

# Stratanalysis Document

## *DPP-IV Inhibitors: Emerging therapy for Type 2 Diabetes*

Stratanalysis  
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# DPP-IV Inhibitors: Emerging therapy for Type 2 Diabetes

## New drugs on the horizon

A novel class of oral Drug for Type 2 Diabetes

- DPP-IV inhibitors are new oral therapies for treatment of Type 2 Diabetes Mellitus
- The first and only DPP-IV inhibitor in the market, Merck's Januvia (Sitagliptin), was approved by the FDA in October 2006 for use as mono therapy or with metformins
- The next drug in this class, Onglyza (Saxagliptin), in this class was approved by FDA on July 31, 2009
  - Onglyza has been jointly developed by Bristol-Myers Squibs (BMS) and Astra Zeneca (AZ)
  - Onglyza has been shown to reduce major adverse cardiovascular events by as much as 55%
- Since DPP-IV inhibitors have oral route of administration and oral medication forms the largest segment of therapy among the anti-diabetics, it appears to be a promising therapy
  - Type 2 Diabetes Mellitus constitutes the main bulk (85%-90%) of the diabetes population in the world. The global diabetes population has been estimated to grow 55% by 2025 compared to what it was in 2007

DPP-IV Inhibitor Drugs in Pipeline

DPP-IV Inhibitors	Company	Stage	Route of Administration	Year of Launch
<b>Alogliptin</b>	Takeda	Phase III	Oral	2010
<b>FDC Onglyza/ Metformin</b>	BMS, AZ	Phase III	Oral	2010
<b>SYR-472</b>	Takeda	Phase II	Oral	
<b>TAK-100</b>	Takeda	Phase I	Oral	

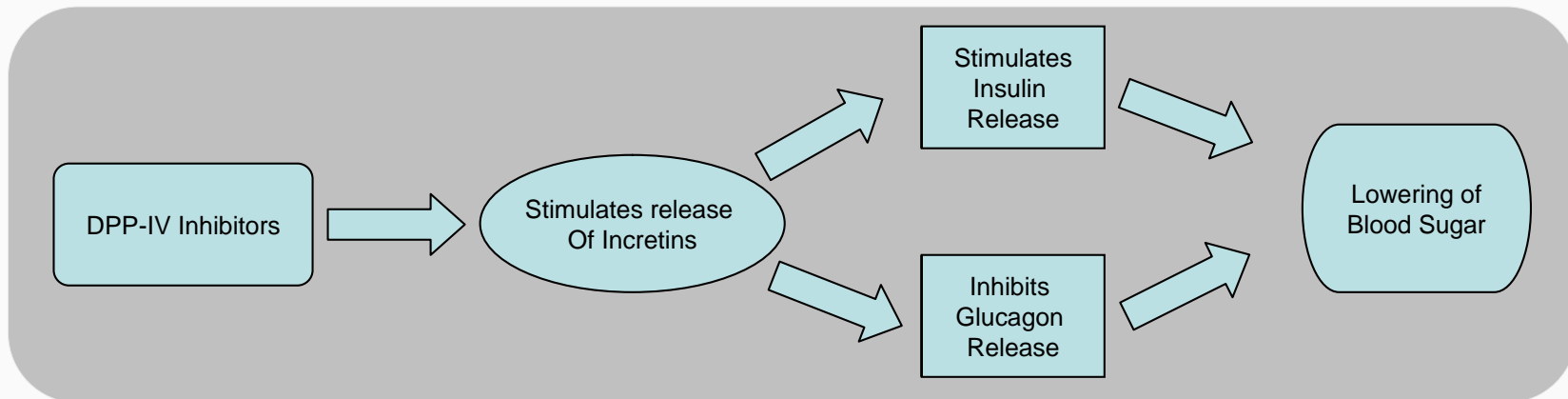
Source: WSJ Health

# DPP-IV Inhibitors: Emerging therapy for Type 2 Diabetes

## New drugs on the horizon

### DPP-IV Inhibitors

- DPP-IV is a member of a family of cell membrane proteins that are expressed in many tissues, including immune cells. DPP-IV inhibitors are small molecules that enhance the effects of GLP-1 and GIP, increasing glucose-mediated insulin secretion and suppressing glucagon secretion
- The mechanism of action of DPP-IV inhibitors is distinctive from that of any other existing class of oral glucose-lowering drugs



