

Oral Diabetes Drugs

Diabetes is a disease caused by high levels of blood glucose resulting from improper production of insulin or action of insulin.

- **Type 1:** In this Diabetes, the cells that make the hormone insulin regulate the blood glucose are destroyed by the body immune system. This is also called as juvenile onset diabetes as it occurs mainly in children and young adults. 5%-10% of all the cases of diabetes have Type I diabetes. Clinical trials are being pursued and planned to prevent type I diabetes. This is also called as Insulin Dependent Diabetes Mellitus (IDDM).
- **Type 2:** In this case, either the cells do not use insulin properly or the body does not produce enough insulin. 90% - 95% of the diabetics have Type 2 diabetes. This type of disease is also called as non-insulin dependent diabetes mellitus (NIDDM) and is mainly observed in people with old age, obese, family history of diabetes, history of gestational diabetes, impaired glucose metabolism, physical inactivity and race/ethnicity.
- **Gestational Diabetes:** Increase in the levels of blood sugar during pregnancy is called gestational diabetes.

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Incidence and prevalence

Incidence

In year 2004, diabetes (Both type I and type II) was diagnosed in 1.4 million adults between the age of 18-79 years (Figure 1). The incidence of diabetes was lower in adults having an age between 18-44 years compared to other groups (Figure 2). From 1997 through 2004, the age adjusted incidence of diagnosed diabetes (Both type I and type II) increased by 35% among men and 46% among women (Figure 3).

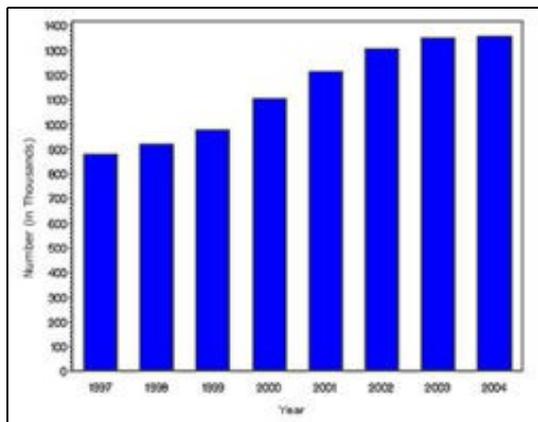


Figure 1. Annual number (in thousands) of new cases of diagnosed diabetes among adults aged 18-79 years, in United States from 1997-2004. [Source](#)

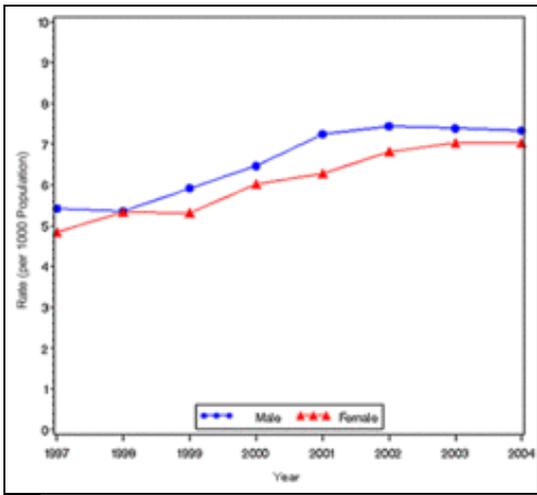


Figure 3. Gender based incidence of diagnosed diabetes per 1000 population aged from 18-79 years in U.S. [Source](#)

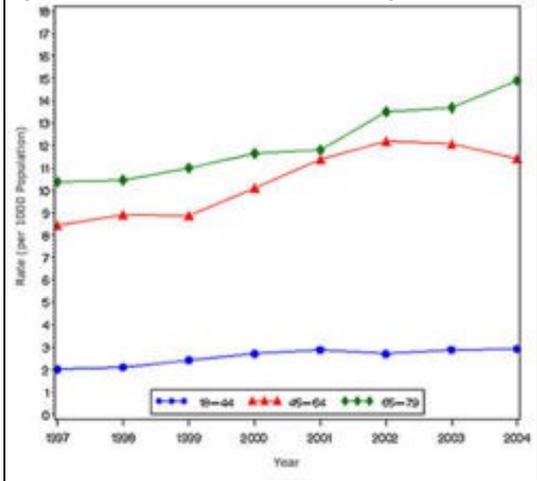


Figure 2. Incidence of diagnosed diabetes per 1000 population aged 18-79 years, by age in U.S. from 1997 to 2004. [Source](#)

- The following table attempts to extrapolate the incidence rate for Diabetes(both type I and type II) to the populations of various countries and regions. [Cure reasearch, Statistics by Country for Diabetes](#)

S.NO	Country/Region	Extrapolated incidence
1	USA	861,533
2	Canada	95,372
3	Europe	1,474,002
4	Asia	10,063,645
5	Africa	1,290,255
6	Middle east	1,055,809
7	Australia and Southern Pacific	70,138

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Prevalence

The prevalence of diabetes(Both type I and type II) in U.S. during the years 1980 to 2005, increased from 5.6 million to 15.8 million (Figure 4). Especially people aged from 65 to 74 had the highest prevalence compared to other age groups (Figure 5). The prevalence of the disease was similar in both men and women till the year 1998 but from 1999, the prevalence of the disease increased highly in men compared to females (Figure 6).

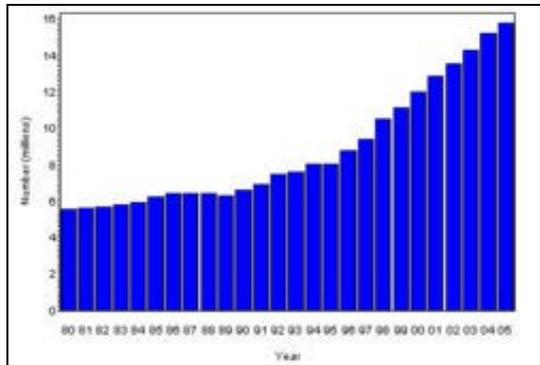


Figure 4. Number (millions) of persons with diagnosed diabetes from year 1980 to 2005 in United States. [Source](#)

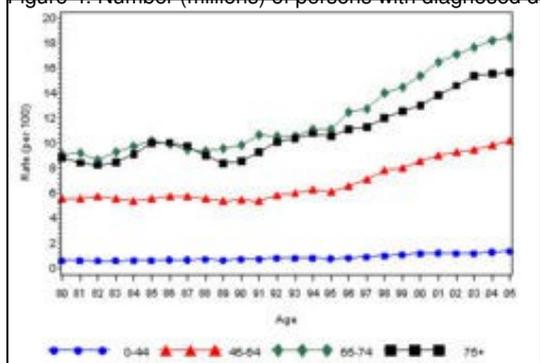


Figure 5. Age dependent Prevalence of diagnosed diabetes in United States from year 1980 to 2005. [Source](#)

