Drugs Fut 2006, 31(8): 719-750

CCC: 0377-8282/2006

Update 2006 - Treatment of Endocrine Disorders

(Source: Prous Science Integrity®)

Treatment of Endocrine Disorders by Condition

Condition	Phase	Drug	Source
Addison's disease	II	Prasterone[2]	Paladin
Adrenal insufficiency	I	Hydrocortisone[1,3]	Phoqus Pharmaceuticals/Diurnal
Amenorrhea	II	Metreleptin	Amgen
Androgen decline in the aging male (andropause)	II	Fispemifene	QuatRx
Cushing's syndrome	II	Pasireotide	Novartis
Diabetes	II	INCB-3284	Pfizer
	II	KRP-101	Kyorin
	II (US)	Ono-5129	Ono Pharmaceutical
	II	TA-6666	Tanabe Seiyaku
	I/II	Encapsulated human islets	AmCyte
	I	Alveair	Coremed
	I	AZD-8677	AstraZeneca
	I	Bay-73-7977	Bayer
	I	CKD-501	Chong Kun Dang
	I	Inhaled insulin	Bristol-Myers Squibb/QDose
	I	MK-0533	Merck & Co.
	I	MK-0893	Merck & Co.
	I	MK-0941	Merck & Co.
	I (JP)	Ono-5129	Ono Pharmaceutical
	I	SRT-501	Sirtris Pharmaceuticals
Diabetes type 1	L-2005	Insulin glulisine[2]	sanofi-aventis
	L-2005	Oral-lyn™	Generex/PharmaBrand
	L-2005	Pramlintide acetate[2]	Amylin
	L-2006	Exubera®[2]	Pfizer
	III	AERx® iDMS[2]	Aradigm/Novo Nordisk
	III	AIR® insulin	Alkermes/Lilly
	III	DiaPep277®	DeveloGen
	III	Technosphere® insulin	MannKind
	II	Basulin®	Flamel Technologies
	II	E1-I.N.T.™	Transition Therapeutics
	II	Intranasal insulin	Bentley Pharmaceuticals/Biocon India/Dong Sung
	II	Mecasermin rinfabate [rDNA origin]	Insmed
	II	NBI-60242	Neurocrine Biosciences
	II	rhGAD65	Diamyd Medical
	II	TRX4	TolerRx
	II	TS-033	Taisho
	I/II	PEG-encapsulated human islets	Novocell
	I	DiabeCell	Living Cell Technologies
	I	Lisofylline[2]	DiaKine Therapeutics
	I	NN-344	Novo Nordisk
	I	NN-5401	Novo Nordisk
Diabetes type 2	L-2005	Exenatide[2]	Amylin/Lilly
	L-2005	Insulin glulisine[2]	sanofi-aventis
	L-2005	Oral-lyn™	Generex/PharmaBrand

Continuation

Treatment of Endocrine Disorders by Condition

Condition	Phase	Drug	Source
Diabetes type 2	L-2005	Pioglitazone hydrochloride/ metformin hydrochloride	Takeda
	L-2005	Pramlintide acetate[2]	Amylin
	L-2006	Exubera®[2]	Pfizer
	L-2006	Glimepiride/rosiglitazone maleate	GlaxoSmithKline
	R-2006	Pioglitazone hydrochloride/glimepiride	Takeda
	R-2006	Sitagliptin phosphate[2]	Merck & Co.
	Prereg.	Sitagliptin phosphate/metformin hydrochloride	Merck & Co.
	Prereg.	Vildagliptin[2]	Novartis
	III	AERx® iDMS[2]	Aradigm/Novo Nordisk
	III	AIR® insulin	Alkermes/Lilly
	III	Colesevelam hydrochloride[1]	Daiichi Sankyo
	III	Liraglutide[2]	Novo Nordisk
	III	Rimonabant hydrochloride[1,2]	sanofi-aventis
	III	Saxagliptin	Bristol-Myers Squibb
	III (JP)	Sitagliptin phosphate[2]	Banyu (Merck & Co.)/Ono Pharmaceutical
	III (EU, US)	SYR-322	Takeda
	III	Technosphere® insulin	MannKind
	II/III	Metaglidasen	Metabolex/Ortho-McNeil
	II/III	rhGAD65	Diamyd Medical
	II/III	Rivoglitazone	Daiichi Sankyo
	II	189075	GlaxoSmithKline
	II	677954	GlaxoSmithKline
	II	AVE-0010	sanofi-aventis/Zealand Pharma
	II	AVE-0847	sanofi-aventis
	II	AVE-2268	sanofi-aventis
	II	Balaglitazone	Dr. Reddy's Laboratories/Rheoscience
	II	Basulin®	Flamel Technologies
	II (I, JP)	BIM-51077 (R-1583, ITM-077)	Ipsen/Roche/Teijin
	II	BLX-1002	Bexel Pharmaceuticals
	II	BMS-512148	Bristol-Myers Squibb
	II	Cetilistat	Alizyme/Takeda
	II	Colestilan[1,2]	Mitsubishi Pharma
	II	CS-917	Daiichi Sankyo/Metabasis Therapeutics
	II	Denagliptin	GlaxoSmithKline
	II	DIO-902	DiObex/Cortendo
	II	E1-I.N.T.™	Transition Therapeutics
	II	GRC-8200	Glenmark Pharmaceuticals
	II	ISIS-113715	Isis Pharmaceuticals
	II	K-111	Kowa
	II	Ketoconazole[1,2]	Cortendo
	II	KI-02212	Kos Pharmaceuticals
	II	KRP-104	ActivX (Kyorin)
	II	Mecasermin rinfabate [rDNA origin]	Insmed
	II	MP-513	Mitsubishi Pharma
	II	N-5984 (KRP-204)	Kyorin/Nisshin Pharma
	II	Naveglitazar	Ligand/Lilly
	II	Netoglitazone[2]	Perlegen Sciences/Mitsubishi Pharma
	II	Oral Insulin	Emisphere
	II	PHX-1149	Phenomix
	II	PN-2034	Wellstat Therapeutics
	II	PSN-357	Prosidion (OSI Pharmaceuticals)
	II	PSN-9301	Prosidion (OSI Pharmaceuticals)
	II	R-1438	Roche
	II	R-1440	Roche
	II	Solabegron hydrochloride	GlaxoSmithKline
	II	Teglicar	Sigma-Tau
	II	TS-033	Taisho
	I/II	PC-DAC™:Exendin-4	ConjuChem
	I	625019	GlaxoSmithKline
	I	716155	GlaxoSmithKline
	I	APD-668	Ortho-McNeil/Arena Pharmaceuticals
	I	AT-1391	Altea Therapeutics

Continuation

Treatment of Endocrine Disorders by Condition

Condition	Phase	Drug	Source
Diabetes type 2	I	ATL-618	Adenosine Therapeutics/Johnson & Johnson
	I	AVE-5376	sanofi-aventis
	I	AVE-8134	sanofi-aventis
	I	EMD-387008	Merck KGaA
	I	INCB-13739	Incyte
	I	JTT-551	Japan Tobacco
	I	MB-07803	Metabasis Therapeutics
	I	NN-344	Novo Nordisk
	I	NN-5401	Novo Nordisk
	I	NN-9101	Novo Nordisk
	I	PSN-010	Prosidion (OSI Pharmaceuticals)
	I	R-1439	Roche
	I	R-1499	Roche
	I	SUN-E7001 (CS-872)	Daiichi Sankyo
	I (JP)	SYR-322	Takeda
	I	TS-021	Lilly/Taisho
	I	ZYH-2	Zydus Cadila
	Discontinued	Sipoglitazar	Takeda
	Discontinued	Tesaglitazar[2]	AstraZeneca
Diabetic complications	III	Insulin glargine[1]	sanofi-aventis
	II/III	Fidarestat[2]	Sanwa
	II	Lidorestat	Alinea Pharmaceuticals
	II	NCX-40162	NicOx
	I	SPR-210	Senju
Dysmenorrhea	I	Lidocaine hydrochloride[1]	Columbia Laboratories
Endocrine disorders	II	Ibutamoren mesilate[2]	Merck & Co.
	I	MK-0974	Merck & Co.
Endometriosis	Prereg. (JP)	Dienogest[1,2]	Mochida
	III	Cetrorelix acetate[1,2]	AEterna Zentaris/Solvay
	III (DE)	Dienogest[1,2]	Schering AG
	III	FP-1096	KV Pharmaceutical/FemmePharma
	II	Asoprisnil[2]	TAP Pharmaceutical
	II	CDB-4124	Repros Therapeutics
	II	NBI-42902	Neurocrine Biosciences
	II	NBI-56418	Neurocrine Biosciences
	II	Prinaberel[2]	Wyeth
	I	Teverelix	Ardana Bioscience
Fibroids, uterine (myoma)	III	Asoprisnil[2]	Schering AG/TAP Pharmaceutical
	II	CDB-4124	Repros Therapeutics
	II	Cetrorelix acetate[1,2]	Nippon Kayaku/Shionogi/AEterna Zentaris
	II	Dienogest[1,2]	Mochida
	II	Mifepristone[1,2]	Université de Poitiers
	II	Uliprisnil acetate	National Institute of Child Health
	I	Teverelix	Ardana Bioscience
Fibrosis, breast	III	IoGen™	Symbollon/Bioaccelerate
Goiter	I	Thyrotropin alfa, recombinant[1]	Genzyme General
Growth hormone deficit	Prereg.	Human growth hormone, recombinant	Cangene
	II	ALTU-238	Altus Pharmaceuticals
	II	Pralmorelin[1,2]	Kaken
	I	EP-01572	Ardana Bioscience/AEterna Zentaris
	I	Somatropin [rDNA origin][1]	Emisphere/Novartis
Gynecomastia	II	Anastrozole[1,2]	AstraZeneca
Hormone replacement therapy	I	LGD-2941	Ligand/TAP Pharmaceutical
Hot flushes	III	Esmirtazapine maleate	Organon
Hypoglycemia	I/II	DIO-901	DiObex

