

Type 2 Diabetes Therapeutics Market to 2019

A Shifting Treatment Algorithm and Intensified Competition Expected to Drive Growth by 2019



GBI Research Report Guidance

- The second chapter provides an introduction to type 2 diabetes, including symptoms, etiology, pathophysiology, methods of initial diagnosis and determination of disease severity, and treatment algorithms.
- The third chapter provides an overview of the type 2 diabetes market landscape, including product profiles for sixteen key marketed products.
- The fourth chapter analyses the type 2 diabetes pipeline, detailing, among other parameters, drug distribution by phase, molecule type and mechanism of action. The clinical trial landscape is also analyzed, with an emphasis on failure rates across phases in addition to trends in clinical trial size and duration.
- The market forecast to 2019 for eight major markets (US, UK, France, Germany, Italy, Spain, and Japan) is displayed in chapter five, and includes prevalence rates, annual cost of treatment and a market size forecast.
- A strategic consolidation analysis is provided in chapter six, including major co-development and licensing deals.

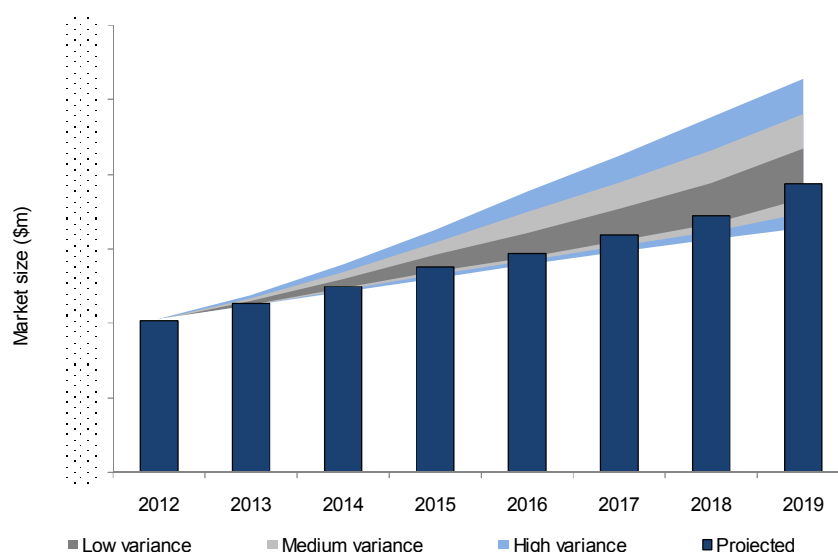
Executive Summary

A Highly Competitive and Growing Market

The market for type 2 diabetes contains a wide range of drugs that are used to treat patients at different points in the treatment algorithm. The market landscape is dense, with a number of drugs competing with one another for different market segments. Although the first-line therapy is usually metformin, a generic drug, it is often unable to bring the disease under control. The second-line therapy involves the use of other drugs in combination with metformin, and at this stage of the treatment algorithm competition between products is very strong. The established second-line therapy involves the use of sulfonylureas, a highly genericized class of drugs, in combination with metformin. The usage of this class of drug is likely to decline in future due to the recent approval of superior products and the anticipated approval of stronger products over the forecast period (2012–2019).

The market for type 2 diabetes is expected to grow from \$XX billion in 2012 to \$XX billion in 2019 at a Compound Annual Growth Rate (CAGR) of XX%. This strong growth is due to the anticipated approval of products in relatively novel treatment classes, such as GLP-1 agonists, DPP-4 inhibitors and SGLT-2 inhibitors. Should these expensive drug classes capture substantial market shares, this would be expected to result in an even more robust level of market growth.

Type 2 Diabetes Market, Market Size (\$m), 2012–2019



Source: GBI Research

1 Table of Contents

1	Table of Contents.....	5
1.1	List of Tables.....	9
1.2	List of Figures.....	10
2	Introduction.....	11
2.1	Epidemiology.....	11
2.2	Symptoms	11
2.3	Etiology	12
2.4	Pathophysiology	12
2.5	Co-morbidities and Complications.....	13
2.6	Classification.....	14
2.7	Prognosis.....	14
2.8	Diagnosis.....	15
2.9	Assessing Treatment Effectiveness	16
2.10	Treatment Algorithm	17
2.10.1	<i>The Role of Insulin in Type 2 Diabetes</i>	19
2.10.2	<i>Non-insulin Diabetic Drugs</i>	20
2.10.3	<i>Other Drugs</i>	22
3	Key Marketed Products.....	23
3.1	Metformin.....	23
3.2	DPP-4 Inhibitors.....	24
3.2.1	<i>Januvia (sitagliptin) – Merck & Co.</i>	24
3.2.2	<i>Tradjenta (linagliptin) – Boehringer Ingelheim</i>	25
3.2.3	<i>Onglyza (saxagliptin) – Bristol-Myers Squibb and AstraZeneca</i>	26
3.2.4	<i>Nesina (alogliptin) – Takeda</i>	26
3.2.5	<i>Galvus (vildagliptin) – Novartis</i>	27
3.2.6	<i>Tenelia (teneligliptin) – Daiichi Sankyo and Mitsubishi Tanabe</i>	28
3.3	GLP-1 Agonists.....	29
3.3.1	<i>Byetta and Bydureon (exenatide) – Bristol-Myers Squibb</i>	29
3.3.2	<i>Lyxumia (lixisenatide) – Sanofi</i>	30
3.3.3	<i>Victoza (liraglutide) – Novo Nordisk</i>	31
3.4	Sulfonylureas.....	32
3.4.1	<i>Glimepiride</i>	32
3.4.2	<i>Gliclazide</i>	32
3.5	Thiazolidinediones	33
3.5.1	<i>Actos (pioglitazone) – Takeda Pharmaceuticals Limited</i>	33
3.5.2	<i>Avandia (rosiglitazone) – GlaxoSmithKline</i>	34
3.6	Long-Acting Insulins	35
3.6.1	<i>Lantus (insulin glargine) – Sanofi</i>	35
3.6.2	<i>Levemir (insulin detemir) – Novo Nordisk</i>	36
3.6.3	<i>Tresiba and Ryzodeg (Insulin degludec) – Novo Nordisk</i>	37
3.7	SGLT-2 Inhibitors	38
3.7.1	<i>Forxiga (dapagliflozin) – Bristol-Myers Squibb</i>	38
3.7.2	<i>Invokana (canagliflozin) – Janssen</i>	38
3.8	Heat Map for Marketed Products.....	39
4	Pipeline for Type 2 Diabetes.....	42
4.1	Overall Pipeline.....	42
4.2	Therapeutic Classes	43
4.3	Rate of Attrition.....	45
4.3.1	<i>Failure Rate by Molecule Type</i>	46
4.3.2	<i>Failure Rate by Therapeutic Class</i>	47

