



DIABETES, METABOLIC  
SYNDROME AND  
CARDIOVASCULAR  
DISEASE  
*(SAMPLE COPY, NOT FOR RESALE)*

Reshaping Tomorrow's Diabetes Market

**TABLE OF CONTENTS**

1.	Overview	9	
1.1	Statement of Report	9	
1.2	About this Report	9	
1.3	Scope of the Report	10	
1.4	Methodology	11	
1.5	Executive Summary	12	
2.	Introduction	16	
2.1	Demographics of Diabetes	17	
2.1.1	Worldwide Diabetes	17	
2.1.2	U.S. Diabetes	20	
2.2	Economics of Diabetes	26	
2.2.1	Worldwide Costs of Diabetes	26	
2.2.2	Costs of Diabetes in the U.S.	27	
3.	Understanding Diabetes	32	
3.1	Pre-Diabetes Syndrome	33	
3.2	Metabolic Syndrome	33	
3.2.1	Prevalence of Metabolic Syndrome	36	
3.2.2	Management of Metabolic Syndrome	37	
3.2.3	The Debate Regarding Metabolic Syndrome	37	
3.3	Diabetes and Inflammation	38	
3.4	Diagnosis of Diabetes Mellitus	39	
3.5	Progression of Diabetes	39	
3.6	Obesity and Diabetes	39	
3.7	Complications and Co-Morbidities in Type 2 Diabetes	41	
3.7.1	Preventing Complications and Co-Morbidities in Diabetes	45	
4.	Pharmaceutical Industry and the Anti-Diabetes Drug Market	47	
4.1	The Worldwide Pharmaceutical Industry	47	
4.1.1	Pharmaceutical R&D Spending by Type, Growth Rate and Expenditure	47	
4.1.2	Global Pharmaceutical Market	49	
4.2	Overall Diabetes Drug Market Size and Growth	55	
4.2.2	Sales Forecast for the Global Anti-diabetes Drug Market	59	
4.3	Diabetic Medications Overview	61	
4.3.1	Recent Trends in Diabetic Drug Usage	63	
4.3.2	Market Influence Factors	65	
5.	Non-Insulin Anti-Diabetes Products and Market	67	
5.1	Non-Insulin Anti-Diabetes Drug Market Drivers and Trends	70	
5.1.1	Market Share and Forecast of Non-Insulin Anti-Diabetic Drugs	71	
5.1.2	Latest Additions to the U.S. Non-Insulin Diabetes Drug Market	73	
5.1.3	GLP-1 Market Revenue, Market Share, Key Players	73	
5.1.4	DPP-4 Inhibitor Market Revenue, Market Share and Key Players	74	
5.1.5	SGLT-2 Inhibitor Market Revenue, Market Share and Key Players	76	
5.2	Sulfonylureas	76	
5.3	Meglitinides	77	
5.4	Biguanides	78	
5.5	Thiazolidinediones (TZDs)	79	
5.6	$\alpha$ -Glucosidase Inhibitors	81	
5.7	Amylin Analog	82	
5.8	GLP-1 (Glucagon-like Peptide) Analogs and Agonists/Incretin Mimetics	82	
5.8.1	Byetta (Exenatide)	83	
5.8.2	Bydureon (Exenatide LAR)	84	

5.8.3	Victoza (Liraglutide)	84	
5.8.4	Tanzeum (Albiglutide)	84	
5.8.5	Trulicity (Dulaglutide)	85	
5.9	DPP-IV Inhibitors	85	
5.9.1	Januvia (Sitagliptin)	87	
5.9.2	Onglyza (Saxagliptin)	87	
5.9.3	Tradjenta (Linagliptin)	87	
5.9.4	Galvus (Vildagliptin)	87	
5.9.5	Nesina (Alogliptin)	88	
5.9.6	Marizev (Omarigliptin)	88	
5.10	SGLT-2 Inhibitors	88	
5.10.1	Invokana (Canagliflozin)	89	
5.10.2	Farxiga (Dapagliflozin)	89	
5.10.3	Jardiance (Empagliflozin)	90	
5.10.4	Suglat (Ipragliflozin)	91	
5.10.5	Lusefi (Luseogliflozin)	91	
5.11	Fixed Dose Combination Therapies on the Market	91	
5.12	Antidiabetic Drug Options for Youth with Recent-Onset Type 2 Diabetes Scarce		93
5.13	Comparisons of the Anti-Diabetes Drugs	93	
5.14	Non-Insulin Anti-Diabetes Products in the Pipeline	94	
5.14.1	Novel GLP-1 Agonists and Analogs	94	
5.14.2	Novel DPP-IV Inhibitors	97	
5.14.3	Sodium Glucose Cotransporter 2 (SGLT-2) Inhibitors		99
5.15	Emerging Anti-Diabetes Targets and Drugs in the Pipeline		100
5.16	Novel Approaches to Finding New Drug Targets	104	
6.	Insulin Markets	105	
6.1	Major Players and Market Share in the Insulin Market		107
6.2	Patent Expirations	109	
6.3	Insulin Biosimilars	109	
6.3.1	Regulatory Avenues for Biosimilar Approval		110
6.3.2	Insulin Biosimilars on the Market	110	
6.3.2.1	Abasaglar (formerly Abasria) and Basaglar		110
6.3.2.2	Other Biosimilars	110	
6.3.2.3	Key Issues for Insulin Biosimilars	110	
6.4	Innovation Strategies	111	
6.5	Overview of Insulin Therapeutics on the Market	111	
6.5.1	Recommendations for Insulin Initiation and Administration		113
6.6	Short-Acting Human Insulin Market	115	
6.7	Rapid-Acting Insulin Analog Market	117	
6.7.1	Ultra Fast-Acting Insulins in Development	118	
6.8	Intermediate-Acting Insulin Market	120	
6.9	Long-Acting Insulin Market	121	
6.9.1	Lantus-Sanofi's Insulin Blockbuster	123	
6.9.2	Toujeo-Sanofi's Bid to Maintain Insulin Market Share		124
6.9.3	Levemir Market	124	
6.9.4	Tresiba Approved for the U.S. Market	125	
6.9.5	Lantus Biosimilars	126	
6.9.5.1	Abasaglar (formerly Abasria) and Basaglar	126	
6.9.5.2	Other Biosimilars	126	
6.10	Insulin Mixtures	127	
6.11	Pipeline Insulins in Development	128	
6.11.1	BIOD-531 (Biodel)	128	
6.11.2	Xultophy (Novo Nordisk)		128
6.11.3	LixiLan (Sanofi)	128	
6.11.4	rHUPH20 and Insulin (Halozyme)		128