Continuation

Treatment of Endocrine Disorders by Condition

Condition	Phase	Drug	Source
Hypogonadism	L-2005	Testosterone, transdermal gel	Cellegy/ProStrakan
	III	AA-2600	Auxilium
	III	Enclomiphene citrate	Repros Therapeutics
	III	Testosterone, transdermal gel	BioSante
	II	Dihydrotestosterone, transdermal gel	Ascend Therapeutics
	II	Testosterone, transdermal cream	Ardana Bioscience
	I	Dutasteride[1,2]	GlaxoSmithKline
	I	LGD-2941	Ligand/TAP Pharmaceutical
	I	Testosterone glucoside	ProStrakan
	I	Testosterone, transdermal cream	MacroChem
Insulin resistance (metabolic syndrome)	III	Nateglinide[1,2]	Novartis
	III	Valsartan[1]	Novartis
	II	BGP-15	N-Gene
	II	BT-16	Quark Biotech
	II	Ketoconazole[1,2]	Cortendo
	I	AMG-221	Amgen/Biovitrum
Latent autoimmune diabetes (LADA)	II	DiaPep277®	DeveloGen
Menorrhagia	III	XP-12-B	Xanodyne
Postmenopausal syndrome	III	Bazedoxifene/conjugated estrogens	Wyeth/Ligand
	III	Desvenlafaxine succinate[2]	Wyeth
	III	Estradiol MDTS®	Acrux/Vivus
	III	Estradiol/progestogen, transdermal gel	Solvay/BioSante
	II	Estradiol glucoside	ProStrakan
	II	Estradiol/testosterone, transdermal gel	Paladin
	II	MF-101	Bionovo
	I/II	Estetrol	Pantarhei Bioscience
	I	232802	GlaxoSmithKline
	I	Org-43228	Organon
Severe primary IGF-I deficiency	L-2006	Mecasermin [rDNA origin]	Tercica/Ipsen
	L-2006	Mecasermin rinfabate [rDNA origin]	Insmed
Sexual dysfunction, female	III	Testosterone, transdermal gel	Cellegy/ProStrakan
	II	Testosterone, transdermal gel	BioSante
	I	Estradiol/testosterone, transdermal gel	BioSante
	I	LGD-2941	Ligand/TAP Pharmaceutical
Urogenital atrophy	III	Ospemifene[2]	QuatRx
Vaginal bleeding	III	Ethinylestradiol/dienogest[1]	Schering AG
Vaginitis, atrophic	Prereg.	Lasofoxifene tartrate[2]	Pfizer/Ligand

[1]Launched for another indication. [2]Monograph previously published in Drugs of the Future. [3]New formulation.

Treatment of Endocrine Disorders by Source

Source	Condition	Drug	Phase
Acrux	Postmenopausal syndrome	Estradiol MDTS®	III
ActivX (Kyorin)	Diabetes type 2	KRP-104	II
Adenosine Therapeutics	Diabetes type 2	ATL-618	I
AEterna Zentaris	Endometriosis	Cetrorelix acetate[1,2]	III
	Fibroids, uterine (myoma)	Cetrorelix acetate[1,2]	II
	Growth hormone deficit	EP-01572	I
Alinea Pharmaceuticals	Diabetic complications	Lidorestat	II
Alizyme	Diabetes type 2	Cetilistat	II
Alkermes	Diabetes type 1	AIR® insulin	III
	Diabetes type 2	AIR® insulin	III
Altea Therapeutics	Diabetes type 2	AT-1391	I
Altus Pharmaceuticals	Growth hormone deficit	ALTU-238	II
AmCyte	Diabetes	Encapsulated human islets	I/II
Amgen	Amenorrhea	Metreleptin	II
	Insulin resistance (metabolic syndrome)	AMG-221	I
Amylin	Diabetes type 1	Pramlintide acetate[2]	L-2005
	Diabetes type 2	Exenatide[2]	L-2005
		Pramlintide acetate[2]	L-2005
Aradigm	Diabetes type 1	AERx® iDMS[2]	III
	Diabetes type 2	AERx® iDMS[2]	III
Ardana Bioscience	Endometriosis	Teverelix	I
	Fibroids, uterine (myoma)	Teverelix	I
	Growth hormone deficit	EP-01572	I
	Hypogonadism	Testosterone, transdermal cream	II
Arena Pharmaceuticals	Diabetes type 2	APD-668	I
Ascend Therapeutics	Hypogonadism	Dihydrotestosterone, transdermal gel	II
AstraZeneca	Diabetes	AZD-8677	I
	Diabetes type 2	Tesaglitazar[2]	Discontinued
	Gynecomastia	Anastrozole[1,2]	II
Auxilium	Hypogonadism	AA-2600	III
Banyu (Merck & Co.)	Diabetes type 2	Sitagliptin phosphate[2]	III (JP)
Bayer	Diabetes	Bay-73-7977	I
Bentley Pharmaceuticals	Diabetes type 1	Intranasal insulin	II
Bexel Pharmaceuticals	Diabetes type 2	BLX-1002	II
Bioaccelerate	Fibrosis, breast	IoGen™	III
Biocon India	Diabetes type 1	Intranasal insulin	II
Bionovo	Postmenopausal syndrome	MF-101	II
BioSante	Hypogonadism	Testosterone, transdermal gel	III
	Postmenopausal syndrome	Estradiol/progestogen, transdermal gel	III
	Sexual dysfunction, female	Estradiol/testosterone, transdermal gel	I
		Testosterone, transdermal gel	II
Biovitrum	Insulin resistance (metabolic syndrome)	AMG-221	I
Bristol-Myers Squibb	Diabetes	Inhaled insulin	I
	Diabetes type 2	BMS-512148	II
		Saxagliptin	III
Cangene	Growth hormone deficit	Human growth hormone, recombinant	Prereg.
Cellegy	Hypogonadism	Testosterone, transdermal gel	L-2005
	Sexual dysfunction, female	Testosterone, transdermal gel	III
Chong Kun Dang	Diabetes	CKD-501	I
Columbia Laboratories	Dysmenorrhea	Lidocaine hydrochloride[1]	I
ConjuChem	Diabetes type 2	PC-DAC™:Exendin-4	I/II
Coremed	Diabetes	Alveair	I
Cortendo	Diabetes type 2	DIO-902	II
		Ketoconazole[1,2]	II
	Insulin resistance (metabolic syndrome)	Ketoconazole[1,2]	II
Daiichi Sankyo	Diabetes type 2	Colesevelam hydrochloride[1]	III
		CS-917	II
		Rivoglitazone	II/III
		SUN-E7001 (CS-872)	I
DeveloGen	Diabetes type 1	DiaPep277®	III
	Latent autoimmune diabetes (LADA)	DiaPep277®	II
DiaKine Therapeutics	Diabetes type 1	Lisofylline[2]	I
Diamyd Medical	Diabetes type 1	rhGAD65	II
	Diabetes type 2	rhGAD65	II/III
DiObex	Diabetes type 2	DIO-902	II

