately treated, are also calculated.

If relevant, the treatment population is then divided into segments using any available inputs from scientific literature. For example, in oncology indications it is common to divide the patient population based on the stage of their disease, as early- to late-stage cancers. Each drug may appear in more than one segment within this model.

The use of each drug within each segment (as a percentage) is estimated as accurately as possible, primarily using treatment guidelines, primary research and any other relevant peer-reviewed data inputs for each indication. The market penetration of pipeline products in their first few years after approval is estimated based primarily on published clinical trial data, with the safety and efficacy profiles of each pipeline drug being compared against any other competitors in their patient segment(s).

Pipeline products that are expected to fulfill an unmet need and perform better than marketed products are typically given higher distributions than those that are not. While efficacy and safety data are usually the most important criteria for making these estimates, other characteristics such as the route of administration and dosing convenience are weighted more strongly in relevant indications.

The cost of each drug is estimated based on the cost per gram of the drug (cost of one unit divided by the size of each unit in grams) and the number of grams taken by each patient in a single year (or a course of therapy). For the purposes of this model, different formulations for a single drug with different dosages (for example, a pediatric and adult formulations) are treated as separate entities.

For pipeline drugs, the cost is estimated based on a benchmark of existing marketed products (typically within the indication). Based on the ability to fulfill unmet needs and compete effectively with marketed products, a percentage markup (or occasionally a mark-down) versus the benchmark is assigned. This benchmark may be an individual product (such as a direct competitor) or an average of existing products. Rarely, the cost of drugs in other indications may be used to estimate the cost of the pipeline product.

The cost is adjusted to take into account inflation of pharmaceutical products and any estimated effects of patent expiries (with biologics having slower and weaker price erosion than small molecules following patent expiry). Finally, based on percentage distributions, a weighted average cost of each drug is estimated for all patients treated for the disease. The weighted average cost of each drug can then be multiplied by the treatment population to arrive at a sales estimate for that drug, and the total sales of all drugs is the overall market size.

From this primary forecast, peak and low market sizes and drug sales are estimated based on potential variations and uncertainties in price inflation, patent expiry, distribution shifts, pipeline product market penetration, and drug pricing for pipeline products. Inherently unpredictable events such as policy changes are not modeled directly in the scenarios, but are accounted for in the numeric inputs. These multiple scenarios aim to supplement the primary forecast with an accurate, transparent picture of the inherent uncertainty of the future market, and the likely range of outcomes.

7.6.5 Geographical Landscape

This GBI Research report covers the following Asia-Pacific markets: Australia, China, India 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.

7.6.6 Pipeline Analysis

This section provides a list of molecules at various stages in the pipeline for various indications. The list is sourced from an 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 used to source information related to the status of the molecule in the pipeline.

7.7 Competitive Landscape

GBI Research aims to cover all major licensing deals and co-development deals related to the market. This section is sourced from company websites, company annual reports and internal databases.

7.8 Expert Panel Validation

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

GBI Research's expert panel includes marketing managers, product specialists, international sales managers from medical device companies, academics from research universities, key opinion leaders from hospitals, consultants from venture capital funds and distributors/suppliers of medical equipment and supplies.

Historic data and forecasts are relayed to GBI Research's expert panel for feedback and adjusted accordingly.

7.10 Disclaimer