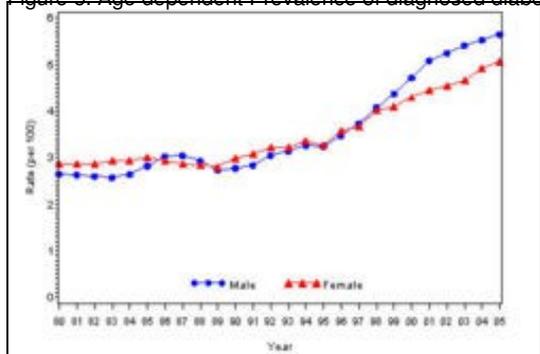


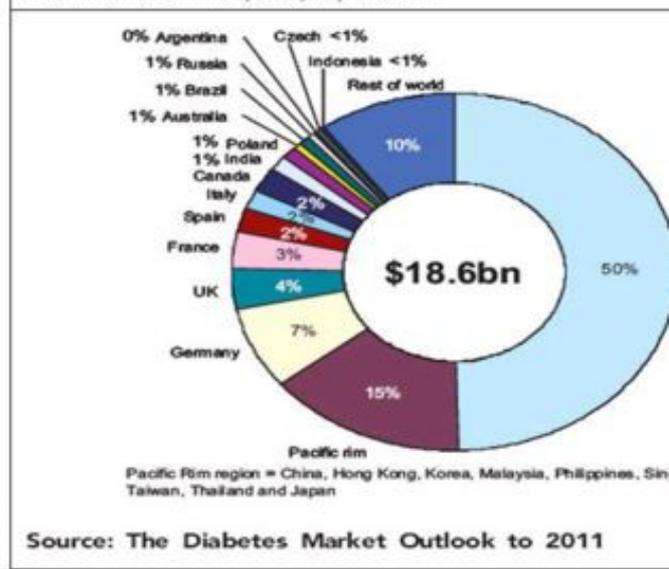
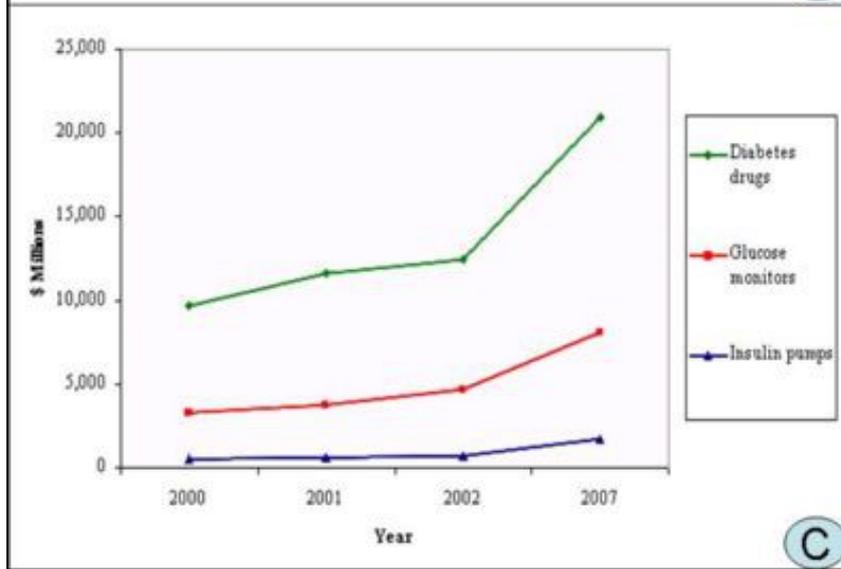
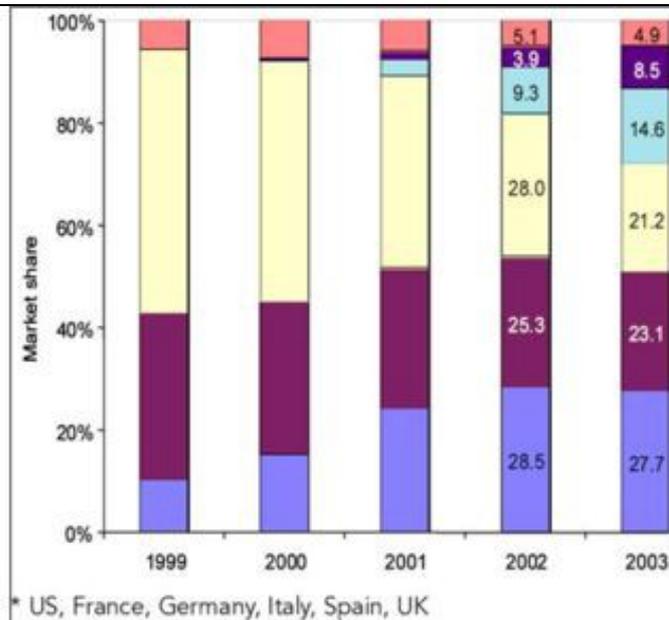
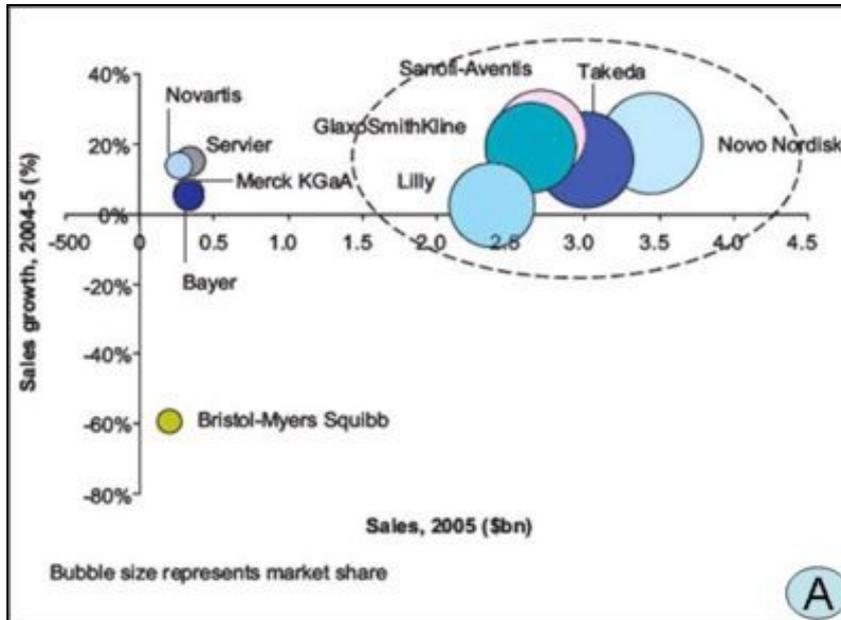
Figure 6. Gender dependent Prevalence of diagnosed diabetes in United States from year 1980 to 2005. [Source](#)

- The following table attempts to extrapolate the prevalence rate for Diabetes(both type I and type II) to the populations of various countries and regions. [Cure research, Statistics by Country for Diabetes.](#)

S.NO	Country/Region	Extrapolated Prevalence
1	USA	17,273,847
2	Canada	1,912,227
3	Europe	33,882,009
4	Asia	201,777,550
5	Africa	25,393,535
6	Middle east	21,169,243
7	Australia and Southern Pacific	1,406,291

