Glioblastoma Multiforme Therapeutics in Major Developed Markets to 2020

Growth to Hinge on the Success of Personalized Vaccine Following Early Approval in Germany

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 2013–2020 period. Eight major markets (US, Canada, Germany, UK, France, Italy, Spain 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.

Executive Summary

The Glioblastoma Multiforme (GBM) market is forecast to grow rapidly from $XXm in 2013 to $XXm in 2020.

Significant Market Growth Driven by Personalized Vaccine DCVax-L

The Glioblastoma Multiforme (GBM) market is forecast to grow rapidly from $XXm in 2013 to $XXm in 2020 at a Compound Annual Growth Rate (CAGR) of XX%. This significant growth comes despite the upcoming patent expiration of Temodar and is primarily contributed to by the market entry of DCVax-L. DCVax-L a dendritic cell-based therapeutic vaccine that demonstrated an Overall Survival (OS) that was around XX times longer that observed with the standard of care in newly diagnosed patients during clinical trials. Currently, surgery, radiotherapy and chemotherapy with Temodar (temozolomide) is the standard initial treatment, but the OS resulting from these treatments does not exceed XX months. DCVax-L, which will be marketed as an add-on to the standard treatment for newly diagnosed patients followed by surgery, is expected to demand a premium price and bear high market potential, given that its efficacy has translated into larger Phase III trials. The vaccine is anticipated to be approved in 2015 in the US and in 2016 in EU. The cancer vaccine Rindopepimut (CDX-110) and targeted therapy Cotara will also enter the GBM market in 2017 and 2016 respectively, but will drive growth to a lesser extent. Despite its high potency in prolonging OS in newly diagnosed patients, the uptake of Rindopepimut is likely to be lower due to its lower efficacy in comparison with DCVax-L. Cotara, developed for treating recurrent GBM, will have limited market uptake due to less favorable cost-effectiveness compared to its competitor Avastin (bevacizumab).

Challenging Clinical Trial Landscape Poses Barrier to Market Entrants

Analysis indicates that GBM clinical trials are of an exceptionally long average duration and have a high attrition rate. These trends pose a huge challenge for the development of new products for the GBM market. These findings indicate that investment in the market is high-risk, and explain the small total of players that are currently active in the market landscape. The clinical trial landscape is characterized by limited efficacy of developmental products due to the limitations in drug delivery techniques and the heterogenous nature of the disease. This is further exacerbated by low prevalence rates, making trial recruitment difficult, resulting in low patient accrual rate, and above-industry average trial durations, leading to a very high cost of drug development. However, attractive opportunities can be found in the market as huge unmet needs remain. This is particularly relevant to recurrent GBM, as the market entrants are not expected to address the unmet needs in this patient segment over the forecast period. Therapies that exhibit high potency against chemotherapy-resistant tumors will remain in high demand, given the limited OS benefits demonstrated by current treatment options.

Significant Presence of Targeted Therapies from Phase II to Phase III of the Pipeline

Targeted therapies and personalized treatments have a significant presence in the late-stages of the pipeline, however, drugs targeting DNA represent only XX% of the total developmental pipeline. This is in contrast to the current market landscape which is dominated by DNA-targeting drugs. This reflects a shift toward treatment strategies with higher tumor specificity and multiple molecular targets. These new treatments can potentially translate into more profound survival improvements with fewer systemic side effects, one of the limitations of Avastin.

1 Table of Contents

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2 Introduction

Glioblastoma Multiforme (GBM), a World Health Organization (WHO) Grade IV tumor, is the most common and aggressive human brain tumor.

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 mostly 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 the prevalence population of GBM, GBM fulfills the criteria for orphan disease under US and EU legislation.

In comparison to the growing diversification of therapeutic options across many indications in oncology, the landscape across most brain cancer types has remained 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 standard of care consists of a combination of three treatment strategies: surgery, radiotherapy and chemotherapy. Temodar (temozolomide), a chemotherapeutic agent, is considered to be the first-line treatment in GBM. Despite these treatments, 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 in GBM patients. 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 since they are too large to penetrate the BBB. The presence of active efflux transporters and tight junctions in the intact BBB are suggested to 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. In addition, 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. In addition, the search for a partnering agent for Avastin therapy is still ongoing and is challenging with regards to efficacy and safety.

