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

Reshaping Tomorrow’s Diabetes Market
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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.
- α-Glucosidase inhibitors.
- Incretin (GLP-1) mimetic.
- Amylin analog.
- Dipeptidyl peptidase IV inhibitors.
- Sodium-glucose co-transporter-2 (SGLT-2) inhibitors.
- 11β-Hydroxysteroid dehydrogenase Type 1 (11β-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 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 90% 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 2015.

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 [Year], the global anti-diabetic market, which includes non-insulin anti-diabetics and human insulin and its analogs, generated sales of $[Amount]. By [Year], it is expected to grow to approximately $[Amount]. In [Year], the anti-diabetic market had [Percentage]% of sales in North America, [Percentage]% in Europe, [Percentage]% in Asia and [Percentage]% 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.