4.4	Reasons for Failure of Developmental Programs	49
4.5	Clinical Trial Duration	49
4.5.1	Duration by Molecule Type	49
4.5.2	Duration by Therapeutic Class	50
4.6	Clinical Trial Size	52
4.6.1	Clinical Trial Size by Molecule Type	53
4.6.2	Clinical Trial Size by Therapeutic Class	54
4.7	Promising Drugs in the Pipeline	56
4.7.1	LY-2189265 (dulaglutide) – Eli Lilly	56
4.7.2	Albiglutide – GlaxoSmithKline	56
4.7.3	LC15-044 (gemigliptin) – LG Life Sciences	57
4.7.4	TAK-875 – Takeda	57
4.7.5	Ipragliflozin – Astellas Pharma	58
4.7.6	LX-4211 – Lexicon Pharmaceuticals	58
4.7.7	Imeglimin – Poxel SA	59
4.7.8	CCX-140-B – ChemoCentryx	59
4.7.9	Semaglutide – Novo Nordisk A/S	60
4.7.10	PC-DAC Exendin-4 – ConjuChem Biotechnologies	60
4.8	Heat Map for Pipeline Products	60
4.9	Conclusion	63
5	Market Forecast to 2019	65
5.1	Global Market	65
5.1.1	Treatment Usage Patterns	65
5.1.2	Market Size	66
5.2	US	67
5.2.1	Treatment Usage Patterns	67
5.2.2	Annual Cost of Therapy	68
5.2.3	Market Size	68
5.3	Top Five Countries of Europe	69
5.3.1	Treatment Usage Patterns	69
5.3.2	Annual Cost of Therapy	70
5.3.3	Market Size	71
5.4	Japan	72
5.4.1	Treatment Usage Patterns	72
5.4.2	Annual Cost of Therapy	73
5.4.3	Market Size	73
5.5	Drivers and Barriers	74
5.5.1	Drivers	74
5.5.2	Barriers	74
6	Deals and Strategic Consolidations	75
6.1	Licensing Deals	75
6.1.1	TransTech Pharma Enters into Licensing Agreement with Forest Laboratories	78
6.1.2	Xoma Enters into Licensing Agreement with Les Laboratoires Servier for Xoma 052	78
6.1.3	Zealand Pharma Enters into a Licensing and Collaboration Agreement with Boehringer Ingelheim	78
6.1.4	Exelixis Enters into Licensing Agreement with Bristol-Myers Squibb for XL475	79
6.1.5	Prosidion Limited Enters into a Licensing Agreement with Eli Lilly and Company	79
6.1.6	Metabolex Enters into Licensing Agreement with Sanofi	79
6.1.7	Wellstat Enters into a License Agreement with Sanofi	79
6.1.8	CureDM and Lankenau Institute Enter into a Licensing Agreement with Sanofi	79
6.1.9	Metabolex Enters into a Development and Licensing Agreement with Janssen Pharmaceuticals	80

6.1.10	Dainippon Sumitomo Pharma Enters into Licensing Agreement with Intercept Pharma for INT-747.....	80
6.1.11	Ipsen Enters into Licensing Agreement with F. Hoffmann-La Roche for BIM 51077	80
6.1.12	Glenmark Pharma Enters into Licensing Agreement with Merck KGaA	80
6.1.13	Euroscreen Enters into Licensing Agreement with Janssen Pharmaceuticals	81
6.1.14	Phenomix Enters into Licensing Agreement with Chiesi Farmaceutici	81
6.1.15	Otsuka Pharma Enters into Licensing Agreement with Kyowa Hakko Kirin for Saxagliptin.....	81
6.1.16	Nastech Pharma Enters into Licensing Agreement with Amylin Pharma	81
6.1.17	Emisphere Technologies Enters into a Licensing Agreement with Novo Nordisk	81
6.1.18	Array BioPharma Enters into a Licensing Agreement with Amgen	82
6.1.19	Theratechnologies Enters into a Licensing Agreement with OctoPlus	82
6.1.20	Diabetica Enters into a Licensing Agreement with Amylin	82
6.1.21	Celtic Therapeutics Enters into a Licensing Agreement with Bellus Health	82
6.1.22	Aradigm Enters into a Licensing Agreement with Novo Nordisk	83
6.1.23	Santarus Enters into a License Agreement with Shore Therapeutics	83
6.1.24	Depomed Enters into a Licensing Agreement with Boehringer Ingelheim.....	83
6.1.25	Depomed Enters into a Licensing Agreement with Merck.....	83
6.1.26	Depomed Enters into a Licensing Agreement with Teva	84
6.2	Co-development Deals	84
6.2.1	Eli Lilly Enters into a Co-development Agreement with Boehringer Ingelheim	85
6.2.2	AstraZeneca Enters into Co-development Agreement with Bristol-Myers Squibb	86
6.2.3	Metabolex Enters into a Co-development Agreement with Janssen Pharmaceuticals.....	86
6.2.4	Amylin Pharma Terminates Co-development Agreement with Eli Lilly for Exenatide	86
6.2.5	Isis Enters into a Collaboration Agreement with Janssen Pharmaceuticals.....	86
6.2.6	Neurocrine Biosciences Enters into a Collaboration Agreement with Boehringer Ingelheim.....	87
6.2.7	Intercept Pharma Enters into Co-development Agreement with Servier.....	87
6.2.8	Transition Therapeutics Enters into an Agreement with Eli Lilly.....	87
6.2.9	Ambrix Enters into a Co-Development Agreement with Bristol-Myers Squibb	87
6.2.10	Biocompatibles Enters into a Co-Development Agreement with AstraZeneca	88
7	Appendix	89
7.1	All Pipeline Drugs by Stage of Development.....	89
7.1.1	Discovery	89
7.1.2	Preclinical and IND-filed	90
7.1.3	Phase I.....	91
7.1.4	Phase II.....	92
7.1.5	Phase III and Pre-registration.....	93
7.1.6	Undisclosed.....	94
7.2	Market Forecasts to 2019	95
7.2.1	Global.....	95
7.2.2	US.....	95
7.2.3	UK	96
7.2.4	France	96
7.2.5	Germany.....	96
7.2.6	Italy.....	97
7.2.7	Spain	97
7.2.8	Japan.....	97
7.3	Market Definitions	98
7.4	Abbreviations	98
7.5	References for Heat Maps.....	101
7.6	References	103
7.7	Research Methodology	109
7.7.1	Coverage	109

7.7.2	Secondary Research	109
7.7.3	Primary Research	109
7.7.4	Therapeutic Landscape.....	110
7.7.5	Epidemiology-based Forecasting.....	110
7.7.6	Pipeline Analysis.....	112
7.7.7	Expert Panel Validation	113
7.7.8	Contact Us	113
8	Disclaimer.....	113

SAMPLE

1.1 List of Tables

Table 1:	The Relationship between HbA _{1c} and Mean Blood Glucose.....	15
Table 2:	Pipeline Drugs (Discovery).....	89
Table 3:	Pipeline Drugs (Preclinical and IND-filed)	90
Table 4:	Pipeline Drugs (Phase I).....	91
Table 5:	Pipeline Drugs (Phase II).....	92
Table 6:	Pipeline Drugs (Phase III).....	93
Table 7:	Pipeline Drugs (Undisclosed stage of development)	94
Table 8:	Type 2 Diabetes Market, Global, Market Forecast, 2012–2019.....	95
Table 9:	Type 2 Diabetes Market, US, Market Forecast, 2012–2019.....	95
Table 10:	Type 2 Diabetes Market, UK, Market Forecast, 2012–2019	96
Table 11:	Type 2 Diabetes Market, France, Market Forecast, 2012–2019.....	96
Table 12:	Type 2 Diabetes Market, Germany, Market Forecast, 2012–2019.....	96
Table 13:	Type 2 Diabetes Market, Italy, Market Forecast, 2012–2019	97
Table 14:	Type 2 Diabetes Market, Spain, Market Forecast, 2012–2019.....	97
Table 15:	Type 2 Diabetes Market, Japan, Market Forecast, 2012–2019	97
Table 16:	Type 2 Diabetes Market, Global, References for Heat Maps, 2013.....	101