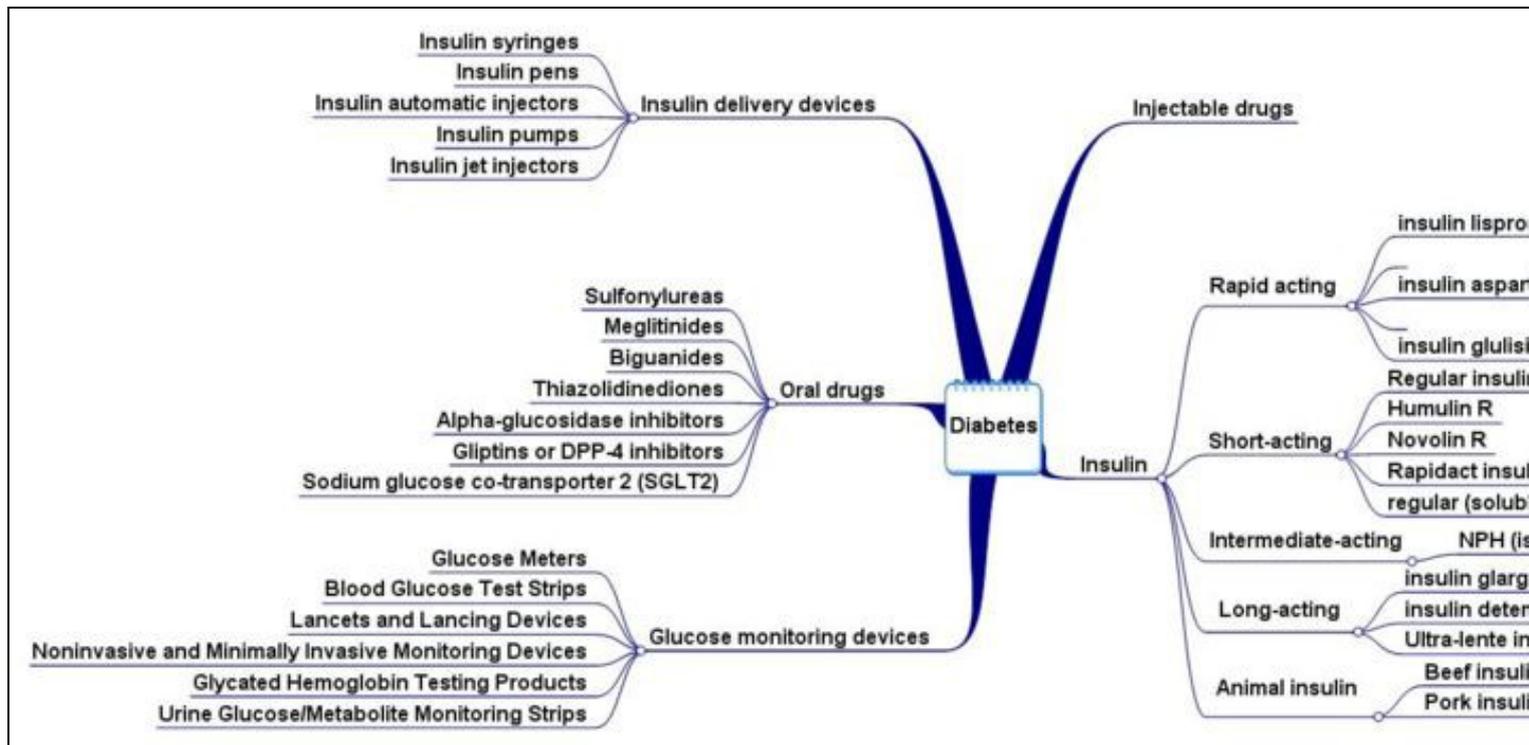
Market Overview

- The Insulin market in 2006 was largely dominated by two players, Novo Nordisk of Denmark and Eli Lilly of USA.
- India and China are emerging as the most potential future markets for insulin delivery devices.
- Growing at a CAGR of 14.09%, global insulin market will reach US\$ 14.5 Billion by 2010 from US\$ 7.5 Billion in 2005.
- Over 60% of the insulin sold in 2006 was sold in pen devices.
- Insulin pen devices dominate the market in Europe and Japan whereas syringes and pumps dominate the US market.
- There was a big improvement in the global diabetes market for innovation particularly in the field of non-invasive methods of insulin delivery, including inhalable, oral and patch technology. [Source](#)
- There are 3 key new OAD classes; PPAR agonists, GLP-1 agonists/DPP IV inhibitors, and amlinomimetic agents. High forecasted sales are anticipated in 2011 for the GLP-1 agonist Exenatide LAR and the DPP-IV inhibitor Galvus at \$2,902.9m and \$1,228.7m, respectively. [Source](#)



A. Competitive dynamics of the leading players in the global diabetes market, 2005 B. Global diabetes market share by geography, 2005] C. Worldwide Diabetes Market, 2000, 2001, 2002 and 2007 D. Global* market share of leading insulins (%), 1999-2003

Product Information



Overall categorization of diabetes treatments
Products: Oral Hypoglycemic Agents

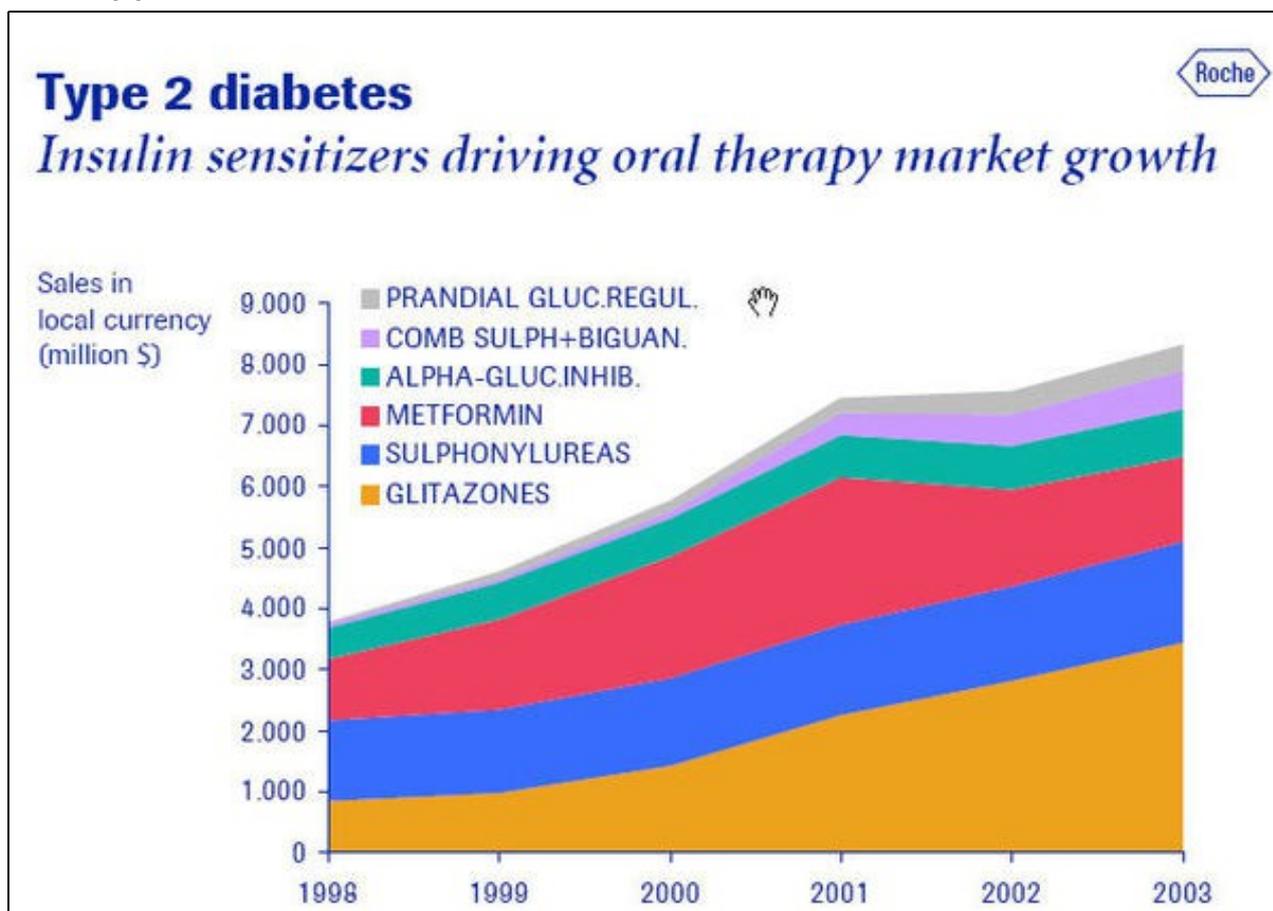
Oral Hypoglycemic Agents			
Drug	Brand	Company	Availability
Sulfonylureas			
First Generation			
Acetohexamide	Dymelor	Eli Lilly	US, F, G, I, S, UK, J
Chlorpropamide, Tolazamide	Diabenase	Pfizer	US, F, G, I, S, UK, J
Second Generation			
Glyburide (Glibenclamide)	Diabeta	Aventis	US, F, G, I, S, UK, J
Glyburide (Glibenclamide)	Micronase	Pharmacia	US, F, G, I, S, UK, J
Glyburide (Glibenclamide)	Glynase	Pharmacia	US, F, G, I, S, UK, J
Glypizide	Glucotrol, Glucotrol XL	Pfizer	US, F, G, I, S, UK, J
Third Generation			
Glimepride	Amaryl	Aventis	US, F, G, I, S, UK, J
Meglitinides			
Repaglinide	Prandin	Novo Nordisk	US, F, G, I, S, UK, J
Nateglinide	Sralix	Novartis	US, UK, J
Biguanides			
Metformin	Glucophage, Glucophage XR	Bristol-Myers Squibb	US
Metformin			
Thiazolidinediones			
Rosiglitazone	Avandia	Glaxosmithkline	US, G, UK
Pioglitazone	Actos	Takeda/ Eli Lilly	US, UK, G, S, J
Alfa-Glucosidase Inhibitors			