Two promising late-stage vaccines possess the potential to fulfill one of these unmet needs. If their superiority in prolonging OS in newly diagnosed patients is established in future trials, they are 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 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 in comparison to Avastin. Therefore, 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). A GBM tumor is 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).

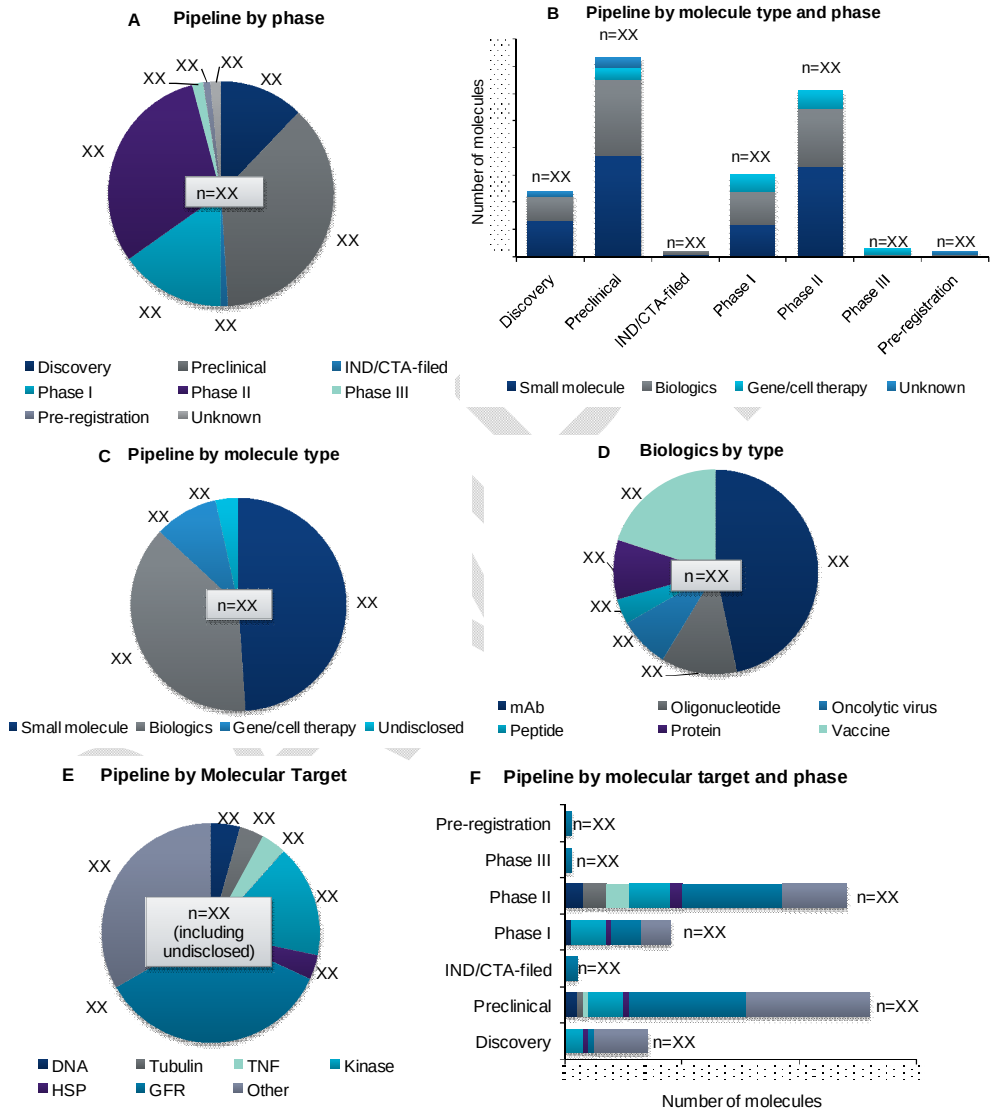
GBM either manifests from astrocytes without any clinical or histologic evidence of a less malignant precursor lesion, or arises from low-grade diffuse astrocytoma or anaplastic astrocytoma, classified as primary and secondary GBM, respectively. There is increasing evidence suggesting that the subtype 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

Overall, there are currently XX drugs in the GBM pipeline.