Continuation

Treatment of Endocrine Disorders by Source

Source	Condition	Drug	Phase
DiObex	Hypoglycemia	DIO-901	I/II
Diurnal	Adrenal insufficiency	Hydrocortisone[1,3]	I
Dong Sung	Diabetes type 1	Intranasal insulin	II
Dr. Reddy's Laboratories	Diabetes type 2	Balaglitazone	II
Emisphere	Diabetes type 2	Oral Insulin	II
	Growth hormone deficit	Somatropin [rDNA origin][1]	I
FemmePharma	Endometriosis	FP-1096	III
Flamel Technologies	Diabetes type 1	Basulin®	II
	Diabetes type 2	Basulin®	II
Generex	Diabetes type 1	Oral-lyn™	L-2005
	Diabetes type 2	Oral-lyn™	L-2005
Genzyme General	Goiter	Thyrotropin alfa, recombinant[1]	I
GlaxoSmithKline	Diabetes type 2	189075	II
		625019	I
		677954	II
		716155	I
		Denagliptin	II
		Glimepiride/rosiglitazone maleate	L-2006
		Solabegron hydrochloride	II
	Hypogonadism	Dutasteride[1,2]	I
	Postmenopausal syndrome	232802	I
Glenmark Pharmaceuticals	Diabetes type 2	GRC-8200	II
Incyte	Diabetes type 2	INCB-13739	I
Insmed	Diabetes type 1	Mecasermin rinfabate [rDNA origin]	II
	Diabetes type 2	Mecasermin rinfabate [rDNA origin]	II
	Severe primary IGF-I deficiency	Mecasermin rinfabate [rDNA origin]	L-2006
Ipsen	Diabetes type 2	BIM-51077 (R-1583, ITM-077)	II (I, JP)
	Severe primary IGF-I deficiency	Mecasermin [rDNA origin]	L-2006
Isis Pharmaceuticals	Diabetes type 2	ISIS-113715	II
Japan Tobacco	Diabetes type 2	JTT-551	I
Johnson & Johnson	Diabetes type 2	ATL-618	I
Kaken	Growth hormone deficit	Pralmorelin[1,2]	II
Kos Pharmaceuticals	Diabetes type 2	KI-02212	II
Kowa	Diabetes type 2	K-111	II
KV Pharmaceutical	Endometriosis	FP-1096	III
Kyorin	Diabetes	KRP-101	II
	Diabetes type 2	N-5984 (KRP-204)	II
Ligand	Diabetes type 2	Naveglitazar	II
	Hormone replacement therapy	LGD-2941	I
	Hypogonadism	LGD-2941	I
	Postmenopausal syndrome	Bazedoxifene/conjugated estrogens	III
	Sexual dysfunction, female	LGD-2941	I
	Vaginitis, atrophic	Lasofoxifene tartrate[2]	Prereg.
Lilly	Diabetes type 1	AIR® insulin	III
	Diabetes type 2	AIR® insulin	III
		Exenatide[2]	L-2005
		Naveglitazar	II
		TS-021	I
Living Cell Technologies	Diabetes type 1	DiabeCell	I
MacroChem	Hypogonadism	Testosterone, transdermal cream	I
MannKind	Diabetes type 1	Technosphere® insulin	III
	Diabetes type 2	Technosphere® insulin	III
Merck & Co.	Diabetes	MK-0533	I
		MK-0893	I
		MK-0941	I
	Diabetes type 2	Sitagliptin phosphate/metformin hydrochloride	Prereg.
		Sitagliptin phosphate[2]	R-2006
	Endocrine disorders	Ibutamoren mesilate[2]	II
		MK-0974	I
Merck KGaA	Diabetes type 2	EMD-387008	I
Metabasis Therapeutics	Diabetes type 2	CS-917	II
		MB-07803	I
Metabolex	Diabetes type 2	Metaglidasen	II/III
Mitsubishi Pharma	Diabetes type 2	Colestilan[1,2]	II
		Netoglitazone[2]	II

Continuation

Treatment of Endocrine Disorders by Source

Source	Condition	Drug	Phase
Mitsubishi Pharma	Diabetes type 2	MP-513	II
Mochida	Endometriosis	Dienogest[1,2]	Prereg. (JP)
	Fibroids, uterine (myoma)	Dienogest[1,2]	II
National Institute of Child Health	Fibroids, uterine (myoma)	Uliprisnil acetate	II
Neurocrine Biosciences	Diabetes type 1	NBI-60242	II
	Endometriosis	NBI-42902	II
		NBI-56418	II
N-Gene	Insulin resistance (metabolic syndrome)	BGP-15	II
NicOx	Diabetic complications	NCX-40162	II
Nippon Kayaku	Fibroids, uterine (myoma)	Cetrorelix acetate[1,2]	II
Nisshin Pharma	Diabetes type 2	N-5984 (KRP-204)	II
Novartis	Cushing's syndrome	Pasireotide	II
	Diabetes type 2	Vildagliptin[2]	Prereg.
	Growth hormone deficit	Somatropin [rDNA origin][1]	I
	Insulin resistance (metabolic syndrome)	Nateglinide[1,2]	III
		Valsartan[1]	III
Novo Nordisk	Diabetes type 1	AERx® iDMS[2]	III
		NN-344	I
		NN-5401	I
	Diabetes type 2	AERx® iDMS[2]	III
		Liraglutide[2]	III
		NN-344	I
		NN-5401	I
		NN-9101	I
Novocell	Diabetes type 1	PEG-encapsulated human islets	I/II
Ono Pharmaceutical	Diabetes	Ono-5129	II (US)
		Ono-5129	I (JP)
	Diabetes type 2	Sitagliptin phosphate[2]	III (JP)
Organon	Hot flushes	Esmirtazapine maleate	III
	Postmenopausal syndrome	Org-43228	I
Ortho-McNeil	Diabetes type 2	APD-668	I
		Metaglidasen	II/III
Paladin	Addison's disease	Prasterone[2]	II
	Postmenopausal syndrome	Estradiol/testosterone, transdermal gel	II
Pantarhei Bioscience	Postmenopausal syndrome	Estetrol	I/II
Perlegen Sciences	Diabetes type 2	Netoglitazone[2]	II
Pfizer	Diabetes	INCB-3284	II
	Diabetes type 1	Exubera®[2]	L-2006
	Diabetes type 2	Exubera®[2]	L-2006
	Vaginitis, atrophic	Lasofoxifene tartrate[2]	Prereg.
PharmaBrand	Diabetes type 1	Oral-lyn™	L-2005
	Diabetes type 2	Oral-lyn™	L-2005
Phenomix	Diabetes type 2	PHX-1149	II
Phoqus Pharmaceutical	Adrenal insufficiency	Hydrocortisone[1,3]	I
Prosidion (OSI Pharmaceuticals)	Diabetes type 2	PSN-010	I
		PSN-357	II
		PSN-9301	II
ProStrakan	Hypogonadism	Testosterone glucoside	I
		Testosterone, transdermal gel	L-2005
	Postmenopausal syndrome	Estradiol glucoside	II
	Sexual dysfunction, female	Testosterone, transdermal gel	III
QDose	Diabetes	Inhaled insulin	I
Quark Biotech	Insulin resistance (metabolic syndrome)	BT-16	II
QuatRx	Androgen decline in the aging male (andropause)	Fispemifene	II
	Urogenital atrophy	Ospemifene[2]	III
Repros Therapeutics	Endometriosis	CDB-4124	II
	Fibroids, uterine (myoma)	CDB-4124	II
	Hypogonadism	Enclomiphene citrate	III
Rheoscience	Diabetes type 2	Balaglitazone	II
Roche	Diabetes type 2	BIM-51077 (R-1583, ITM-077)	II (I, JP)
		R-1438	II
		R-1439	I
		R-1440	II
		R-1499	I

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Treatment of Endocrine Disorders by Source

Source	Condition	Drug	Phase
Roche	Diabetes type 2	AVE-0847	II
sanofi-aventis	Diabetes type 1	Insulin glulisine[2]	L-2005
	Diabetes type 2	AVE-0010	II
		AVE-2268	II
		AVE-5376	I
		AVE-8134	I
		Insulin glulisine[2]	L-2005
		Rimonabant hydrochloride[1,2]	III
	Diabetic complications	Insulin glargine[1]	III
Sanwa	Diabetic complications	Fidarestat[2]	II/III
Schering AG	Endometriosis	Dienogest[1,2]	III (DE)
	Fibroids, uterine (myoma)	Asoprisnil[2]	III
	Vaginal bleeding	Ethinylestradiol/dienogest[1]	III
Senju	Diabetic complications	SPR-210	I
Shionogi	Fibroids, uterine (myoma)	Cetrorelix acetate[1,2]	II
Sigma-Tau	Diabetes type 2	Teglicar	II
Sirtris Pharmaceuticals	Diabetes	SRT-501	I
Solvay	Endometriosis	Cetrorelix acetate[1,2]	III
	Postmenopausal syndrome	Estradiol/progestogen, transdermal gel	III
Symbollon	Fibrosis, breast	IoGen™	III
Taisho	Diabetes type 1	TS-033	II
	Diabetes type 2	TS-021	I
		TS-033	II
Takeda	Diabetes type 2	Cetilistat	II
		Pioglitazone hydrochloride/glimepiride	R-2006
		Pioglitazone hydrochloride/metformin hydrochloride	L-005
		Sipoglitazar	Discontinued
		SYR-322	III (EU, US)
		SYR-322	I (JP)
Tanabe Seiyaku	Diabetes	TA-6666	II
TAP Pharmaceutical	Endometriosis	Asoprisnil[2]	II
	Fibroids, uterine (myoma)	Asoprisnil[2]	III
	Hormone replacement therapy	LGD-2941	I
	Hypogonadism	LGD-2941	I
	Sexual dysfunction, female	LGD-2941	I
Teijin	Diabetes type 2	BIM-51077 (R-1583, ITM-077)	II (I, JP)
Tercica	Severe primary IGF-I deficiency	Mecasermin [rDNA origin]	L-2006
TolerRx	Diabetes type 1	TRX4	II
Transition Therapeutics	Diabetes type 1	E1-I.N.T.™	II
	Diabetes type 2	E1-I.N.T.™	II
Université de Poitiers	Fibroids, uterine (myoma)	Mifepristone[1,2]	II
Vivus	Postmenopausal syndrome	Estradiol MDTS®	III
Wellstat Therapeutics	Diabetes type 2	PN-2034	II
Wyeth	Endometriosis	Prinaberel[2]	II
	Postmenopausal syndrome	Bazedoxifene/conjugated estrogens	III
		Desvenlafaxine succinate[2]	III
Xanodyne	Menorrhagia	XP-12-B	III
Zealand Pharma	Diabetes type 2	AVE-0010	II
Zydus Cadila	Diabetes type 2	ZYH-2	I