Acarbose	Precose	Bayer	US, F, G, I, S, UK, J
Miglitol	Glyset	Pharmacia	US, F, G, S
Voglibose	Basen, Volix, Vogseal	Ranbaxy, Nihon Pharmaceutical Industry Ltd	I, J
Dipeptidyl peptidase-4 (DPP-4) inhibitor			
Sitagliptin	Januvia	Merck	US

Products: Fixed Drug Combinations

Fixed Drug Combinations			
Brand Name	Drug 1	Drug 2	Company
Metaglip	Glipizide	Metformin	Bristol-Myers Squibb
Duetact	Glimepiride	Pioglitazone	Takeda
Avandaryl	Glimepiride	Rosiglitazone	GlaxoSmithKline
ACTOSPlusMet	Pioglitazone	Metformin	Takeda
Avandamet	Rosiglitazone	Metformin	GlaxoSmithKline
Janumet	Sitagliptin	Metformin	Merck

Product pipeline



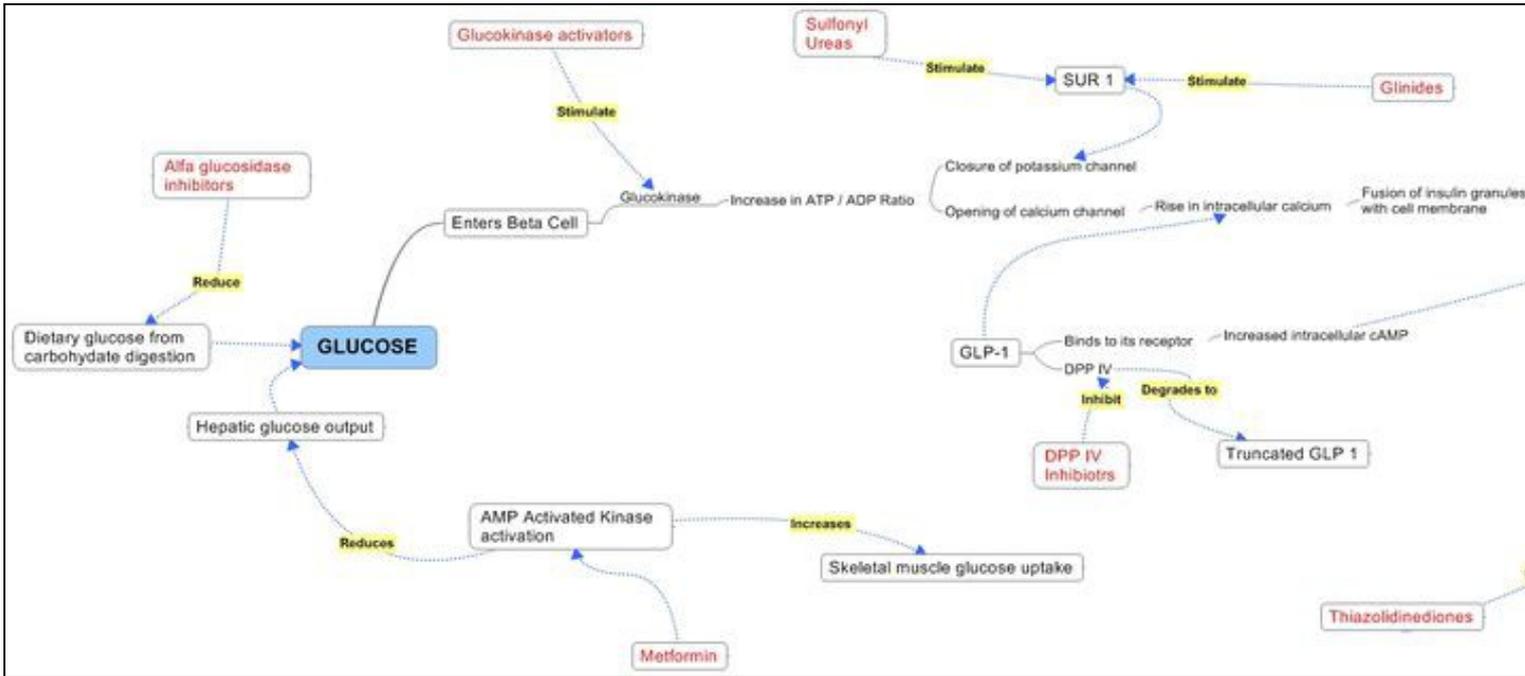
Product Pipeline		
Drug	Company	Stage
Dipeptidyl Peptidase IV (DPP-IV) Inhibitor :DPP-IV inactivates glucagon-like peptide-1 (GLP-1), an important mediator of blood glucose levels following meals. DPP-IV inhibitors have been clinically shown to provide long term improvement of glucose control without the risk of hypoglycemia, and to improve the function of pancreatic beta cells, the cells responsible for the production of insulin.		
ALS 2-0426	Alantos Pharmaceuticals , Amgen , Servier	1
PSN9301	OSI	2