Overall, there are currently XX drugs in the GBM pipeline. Analyses of pipeline products by stage of development have shown that the majority are in the early preclinical stage, XX overall, 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 (Figure 8.A). The pre-registration phase, as expected, constitutes a small proportion of the pipeline, with only 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 only XX%, although disclosure of Research and Development (R&D) activity at this stage is at the discretion of companies and is therefore likely to underestimate the number of programs.

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

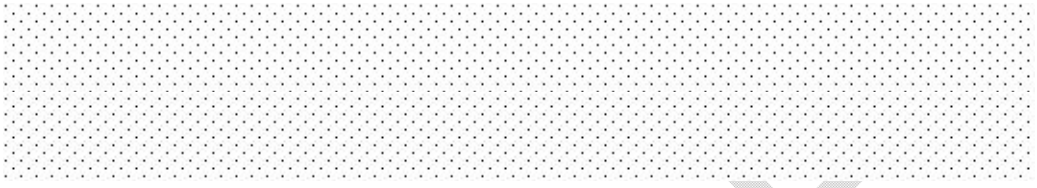


Source: GBI Research Proprietary Database, Pipeline Products

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.

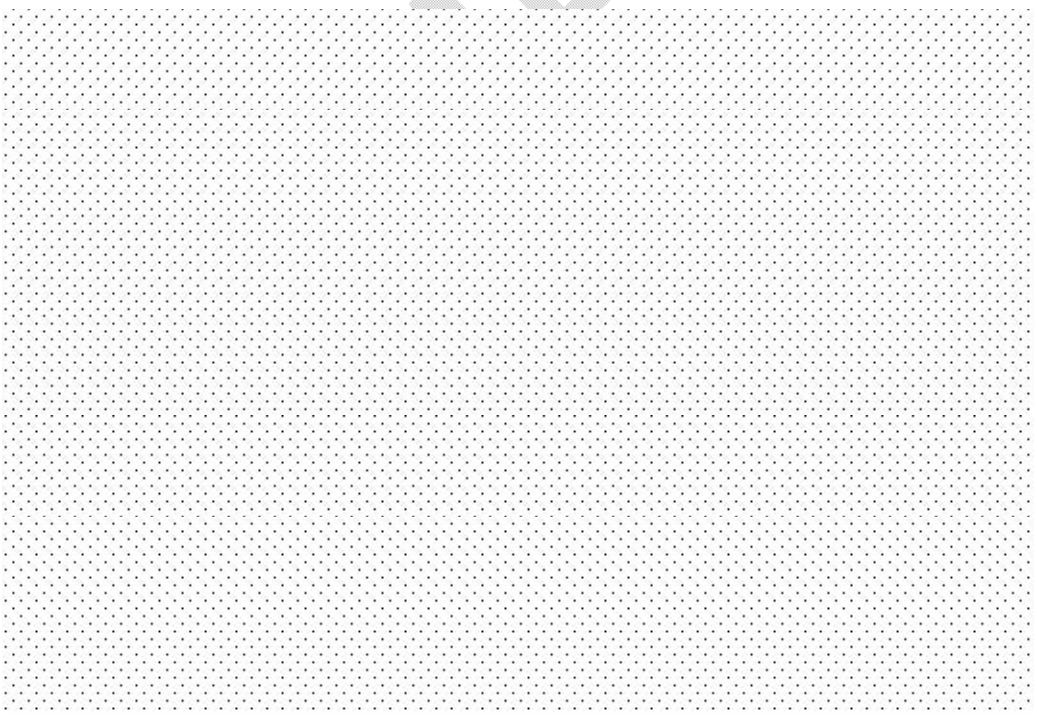
CTA: Clinical Trial Approval; GFR: Growth Factor Receptor; HSP: Heat Shock Protein; IND: Investigational New Drug; mAb: monoclonal Antibody; n: number; TNF: Tumor Necrosis Factor