[1]Launched for another indication. [2]Monograph previously published in Drugs of the Future. [3]New formulation.

Drugs Under Development for the Treatment of Endocrine Disorders

N.E. Mealy, B. Lupone
Prous Science, P.O. Box 540, 08080 Barcelona, Spain

189075

189075 is a sodium-glucose co-transporter SGLT2 inhibitor undergoing phase II clinical evaluation at GlaxoSmithKline for the treatment of type 2 diabetes.

232802

A selective estrogen receptor modulator (SERM), GlaxoSmithKline's 232802 is in phase I clinical trials for the treatment of menopausal symptoms.

625019/677954

GlaxoSmithKline is conducting early clinical trials with 625019, a pan-peroxisome proliferator-activated receptor (PPAR) agonist with potential for the treatment of type 2 diabetes. 677954 is another pan-PPAR agonist in phase II clinical studies at GlaxoSmithKline for the treatment of type 2 diabetes.

716155

716155, a glucagon-like peptide 1 (GLP-1) agonist, is currently undergoing phase I clinical trials at GlaxoSmithKline for the treatment of type 2 diabetes. Originally developed by Human Genome Sciences, the compound was acquired on an exclusive basis in October 2004 by GlaxoSmithKline for development and commercialization.

AA-2600

AA-2600 is a testosterone transmucosal film in phase III clinical trials at Auxilium for the treatment of hypogonadism. AA-2600 was developed using transmucosal film technology licensed from PharmaForm.

AERx® iDMS

The AERx® insulin Diabetes Management System (AERx® iDMS) is currently undergoing phase III clinical trials at Aradigm and Novo Nordisk for the treatment of type 1 and 2 diabetes. AERx® iDMS is an electronic pulmonary delivery system for administering human insulin by inhalation. It converts a proprietary liquid insulin formulation into fine aerosolized particles to be delivered locally to the deep lung and subsequently to the systemic circulation.

Original monograph – Drugs Fut 2005, 30(7): 673.

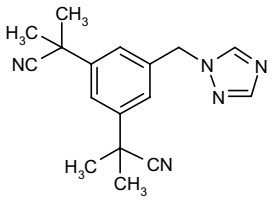
ALTU-238

A crystallized formulation of human growth hormone (hGH), ALTU-238 is in phase II clinical trials at Altus Pharmaceuticals for the once-weekly s.c. treatment of GH deficiency. The drug candidate employs Altus's proprietary protein crystallization and formulation technology, which preserves the structure of the hGH molecule without the need for polymers or encapsulation, and enables ease of administration through a fine gauge needle. Preclinical studies demonstrated that ALTU-238, delivered with a fine 30-gauge needle, results in hGH bioavailability that is capable of stimulating the production of insulin-like growth factor I (IGF-I) levels to the normal range in a dose-dependent manner, consistent with a once-weekly product.

AMG-221

AMG-221 is an 11-β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitor in early clinical trials at Amgen and Biovitrum for the treatment of metabolic insulin resistance. The drug candidate was originally developed at Amgen and later became the subject of a co-development agreement with Biovitrum.

Anastrozole, New Indication



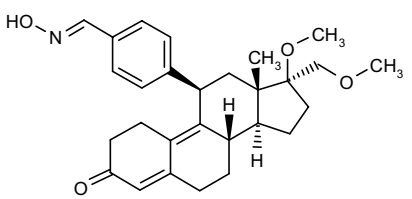
Anastrozole (Arimidex®) is a potent and highly selective, nonsteroidal aromatase inhibitor first launched in 1995 by AstraZeneca for the treatment of advanced breast cancer in postmenopausal women. Currently, the drug is in phase II clinical trials at AstraZeneca for the treatment of gynecomastia, McCune-Albright syndrome and sexual dysfunction in male epileptic patients. It is also undergoing phase II clinical trials at Serono for the treatment of female infertility associated with ovulatory dysfunction. In July 2002, AstraZeneca licensed rights to develop and market the product to Serono.

Original monograph – Drugs Fut 1995, 20(1): 30.

APD-668

Ortho-McNeil is conducting early clinical trials with APD-668, a glucose-dependent insulinotropic receptor (GDIR) agonist, for the oral treatment of type 2 diabetes. The GDIR (previously referred to as 19AJ) is a novel orphan G-protein-coupled receptor discovered by Arena Pharmaceuticals that has the potential to stimulate insulin production in response to increases in blood glucose. Unlike the GLP-1 receptor, the GDIR is amenable to small-molecule, orally active drug development. The GDIR mechanism is glucose-dependent, and as such, Arena's GDIR agonists are not expected to lower normal fasting blood glucose levels or cause hypoglycemia. In addition, GDIR stimulation has been found to increase the levels and activity of intracellular factors thought to be involved in the preservation of β-cells. Ortho-McNeil was granted certain rights to the product pursuant to a collaboration agreement signed by the companies in December 2004.

Asoprisnil



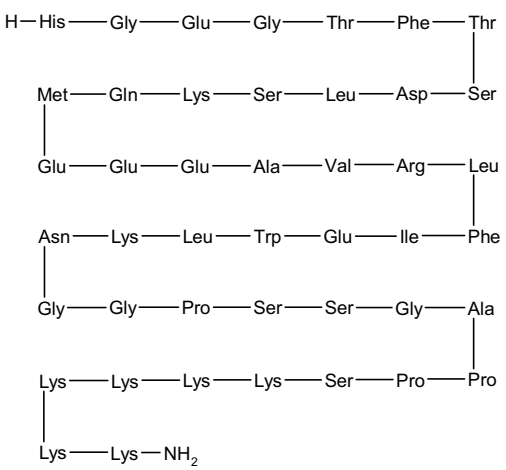
The orally active selective progesterone receptor modulator (SPRM) asoprisnil (J-867) is in phase III clinical trials at Schering AG and TAP Pharmaceutical for the long-term treatment of uterine fibroids. During the clinical study program, some patients experienced endometrial changes, which were reversible in most cases after stopping therapy. In view of these findings, the extension studies were amended and dosing was discontinued in October 2005. Investigators continue to follow up the patients as part of the ongoing extension studies. The drug is also in phase II trials at TAP for the oral treatment of endometriosis. The compound, originally developed at Schering AG, will be co-marketed in the U.S. and Canada by Schering AG and TAP, while Schering retains marketing rights worldwide.

Original monograph – Drugs Fut 2005, 30(10): 985.

ATL-618

ATL-618, an adenosine receptor antagonist, is currently being evaluated in phase I clinical trials at Adenosine Therapeutics in collaboration with Johnson & Johnson Pharmaceutical Research and Development, an affiliate of Ortho-McNeil, for the treatment of type 2 diabetes and asthma. In January 2005, Adenosine Therapeutics signed a worldwide collaboration and option agreement with Ortho-McNeil to further develop adenosine A_{2B} receptor antagonists for the oral treatment of type 2 diabetes, asthma and other disorders.

AVE-0010



Phase II clinical trials are under way for AVE-0010 (ZP-10), a GLP-1 receptor agonist and insulin secretagogue developed at sanofi-aventis, for the treatment of type 2 diabetes. The drug candidate has shown glucose-lowering activity similar to that of competing GLP-1 agonists while being devoid of nausea-related side effects. Originally developed at Zealand Pharma, it was licensed to sanofi-aventis in June 2003.

AVE-0847/AVE-5376

AVE-0847 is a dual PPARα/γ agonist in phase II clinical testing at sanofi-aventis for the treatment of type 2 diabetes and dyslipidemia. AVE-5376 is another dual PPARα/γ agonist in early clinical trials at sanofi-aventis for the treatment of type 2 diabetes.