6.11.5	FIAsp (Novo Nordisk)	129	
6.11.6	BIOD-238, BIOD-250, and BIOD-351 (Biodel)	129	
6.11.7	InsuPatch and InsuPad (Insuline Medical)	129	
6.11.8	MK-1293	130	
6.11.9	Smart Insulins	130	
6.12	Non-Invasive Insulin Delivery	130	
6.12.1	Inhaled Insulin	131	
6.12.1.1	Afrezza	132	
6.12.1.2	Dance Pharmaceuticals and Aerogen (Dance-501)	133	
6.12.1.3	A Chronicle of Inhaled Insulins	134	
6.12.2	Oral Insulin	135	
6.12.3	Transdermal Insulin	138	
6.13	Barriers for Non-Injected Insulin	139	
6.14	Patient Potential for Non-Injected Insulin	140	
6.15	Insulin Delivery Devices	140	
6.15.1	Insulin Pens	142	
6.15.2	Injections Aids	145	
6.15.2.1	Automatic Injectors	146	
6.15.2.2	Syringe Magnifiers	147	
6.15.2.3	Injection Ports	147	
6.15.3	Insulin Jet Injectors	148	
6.15.4	Insulin Pumps	148	
6.15.4.1	External Insulin Pumps	149	
6.15.4.2	Animas OneTouch Ping	152	
6.15.4.3	Animas Vibe	153	
6.15.4.4	Accu-Chek Combo Insulin Pump System (Roche)	153	
6.15.4.5	MiniMed Paradigm Real-Time Revel (Medtronic)	154	
6.15.4.6	MiniMed 530G with Enlite (Medtronic)	154	
6.15.4.7	Insulet Omnipod	154	
6.15.4.8	DANA IIS (Sooil)	155	
6.15.4.9	t:flex (Tandem Diabetes Care)	155	
6.15.4.10	t:slim (Tandem Diabetes Care)	155	
6.15.4.11	Snap (Asante)	155	
6.15.5	Insulin Infusion Sets	156	
6.15.6	Insulin Patch Pumps in Development or Only Available Outside the U.S.	157	
6.15.7	Implantable Insulin Pumps	159	
6.15.8	Insulin Pump Market Share	160	
6.15.9	Drivers of Demand for Pumps	161	
6.16	Market Forecasts for Insulin Administration Technologies	161	
7.	Emerging Anti-Diabetes Technologies and Products	162	
7.1	Projections for the Anti-Diabetes Drug Market	162	
7.2	Artificial Pancreas	166	
7.2.1	MiniMed 530G System	167	
7.2.2	Animas Vibe System	167	
7.2.3	Next Generation Medtronic Artificial Pancreas Systems (MiniMed 640G)	167	
7.2.4	FDA's Artificial Pancreas Guidance Document	168	
7.3	Insulin-Producing Cells	168	
7.3.1	Gene Therapy	169	
7.3.2	Cell Therapy Companies for Diabetes	170	
7.3.2.1	ViaCyte (formerly Novocell, Inc.)	170	
7.3.2.2	Sernova	170	
7.3.2.3	Semma Therapeutics	171	
7.4	Pre-Mixed Glucagon for Self-Treating Hypoglycemia	171	
7.5	Anti-Obesity Drugs to Prevent or Delay Development of Type 2 Diabetes	171	
7.5.1	Xenical (Roche)	171	