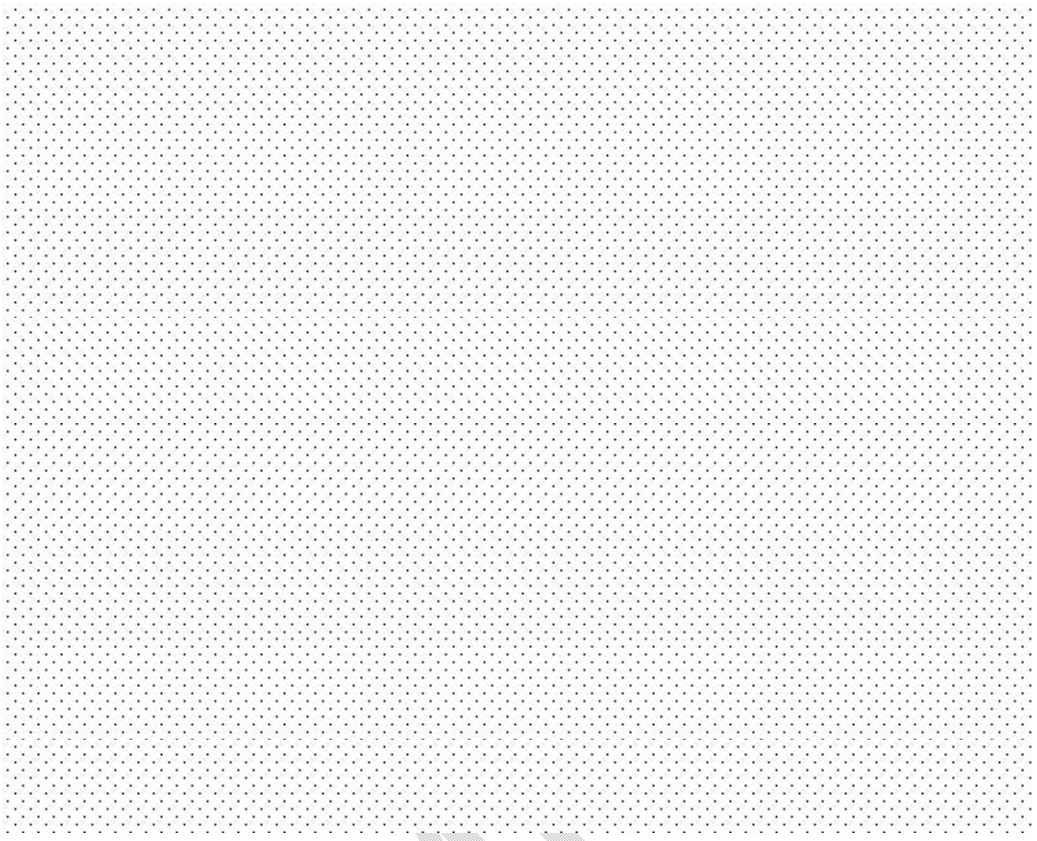
Nearly half of the GBM pipeline is made up of small molecules, with a total of XX pipeline candidates. This is followed by biologics and gene/cell therapies, constituting XX% and XX% of the pipeline respectively (Figure 8.C). A total of XX drugs did not disclose their molecule type. With a significant presence in the overall GBM pipeline, small molecules are found throughout all the developmental stages, and their presence is particularly apparent in the discovery phase and Phase II. Apart from the discovery stage and Phase II, they are equally distributed throughout each phase, representing XX–XX% in each of the other phases except Phase III, where no small molecule is found (Figure 8.B). Biologics in the GBM pipeline mainly consist of a mixture of mAbs, vaccines and oncolytic virus. As shown in Figure 8.D, the majority of the biologics are mAbs, representing XX% of all biologics. This is followed by vaccines and oligonucleotide, constituting 20% and XX% of all the biologic products, respectively. The remaining biologics which have comparatively lower presence in the pipeline are oncolytic virus, proteins and peptides.



4.2 Molecular Targets

The GBM pipeline products are categorized into seven groups in terms of their molecular targets (Figure 8.D). 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.





When the pipeline products are analyzed by program type, defined as either novel, repositioned or generic/biosimilar, the majority are novel. As shown in Figure 9.A, XX drugs are classed as novel, accounting for XX%, whereas repositioned drugs only represent XX% of the entire pipeline. These results align with the findings from earlier, indicating a high degree of innovation in the GBM pipeline and limitations in the repositioning potential of products already established in the market. Novel drugs are distributed equally and represent the majority across all stages of development. There are XX generic drugs in the pipeline, XX in preclinical development and the other in Phase II. (Figure 9.B). All nine biosimilars for Avastin are found across the discovery phase and Phase I.