SYR-322	Takeda	3
R1579	Roche	1
vildagliptin (Galvus)	novartis	NDA submitted in March 2006
MP-513	Mitsubishi Pharma	2
Gastrin + DPP IV Inhibitor	Transition Therapeutics	Preclinical
Saxagliptin	Otsuka Pharmaceutical Co. Bristol-Myers Squibb	3
Insulin sensitizer		
ISIS 113715	Isis	3
NCX 4016 (Nitric Oxide donating derivative of Acetyl Salicylic acid)	NicOx	2
DG070 inhibitors	Develogen AG	Preclinical
NovoNorm® (repaglinide)/Metformin	Novo Nordisk	3
Biguanides		
Gastrin + Metformin	Transition Therapeutics	1
GLP 1 Analogue / Agonists GLP 1 Analogues have to be injected subcutaneously, Emisphere is working on an oral analogue		
Abiglutide (716155)	glaxosmithkline	2
TH0318	Theratechnologies	1
Liraglutide (NN2211)	Novo Nordisk	3
R1583	Roche	2
Oral GLP	Emisphere Technologies	1
PC-DAC?:Exendin-4	ConjuChem	2
	Bristol-Myers Squibb	Exploratory development
AVE0001A	Sanofi Aventis	2
Gastrin +GLP 1 Agonist	Transition Therapeutics	2
Peroxisome Proliferator-Activated Receptor (PPAR) agonist/analogue		
CS-011 (Rivoglitazone)	Sankyo	2
Metaglidase(MBX 102)	Metabolex	2
MBX-2044	Metabolex	1
AVE8134	Sanofi Aventis	2
AVE0897	Sanofi Aventis	1
R1439, aleglitazar	Roche	2
AVE0847	Sanofi Aventis	2
SAR351034	Sanofi Aventis	Preclinical
376501	Glaxosmithkline	1
625019	Glaxosmithkline	1
677954	Glaxosmithkline	2
Avandia	Glaxosmithkline	2
Avandia XR	Glaxosmithkline	2
PPAR Gamma Agonist + simvastatin	Glaxosmithkline	3
MCC-555, Netoglitazone	Mitsubishi Pharma. Novartis	
Muraglitazar	Bristol-Myers Squibb	3
R483	Roche	2

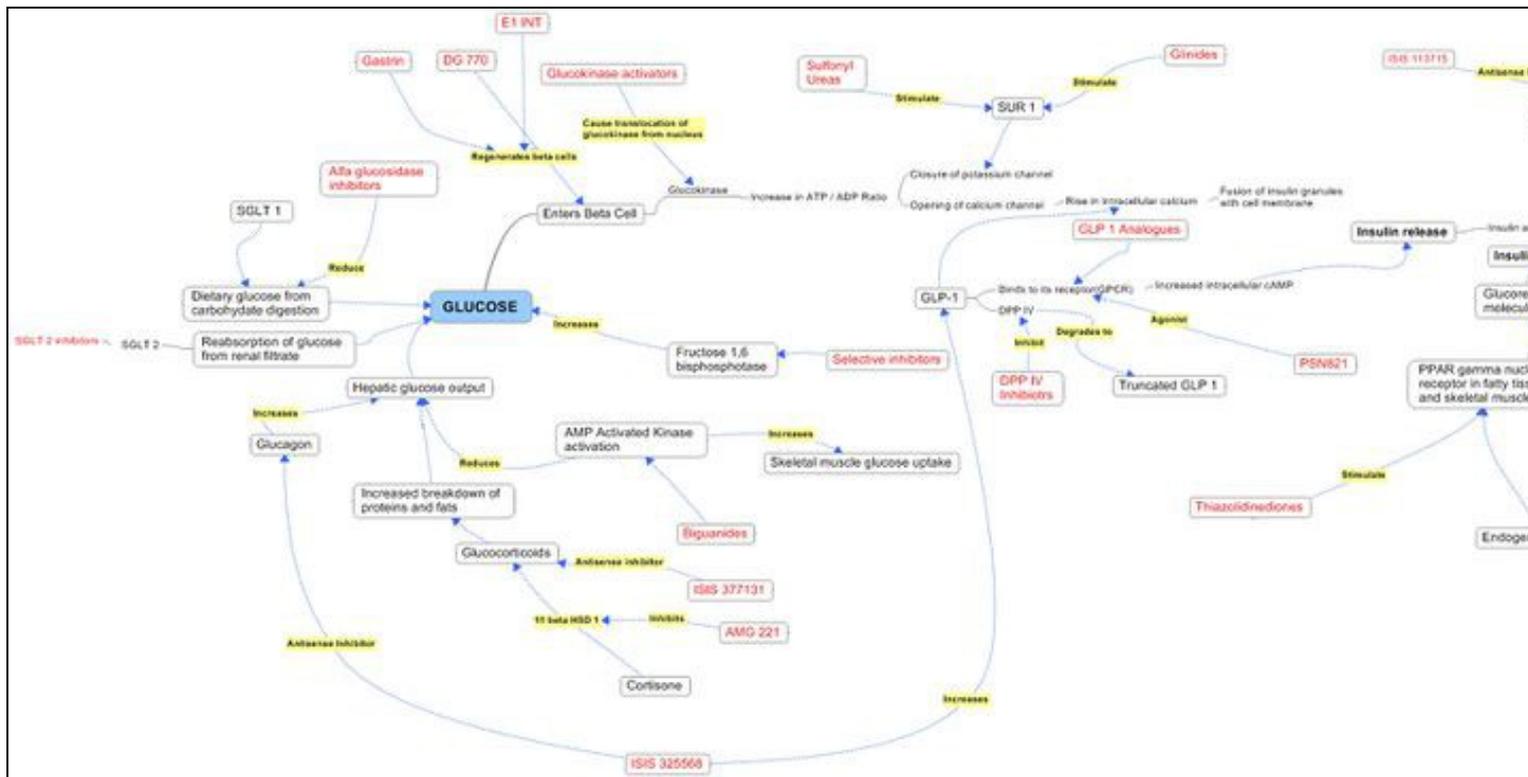
PPM-204	Wyeth, Plexikon	2
Oral glucokinase activator (GKA)		
PSN010	OSI	1
R1511	Roche	1
G protein-coupled Receptor(GPR) 119 Agonist		
PSN821	OSI	
Antisense drug for Glucagon Receptor (GCGR)		
ISIS 325568	Isis	1
Antisense drug for Glucocorticoid Receptor (GCCR)		
ISIS 377131	Isis	Preclinical
Sodium Glucose Transporter 2 (SGLT2) inhibitor		
AVE2268	Sanofi Aventis	2
SAR 7226	Sanofi Aventis	Preclinical
189075	Glaxosmithkline	2
869682	Glaxosmithkline	2
Growth hormone releasing analogue		
TH 9507	Theratechnologies	
Nitric oxide (NO) blocking agent		
NOX-700	Medinor	1 started in 2002
Antibody		
TRX4	BTG	2
Selective inhibitor of fructose-1, 6-bisphosphatase (FBPase)		
CS-917	Sankyo, Metabasis	2
MB07803	metabasis, Daiichi Sankyo	2
11-beta hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitor		
AMG 221	Amgen, Biovitrum	1
Polypyrimidine tract binding protein (PTB, also named hnRNP) inhibitor		
	Serono	1
Insulin Like Growth Factor 1		
IPLX (Mecasermin rinfabate)	Glen Allen	Orphan Drug Status
Newer Meglitinides		
Nateglinide with insulin sensitizers	Astellas pharma	SNDA Filed
Nateglinide with biguanides	Astellas pharma	SNDA Filed
Islet Regeneration Factors		
DG770 (beta cell regeneration factor)	Develogen AG	3
E1 INT (Islet regeneration)	Transition Therapeutics	2
Miscellaneous		
AMG 837 (Potentiates Glucose Dependent Insulin Secretion)	Amgen	1
MBX 213	Metabolex	1
R 1499	Roche	1