1.2 List of Figures

Figure 1:	Type 2 Diabetes Market, Global, Composite Treatment Algorithm, 2013	18
Figure 2:	Type 2 Diabetes Market, Global, Sales of Januvia and Janumet (\$m), 2006–2012	24
Figure 3:	Type 2 Diabetes Market, Global, Sales of Onglyza (\$m), 2009–2012	26
Figure 4:	Type 2 Diabetes Market, Global, Sales of Galvus (\$m), 2007–2012	27
Figure 5:	Type 2 Diabetes Market, Global, Sales of Byetta (\$m), 2005–2010	29
Figure 6:	Type 2 Diabetes Market, Global, Sales of Victoza (\$m), 2009–2012	31
Figure 7:	Type 2 Diabetes Market, Global, Sales of Actos (\$m), 2003–2011	33
Figure 8:	Type 2 Diabetes Market, Global, Sales of Avandia (\$m), 1999–2012	34
Figure 9:	Type 2 Diabetes Market, Global, Sales of Lantus (\$m), 2003–2012	35
Figure 10:	Type 2 Diabetes Market, Global, Sales of Levemir (As reported by Novo Nordisk), 2008–2012	36
Figure 11:	Type 2 Diabetes Market, Global, Heat Map of Marketed Products, 2013	40
Figure 12:	Type 2 Diabetes Market, Global, Sales of Novel Products (\$m, Years after Approval), 1998–2012	41
Figure 13:	Type 2 Diabetes Pipeline Overview	42
Figure 14:	Type 2 Diabetes Market, Global, Therapeutic Classes	43
Figure 15:	Type 2 Diabetes Market, Global, Clinical Trial Failure Rate (%), 2006–2013	45
Figure 16:	Type 2 Diabetes Market, Global, Failure Rate by Molecule Type, 2006–2013	46
Figure 17:	Type 2 Diabetes Market, Global, Failure Rate by Therapeutic Class, 2006–2013	47
Figure 18:	Type 2 Diabetes Market, Global, Reasons for Clinical Trial Failure (%), 2006–2013	49
Figure 19:	Type 2 Diabetes Market, Global, Clinical Trial Duration, 2006–2013	50
Figure 20:	Type 2 Diabetes Market, Mean Clinical Trial Duration by Therapeutic Class, Global, 2006–2013	51
Figure 21:	Type 2 Diabetes Market, Mean and Median Clinical Trial Size, Global, 2006–2013	52
Figure 22:	Type 2 Diabetes Market, Clinical Trial Size by Molecule Type, Global, 2006–2013	53
Figure 23:	Type 2 Diabetes Market, Clinical Trial Size by Therapeutic Class, Global, 2006–2013	54
Figure 24:	Type 2 Diabetes Market, Heat Map of Pipeline Products	61
Figure 25:	Type 2 Diabetes Market, Global, Heat Map of Marketed Products, 2013	62
Figure 26:	Type 2 Diabetes Market, Global, Treatment Usage Patterns ('000), 2012–2019	65
Figure 27:	Type 2 Diabetes Market, Global, Market Size (\$m), 2012–2019	66
Figure 28:	Type 2 Diabetes Market, US, Treatment Usage Patterns, 2012–2019	67
Figure 29:	Type 2 Diabetes Market, Global, Market Size (\$m), 2012–2019	68
Figure 30:	Type 2 Diabetes Market, Top Five Countries of Europe, Treatment Usage Patterns, 2012–2019	69
Figure 31:	Type 2 Diabetes Market, Top Five Countries of Europe, Annual Cost of Therapy (\$), 2012–2019	70
Figure 32:	Type 2 Diabetes Market, Top Five Countries of Europe, Market Size (\$m), 2012–2019	71
Figure 33:	Type 2 Diabetes Market, Japan, Treatment Usage Patterns, 2012–2019	72
Figure 34:	Type 2 Diabetes Market, Japan, Market Size (\$m), 2012–2019	73
Figure 35:	Type 2 Diabetes Market, Global, Licensing Deals by Country, 2006–2013	75
Figure 36:	Type 2 Diabetes Market, Global, Licensing Deals, 2006–2013	76
Figure 37:	Type 2 Diabetes Market, Global, Licensing Deals, 2006–2013	77
Figure 38:	Type 2 Diabetes Market, Global, Licensing Deals by Country, 2006–2013	84
Figure 39:	Type 2 Diabetes Market, Global, Co-development Deals, 2006–2012	85
Figure 40:	GBI Research Market Forecasting Model	112

2 Introduction

Diabetes mellitus refers to a group of three metabolic diseases, categorized as type 1, type 2, and gestational diabetes, that are characterized by persistently high blood glucose concentrations. If not adequately controlled, type 2 diabetes leads to a number of complications including stroke, blindness, amputation, kidney failure and heart attack, which can ultimately be fatal and highlight how important it is to manage and treat this disease.

In type 1 diabetes, which can only be treated by injection of insulin or insulin analogs, the pancreas fails to produce enough insulin. This form usually has a childhood onset and is the result of auto-immune destruction of the pancreatic β cells (Eizirik et al., 2009).

2.1 Epidemiology

Type 2 diabetes is the most prevalent type of diabetes, accounting for XX% of all cases (Srinivasan et al., 2008). The prevalence in the population has been shown to increase with age, although incidence is increasing in younger sections of the population. It is currently estimated to be present in XX% of adults aged 20 years and older, and XX% of persons aged 65 and older (CDC, 2011).

2.2 Symptoms

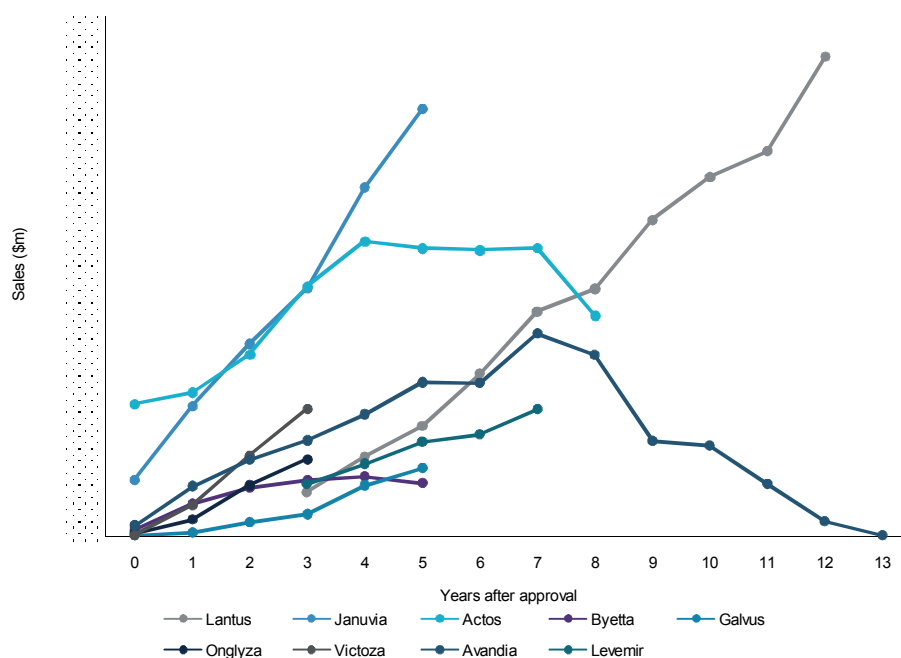
The most common symptoms of this disease are listed below:

- Regular thirst
- Frequent urination
- Blurred vision
- Irritability
- Tingling or numbness in the hands or feet
- Frequent skin, bladder or gum infections
- Slow wound healing
- Extreme, unexplained fatigue- particularly following meals

Although these symptoms are usually apparent in type 2 diabetes sufferers, the disease can also remain asymptomatic for months or even years. These symptoms can be controlled with appropriate disease management, but may grow increasingly worse as the disease progresses.

When sales following marketing approval are compared, Januvia emerges as the fastest-growing product following its launch. While Lantus generates the largest annual revenues, its growth was slower, and it took over a decade to reach the sales peak Januvia reached after five years.

Figure 12: Type 2 Diabetes Market, Global, Sales of Novel Products (\$m, Years after Approval), 1998–2012



Source: Company Annual Reports, 10-K and 20-F Filings, 1998–2012

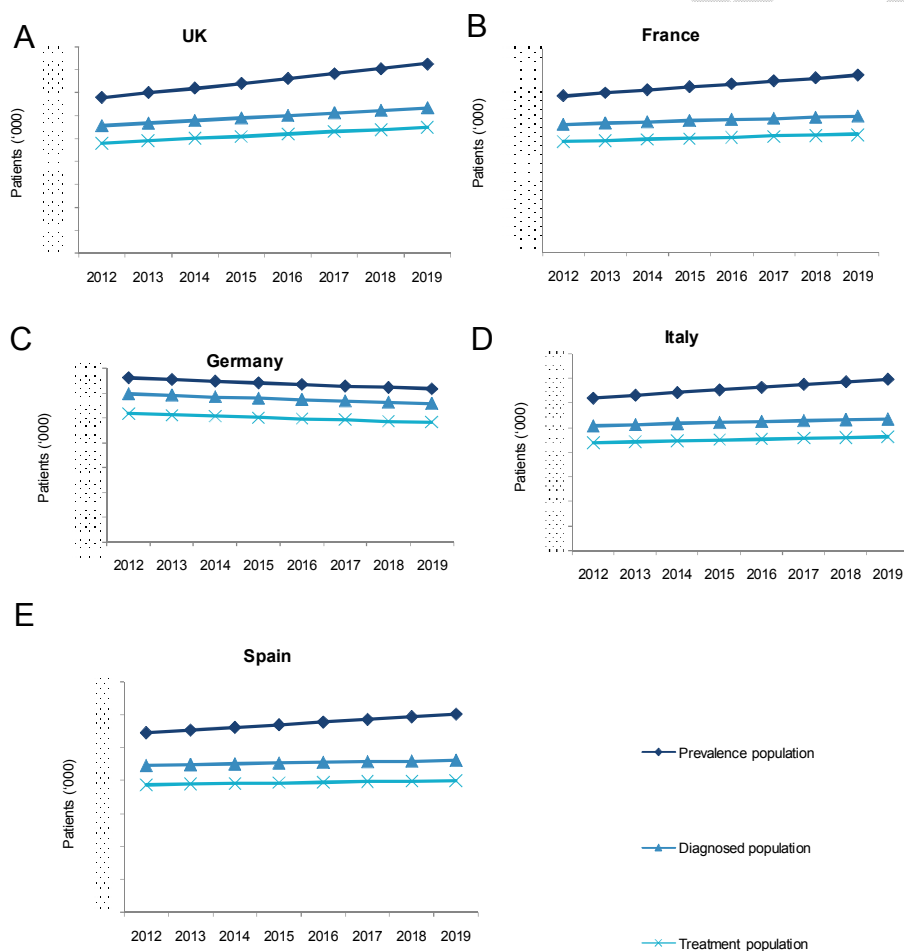
5.3 Top Five Countries of Europe

5.3.1 Treatment Usage Patterns

The general trend in the EU is one of increasing prevalence of type 2 diabetes, caused by worsening diets and increasingly sedentary lifestyles. Additionally, no significant changes are expected to the proportion of patients who are treated with pharmaceutical products.



Figure 30: Type 2 Diabetes Market, Top Five Countries of Europe, Treatment Usage Patterns, 2012–2019



Source: GBI Research

6 Deals and Strategic Consolidations

6.1 Licensing Deals

Licensing deals involving products for the treatment of Type 2 diabetes were mostly situated in North America, with the remainder being largely situated in Europe or the Asia-Pacific region, in terms of the licensor headquarters.