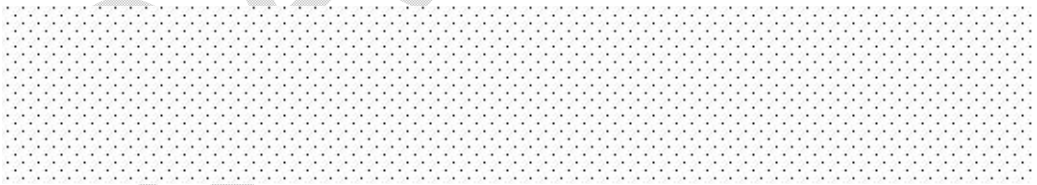
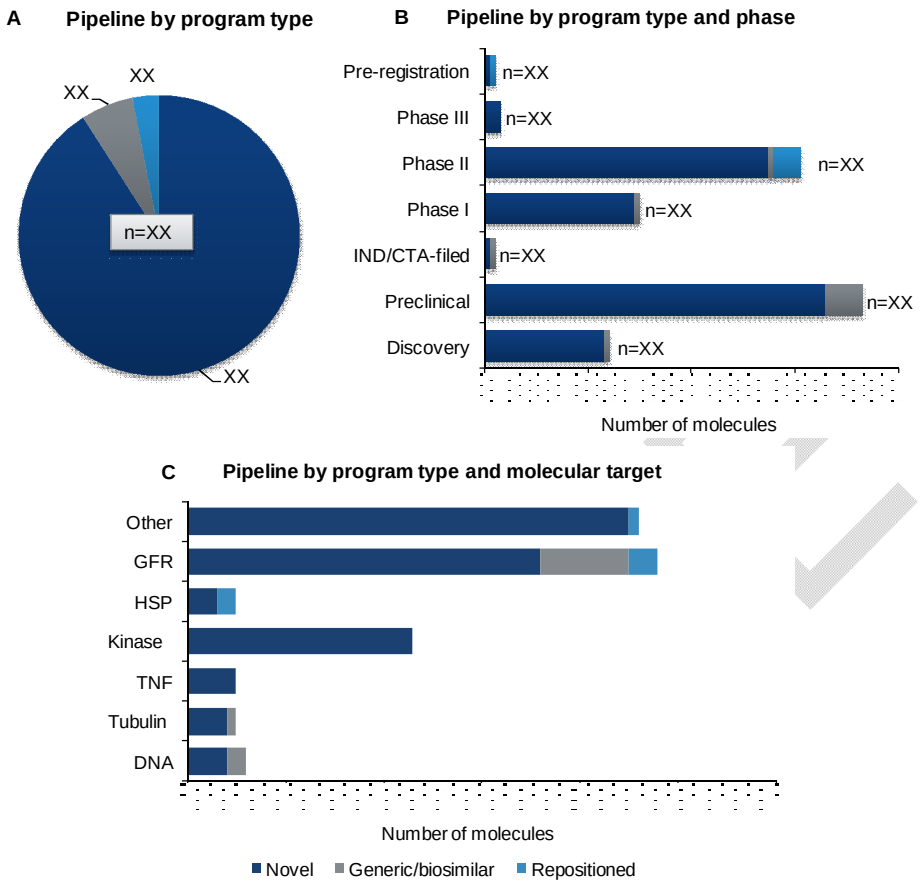


Figure 9: Glioblastoma Multiforme, Global, Program Type by Phase and Molecular Targets, 2013