AVE-2268

The SGLT2 inhibitor AVE-2268 is being evaluated in phase II clinical trials at sanofi-aventis for the treatment of type 2 diabetes.

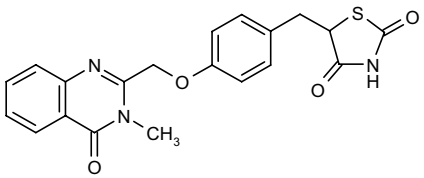
AVE-8134

A PPARα agonist developed at sanofi-aventis, AVE-8134 is currently undergoing phase I clinical trials for the treatment of type 2 diabetes. It is also being evaluated in early clinical studies for the treatment of dyslipidemia and chronic heart failure (CHF).

AZD-8677

AZD-8677 is in early clinical trials at AstraZeneca for the treatment of diabetes and dyslipidemia.

Balaglitazone

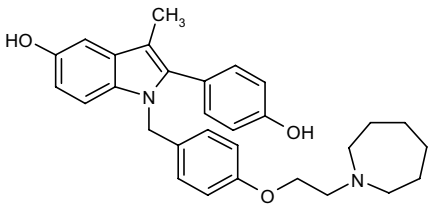


Balaglitazone (DRF-2593), a partial PPARγ agonist, is currently being evaluated in phase II clinical trials at Dr. Reddy's Laboratories for the treatment of type 2 diabetes. The compound was licensed to Novo Nordisk for development in 1997. However, Novo Nordisk decided to terminate further clinical development based on preclinical results which did not suggest a sufficient competitive advantage compared to similar marketed products. In 2005, Dr. Reddy's Laboratories established an agreement with Rheoscience for the joint development and commercialization of balaglitazone.

Bay-73-7977

Bayer's Bay-73-7977 is currently in early clinical trials for the treatment of diabetes mellitus.

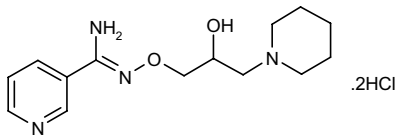
Bazedoxifene/Conjugated Estrogens



Bazedoxifene

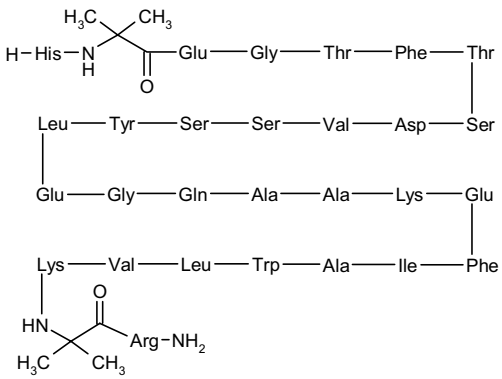
The combination of the SERM bazedoxifene and conjugated estrogens (Premarin®) is in phase III clinical trials at Wyeth and Ligand for the treatment of the vasomotor symptoms associated with menopause and for the prevention of osteoporosis in postmenopausal women.

BGP-15



BGP-15 is an insulin sensitizer in phase II clinical trials at N-Gene for the treatment of metabolic insulin resistance in nondiabetic patients. BGP-15 is thought to increase insulin sensitivity by improving mitochondrial function via inducible heat shock protein (HSP) production and restoring constitutive nitric oxide synthase (NOS) function.

BIM-51077 (R-1583, ITM-077)



The GLP-1 receptor agonist BIM-51077 is in phase II clinical trials at Ipsen and Roche (R-1583) and phase I trials at Teijin (ITM-077) for the treatment of type 2 diabetes. The compound has an extended duration of action compared to the endogenous hormone. Developed under a collaboration between Ipsen and SCRAS, BIM-51077 was licensed to Teijin in July 2003 under a development

and marketing agreement pursuant to which Teijin obtained co-exclusive rights in Japan. In October 2003, Roche and Ipsen entered into an agreement whereby Roche gained exclusive rights to market and sell BIM-51077 worldwide, except in Japan and France.

BLX-1002

Phase II clinical trials are in progress at Bexel Pharmaceuticals with the novel orally active thiazolidinedione BLX-1002 for the treatment of type 2 diabetes.

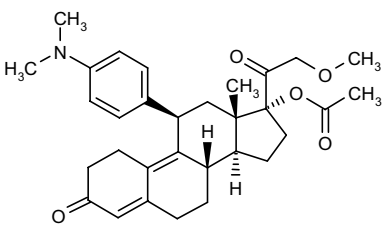
BMS-512148

Bristol-Myers Squibb's BMS-512148 is in phase II clinical trials as a potential new treatment for type 2 diabetes.

BT-16

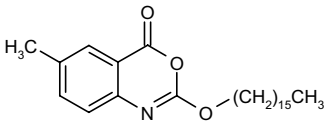
Quark Biotech is evaluating BT-16 in phase II clinical trials for the treatment of dyslipidemia and metabolic syndrome. The compound, which acts on a novel proprietary orphan nuclear receptor, has shown potent efficacy in suppressing triglyceride levels, as well as in sensitizing tissues to insulin. BT-16 was licensed to Sanwa (SK-0412) in February 2005, providing that company exclusive development, manufacturing and marketing rights for the use of the drug candidate in the treatment of dyslipidemia in Japan and other Asian countries. Quark continues to seek additional licensees in Europe and the U.S.

CDB-4124



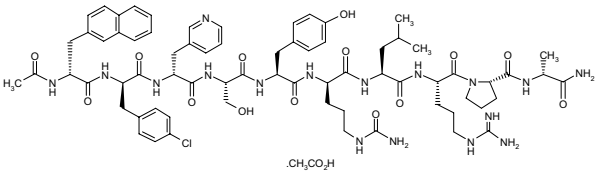
CDB-4124 (Proellex™), a progesterone receptor antagonist, is currently undergoing phase II clinical trials at Repros Therapeutics (formerly Zonagen) for the once-daily oral treatment of uterine fibroids and endometriosis. In studies to date in women with uterine fibroids, CDB-4124 has shown positive effects on fibroid size, bleeding and pain associated with the condition. The compound is being developed under an exclusive license from the National Institutes of Health (NIH).

Cetilistat



A triacylglycerol lipase inhibitor, cetilistat (ATL-962) is currently being evaluated in phase II clinical trials for the treatment of type 2 diabetes in obese patients and obesity. Discovered by Alizyme, the company granted exclusive rights to Takeda for development and commercialization of the compound for obesity in Japan.

Cetrorelix Acetate, New Indication



Cetrorelix acetate is a peptide-based luteinizing hormone-releasing hormone (LHRH) antagonist that blocks LHRH receptors in the pituitary and rapidly and dose-dependently decreases sex hormone levels. The product (Cetrotide®), originated by the former Asta Medica, now AEterna Zentaris, was launched by Serono in 1999 for the prevention of premature ovulation in controlled ovarian stimulation and assisted reproductive techniques, and is approved in several countries for this indication, including the U.S., the E.U. and Japan. Currently, AEterna Zentaris and partner Solvay are conducting phase III clinical trials with cetrorelix for the treatment of endometriosis, and AEterna Zentaris is also conducting phase II trials for benign prostatic hypertrophy (BPH) in men. Shionogi and Nippon Kayaku (NS-75A) are the licensees for Japan, where the companies are conducting phase II trials for the treatment of uterine fibroids.

Original monograph – Drugs Fut 1994, 19(3): 228.

CKD-501

CKD-501, a dual PPARα/γ agonist, is currently being evaluated in phase I clinical trials at Chong Kun Dang for the treatment of diabetes.

Colesevelam Hydrochloride, New Indication

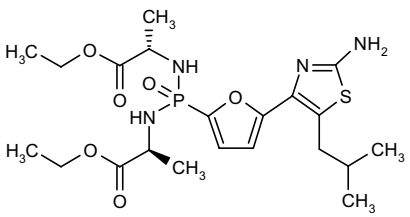
Colesevelam hydrochloride (WelChol®) is a bile acid sequestrant that was launched in 2000 by the former GelTex, now Genzyme, the former Sankyo (now Daiichi Sankyo) and Pfizer as an oral adjunct to diet and exercise for the reduction of elevated low-density lipoprotein (LDL) cholesterol with or without statins in patients with primary hypercholesterolemia. The drug is currently in phase III clinical trials at Daiichi Sankyo for the treatment of type 2 diabetes, alone or in combination with other antidiabetic agents. Colesevelam was originally developed at GelTex. In December 1999, GelTex granted Sankyo exclusive U.S. marketing rights to the drug. Sankyo in turn licensed the product to a joint venture the company had formed with Parke-Davis, a division of Warner-Lambert, which was subsequently acquired by Pfizer.