R1438	Roche	2
R1440	Roche	2
PSN 357	OSI	1
NBI 6024	Neurocrine Biosciences	2
MK 0941	Merck	1
MK 1642	Merck	1
Mk 0533	Merck	2
MK0893	Merck	2
Insulins		
Oral Insulin	Emisphere Technologies	2
Technosphere	Mannkind corporation	3
NN344 (Insulin analogue)	Novo Nordisk	1
NN5401(Insulin analogue)	Novo Nordisk	1
AERx® iDMS (Insulin Inhalation system)	Novo Nordisk	3
Inhaled insulin	Bristol Meyers Squibb	1
Inhaled insulin	Eli Lilly	2
Exubera (Inhaled insulin)	Pfizer	4
Oal Lyn (Inhaled insulin)	http://www.generex.com/products/oral-lyn/	Approved in Ecuador
Nasulin	Bentley	2

Product Pathways



Product

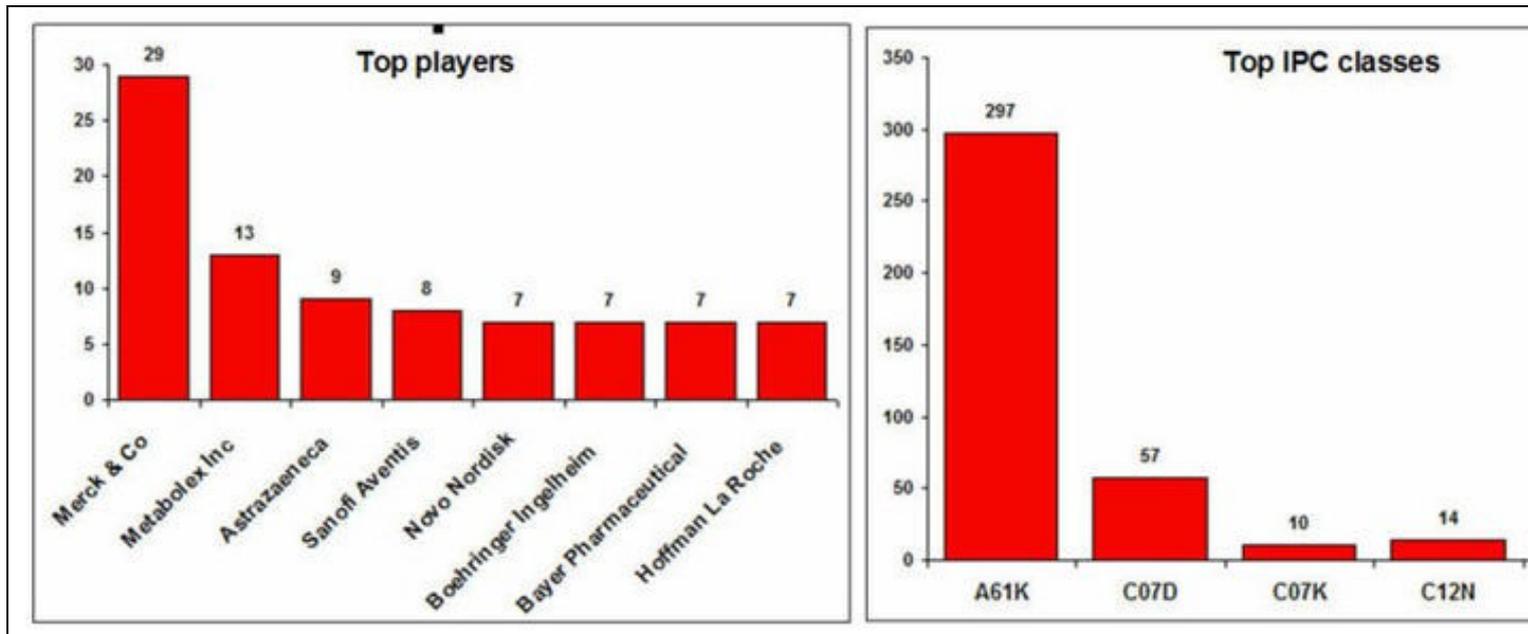


Product pipeline
Intellectual Property

Search strategy

- **Database/Vendor:** Micropat
- **Search scope:** US Granted US Applications EP-A EP-B WO JP (bibliographic data only) DE-C,B DE-A DE-T DE-U GB-A FR-A; **English Title**
- **Years: Issue/Publication Date:** >20051231
- **Search String:** (Diabetes OR diabetic) AND (treatment OR treating)
- **Hits:** 618/217 patents (with/with out family members)
- **Date of search:** 11 July 2007

Top players and IPC classes

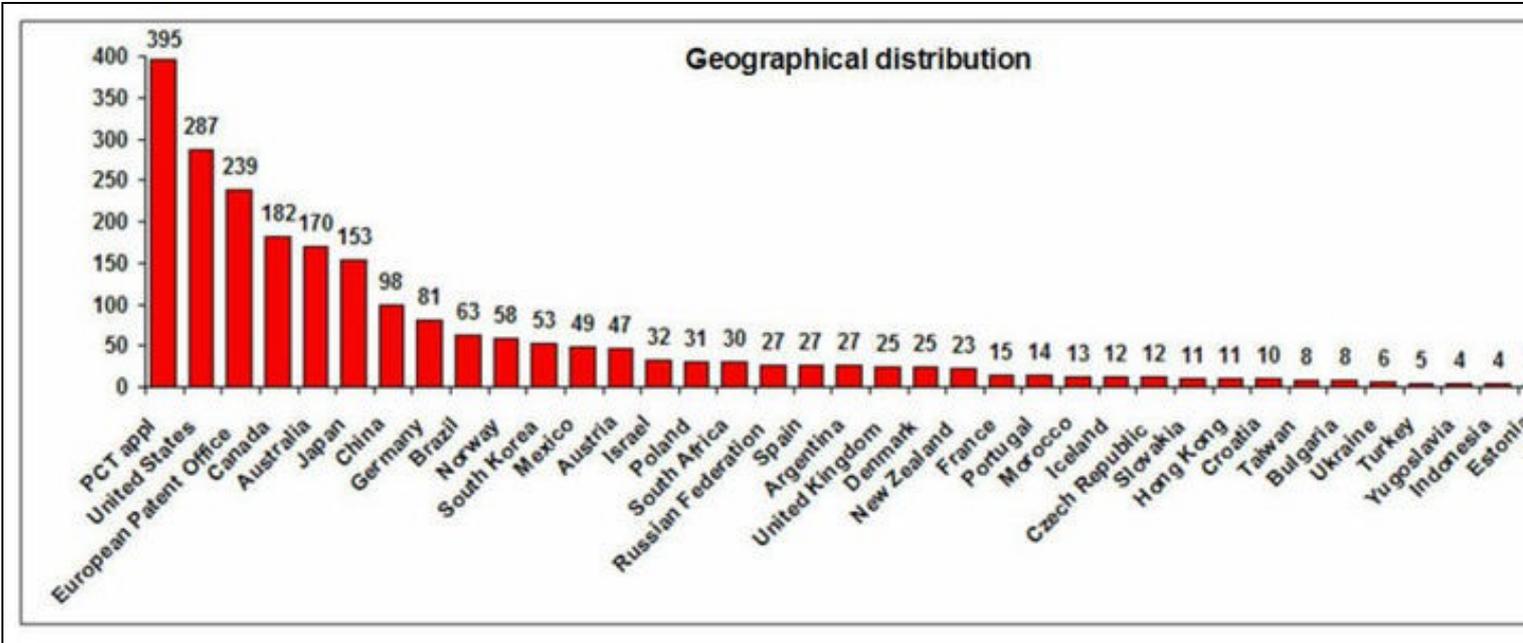


IPC code definition

- A61K** Preparations for medical, dental, or toilet purposes
- C07D** Heterocyclic compounds
- C07K** Peptides
- C12N** Micro-organisms or enzymes; compositions thereof