7.5.2	Qsymia (Vivus)	171	
7.5.3	Belviq (Arena Pharmaceuticals)	171	
7.5.4	Contrave (Orexigen Therapeutics)	172	
7.5.5	Saxenda	172	
7.5.6	Anti-Obesity Drugs in Development	172	
7.6	Insulin and Anti-Diabetes Drug Combinations	172	
7.6.1	Xultophy (Novo Nordisk)	172	
7.6.2	LixiLan (Sanofi)	173	
8.	Market Trends, Challenges and Strategic Options	174	
8.1	Overview	174	
8.2	Diabetes Drug Market Trends	174	
8.2.1	Overview	174	
8.2.2	Emergence of Therapeutics with Improved Administration Characteristics	174	
8.2.2.1	Barriers to the Initiation of Insulin Therapy in Type 2 Diabetics	176	
8.2.3	Increasing Prevalence of Obesity	176	
8.2.4	Consumer Preference Drives Product Development in Invasive Technology Segment	177	
8.3	Diabetes Mellitus Market Challenges	177	
8.3.1	Overview	177	
8.3.2	Patent Expirations	178	
8.3.3	Market Prospects of Inhalable Insulin	178	
8.4	Strategic Options	179	
8.4.1	Developing Countries are Key Markets for Growth	180	
8.4.2	Consumer-Driven Marketing Campaigns	181	
8.4.3	Strategies for Successful New Product Launches	181	
8.4.4	Collaborations and Strategic Alliances	182	
8.5	FDA Guidelines for Developing Anti-Diabetic Drugs	183	
8.6	Recent Industry Activity	183	
9.	Company Profiles	187	
9.1	A. Menarini	187	
9.2	Abbott Laboratories	187	
9.3	Abbvie	191	
9.4	Amgen	191	
9.5	Amylin Pharmaceuticals (bought by Bristol-Myers Squibb)	192	
9.6	Animas (part of Johnson & Johnson)	192	
9.7	Asante	192	
9.8	Astellas Pharma, Inc.	192	
9.9	AstraZeneca PLC	193	
9.10	Bayer	194	
9.11	Becton, Dickinson and Company	196	
9.12	Biocon	197	
9.13	Biodel	198	
9.14	BodyMedia	198	
9.15	Boehringer Ingelheim	198	
9.16	Bristol Myers Squibb	199	
9.17	Cellnovo	199	
9.18	CeQur	199	
9.19	ConjuChem	199	
9.20	Daiichi Sankyo	200	
9.21	Dance Biopharm	200	
9.22	Debiotech	200	
9.23	DexCom	200	
9.24	Echo Therapeutics, Inc.	202	
9.25	Eli Lilly	203	
9.26	FIFTY50 Medical, Inc.	204	

9.27	Flamel Technologies	204	
9.28	Generex Biotechnology Corporation		204
9.29	GlaxoSmithKline PLC	205	
9.30	Halozyme Therapeutics	205	
9.31	Insulet	205	
9.32	Insuline Medical Ltd.	206	
9.33	Intarcia Therapeutics, Inc.		206
9.34	Janssen Research & Development		206
9.35	Johnson & Johnson	207	
9.36	Kowa Pharmaceuticals	208	
9.37	Lexicon Pharmaceuticals	208	
9.38	MannKind Corporation	209	
9.39	Medipacs	209	
9.40	Medtronic	209	
9.41	Merck & Company, Inc.	210	
9.42	Mitsubishi Tanabe Pharma Corporation		211
9.43	Novartis	211	
9.44	Novo Nordisk	211	
9.45	Oramed Pharmaceuticals	212	
9.46	Orexigen Therapeutics, Inc.		212
9.47	Owen Mumford	213	
9.48	PhaseBio Pharmaceuticals		213
9.49	Pfizer	213	
9.50	Promethion Pharma	214	
9.51	Roche Diagnostics	214	
9.52	Sanofi	216	
9.53	Sernova	217	
9.54	Smiths Medical		217
9.55	SOOIL Development	218	
9.56	Taisho Pharmaceuticals	218	
9.57	Takeda	218	
9.58	Tandem Diabetes Care, Inc.		218
9.59	Theracos, Inc.	219	
9.60	Transdermal Specialties, Inc.		219
9.61	Valeritas	219	
9.62	ViaCyte, Inc. (formerly Novocell)		219
9.63	Vivus, Inc.	220	
9.64	vTv Therapeutics (formerly TransTech Pharma)		220
9.65	Ypsomed Holding	220	
9.66	Zealand Pharma	220	

## INDEX OF FIGURES

Figure 2.1:	Worldwide Diabetes Cases, 2015 and 2035	17
Figure 2.2:	Worldwide Prevalence of Diabetes (%) in Adults (20-79 Years), 2013	18
Figure 2.3:	Annual Number of New Cases of Diagnosed Diabetes Among U.S. Adults Aged 18-79 Years, 1980-2012	21
Figure 2.4:	New Adult Cases of Diabetes Diagnosed in the U.S., 2012	22
Figure 2.5:	Diagnosed and Undiagnosed Diabetes by Age in the U.S., 2013	22
Figure 2.6:	Percentage of U.S. Adults Diagnosed Diabetes by State, 2013	24
Figure 2.7:	Number of Deaths from Diabetes by Age in the U.S., 2013	25
Figure 2.8:	Number of Diabetes Deaths by Race and Sex in the U.S., 2013	25
Figure 2.9:	Mean Diabetes Healthcare-Related Expenditures Per Adult (20-79 Years) with Diabetes (USD), 2013	26
Figure 2.10:	How Diabetes Dollars are Spent in the U.S.	28