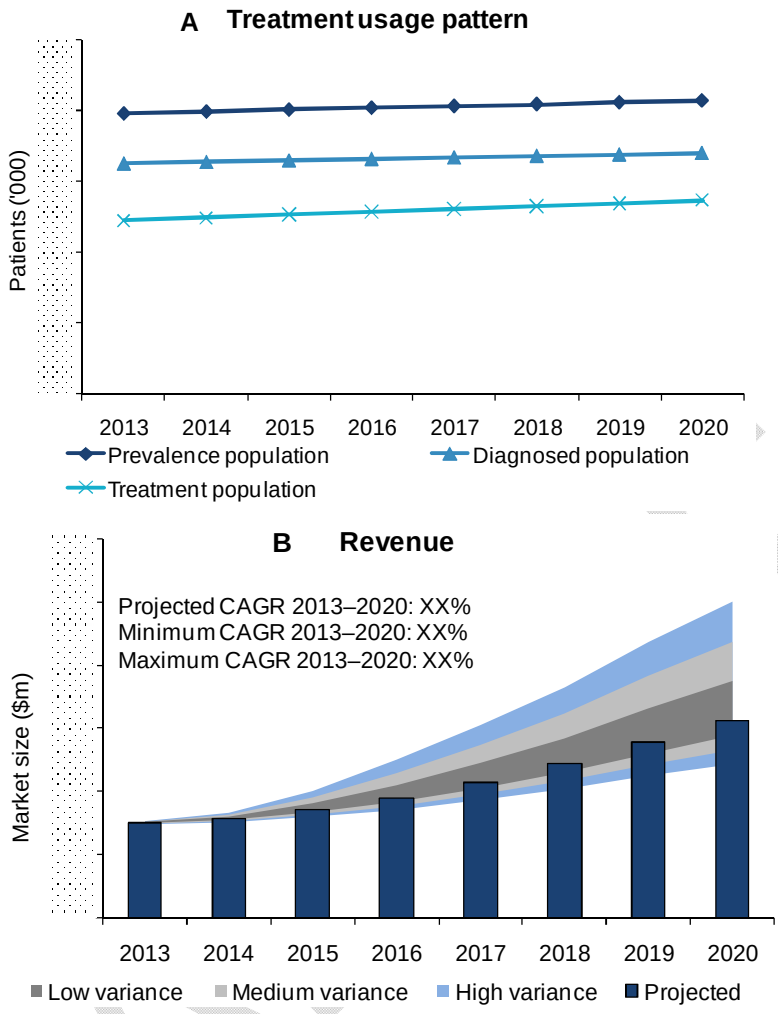
Source: GBI Research Proprietary Database, Pipeline Products

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

5.1.1 Global Market

During the 2015–2020 period, the global market size is expected to nearly double. This dramatic increase is mainly due to the launch of DCVax-L in 2015 in the US. Pipeline drugs Rindopepimut and Cotara, which will become available in 2017 and 2016, will drive growth in a lesser extent. The three market entrants will lead to an increase in the ACoT, which is expected to offset generic erosion as a result of the patent expiration of Temodar, resulting in the market growth between 2015 and 2020. In clinical trials, both DCVax-L and Rindopepimut demonstrated superior OS benefit than the standard of care alone, although DCVax-L appears to be a stronger product clinically. Due to their superior OS improvements in clinical trials, both DCVax-L and Rindopepimut are expected to command premium prices. Due to a lower improvement in median OS than DCVax-L and label restrictions, it is likely that Rindopepimut will cost less than DCVax-L. Both vaccines are expected to contribute to significant market growth once approved, providing they continue to exhibit remarkable OS benefit in Phase III trials.

Figure 18: Glioblastoma Multiforme, Global, Treatment Usage Patterns and Market Size, 2013–2020



Source: GBI Research

7 Appendix

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7.2 Market Definition

- The global HIV market is defined as the top eight markets: the US, the UK, Germany, France, Spain, Italy, Japan and Canada.
- The top five European countries are the UK, Germany, France, Spain and Italy.
- The prevalence population is the estimated number of people at any given time who have HIV-1 infection.

7.3 Abbreviations

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

2-HG: 2-Hydroxyglutarate

ACoT: Annual Cost of Treatment

AE: Adverse Event

AIM: Antigen isolated from Immunoselected Melanoma

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

CDK4 : Cyclin-Dependent Kinase 4
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: Dysembroplastic 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
EU: European Union
FDA: Food and Drug Administration
Flt3L: FMS-like tyrosine kinase-3 Lligand
G1: Gap 1
GBM: Glioblastoma Multiforme
GFR: Growth Factor Receptor
gp: glycoprotein
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
MAGE: Melanoma-Associated Antigen
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
OR:	Objective Response
OS:	Overall Survival
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
R&D:	Research and Development
RB:	Retinoblastoma
RoA:	Route of Administration
ROI:	Return On Investment
RT:	Radiotherapy
S:	Synthesis
SEER:	Surveillance, Epidemiology, and End Results
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
VEGF:	Vascular Endothelial Growth Factor
VEGFR:	Vascular Endothelial Growth Factor Receptor