Colestilan, New Indication

The bile acid sequestrant and cholesterol absorption inhibitor colestilan (Cholebine®) was launched in 1999 by the former Mitsubishi Chemical (now Mitsubishi Pharma) and licensee Astellas Pharma (formerly Yamanouchi) for the treatment of hypercholesterolemia. The drug is also in phase III trials at Mitsubishi Pharma for the treatment of hyperphosphatemia and in phase II trials for the treatment of type 2 diabetes. Astellas Pharma returned the rights to the product to Mitsubishi several years ago and no longer markets it.

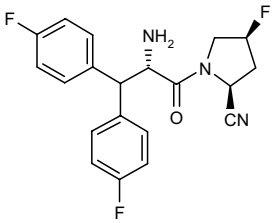
Original monograph – Drugs Fut 1993, 18(1): 15.

CS-917



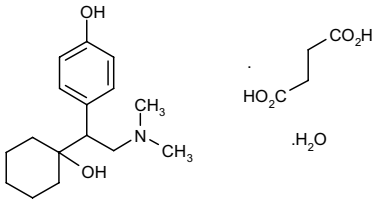
Phase II clinical trials are being conducted with CS-917 (formerly MB-6322), a gluconeogenesis inhibitor for the oral treatment of type 2 diabetes, under a partnership between Metabasis and Daiichi Sankyo. The compound works through inhibition of fructose-1,6-bisphosphatase, an enzyme that regulates the production of glucose in the liver. Previous studies demonstrated that inhibiting the gluconeogenesis pathway results in clinically and statistically significant reductions in blood sugar levels. Metabasis retains co-promotion rights in North America.

Denagliptin



The dipeptidyl-peptidase IV (DPP-IV) inhibitor denagliptin (832093) is in phase II clinical development for the treatment of type 2 diabetes at GlaxoSmithKline.

Desvenlafaxine Succinate



Desvenlafaxine succinate (DVS-233), a norepinephrine and 5-HT reuptake inhibitor, has been submitted for approval in the U.S. by Wyeth for the treatment of major depression. Phase III trials are also under way at the company for the relief of vasomotor symptoms associated with menopause, neuropathic pain and fibromyalgia. The drug is expected to achieve a different balance of 5-HT and norepinephrine reuptake inhibition compared to other antidepressant agents.

Original monograph – Drugs Fut 2006, 31(4): 304.

DiabeCell

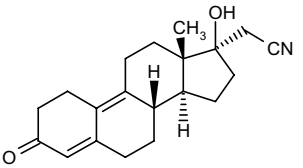
DiabeCell is an insulin-delivering drug candidate composed of live porcine pancreatic cells covered in a seaweed-derived coating (alginate encapsulation) to form capsules which isolate the transplanted cells from the patient's immune system, while allowing for free passage of small nutrient molecules, oxygen and cell products. DiabeCell is currently undergoing early clinical trials at Living Cell Technologies for the treatment of type 1 diabetes.

DiaPep277®

DiaPep277® is undergoing phase III clinical trials for the treatment of type 1 diabetes. It is also being evaluat-

ed in phase II for the treatment of latent autoimmune diabetes in adults (LADA). Originally discovered by researchers at the Weizmann Institute of Science, the compound is being developed at DeveloGen.

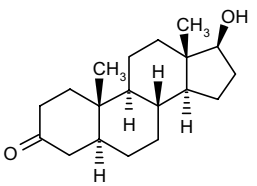
Dienogest



Dienogest is a synthetic steroid with progestational activity that was launched over 15 years ago by Jenapharm (a subsidiary of Schering AG) in combination with ethinylestradiol for use as an oral contraceptive, and was launched again by Schering AG in 2001 in combination with estradiol valerate for the treatment of the symptoms of menopause. The drug was submitted for approval in Japan by licensee Mochida (MJR-35) in April for the treatment of endometriosis and Schering (Visanne®, formerly Endometrion®) is conducting phase III trials for this indication; it is also in phase II trials at Mochida for the oral treatment of uterine fibroids. *In vitro* studies revealed an antiproliferative effect for dienogest on rat endometrial cells due to inhibition of protein kinase C (PKC) activity. Dienogest was originally developed by Jenapharm and Schering AG, and is currently marketed by those companies in Germany and Europe, respectively. Mochida acquired rights to the drug in Japan from Jenapharm, and Innothera also holds rights to the compound.

Original monograph – Drugs Fut 1980, 5(6): 311.

Dihydrotestosterone, Transdermal Gel

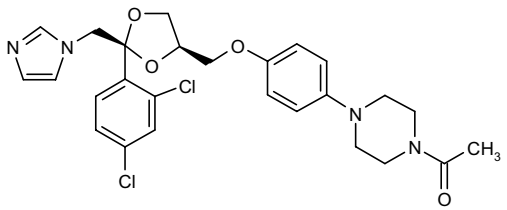


Ascend Therapeutics is evaluating a transdermal gel formulation of dihydrotestosterone (DHT), based on Besins' Enhanced Hypoalcoholic Gel (EHG™) technology, in phase II clinical trials for late-onset hypogonadism.

DIO-901

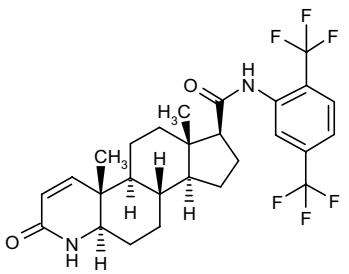
DIO-901 (VLD-glucagon, or very-low-dose glucagon), a natural occurring hormone, is in early clinical development at DiObex for the prevention of hypoglycemia associated with insulin intensification in type 1 diabetes patients. In 2005, fast track designation was received in the U.S. for the treatment of hypoglycemia.

DIO-902



DIO-902, the (–)-enantiomer of the racemate ketoconazole, is in phase II clinical trials at DiObex for the treatment of type 2 diabetes. Preclinical studies have demonstrated the drug candidate's ability to inhibit the synthesis of cortisol, resulting in substantial clinical benefits, including lowering both blood pressure and cholesterol, in addition to controlling glucose levels. It has also been shown that (–)-ketoconazole is responsible for virtually all of the cortisol synthesis-inhibitory activity present in the racemate. Rights to the compound were licensed from Cortendo.

Dutasteride, New Indication



GlaxoSmithKline's dutasteride (Avodart®) is a selective inhibitor of both type 1 and type 2 isoforms of steroid 5α-reductase, an intracellular enzyme that converts testosterone to DHT, thereby further reducing serum DHT levels in patients with BPH as compared to specific type 2 5α-reductase inhibitors. Dutasteride was launched in 2003 in the U.S. and the E.U. for the treatment of BPH. Phase III development to evaluate the efficacy of dutasteride in combination with an α-adrenoceptor blocker for the treatment of BPH is ongoing at GlaxoSmithKline. Additional phase III trials are under way at the company for reducing the risk of prostate cancer. Early clinical trials with dutasteride in combination with testosterone for the treatment of hypogonadism are currently under way.

Original monograph – Drugs Fut 1999, 24(3): 246.

E1-I.N.T.™

E1-I.N.T.™ is Transition Therapeutics' lead regenerative therapy in phase II clinical development for the treatment of type 1 and type 2 diabetes. This product candidate, a combination of an epidermal growth factor (EGF) analogue (E1) and a gastrin analogue (G1), is a short-course combination therapy aimed at stimulating the regeneration of islet cells. For type 2 diabetes patients, islet cell regeneration therapy could eliminate the need for daily insulin injections. The Islet Neogenesis Therapy (I.N.T.™) technology platform is based on the discovery that a short course of injections of naturally occurring peptides can regenerate insulin-producing cells in the body.

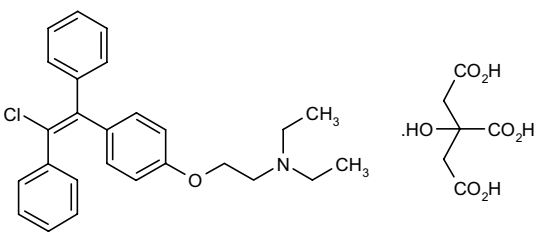
EMD-387008

EMD-387008 is in early clinical trials at Merck KGaA for the oral treatment of type 2 diabetes.

Encapsulated Human Islets

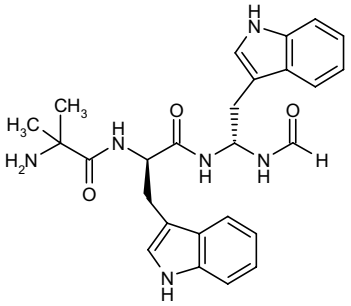
AmCyte is conducting phase I/II clinical trials with encapsulated isolated primary human pancreatic islet cells for the treatment of diabetes. AmCyte has developed a proprietary method of protecting the islets through encapsulation to increase and sustain insulin output without the need for life-long immune suppression subsequent to intraperitoneal transplantation.