Figure 3.1: Maintenance of Normal Blood Sugar Levels	32
Figure 3.2: Prevalence of Self-Reported Obesity (BMI $\geq$ 30) Among U.S. Adults, 2013	40
Figure 3.3: Prevalence of Obesity Among Adults in the U.S., 2012	40
Figure 3.4: Percentage of Obese Children and Adolescents in the U.S., 1999-2012	41
Figure 4.1: Sales Forecast for the Global Diabetes Drug Market, 2012-2019	60
Figure 4.2: Sales Forecast for the U.S. Diabetes Drug Market, 2012-2019	60
Figure 4.3: Percentage of U.S. Diabetics Taking Medications, 2010-2012	62
Figure 4.4: U.S. Non-Insulin Anti-Diabetic Drug Market by Volume, 2014	64
Figure 5.1: Global Non-Insulin Anti-Diabetes Prescriptions by Drug Class, 2014	71
Figure 5.2: Global Non-Insulin Anti-Diabetes Sales by Drug Class, 2014	71
Figure 5.3: GLP-1 Market Share by Brand, 2014	73
Figure 5.4: GLP-1 Market Share of Key Players, 2014	74
Figure 5.5: DPP-4 Inhibitor Market Share by Brand, 2014	75
Figure 5.6: DPP-4 Inhibitor Market Share of Key Players, 2014	76
Figure 5.7: Overview of GLP-1 and Blood Glucose	82
Figure 5.8: Overview of DPP-4 Inhibitors and Blood Glucose	86
Figure 5.9: SGLT-2 Inhibitor Mechanism of Action	89
Figure 6.1: Worldwide Insulin Market Share (Value), 2014	108
Figure 6.2: U.S. Insulin Market Share (Value), 2014	108
Figure 6.3: Short-Acting Human Insulin Worldwide Market Share by Company, 2014	116
Figure 6.4: Rapid-Acting Insulin Worldwide Market Share by Company, 2014	118
Figure 6.5: Intermediate-Acting Human Insulin Worldwide Market Share by Company, 2014	121
Figure 6.6: Long-Acting Insulin Worldwide Market Share by Company, 2014	122
Figure 6.7: Market Share of Basal Insulins in Emerging Markets, 2014	123
Figure 6.8: Global Sales of Lantus, 2005-2014	124
Figure 6.9: Global Sales of Levemir, 2011-2014	125
Figure 6.10: Insulin Pump Market Share, 2014	160

## INDEX OF TABLES

Table 2.1: Regional Estimates of the Number of Diabetes (20-79 Years) in Millions, 2015 and 2035	18
Table 2.2: Top Ten Countries with the Largest Estimated Number of Diabetics (20 to 79 Years Age Group), 2015 and 2035	19
Table 2.3: Worldwide Undiagnosed Diabetes in Adults (20-79 Years) by Region and Income Group, 2013	19
Table 2.4: Countries with the Largest Number of Deaths Attributable to Diabetes, 2013	20
Table 2.5: U.S. Population of Diagnosed Diabetics Aged 20-79 Years, 2013	22
Table 2.6: Percentage of U.S. Adults with Diagnosed Diabetes by State, 2010	23
Table 2.7: Cost of Diagnosed Diabetes in the U.S.	27
Table 2.8: Annual Cost of Care of United Healthcare Adult Members with Diabetes	29
Table 2.9: Healthcare Utilization by Diabetic Patients	29
Table 3.1: International Diabetes Federation (IDF) Diagnostic Criteria for Metabolic Syndrome	34
Table 3.2: Ethnic Specific Values for Waist Circumference in IDF's Metabolic Syndrome Criteria	34
Table 3.3: American Heart Association and National Heart, Lung, and Blood Institute (AHA/NHLBI) Diagnostic Criteria for Metabolic Syndrome	34
Table 3.4: Additional Metabolic Criteria for Research	36
Table 3.5: Ten Leading Diagnoses for Co-Morbid Chronic Diseases in the U.S.	42
Table 3.6: Prevalence of Complications Among Patients with Diabetes	43
Table 3.7: Odds Ratio of Progression to Complications Associated with Type 2 Diabetes	44
Table 3.8: Novel Risk Factors and Possible Mechanisms of the Excess Risk of Coronary Heart Disease in Type 2 Diabetes Mellitus	44
Table 3.9: Major Causes of End-Stage Renal Disease	44
Table 3.10: Clinical Recommendations for Adults with Diabetes	45
Table 3.11: Laboratory Assessment of Diabetic Vascular Disease	45
Table 3.12: Average Years Gained Free of Diabetes-Related Disease with Intensive Management	46
Table 4.1: Global R&D Spending in the Pharmaceutical Industry, 2010-2014	47