Figure 35: Type 2 Diabetes Market, Global, Licensing Deals by Country, 2006–2013

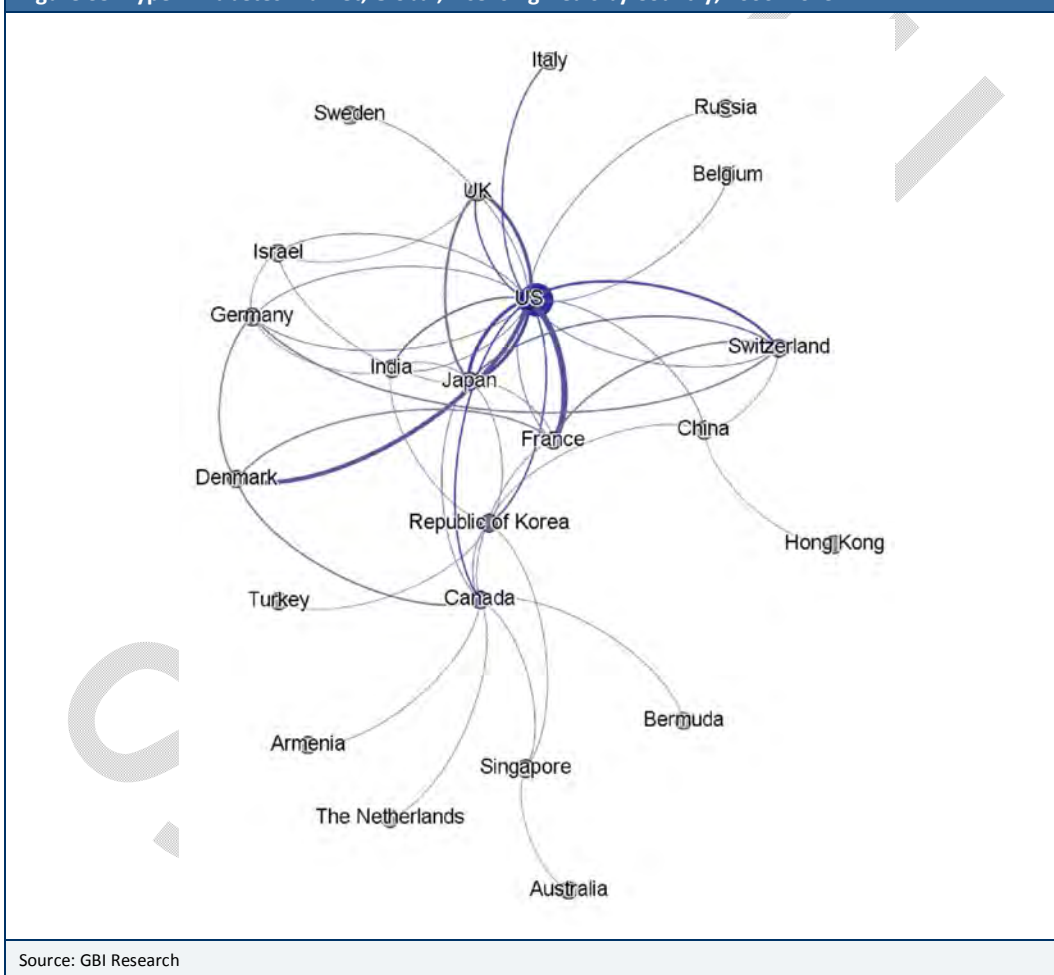
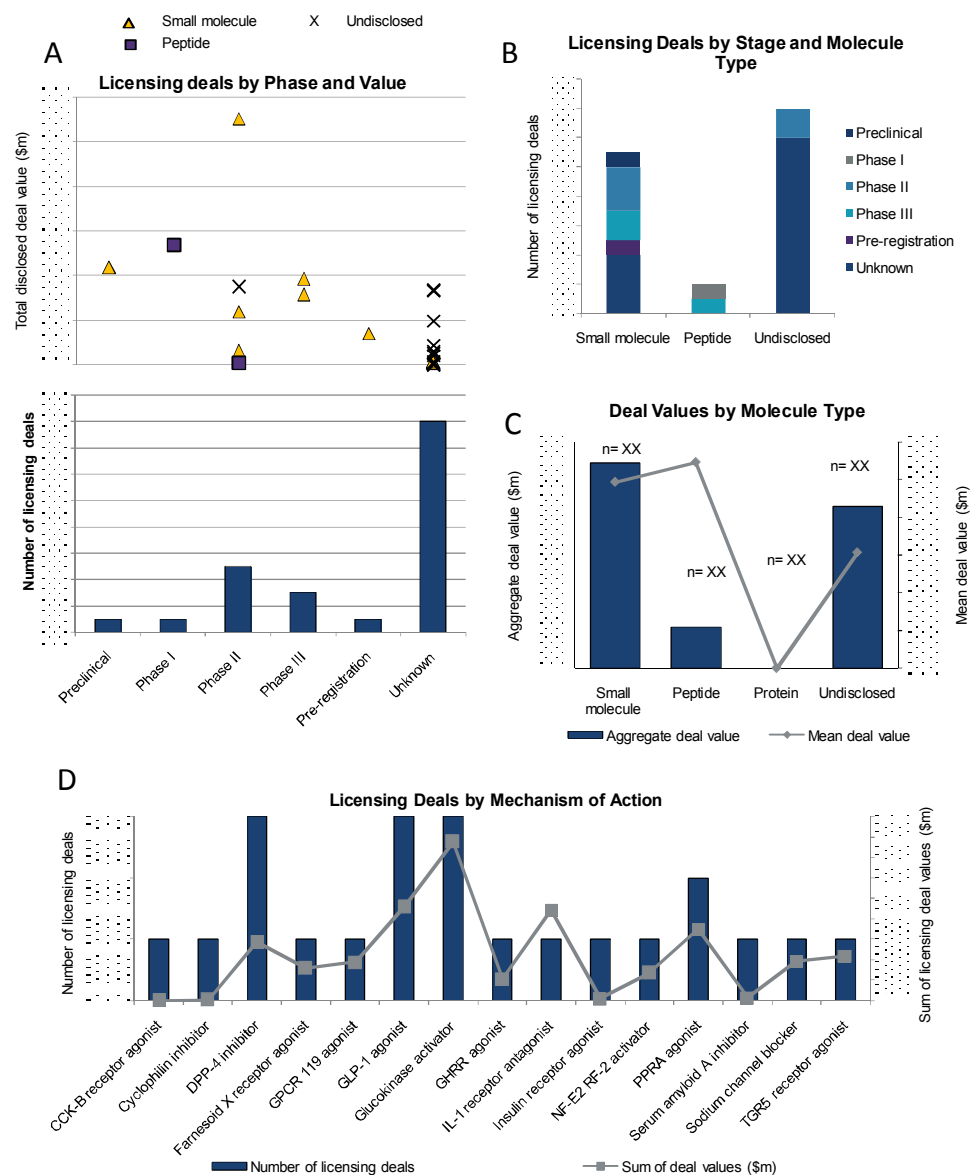


Figure 37: Type 2 Diabetes Market, Global, Licensing Deals, 2006–2013



Source: GBI Research

7.1.3 Phase I

Table 4: Pipeline Drugs (Phase I)

[illegible]

7.1.4 Phase II

Table 5: Pipeline Drugs (Phase II)

[illegible]

7.2 Market Forecasts to 2019

7.2.1 Global

Table 8: Type 2 Diabetes Market, Global, Market Forecast, 2012–2019									
Year	2012	2013	2014	2015	2016	2017	2018	2019	CAGR (%)
Prevalence population ('000)									
Diagnosed population ('000)									
Treatment population ('000)									
Maximum projected revenue (\$m)									
Projected revenue (\$m)									
Minimum projected revenue (\$m)									
Source: GBI Research									

7.2.2 US

Table 9: Type 2 Diabetes Market, US, Market Forecast, 2012–2019									
Year	2012	2013	2014	2015	2016	2017	2018	2019	CAGR (%)
Prevalence population ('000)									
Diagnosed population ('000)									
Treatment population ('000)									
ACoT (\$)									
Maximum projected revenue (\$m)									
projected revenue (\$m)									
Minimum projected revenue (\$m)									
Source: GBI Research									

7.2.3 UK

Table 10: Type 2 Diabetes Market, UK, Market Forecast, 2012–2019

Year	2012	2013	2014	2015	2016	2017	2018	2019	CAGR (%)
Prevalence population ('000)									
Diagnosed population ('000)									
Treatment population ('000)									
ACoT (\$)									
Maximum projected revenue (\$m)									
Projected revenue (\$m)									
Minimum projected revenue (\$m)									
Source: GBI Research									

7.2.4 France

Table 11: Type 2 Diabetes Market, France, Market Forecast, 2012–2019

Year	2012	2013	2014	2015	2016	2017	2018	2019	CAGR (%)
Prevalence population ('000)									
Diagnosed population ('000)									
Treatment population ('000)									
ACoT (\$)									
Maximum projected revenue (\$m)									
projected revenue (\$m)									
Minimum projected revenue (\$m)									
Source: GBI Research									