Enclomiphene Citrate



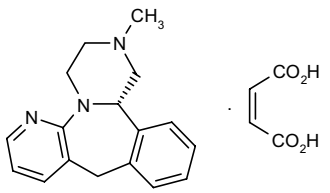
Enclomiphene citrate (Androxal™) is a proprietary, small-molecule, orally active product candidate being tested at Repros Therapeutics in phase III clinical trials for the treatment of testosterone deficiency in men with secondary hypogonadism in a once-daily formulation. Androxal™ is designed to act centrally to restore normal testicular function in the body, thereby achieving normal levels of endogenous or self-produced testosterone, rather than externally replacing diminished testosterone.

EP-01572



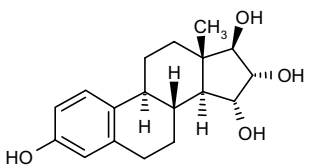
The orally available peptidomimetic GH secretagogue EP-01572 (EP-1572) is currently undergoing phase I clinical trials for the treatment of short stature and other conditions associated with GH deficiency. Ardana Bioscience licensed exclusive worldwide rights to the product from AEterna Zentaris in 2002.

Esmirtazapine Maleate



Organon is developing esmirtazapine maleate (Org-50081), a 5-HT_2 receptor antagonist, for two different indications. It is in phase III clinical development for the treatment of hot flushes and in phase II clinical trials for the treatment of sleep disorders. Org-50081 may become the first nonhormonal menopausal therapy for the relief of hot flushes.

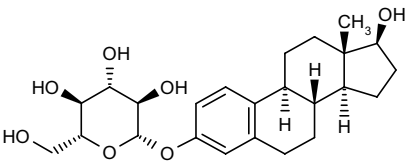
Estetrol



Estetrol is a SERM in phase I/II clinical trials at Pantarhei Bioscience for the treatment of breast cancer, osteoporosis, postmenopausal syndrome and for the prevention of pregnancy. When administered orally, estetrol, a natural human estrogen which is solely produced in large quantities during human pregnancy by the male and female fetal liver, acts as an estrogen agonist on the vagina, uterus and bone. It has been shown to suppress hot flushes and inhibit ovulation. Furthermore, the finding that estetrol dose-dependently prevented the development of

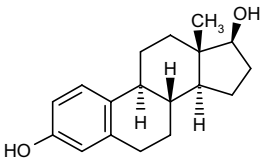
breast tumors and inhibited pre-existing breast tumors in the DMBA rat model suggests that it also acts as an estrogen antagonist on the breast.

Estradiol Glucoside



Estradiol glucoside, originally developed at Boston University, is currently undergoing phase II clinical trials at ProStrakan for the treatment of postmenopausal syndrome.

Estradiol MDTS®

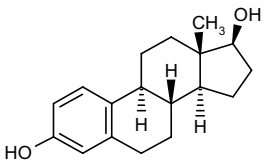


A once-daily transdermal spray using Acrux's metered-dose transdermal system (MDTS), estradiol MDTS® (Evamist™) is currently undergoing phase III clinical trials for the treatment of postmenopausal syndrome. The product was licensed to Vivus in 2004 for marketing in the U.S. Acrux retains the rights to estradiol MDTS® for the rest of the world and is seeking marketing partners for major markets.

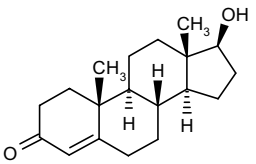
Estradiol/Progestogen, Transdermal Gel

A transdermal gel formulation of the estradiol/progestogen combination known as Bio-E/P-Gel™ is being tested in phase III clinical trials at BioSante for the treatment of vasomotor symptoms associated with postmenopausal syndrome. Designed to be applied once daily on the arms, abdomen or thighs and to be absorbed quickly through the skin without a trace of residue, the gel delivers the hormones to the bloodstream in a painless, noninvasive manner. The progestogen is added to reduce the risk of endometrial hyperplasia. Originally developed at Antares Pharma using its Advanced Transdermal Delivery (ATD™) gel technology, transdermal estradiol/progestogen was licensed to BioSante in June 2000. Under the terms of the agreement, BioSante acquired exclusive marketing rights for the combination drug candidate in the U.S. and Canada. In August 2001, BioSante granted Solvay development and marketing rights in the U.S. and Canada, while retaining co-promotion rights in those areas, but further development at Solvay has not been reported.

Estradiol/Testosterone, Transdermal Gel



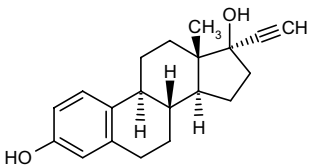
Estradiol



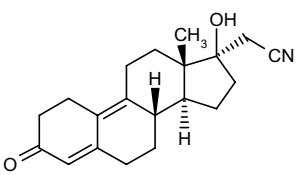
Testosterone

An estradiol/testosterone transdermal gel is currently undergoing phase II clinical trials at Paladin for the treatment of postmenopausal syndrome. The once-daily transdermal gel (LibiGel ET™) is also being evaluated in phase I clinical trials at BioSante for the treatment of female sexual dysfunction. The transdermal gel formulations, based on Antares Pharma's ATD™ gel technology, were licensed to BioSante, which later sublicensed marketing rights to Paladin.

Ethinylestradiol/Dienogest, New Indication



Ethinylestradiol

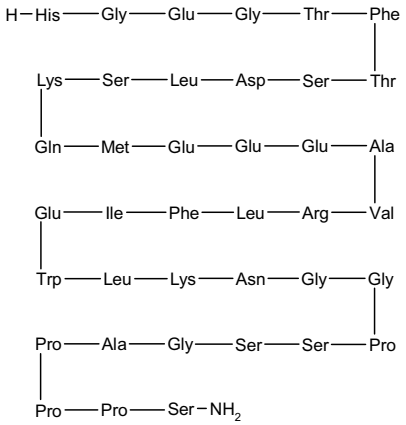


Dienogest

Ethinylestradiol/dienogest is a combination estrogen/progestogen product that has been marketed in Germany for over 15 years by Jenapharm (a subsidiary of Schering AG) for use as an oral contraceptive under the trade name Valette®. It is currently undergoing phase III

clinical trials at Schering AG for the treatment of vaginal bleeding.

Exenatide



The first in a new class of drugs known as incretin mimetics, exenatide (Byetta™) was launched by Amylin and Lilly in 2005 in the U.S. as adjunctive therapy to improve blood sugar control in patients with type 2 diabetes who have not achieved adequate control with metformin and/or sulfonylurea therapy. A regulatory application has been filed for the product in the E.U. Exenatide is formulated for self-administration as a fixed-dose subcutaneous injection given prior to the morning and evening meals. Amylin licensed rights to Nastech to develop a nasal spray formulation for the treatment of type 2 diabetes in 2006 and preclinical studies are currently under way.

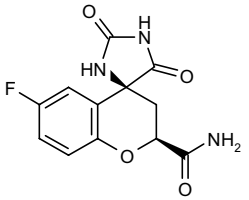
Original monograph – Drugs Fut 2004, 29(1): 23.

Exubera®

Exubera®, an inhalable, rapid-acting, dry powder formulation of human insulin [rDNA origin], has been registered in the E.U. and the U.S. for the treatment of type 1 and type 2 diabetes. The product is currently available in Germany and Ireland and is expected to be introduced in the U.S. in September. Specifically, Exubera® has been approved for type 2 diabetes in adults not adequately controlled with oral antidiabetic agents and requiring insulin therapy. In type 1 diabetes, Exubera® is approved in addition to long- or intermediate-acting injectable insulin in adults for whom the potential benefits of adding inhaled insulin outweigh the potential safety concerns. Jointly developed by Pfizer and sanofi-aventis, the product is inhaled through the mouth into the lungs prior to eating, using a simple-to-use, hand-held inhalation device that does not require batteries or electricity and a powdered insulin formulation developed by Nektar Therapeutics. Exubera® closely mimics the normal physiological insulin response to meals due to its rapid related spikes in glucose levels in people with diabetes. In March 2006, Pfizer completed the acquisition of sanofi-aventis's worldwide rights to Exubera®.

Original monograph – Drugs Fut 2004, 29(12): 1206.

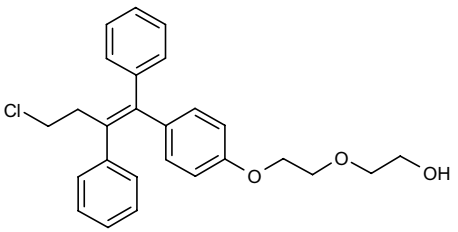
Fidarestat



Fidarestat (SNK-860, Aldos), an aldose reductase inhibitor, is currently in phase II/III development at Sanwa for the treatment of diabetic complications, including peripheral diabetic neuropathy. The drug was co-developed with N.K. Curex (a joint venture of Kaken and Japan Energy) and an NDA was submitted to the Japanese authorities several years ago. Based on results from U.S. trials carried out by the former Sankyo (now Daiichi Sankyo), leading that company to discontinue its development, Kaken was last reported to be re-considering its development strategy for the compound.