Table 4.2: Pharmaceutical Companies Ranked by Total R&D Expenditures, 2014	47
Table 4.3: Leading Therapy Classes for R&D, 2014	48
Table 4.4: Leading Disease Indications for R&D, 2014	49
Table 4.5: Cost of Clinical Trial Protocol Procedure by Endpoint Type, 2012	49
Table 4.6: Global Pharmaceutical Sales by Region and Country, 2013 and 2018 (estimated) and CAGR 2009-2013 and 2014-2018 (estimated)	50
Table 4.7: World Pharmaceutical Sales Share by Region, 2013	51
Table 4.8: Leading Ten Therapeutic Classes by Global Sales, 2010-2014	52
Table 4.9: Estimated Leading Therapy Classes by Global Sales in the Developed Market, 2018	52
Table 4.10: Estimated Leading Therapy Classes by Global Sales in the Pharming Market, 2018	53
Table 4.11: Leading Therapeutic Classes by U.S. Sales, 2010-2014	53
Table 4.12: Top Selling Drugs Worldwide by Sales, 2014	53
Table 4.13: Top Selling Drugs in the U.S. by Sales, 2014	54
Table 4.14: Top Ten Global Pharmaceutical Companies by Global Sales, 2014	54
Table 4.15: Worldwide Anti-Diabetes (Insulin and Non-Insulin) Drug Market, 2012-2019	55
Table 4.16: U.S. Anti-Diabetes (Insulin and Non-Insulin) Drug Market, 2012-2019	55
Table 4.17: Anti-Diabetic Therapy Markets, 2014	56
Table 4.18: Top Ten Branded Anti-Diabetics by Sales Worldwide, 2014	59
Table 4.19: Top Ten Branded Anti-Diabetics by Monthly Prescriptions Worldwide, 2014	59
Table 4.20: American College of Physicians 2012 Practical Guideline for the Use of Anti-Diabetes Drugs for Type 2 Diabetes	61
Table 4.21: Summary of Glucose-Lowering Interventions as Monotherapy	62
Table 5.1: Classes of Non-Insulin Hypoglycemic Agents	68
Table 5.2: Branded Non-Insulin Hypoglycemic Drugs Used to Treat Type 2 Diabetes in the U.S., 2014	69
Table 5.3: Relative Efficacy of Diabetes Drugs	70
Table 5.4: Worldwide Non-Insulin Anti-Diabetes Drug Market, 2012-2019	72
Table 5.5: U.S. Non-Insulin Anti-Diabetes Drug Market, 2012-2019	72
Table 5.6: Diabetes Drugs Approved for U.S. Market, 2014 and 2015	73
Table 5.7: GLP-1 Drug Revenues in 2014	74
Table 5.8: DPP-4 Inhibitor Revenues in 2014	75
Table 5.9: SGLT-2 Inhibitor Revenues in 2014	76
Table 5.10: Fixed-Dose Oral Anti-Diabetes Drug Combinations	92
Table 5.11: GLP-1 Agonist Pipeline: Selected Drugs in Development	95
Table 5.12: DPP-IV Inhibitor Pipeline: Selected Drugs in Development	98
Table 5.13: SGLT-2 Inhibitor Pipeline: Selected Drugs in Development	99
Table 5.14: Fixed-Dose Combination Drugs with SGLT-2 Inhibitor: Selected Drugs in Development	99
Table 5.15: Summary of Emerging Non-Insulin Anti-Diabetes Drug Categories	101
Table 6.1: Value Market Shares of Animal, Human and Modern Insulin, 1995-2014	105
Table 6.2: Worldwide Insulin Market, 2012-2019	106
Table 6.3: Worldwide Insulin Sales and Market Share by World Region, 2014	106
Table 6.4: U.S. Insulin Market, 2012-2019	106
Table 6.5: Key Drivers of the Type 2 Diabetes Insulin Market, 2014	107
Table 6.6: Worldwide Insulin Market by Type (% Market Value), 2014	107
Table 6.7: Worldwide Insulin Sales and Value Market Share by Company, 2014	107
Table 6.8: U.S. Insulin Sales and Value Market Share by Company, 2014	108
Table 6.9: Insulins on the U.S. Market	112
Table 6.10: Pharmacokinetics of Therapeutic Insulins on the U.S. Market	113
Table 6.11: Comparison of Recommendations from Existing Guidelines	115
Table 6.12: Pharmacokinetics of Short-Acting Human Insulins	115
Table 6.13: Short-Acting Human Insulin Worldwide Market Revenues, 2011-2014	116
Table 6.14: Pharmacokinetics of Rapid-Acting Insulins	117
Table 6.15: Rapid-Acting Insulin Worldwide Market Revenues, 2011-2014	118
Table 6.16: Pharmacokinetics of Intermediate-Acting Insulins	120
Table 6.17: Intermediate-Acting Human Insulin Worldwide Market Revenues, 2011-2014	120
Table 6.18: Pharmacokinetics of Long-Acting Insulins	121
Table 6.19: Long-Acting Insulin Worldwide Market Revenues, 2011-2014	122



Table 6.20: Pharmacokinetics of Insulin Mixtures	127
Table 6.21: A Comparison of Existing Insulin Delivery Devices	141
Table 6.22: Insulin Pens	143
Table 6.23: Estimated Worldwide Demand for Insulin Pens by Volume, 2013-2018	145
Table 6.24: Injection Aids	146
Table 6.25: Jet Injectors	148
Table 6.26: Control Averages by Treatment	149
Table 6.27: Reduced Risk for Various Diseases When Blood Glucose is Near Normal	149
Table 6.28: Leading Insulin Pump Manufacturers	150
Table 6.29: Comparison of Current External Insulin Pumps on the Market	150
Table 6.30: Insulin Infusion Sets	156
Table 6.31: Worldwide Insulin Pump Market, 2013-2019	160
Table 7.1: Advantages and Disadvantages of Newer Type 2 Diabetes Therapies	163
Table 7.2: Cells of the Pancreas	169
Table 8.1: BRIC Countries, Percentage of GDP Spent on Healthcare, 2013	180

SAMPLE

## 1. Overview

### 1.1 Statement of Report

As the diabetes epidemic escalates, a new sense of urgency has taken hold. Proactive strategies for prevention of the disease are being put in place by international health organizations such as the World Health Organization, as well as by the health departments of industrialized and developing countries, and even at the local level where food ingredients regulations are being passed. This report evaluates widely-accepted therapeutic approaches to diabetes that are currently in use, while providing an in-depth analysis of emerging technologies that will be used to treat diabetes in the future.

### 1.2 About this Report

The main objectives of this report are to:

- Identify viable technology drivers through a comprehensive look at various platform technologies for diabetes.
- Discover feasible market opportunities via an identification of high-growth applications in different therapeutic areas, with a focus on the largest and most rapidly expanding markets for diabetes.
- Focus on global industry development through an in-depth analysis of the major world markets for diabetes therapeutics, including forecasts for growth.