WHO: World Health Organization

7.4 All Pipeline Products, by Phase

7.4.1 Discovery

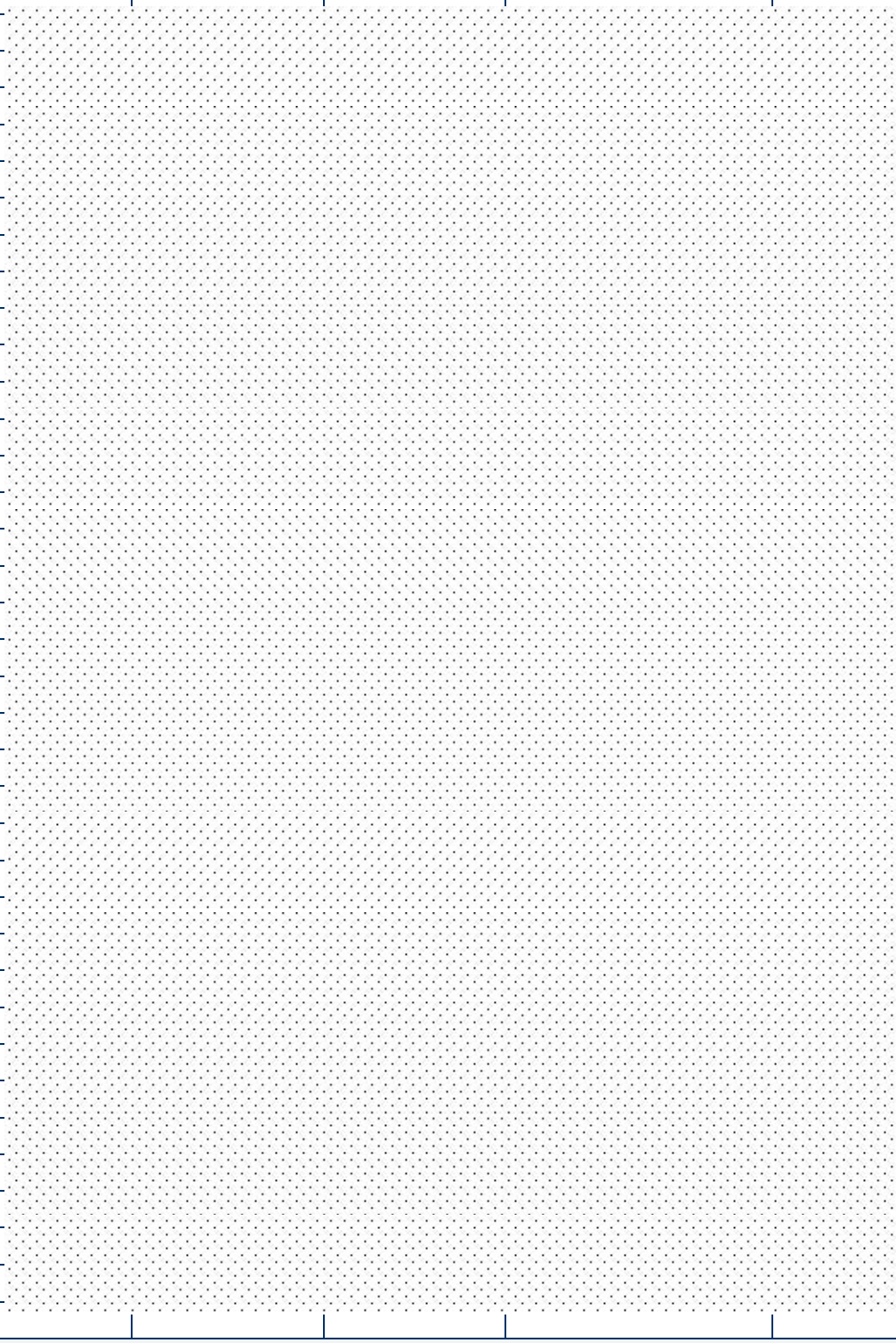
Table 5: Discovery

Product Name	Company	Molecule Type	Mechanism of Action	Stage of Development

Source: GBI Research

7.4.2 Preclinical

Table 6: 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 7: Phase I

Product Name	Company	Molecule Type	Mechanism of Action	Stage of Development

Source: GBI Research

7.4.4 Phase II

Table 8: Phase II

Product Name	Company	Molecule Type	Mechanism of Action	Stage of Development

Source: GBI Research

7.4.5 Phase III and Pre-registration

Table 9: 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 10: Undisclosed stage of development				
Product Name	Company	Molecule Type	Mechanism of Action	Stage of Development