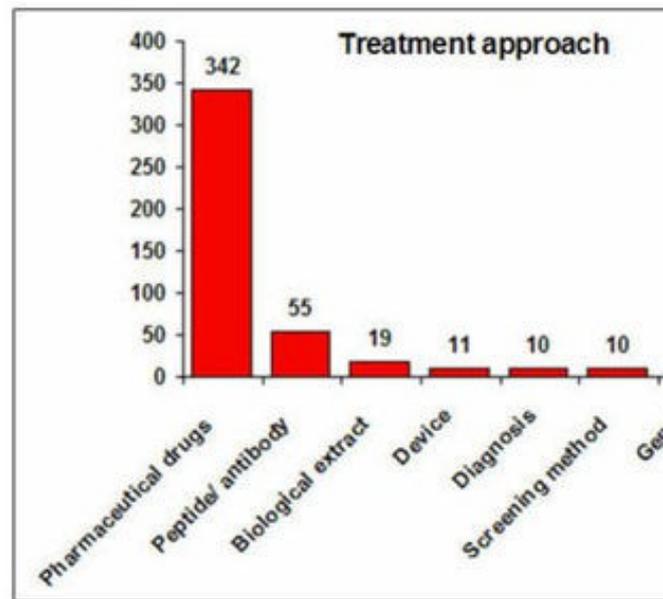
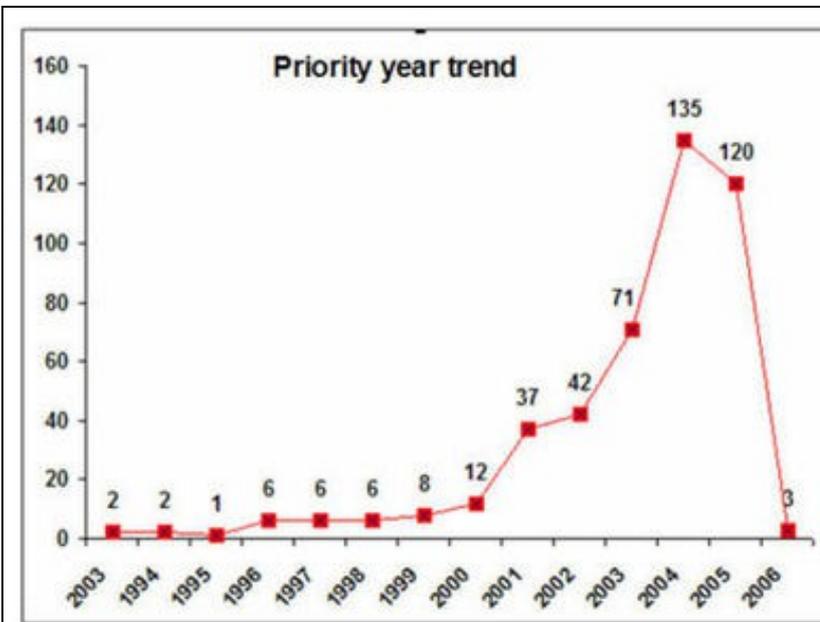
C12Q Measuring or testing processes involving enzymes or micro-organisms (immunoassay); compositions or test papers therefor; processes of preparing such compositions; condition-responsive control in microbiological or enzymological processes

Geographical Distribution and Treatment Approaches



IP activity and Treatment Approaches

- Decline in the IP activity during 2005 and 2006 is due 18 months publication delay of patent document.



Clinical Trials

Approved/On-going

Clinical trials				
Drug	Sponsors	Description	Phase	Date of Start
Oral Drugs				
Cannabinoid receptor antagonist				
Rimonabant	Sanofi-Aventis	The primary objective of this study is to assess the efficacy of SR141716 (rimonabant) compared to placebo on change in HbA1c and on relative change in body weight over 52 weeks in obese type 2 diabetic patients on monotherapy inadequately controlled with oral anti-diabetic drug (sulfonylurea	3	May-07

or α -glucosidase inhibitor).

Insulin Sensitisers

Metaglidasen	Metabolex		2, 3	May-06
Thioglitazone				
Rosiglitazone maleate/metformin hydrochloride (AVANDAMET)	GlaxoSmithKline	This study will evaluate the longer-term glycemic effect of two medicines approved for initial treatment of type 2 diabetes.	4	Oct-06
Balaglitazone	Rheoscience A/S	Balaglitazone is a thiazolidinedione derivative that is being developed as an oral anti-diabetic drug to improve blood glucose control in patients with type 2 diabetes. The purpose of this study is to assess if additional treatment with balaglitazone in patients with type 2 diabetes on stable insulin treatment will improve blood glucose control and decrease the daily insulin dose, but with less impact on weight gain and oedema.	3	Jul-07
(DPP-4) inhibitor				
Vildagliptin	Novartis	This is a 24-week study to assess the efficacy on HbA1c of 100 mg vildagliptin once daily as compared to placebo as add-on to metformin in patients with type 2 diabetes inadequately controlled with metformin.	3	May-06
Insulin				
Oral Insulin	NIDDK, NICHD, NIAID, NICR, ADA, JDRF	N/A	3	Feb-07
Potassium Channel Blocker				
Diazoxide	Grill, Valdemar, M.D.	The purpose of this study is to find out if Diazoxide can partly retain insulin production in newly diagnosed type 1 diabetes patients.	4	Feb-05
Nutritional Agents				
Benfotiamine (Vitamin B1)	University Hospital, Aker, The Research Council of Norway	N/A	1, 2	Aug-05
Docosahexaenoic acid (DHA)	NIDDK	N/A	2	June 2006
Vitamin D	University of Tromso	The purpose of the study is to evaluate if supplementation with vitamin D in a dose of 40.000 IU per week will result in improved metabolic control in patients with type 2 diabetes.	2	Jun-06
Carnitine Supplementation	Children's Mercy Hospital Kansas City, Sigma Tau Pharmaceuticals, Inc, Minimed Pharmaceuticals, Pharmacia/Upjohn Career Development Award	The purpose of this study is to determine whether type I diabetics with carnitine deficiency exhibit increased numbers of hypoglycemic (low blood sugars) events and if unrecognized hypoglycemia occurs during continuous 72-hour glucose monitoring. If they are determined to have unrecognized hypoglycemia, then oral carnitine supplementation will be given to those subjects and they will be reassessed for the number of hypoglycemic events in a 72-hour glucose monitoring.		Oct-04
Antiinflammatory				
Salsalate	NIDDK, National Institutes of Health Clinical Center	This study, conducted at the Phoenix Indian Medical Center, Phoenix, Arizona, will determine whether reducing subclinical inflammation lessens insulin resistance in healthy, obese volunteers.	4	Mar-03
Angiotensin (AT 2) Antagonist/blocker				
Olmесartan	Daiichi Sankyo Inc	N/A	3	Oct-04
MBX-2044	Metabolex	The purpose of this study is to collect important information regarding the glucose-lowering efficacy of MBX-2044 and the safety of MBX-2044 (especially weight gain and edema) in diabetics. It will also provide important information about the appropriate doses to be used in subsequent longer-term studies to evaluate the safety and efficacy of MBX-2044 alone and in combination with other anti-diabetic agents.	2	Oct-06
PF-00734200	Pfizer	The purpose of this Phase 2a study is to evaluate the efficacy, safety and tolerability, of multiple parallel doses of PF-00734200 following oral administration to adult human subjects with T2DM who currently are on a stable dose of metformin.	2	Jun-07
CP-945,598	Pfizer	The purpose of this study is to determine if CP-945,598 is effective in the treatment of obesity in type 2 diabetic patients	3	Nov-06