### Mechanism of Action

- DPP-IV inhibitors are oral hypoglycemics that block DPP-IV by increasing incretin levels. Incretins stimulate the release of insulin and inhibit the release of glucagon and hence lower blood sugar level
  - DPP-IV breaks down proteins responsible for stimulation of insulin producing cells. If DPP-IV is subdued then the proteins can trigger the release of insulin for an enhanced period of time thereby reducing glucose levels in the blood

# DPP-IV Inhibitors: Emerging therapy for Type 2 Diabetes

## Market Analysis for Diabetes – Market Potential

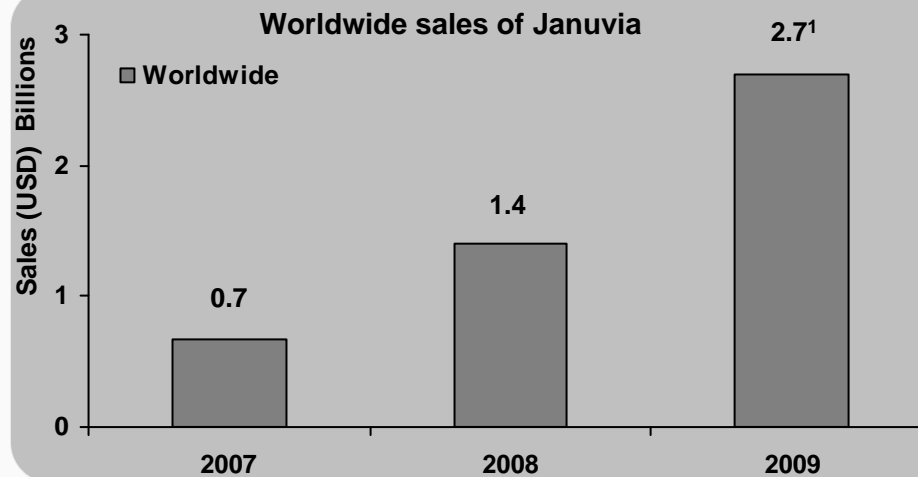
### Market Potential

#### ➤ Global Market:

- The revenue generated worldwide by anti-diabetic drugs in 2008 was USD 26.1 Bn
  - The revenue generated by the top 10 drugs in diabetes was USD 21 Bn
  - Januvia on its own sold USD 1.4 Bn worldwide in 2008

➤ **Growth Rate:** Januvia is the only drug in the class of DPP-IV inhibitors. Januvia was predicted to reach USD 1 Bn in sales by 2010 but it exceeded expectations and became a blockbuster drug in 2008 with worldwide sales of USD 1.4 Bn

- Merck expects to add around USD 2.4 to 2.7 Bn to its topline through Januvia alone
- Januvia has shown an increase in sales of 51% and 38% in Q1 2009 and Q2 2009 respectively compared to the same quarters in the previous year



➤ **US Market:** Approximately 23.6 million children and adults (8% of total population) have diabetes, of whom more than 90% have Type 2 Diabetes Mellitus. Nearly 1.6 million new cases of diabetes were diagnosed among people 20 years and older in 2007

Note: <sup>1</sup>As expected by Merck

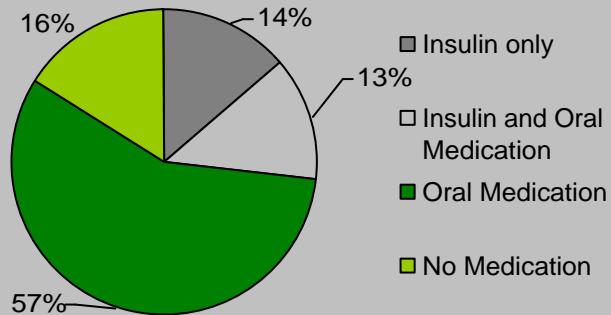
Source: Global Diabetes Market Review 2008, Merck Financials,

Strategic Analysis and Tech Solutions Limited [www.stratanalysis.com](http://www.stratanalysis.com)

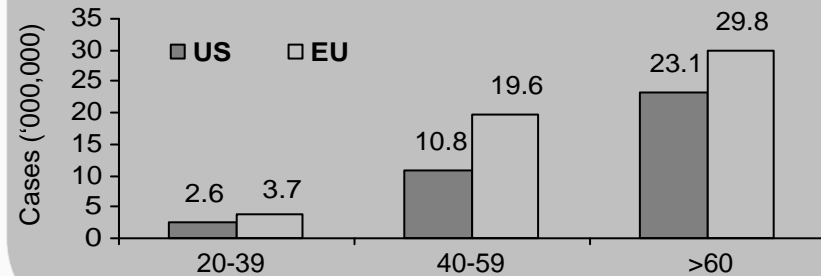
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## Market Analysis for Diabetes – Market Potential