Source: GBI Research

7.5 Tabular Forecast Data

7.5.1 Global

Table 11: Glioblastoma Multiforme, Global, Market Forecast, 2013-2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
Prevalence population (000')									
Treatment population (000')									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									

Source: GBI Research

7.5.2 US

Table 12: Glioblastoma Multiforme, US, Market Forecast, 2013-2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
Prevalence population (000')									
Treatment population (000')									
Maximum ACOT ($)									
Projected ACOT ($)									
Minimium ACOT ($)									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									

Source: GBI Research

7.5.3 Canada

Table 13: Glioblastoma Multiforme, Canada, Market Forecast, 2013-2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
Prevalence population (000')									
Treatment population (000')									
Maximum ACOT ($)									
Projected ACOT ($)									
Minimium ACOT ($)									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									
Source: GBI Research									

7.5.4 UK

Table 14: Glioblastoma Multiforme, UK, Market Forecast, 2013-2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
Prevalence population (000')									
Treatment population (000')									
Maximum ACOT ($)									
Projected ACOT ($)									
Minimium ACOT ($)									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									
Source: GBI Research									

7.5.5 France

Table 15: Glioblastoma Multiforme, France, Market Forecast, 2013-2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
Prevalence population (000')									
Treatment population (000')									
Maximum ACOT ($)									
Projected ACOT ($)									
Minimium ACOT ($)									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									
Source: GBI Research									

7.5.6 Germany

Table 16: Glioblastoma Multiforme, Germany, Market Forecast, 2013-2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
Prevalence population (000')									
Treatment population (000')									
Maximum ACOT ($)									
Projected ACOT ($)									
Minimium ACOT ($)									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									
Source: GBI Research									

7.5.7 Italy

Table 17: Glioblastoma Multiforme, Italy, Market Forecast, 2013-2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
Prevalence population (000')									
Treatment population (000')									
Maximum ACOT ($)									
Projected ACOT ($)									
Minimium ACOT ($)									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									

Source: GBI Research

7.5.8 Spain

Table 18: Glioblastoma Multiforme, Spain, Market Forecast, 2013-2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
Prevalence population (000')									
Treatment population (000')									
Maximum ACOT ($)									
Projected ACOT ($)									
Minimium ACOT ($)									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									

Source: GBI Research

7.5.9 Japan

Table 19: Glioblastoma Multiforme, Japan, Market Forecast, 2013-2020									
Year	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
Prevalence population (000')									
Treatment population (000')									
Maximum ACOT ($)									
Projected ACOT ($)									
Minimium ACOT ($)									
Maximum revenue ($m)									
Projected revenue ($m)									
Minimum revenue ($m)									
Source: GBI Research									

7.6 Research Methodology

GBI Research's dedicated research and analysis teams consist of experienced professionals with marketing, market research and consulting backgrounds in the pharmaceutical 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.

7.7 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).

7.7.1 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

7.8 Therapeutic Landscape

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

7.8.1 Forecasting

Our 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 each.

Initially, based on peer-reviewed literature, the disease prevalence is calculated and extrapolated with historic trends and any other relevant inputs which have been gathered from the literature. In the same way, the fraction of prevalent patients who 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 for us to divide the patient population based on the stage of their disease, into early- to late-stage cancers. Each drug may appear in more than one segment within this model.

The usage 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 which are expected to fulfill and unmet need and perform better than marketed products are typically given higher distributions than those which 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 again on its ability to fulfill unmet needs and compete effectively with marketed products, a percentage markup (or occasionally a mark-down) versus its 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 a 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 then 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.

7.9 Geographical Landscape

This GBI Research report covers the following major developed markets: the US, Canada, 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.

7.10 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 that 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.

7.11 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.

7.11.1 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 pharmaceutical companies, academics from research universities, and key opinion leaders from hospitals.

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

7.13 Disclaimer