WelChol® (colesevelam)	Daiichi Sankyo Inc	This study is designed to assess the potential mechanism of action by which WelChol® (colesevelam) may improve blood glucose control in patients with type 2 diabetes	2	May-05
Aleglitazar and Actos®	Hoffmann-La Roche	This study will compare the effects of aleglitazar and Actos®, added to preexisting oral antihyperglycemic therapy and/or diet and exercise, on renal function in patients with type 2 diabetes, and normal or mildly impaired renal function.	2	June 2007
BI 1356 BS	Boehringer Ingelheim Pharmaceuticals	The objective of this monotherapy study is to investigate the efficacy, safety, and tolerability of 3 doses of BI 1356 BS compared to placebo over 12 weeks of treatment in patients with type 2 diabetes and insufficient control of their blood glucose. In addition, there will be an open-label treatment arm with metformin. The hypothesis of the trial is that the test drug, BI 1356 BS will lead to better control of blood glucose compared to placebo after 12 weeks of treatment.	2	May-06
BMS-512148	Bristol-Myers Squibb	The purpose of this clinical research study is to learn if BMS-512148, added to insulin and one or two anti-diabetes medications (metformin and/or pioglitazone or rosiglitazone), can help reduce the blood sugar levels compared to insulin and one or two anti-diabetes medications (metformin and/or pioglitazone or rosiglitazone) alone, in subjects with type 2 diabetes.	2, 3	October 2006
Parenteral routes				
Insulins				
Insuline glargine	Sanofi-Aventis	Purpose of this study is to determine the first dose and titration of basal insulin	4	May-06
Basal Insulin Plus Insulin Glulisine	Sanofi-Aventis	To evaluate the efficacy of a single injection of glulisine before the main meal added to insulin glargine plus oral antidiabetic drugs (OADs) compared to insulin glargine plus OADs in Type 2 diabetic patients poorly controlled with basal insulin plus OADs.	4	Jul-06
Inhaled Insulin (Exubera)	Pfizer	To assess the impact on glucose control by inhaled insulin in patients with type 2 diabetes who are not well controlled on 2 or more oral anti-diabetic agents	3	Mar-06
Insulin Inhalation Powder	Eli Lilly and Company	This is a phase 3, open-label, randomized study to evaluate the safety and efficacy of the Lilly/Alkermes inhaled insulin system compared to injected pre-meal insulin in non-smoking patients with type 2 diabetes. Patients will be treated for 24 months with a 2-month follow-up period.	3	Apr-06
Levemir	Novo Nordisk	This trial aims for a comparison of the effect on glycaemic control in subjects with type 2 diabetes under both established Western algorithm and Korean practical algorithm, given in combination with oral diabetic drug(s)	4	Aug-07
Pulsatile IV Insulin	Florida Atlantic University	The purpose of this study is to determine if restoring normal metabolic function in patients with either type I or type II diabetes can improve the impact of the consequences of diabetic complications on the overall quality of life of diabetic patients. Patients are treated once a week with pulsatile intravenous insulin therapy mimicking normal insulin secretion.	2, 3	Mar-03
Incretin Minetic				
Exenatide With Basal Insulin	Amylin Pharmaceuticals, Eli Lilly	This is a phase 3 trial designed to compare the effects of twice daily exenatide plus oral antidiabetic agents (OADs) and once-daily insulin glargine plus OADs with respect to glycemic control, as measured by hemoglobin A1c, with minimum weight gain, in patients with uncontrolled type 2 diabetes on OADs.	3	Jun-06
Exenatide	Baylor College of Medicine, NIH	The purpose of this study is to see if giving exenatide and insulin before a meal would lower blood sugars after the meal.	4	Mar-07
Exenatide Plus Metformin vs. Insulin Aspart Plus Metformin	Amylin Pharmaceuticals, Eli Lilly	This study in Germany is designed to compare the effects of twice-daily exenatide plus metformin and twice-daily premixed human insulin aspart plus metformin with respect to glycemic control, as measured by HbA1c, combined with the percentage of patients with at least one treatment-emergent hypoglycemic episode. Patients will be treated with study therapy for approximately 26 weeks.	3	Feb-07
Sitigliptin	Merck Frosst Canada Ltd, University of British Columbia		2	Nov-06
Antibodies				
hO K T 3 g a m m a 1 (Ala-Ala)	NIAID	hO K T 3 g a m m a 1 (Ala-Ala) is a man-made antibody that is commonly used to prevent organ rejection. The purpose of this study is determine whether hO K T 3 g a m m a 1 (Ala-Ala) can halt the progression of newly diagnosed type 1 diabetes.	2	Sep-05

Anti-CD20 (rituximab)	NIDDK, NICHD, NIAID, NICR, ADA, JDRF	This study will investigate the use of rituximab to see if it can help lower the number of immune B cells thereby preventing the destruction of any remaining insulin producing beta cells that remain at diagnosis.	2, 3	Dec-06
Surgical				
Islet Cell Transplants	Weill Medical College of Cornell University		1	Aug-03

Conferences

- [Diabetes Mellitus, Insulin Action and Resistance](#) at Breckenridge, Colorado from January 22 - 27, 2008
- [Diabetes UK Annual Professional Conference 2008](#) at Glasgow from 05 Mar 2008 09:00 to 07 Mar 2008 17:00
- [7th International Diabetes Federation Western Pacific Region Congress](#) at Wellington, New Zealand on 30 Mar 2008.
- [1st International Conference on Advanced Technologies & Treatments for Diabetes](#) at Czech Republic during 27 Feb to 01 Mar 2008.
- [Discovery Strategies Conference: Modeling Human Metabolic Syndrome and Type 2 Diabetes in Rodents](#) at US during Aug-05-2007.
- [7th International Conference for Clinical Endocrinology, Diabetes and Infertility](#) at Egypt during Sep-06-2007.
- [CDA/CSEM Professional Conference and Annual Meetings](#) at British Columbia during October 24-27, 2007.

Conference Update: [American Diabetic Association 2007](#)

Conference highlights for Oral Hypoglycemic Agents

1. [Oral hypoglycemic agents](#) and their role in diabetes treatment. The focus was the recent meta analysis published in [NEJM](#), showing increase CV mortality with Rosiglitazone. The panel consensus was that while awaiting more safety data, for now those patients who are tolerating Rosiglitazone should continue taking them, whereas newly diagnosed patients should try alternative treatment. Also all PPAR agonists should be treated as distinct entities rather than having class effect.
2. 12 different [diabetes products](#) are in various stages of development, and there were about 55 abstracts talking about DPP-IV inhibitors. They are especially useful for:
 - ◆ The elderly
 - ◆ Those with renal insufficiency
 - ◆ Heart failure patients
3. [Amyline](#) analogue (Pramlintide) was combined with Insulin for treatment of Type 2 DM and results were favorable.
4. Continuous glucose monitoring using implanted glucose sensors is a step forward in evolving technology. Yet it is still very expensive and best for highly trained patients on intensive insulin therapy.

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