Market figures regarding the current value of the diabetes drug market are taken from the most recently available data of the global pharmaceutical industry. The following categories of diabetes drugs will be covered herein:

- Rapid-acting insulin.
- Short-activity insulin.
- Intermediate-acting insulin.
- Long-acting insulin.
- Ultra-long-acting insulin.
- Insulin mixtures.
- Sulfonylureas.
- Meglitinides.
- Biguanides.
- Thiazolidinediones.
- $\alpha$ -Glucosidase inhibitors.
- Incretin (GLP-1) mimetic.
- Amylin analog.
- Dipeptidyl peptidase IV inhibitors.
- Sodium-glucose co-transporter-2 (SGLT-2) inhibitors.
- $11\beta$ -Hydroxysteroid dehydrogenase Type 1 ( $11\beta$ -HSD1) inhibitors.
- AMP-activated protein kinase (AMPK) activators.
- Combination drugs.

This report will cover the top brands for lowering elevated blood sugar including:

- Lantus.
- Januvia.
- NovoLog and NovoMix.
- Levemir.
- Humalog.
- Victoza.
- Janumet.
- Humulin

This market analysis includes the use of charts and graphs to show product growth and marketplace trends. In addition, a discussion of the biology underlying diabetes provides the reader with a more comprehensive understanding of the possibilities for future treatment as well as avenues for possible research and development (R&D) budgets. In addition, this report will:

- Assess the diabetes market drivers and bottlenecks, from the perspective of the medical and scientific research communities.
- Discuss the potential opportunities of the diabetes sectors of the medical community.
- Establish the current total market size and future growth of the diabetes market, and analyze the current size and growth of therapeutic segments.
- Provide current and forecasted growth rates and market shares for each participating company.
- Discuss profit and business opportunities for each therapeutic segment.
- Provide strategic recommendations for near-term business opportunities.

The analysis includes top companies in the diabetes space:

- Novo Nordisk.
- Eli Lilly.
- AstraZeneca.
- Merck & Co.
- Boehringer Ingelheim.
- Takeda.
- GlaxoSmithKline.
- Sanofi.
- Pfizer.
- Medtronic.
- Insulet.
- Roche.
- Animas (Johnson & Johnson).

### 1.3 Scope of the Report

This report concentrates on the diabetes therapies market segment in major worldwide markets.

- It will discuss the market size, growth rates used in treating diabetes.
- Business trends, technology trends, and developing areas of pharmaceutical therapies for diabetes will also be addressed. The market for such therapies in clinical use is presented here in detail.
- In addition, the dollar volume of sales, both worldwide and in the U.S., are reported, and the factors that influence the size and growth of individual market segments are discussed.
- The market sizes and growth rates for the U.S. and world markets are described in detail. Emphasis is on those companies that are actively developing and marketing therapies for diabetes.
- Leading companies are discussed in depth with a section on the history of the company, the product line, business and marketing analysis, and a subjective commentary of the position of the company in its market.

The reader is encouraged to consult other TriMark Publications reports at [www.trimarkpublications.com](http://www.trimarkpublications.com) for a detailed discussion of important individual market segments related to diabetes, such as TriMark's *Blood Glucose Testing and Diabetes Management* and *U.S. Glucose Testing Markets* reports, which provide more in-depth information on blood glucose testing for diagnosis and management of diabetes. Additionally, TriMark's *World Glucose Self-Testing Markets* covers the substantial market composed of diabetics who self-test in order to manage their disease on a daily basis.

## 1.4 Methodology

The author of this report holds a Ph.D. in biochemistry from the University of Minnesota, with many decades of experience in science writing and as a medical industry analyst. He has over 30 years of experience in laboratory testing and instrument and reagent development technology, as well as extensive experience in senior level positions in biotech and medical service companies. The senior editor of this report holds a Master's degree in immunology, and has substantial experience in science writing and as a medical industry analyst. She also has many years of laboratory experience investigating cancer immunotherapies and *in vitro* assay development for biotech companies.

Company-specific information is obtained mainly from industry trade publications, academic journals, news and research articles, press releases and corporate websites, as well as annual reports for publicly-held firms. Additionally, sources of information include the non-governmental organizations (NGOs) such as the World Health Organization (WHO), governmental entities like the U.S. Department of Health and Human Services (HHS), and U.S. federal agencies such as National Institutes of Health (NIH), Food and Drug Administration (FDA), and the Centers of Disease Control and Prevention (CDC). Where possible and practicable, the most recent data available have been used.

Some of the statistical information was taken from Biotechnology Associates' databases and from TriMark's private data stores. The information in this study was obtained from sources that we believe to be reliable, but we do not guarantee the accuracy, adequacy or completeness of any information or omission or for the results obtained by the use of such information. Key information from the business literature was used as a basis to conduct dialogue with and obtain expert opinion from market professionals regarding commercial potential and market sizes.

### ***Primary Sources***

TriMark collects information from hundreds of Database Tables and many comprehensive multi-client research projects, as well as Sector Snapshots that it publishes annually. TriMark extracts relevant data and analytics from its research as part of this data collection.

### ***Secondary Sources***

TriMark uses research publications, journals, magazines, newspapers, newsletters, industry reports, investment research reports, trade and industry association reports, government-affiliated trade releases and other published information as part of its secondary research materials. The information is then analyzed and translated by the Industry Research Group into a TriMark study. The Editorial Group reviews the complete package with product and market forecasts, critical industry trends, threats and opportunities, competitive strategies and market share determinations.