7.2.5 Germany

Table 12: Type 2 Diabetes Market, Germany, Market Forecast, 2012–2019

Year	2012	2013	2014	2015	2016	2017	2018	2019	CAGR (%)
Prevalence population ('000)									
Diagnosed population ('000)									
Treatment population ('000)									
ACoT (\$)									
Maximum projected revenue (\$m)									
Projected revenue (\$m)									
Minimum projected revenue (\$m)									
Source: GBI Research									

7.2.6 Italy

Table 13: Type 2 Diabetes Market, Italy, Market Forecast, 2012–2019

Year	2012	2013	2014	2015	2016	2017	2018	2019	CAGR (%)
Prevalence population ('000)									
Diagnosed population ('000)									
Treatment population ('000)									
ACoT (\$)									
Maximum projected revenue (\$m)									
Projected revenue (\$m)									
Minimum projected revenue (\$m)									
Source: GBI Research									

7.2.7 Spain

Table 14: Type 2 Diabetes Market, Spain, Market Forecast, 2012–2019

Year	2012	2013	2014	2015	2016	2017	2018	2019	CAGR (%)
Prevalence population ('000)									
Diagnosed population ('000)									
Treatment population ('000)									
ACoT (\$)									
Maximum projected revenue (\$m)									
Projected revenue (\$m)									
Minimum projected revenue (\$m)									
Source: GBI Research									

7.2.8 Japan

Table 15: Type 2 Diabetes Market, Japan, Market Forecast, 2012–2019

Year	2012	2013	2014	2015	2016	2017	2018	2019	CAGR (%)
Prevalence population ('000)									
Diagnosed population ('000)									
Treatment population ('000)									
ACoT (\$)									
Maximum projected revenue (\$m)									
Projected revenue (\$m)									
Minimum projected revenue (\$m)									
Source: GBI Research									

7.3 Market Definitions

The global type 2 diabetes therapeutics market covers type 2 diabetes in the top seven markets: 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 type 2 diabetes.
- The prescription rate is the percentage of the diabetes-suffering population that has been prescribed pharmacological therapeutics for type 2 diabetes.
- The prescription population refers to the number of people using pharmacological products for type 2 diabetes.

7.4 Abbreviations

- 11 β HSD: 11 β -Hydroxysteroid Dehydrogenase
- ACoT: Annual Cost of Therapy
- ADP: Adenosine Diphosphate
- AGTR2: Angiotensin II Receptor Type 2
- AMP: Adenosine Monophosphate
- AMPK: Adenosine Monophosphate-activated Protein Kinase
- AMPK beta: Adenosine Monophosphate-activated Protein Kinase beta
- ASBT: Apical Sodium-dependent Bile Acid Transporter
- AWARD: Assessment of Weekly Administration (A Clinical trial for Insulin Glargine)
- BMI: Body Mass Index
- CAGR: Compound Annual Growth Rate
- CB1: Cannabinoid receptor type 1
- CB2: Cannabinoid receptor type 2
- CCR2: C-C Chemokine Receptor type 2
- COX: Cyclooxygenase
- CPT 1: Carnitine Palmitoyltransferase I
- CRADA: Cooperative Research and Development Agreement
- CTA: Clinical Trial Authorization
- CMC: Chemistry, Manufacturing and Controls
- DGAT-1: Diglyceride Acyltransferase-1
- DPP-4: Dipeptidyl-Peptidase Four
- DRI: Dopamine Reuptake Inhibitor
- ECG: Electrocardiogram
- EGFR: Epidermal Growth Factor Receptor
- EMA: European Medicines Agency
- EU: European Union
- FBPase: Fructose-2,6-Biphosphatase

- Fc: Fragment crystallizable
- FDA: Food and Drug Administration
- FGFR: Fibroblast Growth Factor Receptor
- FGFR-1: Fibroblast Growth Factor Receptor 1
- FPG: Fasting Plasma Glucose
- FXR: Farnesoid X Receptor
- GABA: Gamma-Aminobutyric Acid
- GI: Gastrointestinal
- GIP: Gastric Inhibitory Polypeptide
- GIPR: Gastric Inhibitory Polypeptide Receptor
- GKA: Glucokinase Activator
- GLP-1: Glucagon-Like Peptide One
- GPBAR-1: G Protein-coupled Bile Acid Receptor 1
- GPCR: G-Protein Coupled Receptor
- GPR40: G Protein-Coupled Receptor 40
- GPR120: G-Protein Coupled Receptor 120
- GR: Glucocorticoid Receptor
- GSK3b: Glycogen Synthase Kinase 3b
- HbA_{1c}: Glycated Hemoglobin level
- IL-2: Interleukin 2
- IMC: Intramyocellular
- IND: Investigational New Drug
- IR: Immediate Release
- LPS: Lipopolysaccharide-binding Protein
- mAChR: muscarinic Acetylcholine Receptor
- MAOI: Monoamine Oxidase Inhibitor
- mg: milligrams
- mg/dl: milligrams per deciliter
- mmol/mol: millimoles per mole
- MR: Modified Release
- MTP: Microsomal Triglyceride Transfer Protein
- nAChR: nicotinic Acetylcholine Receptor
- NAFLD: Non-Alcoholic Fatty Liver Disease
- NF- κ B: Nuclear Factor Kappa-light-chain-enhancer of activated B cells
- NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases
- NIDDM: Non-Insulin Dependent Diabetes Mellitus
- NPH: Neutral Protamine Hagedorn

- NPYR2: Neuropeptide Y receptor Y2
- NRI: Norepinephrine Reuptake Inhibitor
- OCA: Obeticholic Acid
- OGTT: Oral Glucose Tolerance Test
- PARP: Poly-Adenosine diphosphate Ribose Polymerase
- PKC: Protein Kinase C
- PPAR: Peroxisome Proliferator-Activated Receptor
- PPAR-alpha: Peroxisome Proliferator-Activated Receptor alpha
- PPAR-beta/delta: Peroxisome Proliferator-Activated Receptor beta/delta
- PPAR-gamma: Peroxisome Proliferator-Activated Receptor gamma
- PPRE: Peroxisome Proliferator Responsive Elements
- PTP: Protein Tyrosine Phosphatase
- PTP1B: Protein Tyrosine Phosphatase 1B
- SCr: Serum Creatine
- SGLT: Sodium-dependent Glucose Co-transporter
- SGLT-1: Sodium-dependent Glucose Co-transporter 1
- SGLT-2: Sodium-dependent Glucose Co-transporter 2
- SIRT-1: Sirtuin-1
- SIR2: Silent Information Regulator 2 Protein
- STAT4: Signal Transducer and Activator of Transcription 4
- TNF- α : Tumor Necrosis Factor-alpha
- TPK1: Thiamin Pyrophosphokinase 1
- μ g: micrograms
- VEGF-B: Vascular Endothelial Growth Factor B
- WHO: World Health Organization