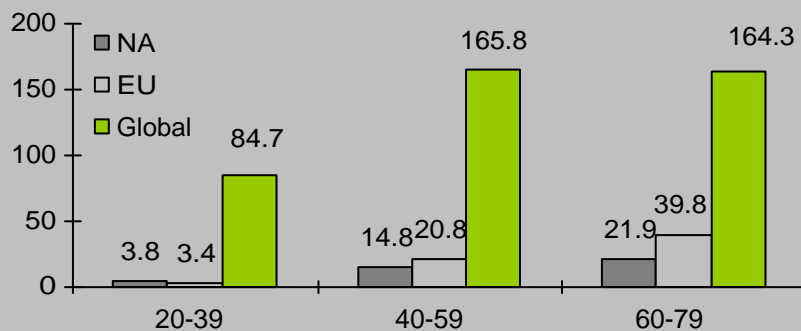
Treatment with Insulin or Oral Medication among adults with diagnosed Diabetes, US, 2004-2006



Prevalence of Diabetes by Age Group, 2007



Estimated Prevalence of Diabetes by Age Group, 2025



- It is estimated that the global diabetes prevalence would be around 380 million by 2025
  - The highest percentage increase in prevalence of 102% and 81% would be in South America and the Middle-east respectively
  - NA and EU will show an increase in prevalence of about 43% and 21% respectively

Source: 2004-2006 National Health Interview Survey, IDF

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## Focus Onglyza

### Issues: Safety Profile

- Clinical trials with Onglyza have reported lymphocytopenia, thrombocytopenia and a cardiovascular signal
  - Lymphocytopenias reported did not result in any clinical side effects
  - Thrombocytopenias reported were observed at doses that were not used in the Phase III clinical trials
  - The company has also said that it is extremely confident that there is no cardiovascular signal

### Downward Dose Adjustment

- Onglyza, unlike the two downward dose adjustments with Januvia, may end up with only one downward dose adjustment (in case of renal failure)

### Clinical Studies for Combination Therapy

- In combination with metformin
  - In a 24 week, randomized double blind study in 1,300 people with type II diabetes, patients on Onglyza+metformin showed a significant change in A1C from baseline of -2.5% for Onglyza 5mg/ 10mg + metformin compared to -1.7% for Onglyza 10mg + placebo and 2.0% for metformin + placebo. Also, the incidence of adverse events for Onglyza 5mg + metformin was slightly lower than that for metformin + placebo
- In combination with TZD (thiazolidinediones)
  - A 24 week, randomized, double blind study in 550 people with Type 2 diabetes demonstrated that patients on Onglyza+TZD treatment arms demonstrated significant change in HbA1C from baseline

### Peak Sales

- Early estimates put peak sales of Onglyza at around USD 1.4 Bn by 2016

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## Stratanalysis Viewpoints and Analysis

### Januvia Outperforming

- Despite the slowdown in US diabetes market, Januvia continues to grow both in volume and share
  - Analysts had predicted Januvia to touch USD 1 Bn mark by 2010 but it outperformed and sold USD 1.4 Bn in 2008 itself
  - Januvia is the fastest growing product in the family of oral drugs for Type 2 Diabetes Mellitus

### Benefit

- Owing to its oral route of administration and oral medications constituting 57% of all therapies in diabetes, DPP-IV inhibitors promise to achieve wide acceptance among both physicians and patients

### Market Potential

- In most established and emerging markets, ageing population, sedentary lifestyle and availability of advanced diagnostic techniques are leading to increased incidence and diagnosis of diabetes which requires long term management
  - Type 2 Diabetes often goes unnoticed for 7 years on average before diagnosis
- There is a huge increase predicted in the prevalence of diabetes in both developed and developing countries in the next 2 decades
- Looking at the outperformance of Merck's Januvia that achieved a billion dollar in sales well before expected (2008 instead of 2010) and the excellent results with Onglyza in clinical studies, DPP-IV inhibitors are here to stay in the ever-increasing diabetes market

Website: [www.stratanalysis.com](http://www.stratanalysis.com)

Phone:  
+44 7950 324483

EMAIL:  
[hari@stratanalysis.com](mailto:hari@stratanalysis.com)

SKYPE ID: harithrividikramji

**Thank You**