### ***TriMark Publications Report, Research and Data Acquisition Structure***

The general sequence of research and analysis activity prior to the publication of every report in TriMark Publications includes the following items:

- Completing an extensive secondary research effort on an important market sector, including gathering all relevant information from corporate reporting, publicly-available data and proprietary databases.
- Formulating a study outline with the assigned writer, including important items, as follows:
  - Market and product segment grouping, and evaluating their relative significance.
  - Key competitors' evaluations, including their relative positions in the business and other relevant facts to prioritize diligence levels and assist in designing a primary research strategy.
  - End-user research to evaluate analytical significance in market estimation.
  - Supply chain research and analysis to identify any factors affecting the market.
  - New technology platforms and cutting-edge applications.
- Identifying the key technology and market trends that drive or affect these markets.

- Assessing the regional significance for each product and market segment for proper emphasis of further regional/national primary and secondary research.
- Completing a confirmatory primary research assessment of the report's findings with the assistance of expert panel partners from the industry being analyzed.

## 1.5 Executive Summary

Diabetes mellitus is a disease characterized by dysregulated levels of insulin, a pivotal hormone that regulates blood glucose levels, and insulin resistance in the peripheral tissues. There are two main forms of diabetes: Type 1 and Type 2. Type 1 diabetes, once referred to as juvenile diabetes, is an autoimmune disease that is typically manifested in early childhood and results from the rapid and complete obliteration of the pancreatic beta cells that produce insulin. Delivery of insulin into the bloodstream is required, or else death will ensue. Type 2 diabetes, is heralded by a slow but progressive loss of pancreatic beta cell function and characterized by decreased responsiveness to insulin of many tissues responsible for central metabolism. Type 2 diabetes is commonly treated with oral anti-diabetes drugs that supplement endogenous uptake of glucose by peripheral tissues in order to clear the glucose from circulation as rapidly as possible. In addition, the Centers for Disease Control and Prevention (CDC) recently reported that nearly █% of people aged 18 and older with Type 1 and Type 2 diabetes currently taking medication in the U.S. are treated with insulin while █% are currently prescribed oral medication only. In addition, █% of these individuals are being medicated with both insulin and oral drugs.

According to the International Diabetes Federation (IDF), worldwide, there were about █ diabetics in █, representing roughly █% of the adult population (20 to 79 years age group). Biotechnology Associates estimates that there will be at least █ more diabetics by █. The global incidence of diabetes is expected by industry experts to increase dramatically, reaching █ by █. Of these, only about █% to █% are Type 1 diabetes cases, whereas the vast majority has Type 2 diabetes, which is strongly linked to obesity. Due to lifestyle changes, rising rates of obesity, and increased lifespan, the prevalence of Type 2 diabetes is on the rise. Because the prevalence of Type 2 diabetes has recently been described as epidemic, the impact of this disease in the near future will exceed current influence.

Despite this large patient population, physician research reveals that, even now, only █% of Type 2 diabetics have been diagnosed. In light of this staggering worldwide prevalence of diabetes mellitus, there is increasing demand for effective therapeutics to delay disease progression, prevent diabetic complications and improve the quality of life for patients.

Two of the main areas of pharmaceutical development within the diabetes market are delivery technologies for treatment of Type 1 diabetes and new drugs for the treatment of Type 2 diabetes. In █, the FDA approved a rapid acting inhaled insulin, Afrezza, which is given at the start of each meal. Sales of Afrezza commenced in █, with Sanofi winning the bid to market the drug. Sales of insulin sensitizers also continue to grow and combination therapy is common in the treatment of Type 2 diabetes.

Modern diabetes drugs can successfully treat the symptoms of diabetes but fail to suppress the progression of diabetes and diabetic complications. There are many consequences of this dramatic increase in the number of patients of diabetes. Foremost, diabetes is a disease for which long-term pharmacological maintenance is a necessity in virtually all cases. Moreover, this condition inexorably worsens over time and must be remedied by increased medication, including combination therapy. Secondly, diabetes is typically associated with a host of co-morbidities, including:

- Cardiovascular disease (CVD).
- Renal function.
- Deterioration of vision.
- Neuropathy.

These co-morbidities require vigilant surveillance and management, and in most cases, require pharmacological intervention that can incur high medical care costs. Key opinion leaders recognize these precipitating or interrelated conditions as a disease state called "metabolic syndrome". These efforts are intended to assist in early recognition

and pharmacological intervention of patients at risk for diabetes. Of particular interest is the strong correlation between diabetes and CVD, a component of metabolic syndrome. As a result, diabetes experts are increasingly urging diabetes screening by cardiologists, and conversely, that endocrinologists prescribe CVD agents when diagnosing Type 2 diabetes. The net outcome of this trend will be an increased number of prescriptions written for both disease states.

Among the growing number of patients with diabetes are new patient subpopulations. Specifically, the indoctrination of an “American” lifestyle in many growing economies is resulting in increased prevalence of diabetes, even in developing nations. In addition, whereas diabetes was previously a health concern of the elderly, epidemiological data have shown that record numbers of middle-aged adults and children are now at risk or patients of this condition. Not only are the needs of these groups somewhat unique, their predominance also means that the average patient will require medical attention for decades longer than the typical diabetes patient in the past. This can have grave ramifications for the prevalence of co-morbidities such as:

- Dyslipidemia.
- Hypertension.
- Kidney failure.
- Psychological outcomes such as depression.