7.5 References for Heat Maps

Table 16: Type 2 Diabetes Market, Global, References for Heat Maps, 2013	
1	Grunberger G, et al. (2012). Mono-therapy with the once-weekly GLP-1 analogue dulaglutide for 12 weeks in patients with Type 2 diabetes: dose-dependent effects on glycaemic control in a randomized, double-blind, placebo-controlled study. <i>Diabetic Medicine</i> ; 29 (10): 1,464–5,491.
2a	GlaxoSmithKline Press Release (April 3, 2012). GSK receives further data from Phase III studies of albiglutide in type 2 diabetes.
2b	GlaxoSmithKline Press Release (July 11, 2012). GSK announces positive data from Harmony 8 and completion of clinical registration package for albiglutide in type 2 diabetes.
2c	Rosenstock, et al. (2009). Potential of Albiglutide, a long-acting GLP-1 receptor agonist, in type 2 diabetes. <i>Diabetes Care</i> ; 32 (10): 1,880–1,886
3	Yang S, et al. (2012). A multicentre, multinational, randomized, placebo-controlled, double-blind, phase 3 trial to evaluate the efficacy and safety of gemigliptin (LC15-0444) in patients with type 2 diabetes. <i>Diabetes, Obesity and Metabolism</i> ; 15 (5): 410–416.
4	Burant C, et al. (2012). TAK-875 versus placebo or glimepiride in type 2 diabetes mellitus: a phase 2, randomised, double-blind, placebo-controlled trial. <i>Lancet</i> ; 379 (9,824): 1,403–1,411
5	Fonseca V (2012). Efficacy and Safety of the Once-Daily GLP-1 Receptor Agonist Lixisenatide in Mono-therapy, A randomized, double-blind, placebo-controlled trial in patients with type 2 diabetes (GetGoal-Mono). <i>Diabetes Care</i> ; 35 (6): 1,225–1,231.
6	Wilding J, et al. (2013). Efficacy and safety of ipragliflozin in patients with type 2 diabetes inadequately controlled on metformin: a dose-finding study. <i>Diabetes, Obesity and Metabolism</i> ; 15 (5): 403–409.
7	Astellas Pharma Press Release (October 3, 2012). Astellas Announces Poster Presentation of SGLT2 Inhibitor (Ipragliflozin) Detailing Efficacy and Safety in Combination with Other Hypoglycemic Agents in Patients with Type 2 Diabetes at the European Association for the Study of Diabetes Meeting.
8	FDA (2013). Briefing Document for Invokana (canagliflozin) tablets. Food and Drug Administration. Available from: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM334550.pdf
9	Boehringer Ingelheim Press Release (June 9, 2012). Safety and Efficacy of Empagliflozin as Monotherapy or Add-On to Metformin in a 78-Week Open-Label Extension Study in Patients with Type 2 Diabetes.
10	Zambrowicz B, et al. (2012). LX4211, a Dual SG LT1/SG LT2 Inhibitor, Improved Glycemic Control in Patients With Type 2 Diabetes in a Randomized, Placebo-Controlled Trial. <i>Clinical Pharmacology & Therapeutics</i> ; 92 (2): 158–169.
11	Hanefeld M, et al. (2012). The CCX140-B Diabetes Study Group. Orally-Administered Chemokine Receptor CCR2 Antagonist CCX140-B in type 2 Diabetes: A Pilot Double-Blind, Randomized Clinical Trial. <i>Diabetes & Metabolism</i> ; 3 (9): (epub)
12	Nauck M, et al. (2012). The once-weekly human GLP-1 analogue Semaglutide provides significant reductions in HbA1c and body weight in patients with type 2 diabetes. Available from: http://novonordiskscientificmaterial2012.com/EASD/Presentations/2.pdf
13	Conjuchem, Press Release (March 26, 2007). PC-DAC(TM): Exendin-4 Phase I/II Multiple-Dose Study Preliminary Results Demonstrate Safety and Efficacy at Once-Weekly Dosing.
14	Hermansen K (2007). Efficacy and safety of the dipeptidyl peptidase-4 inhibitor, sitagliptin, in patients with type 2 diabetes mellitus inadequately controlled on glimepiride alone or on glimepiride and metformin. <i>Diabetes, Obesity and Metabolism</i> ; 9 (5): 733–745.
15	DeFronzo R, et al. (2011). The Efficacy and Safety of Saxagliptin When Added to Metformin Therapy in Patients With Inadequately Controlled Type 2 Diabetes With Metformin Alone. <i>Diabetes Care</i> ; 32: 1,649–1,655.
16	DeFronzo R, et al. (2008). Efficacy and Safety of the Dipeptidyl Peptidase-4 Inhibitor Alogliptin in Patients With Type 2 Diabetes and Inadequate Glycemic Control. <i>Diabetes Care</i> ; 31 (12): 2,315–2,317.
17	Takinsen M, et al. (2010). Safety and efficacy of linagliptin as add-on therapy to metformin in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study. <i>Diabetes, Obesity and Metabolism</i> ; 13 (1): 65–74.
18	Owens D, et al. (2011). Efficacy and safety of linagliptin in persons with Type 2 diabetes inadequately controlled by a combination of metformin and sulphonylurea: a 24-week randomized study. <i>Diabetic</i>

	Medicine; 28 (11): 1,352–1,361.
19	Filozof C, et al. (2010). Effect of vildagliptin as add-on therapy to a low-dose metformin. World Journal of Diabetes; 1 (1): 19–26.
20	Filozof C and Gautier J (2010). A comparison of efficacy and safety of vildagliptin and gliclazide in combination with metformin in patients with Type 2 diabetes inadequately controlled with metformin alone: a 52-week, randomized study. Diabetic Medicine; 27 (3): 318–326.
21	Guerzi B, et al. (2012). Continuous glucose profiles with vildagliptin versus sitagliptin in add-on to metformin: Results from the randomized Optima study. Diabetes and Metabolism; 38 (4): 359–366.
22	DeFronzo R, et al. (2005). Effects of exenatide (exendin-4) on glycemic control and weight over 30 weeks in metformin-treated patients with type 2 diabetes. Diabetes Care; 28 (5): 1,092–1,100.
23	Russell-Jones D, et al. (2011). Efficacy and Safety of Exenatide Once Weekly Versus Metformin, Pioglitazone, and Sitagliptin Used as Mono-therapy in Drug-Naive Patients With Type 2 Diabetes. Diabetes Care; 35 (2): 252–258.
24	Garber A, et al. (2009). Liraglutide versus glimepiride mono-therapy for type 2 diabetes (LEAD-3 Mono): a randomised, 52-week, Phase III, double-blind, parallel-treatment trial. Lancet; 373: 473–481.
25	Buse J, et al. (2013). Exenatide once weekly versus liraglutide once daily in patients with type 2 diabetes (DURATION-6): a randomised, open-label study. Lancet; 381 (9,861): 117–124.
26	Seino Y et al., (2012). Randomized, double-blind, placebo-controlled trial of the once-daily GLP-1 receptor agonist lixisenatide in Asian patients with type 2 diabetes insufficiently controlled on basal insulin with or without a sulfonylurea (GetGoal-L-Asia). Diabetes, Obesity and Metabolism; 14 (10): 910–917.
27	Strowig S, et al. (2002). Comparison of Insulin Mono-therapy and Combination Therapy with Insulin and Metformin or Insulin and Troglitazone in Type 2 Diabetes. Diabetes Care; 25 (10): 1,619–1,698.
28	Ferrannini E, et al. (2010). Dapagliflozin Mono-therapy in Type 2 Diabetic Patients With Inadequate Glycemic Control by Diet and Exercise. Diabetes Care; 33 (10): 2,217–2,224.
29	Wilding J, et al. (2012). Long-Term Efficacy of Dapagliflozin in Patients With Type 2 Diabetes Mellitus Receiving High Doses of Insulin. Annals of Internal Medicine; 156 (6): 405–415.
30	Aronoff S, et al. (2000). Pioglitazone hydrochloride monotherapy improves glycemic control in the treatment of patients with type 2 diabetes: a 6-month randomized placebo-controlled dose-response study. The Pioglitazone 001 Study Group. Diabetes Care; 23: 1,605–1,611.
31	Rosenstock J, et al. (2001). Basal Insulin Therapy in Type 2 Diabetes 28-week comparison of insulin glargine (HOE 901) and NPH insulin. Diabetes Care; 24 (4): 631–636.
Source: GBI Research	