The societal burden for uncontrolled diabetes and/or debilitating diabetes-related complications extend beyond medical care: worker’s disability, unemployment and disturbance to family structure are just a few. As such, there has been mounting concern among policy-makers. In fact, the U.S. government has declared “war” on obesity, since it is a major health risk precipitating Type 2 diabetes. Quality of life and the monetary ramifications for government-supported healthcare are two key reasons for the government’s commitment to this issue. It is widely accepted that Type 2 diabetes is a largely preventable disorder, and research clearly confirms that the co-morbidities of diabetes can be forestalled or prevented with early and aggressive management of elevated glucose levels, the primary contributor to the co-morbid conditions of diabetes.

The diabetes therapeutics market is divided into two primary pharmacological interventions:

- Non-insulin, including oral anti-hyperglycemic agents and the injected GLP-1 drugs.
- Insulin and its delivery technologies.

Excessively high levels of circulating glucose are toxic to many organ systems. Hence, diabetes-related complications can arise when blood glucose levels go unchecked. To date, oral anti-diabetes agents address elevated glucose levels through a number of different mechanisms of action that are expanding rapidly as improved therapies enter the marketplace.

In the category of insulin delivery, modifications are being developed to improve the rate of onset and duration of effect. Additionally, entirely novel types of delivery systems are also being developed. These non-injectable formulations are intended to provide alternatives to the pain, inconvenience and social stigma associated with the traditional method of needle-injections.

Currently, the key players in the diabetes market (and their principal products in this market) are:

- Novo Nordisk (broad range of insulin products and a robust non-insulin anti-diabetic pipeline).
- Eli Lilly (Humulin, Humalog, Victoza, Jardiance, Tradjenta, Trulicity).
- Takeda (Nesina, Kazano, Oseni).
- GlaxoSmithKline (Tanzeum).
- Merck (Januvia, Janumet).
- Sanofi (Lantus, Amaryl, Apidra, Insuman, Lyxumia).
- Johnson & Johnson (Invokana).
- AstraZeneca (Byetta, Bydureon, Farxiga, Onglyza, Kombiglyze, Kombiglyze XR, Xigduo XR).

A number of manufacturers also benefit from the wide use of anti-diabetes drugs that are already produced as generic medications (e.g., metformin and most sulfonylureas).

While currently available anti-diabetes agents are indispensable, such approaches are not free of clinical disadvantages. Hence, there is certainly room for new agents. For example, new options are emerging that are not associated with classical side effects of existing therapies, such as weight gain. Drugs that are able to address multiple co-morbidities associated with diabetes will also draw the attention of prescribers. Agents currently in the pipeline may enhance the ability to manage this condition at a premium acquisition cost, but are not likely to cure diabetes. Amelioration of diabetes-related complications will come more from early and aggressive intervention, a second factor that will expand the market.

Management of incretin levels represents a novel treatment among emerging oral agents. Increased levels of incretins have the potential to cause delayed gastric emptying and to stimulate insulin secretion, two processes that are favorable for diabetes management. Glucagon-like peptide 1 (GLP-1) has been found to be impaired in patients with Type 2 diabetes. GLP-1 and Dipeptidyl peptidase IV (DPP-IV) are two endogenous compounds that regulate incretins and are being utilized for clinical use. DPP-IV is an enzyme that degrades endogenous GLP-1.

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors are the newest class of diabetic medications indicated for the treatment of Type 2 diabetes. SGLT-2, which is a low-affinity, high capacity glucose transporter located in the proximal tubule in the kidneys, is responsible for █% of glucose reabsorption. SGLT-2 inhibitors function by blocking the reabsorption of glucose within the kidneys, resulting in increased glucose excretion and thereby lowering blood glucose levels. In conjunction with exercise and a healthy diet, they can improve glycemic control.

Non-injectable insulin delivery methods will prove valuable in needle-fearing patients who are non-compliant. This technology platform will also constitute an advance in convenience for all insulin-requiring patients in situations where injection is not preferable, such as on airplanes (where syringes may raise security issues), schools or other public places. Diabetics may choose to replace one or more of their insulin injections per day with this less painful mode, as long as the loss of glucose control for a given delivery method does not outweigh the benefits of a more facile delivery method. After its recent approval, the inhaled insulin Afrezza has launched in early █.

In summary, the following drivers will shape the U.S. anti-diabetes market:

- Changes in diagnostic criteria for hyperglycemia and related metabolic disorders.
- Government-waged war on obesity and diabetes.
- Longer lifespan.
- Introduction of new agents, including those with novel mechanisms of action.
- Greater reliance on newer, vastly more expensive drugs that can increase attention on pharmacological intervention.
- Augmented efforts for patient compliance.
- Changes in Medicare pharmacy benefit.

In █, the global anti-diabetic market, which includes non-insulin anti-diabetics and human insulin and its analogs, generated sales of \$█. By █, it is expected to grow to approximately \$█. In █, the anti-diabetic market had █% of sales in North America, █% in Europe, █% in Asia and █% in the rest of the world. Given the size and potential of the market, pharmaceutical companies are now in a race to capture share in combating both Type 1 and Type 2 diabetes. The overall market growth is expected to be driven by the increasing number of diabetes patients, population growth and the increasing use of combination therapy. The global diabetes market is slated to become one of the largest healthcare markets over the next five years, second only to oncology.

- However, the market will also be shaped by strong government and payer pressure towards the use of generic drugs that are tried and proven, or less expensive. On the international front, westernization of lifestyle and increasing population size in developing economies will reshape the global market place. In addition, greater assets and initiative of industrial nations to invest in healthcare will also add to the growth of this market.