7.6 References

- Adams C and Brantner I (2010). Spending on new drug development. *Health Economics*; 19 (2): 130–141.
- Ajjan A and Grant P (2008). The cardiovascular safety of rosiglitazone. *Expert Opinion on Drug Safety*; 7 (4): 367–376.
- American Diabetes Association (2004). Nephropathy in Diabetes. *Diabetes Care*; 27: s79–s83.
- American Diabetes Association (2007). Screening for Diabetes. *Diabetes Care*; 25: s21–s24.
- American Diabetes Association (2013). Guide to HbA1c. Available from: <http://www.diabetes.org/living-with-diabetes/treatment-and-care/blood-glucose-control/a1c/> [Accessed on April 22, 2013].
- Andersson C, et al. (2010). Metformin treatment is associated with a low risk of mortality in diabetic patients with heart failure: a retrospective nationwide cohort study. *Diabetologia*; 53: 2,546–2,553.
- Aronoff S, et al. (2000). Pioglitazone hydrochloride monotherapy improves glycemic control in the treatment of patients with type 2 diabetes: a 6-month randomized placebo-controlled dose-response study. The Pioglitazone 001 Study Group. *Diabetes Care*; 23 (11): 1,605–1,611.
- Ascher P, et al. (2006). Efficacy and safety of mono-therapy of sitagliptin compared with metformin in patients with type 2 diabetes. *Diabetes, Obesity and Metabolism*; 12 (3): 252–261.
- Bachmann O, et al. (2001). Effects of Intravenous and Dietary Lipid Challenge on Intramyocellular Lipid Content and the Relation with Insulin Sensitivity in Humans. *Diabetes*; 50: 2,579–2,584.
- Barthel A and Schmoll D (2003). Novel concepts in insulin regulation of hepatic gluconeogenesis. *American Journal of Physiology*; 285 (4): 685–692.
- Belcher G, et al. (2005). Safety and tolerability of pioglitazone, metformin, and gliclazide in the treatment of type 2 diabetes. *Diabetes Research and Clinical Practice*; 70: 53–62.
- Bunck M, et al. (2009). One-Year Treatment With Exenatide Improves β -Cell Function, Compared With Insulin Glargine, in Metformin-Treated Type 2 Diabetic Patients. *Diabetes Care*; 32 (5): 762–768.
- Burant C, et al. (2012). TAK-875 versus placebo or glimepiride in type 2 diabetes mellitus: a phase 2, randomised, double-blind, placebo-controlled trial. *Lancet*; 379: 1,403–1,411.
- Buse J, et al. (2013). Exenatide once weekly versus liraglutide once daily in patients with type 2 diabetes (DURATION-6): a randomised, open-label study. *Lancet*; 381 (9,861): 117–124.
- Caring for Diabetes Foundation (2006). Epidemiology, Screening, and Diagnosis of Diabetes in Spain. Available from: http://www.caringfordiabetes.com/Global/Spain/ESD_Diabetes.cfm [Accessed on May 1, 2013].
- Cefalu W, et al. (2013). Efficacy and safety of canagliflozin versus glimepiride in patients with type 2 diabetes inadequately controlled with metformin (CANTATA-SU): 52 week results from a randomised, double-blind, phase 3 non-inferiority trial. *Lancet*; 382 (9896): 941–950.
- Cowie C, et al. (2010). Prevalence of Diabetes and High Risk for Diabetes Using A1C Criteria in the U.S. Population in 1988–2006. *Diabetes Care*; 33 (3): 562–568.
- Crawford T, et al. (2009). Diabetic retinopathy and angiogenesis. *Current Diabetes Reviews*; 5 (1): 8–13.
- Cree-Green M, et al. (2012). Etiology of Insulin Resistance in youth with type 2 Diabetes. *Current Diabetes Reports*; 13: 81–88.
- Dall T, et al. (2009). Distinguishing the economic costs associated with type 1 and type 2 diabetes. *Population Health Management*; 12 (2): 103–110.
- DeFronzo R, et al. (1979). Glucose clamp technique: a method for quantifying Insulin secretion and resistance. *The American Journal of Physiology*; 237 (3): 214–223.

7.7 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.

7.7.1 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 pharmaceutical industry, updated on a daily basis.

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

7.7.2 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 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

7.7.3 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, 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

7.7.4 Therapeutic Landscape

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

The annual cost of therapy for each indication is arrived at by considering the cost of the drugs, 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 an epidemiology-based treatment flow model to forecast market size for therapeutic indications.

7.7.5 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). The diagnosis population is the population diagnosed with a disease expressed as a percentage of the population that is seeking treatment (treatment-seeking population). The prevalence of a disease (diseased population) is the percentage of the total population that suffers from a disease/condition.

Data on the 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 into the forecasting model to account for patient switching and compliance behavior.

To account for differences in the affordability of drugs for patients 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.

The 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 and the British National Formulary.

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.

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.

Diseased Population

The diseased population for any indication is the prevalence. The prevalence population for this report is taken from articles published in various journals including the Annals of the Rheumatic Diseases, British Medical Journal and Rheumatology.

Prescription Population

RA has multiple treatment options depending upon the stage of the disease and the previous effectiveness of other similar treatments. Options for the treatment of type 2 diabetes include lifestyle modification, non-biologic drug therapy and biologic drug therapy. 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. The prescription population proportion is taken from articles published in various journals including the Annals of the Rheumatic Diseases, British Medical Journal and Rheumatology.

7.7.5.1 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.

Forecasting Model for Therapeutic Areas

Figure 40: 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/M ed/N one)		-
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.

7.7.5.2 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. The maximum and minimum estimated market sizes are then provided by adjusting all variables expected to impact upon the market during the forecast period in order to provide the best- and worst-case scenarios.

7.7.6 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. A heat map, sourced from relevant clinical trials, is provided in order to compare these products to one another in addition to currently marketed products. 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. This list of pipeline molecules, in conjunction with a list of ongoing and completed clinical trials, is analyzed in this section, and a full breakdown of pipeline molecules and clinical trials by Phase, molecule type and molecular target is provided.

7.7.7 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.

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

8 Disclaimer

All Rights Reserved.

No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form by any means, electronic, mechanical, photocopying, recording or otherwise, without the prior permission of the publisher, GBI Research.