Original monograph – Drugs Fut 1996, 21(3): 261.

Fispemifene



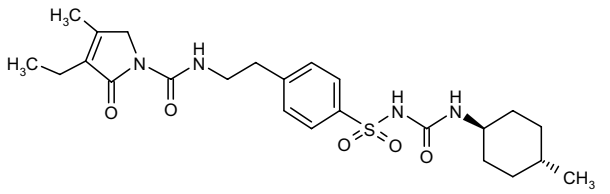
The SERM fispemifene is undergoing phase II clinical trials at QuatRx for the treatment of androgen decline in the aging male. Unlike testosterone replacement therapies that are typically administered topically or by injection, fispemifene is an oral treatment and is not a formulation of testosterone. Fispemifene utilizes the body's normal feedback mechanism to increase testosterone levels. Originally developed at Hormos, QuatRx gained rights to the drug candidate following its 2005 merger with Hormos.

FP-1096

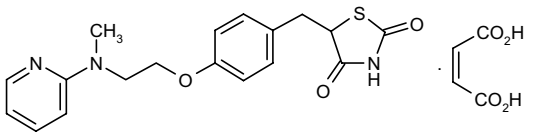
FP-1096 is an investigational endometriosis therapy delivered intravaginally directly to the target region. Originally developed by FemmePharma, KV Pharmaceutical obtained worldwide marketing rights to

the product in 2005 and is currently conducting phase III clinical trials.

Glimepiride/Rosiglitazone Maleate



Glimepiride



Rosiglitazone Maleate

The sulfonylurea/thiazolidinedione combination glimepiride/rosiglitazone maleate (Avandaryl™) was launched in 2006 by GlaxoSmithKline for the control of blood sugar in patients with type 2 diabetes. Sulfonylureas act primarily by stimulating the release of insulin from functioning pancreatic β-cells, and thiazolidinediones are insulin-sensitizing agents that act primarily by enhancing peripheral glucose utilization. Extrapancreatic effects may also play a role in the activity of sulfonylureas such as glimepiride. This is supported by both preclinical and clinical studies demonstrating that glimepiride administration can lead to increased sensitivity of peripheral tissues to insulin. Rosiglitazone improves glycemic control by improving insulin sensitivity. It is a highly selective and potent PPARγ agonist.

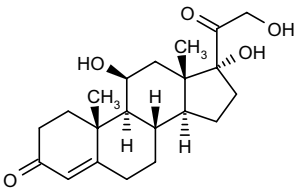
GRC-8200

GRC-8200, a DPP-IV inhibitor, is in phase II clinical development at Glenmark Pharmaceuticals for the treatment of type 2 diabetes. Glenmark is in early discussions with potential partners for this product

Human Growth Hormone, Recombinant

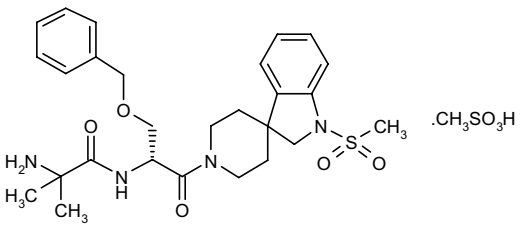
Cangene's recombinant human growth hormone (rhGH) drug candidate Accretropin™ has been submitted and accepted for review at the FDA for children with short stature due to GH deficiency and girls with Turner syndrome. The company's product is identical in sequence to naturally produced human GH of pituitary origin.

Hydrocortisone, New Formulation/Indication



A new circadian-release formulation of hydrocortisone (cortisol), a corticosteroid marketed for the treatment of skin inflammation, is currently in early clinical trials at Phoqus Pharmaceuticals, in collaboration with Diurnal (a subsidiary of Biofusion), for the oral treatment of adrenal insufficiency. Known as Chronocort, the once-daily, modified-release product was shown in a recently completed phase I trial to release drug and provide blood levels of hydrocortisone that closely mimic levels of the natural product seen in healthy subjects. Orphan medicinal product designation has been obtained in the E.U. and Phoqus plans to seek a licensing partner for further development.

Ibutamoren Mesilate



Ibutamoren mesilate (MK-0677, Crescendo®) is an orally administered GH secretagogue in phase II/III trials at Merck & Co. for the treatment of sarcopenia in post-hip fracture patients and in phase II trials for the treatment of fibromyalgia, endocrine disorders and Alzheimer's-type dementia. The drug candidate acts on the GH secretagogue receptor in the anterior pituitary to stimulate the release of GH, a different regulatory pathway for GH release from pituitary somatotrophs to that mediated by GHRH and somatostatin.

Original monograph – Drugs Fut 2006, 31(5): 390.

INCB-13739

Clinical trials were recently initiated with Incyte's INCB-13739, an inhibitor of 11-β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) for the treatment of type 2 diabetes and conditions commonly associated with this disease. Recently published data suggest that

11β-HSD1-mediated production of cortisol within adipose tissue and the liver may play a key role in regulating the body's resistance to insulin in people with type 2 diabetes. INCB-13739 has been shown to selectively inhibit 11β-HSD1 and subsequently reduce cortisol levels in multiple tissues.

INCB-3284

INCB-3284 is a novel, orally active chemokine CCR2 (MCP-1) antagonist developed at Incyte and licensed to Pfizer in 2005 for the treatment of inflammation, with the exception of multiple sclerosis and another undisclosed indication, for which Incyte has retained exclusive worldwide rights. Pfizer is currently conducting phase II trials for the treatment of rheumatoid arthritis in patients who have active disease and are receiving methotrexate and for the treatment of diabetes in obese insulin-resistant patients.

Insulin, New Formulations

A liquid formulation of regular human insulin was launched in 2005 by Generex under the trade name Oral-lyn™. The drug is marketed for the treatment of type 1 and type 2 diabetes as a buccal spray in Ecuador. This formulation involves the aerosolization of liquid insulin with a pharmaceutical-grade chemical propellant for delivery to the buccal mucosa by way of Generex's proprietary RapidMist™ device. In this fashion, absorption is limited to the mouth, with no entry into the lungs. The rich vascularity of the buccal mucosa allows for much faster absorption of insulin and a shorter total duration of activity, making the product an ideal prandial insulin. Developed by Generex, rights to Oral-lyn™ were acquired by Lilly in September 2000 when a development and commercialization agreement was signed by the companies. A termination agreement was subsequently signed by the companies in November 2003, pursuant to which all intellectual property and commercialization rights were retained by Generex, while Lilly agreed to supply Generex with human insulin crystals over a 3-year period. Generex also has a joint venture partner in PharmaBrand, the company responsible for the commercial launch of Oral-lyn™ in Ecuador.

The Technosphere® insulin system, a drug delivery system for pulmonary administration, is currently being evaluated in phase III clinical trials at MannKind for the treatment of type 1 and 2 diabetes. This inhaled insulin delivery system consists of a proprietary dry powder formulation of Technosphere® insulin that is inhaled into the deep lung using the company's proprietary MedTone™ inhaler.

AIR® insulin is an inhaled insulin system that delivers human insulin inhalation powder (HIIP) using Alkermes' AIR® pulmonary drug delivery technology. It is currently in phase III trials at Alkermes and Lilly for the treatment of type 1 and type 2 diabetes, and has been developed under a collaboration alliance between the two companies since 2001. Clinical trials have demonstrated an absence of statistically significant differences between inhaled and injected insulin study groups with respect to fasting blood glucose, carbon monoxide lung-diffusing capacity and severe hypoglycemia.

An inhaled insulin product candidate using MicroDose Technologies' dry powder inhaler is currently undergoing phase I clinical trials for the treatment of diabetes at Bristol-Myers Squibb and QDose, a joint venture between MicroDose and Quadrant Drug Delivery.

Kos Pharmaceuticals is developing an inhaled insulin product (KI-02212) in phase II clinical trials for the treatment of type 2 diabetes. The product will be administered using Kos's Breath Actuated Inhaler (BAI) device, a breath-coordinated, spacerless, metered-dose inhaler (MDI) that generates low plume force.

Alveair, an inhaled insulin delivery system, is currently being evaluated in phase I clinical trials at Coremed for the treatment of diabetes.

An intranasal formulation of insulin using the company's proprietary drug delivery technology is being tested in phase II clinical trials at Bentley Pharmaceuticals for the treatment of type 1 diabetes. In preclinical studies, the formulation was characterized by a rapid absorption and onset of action, and was effective in blunting postprandial hyperglycemia for more than 2 h. Rights to intranasal insulin were acquired by Dong Sung in South Korea in April 2005 pursuant to a development agreement signed by the companies. In November 2005, Biocon signed a licensing agreement with Bentley, obtaining exclusive as well as co-exclusive rights to develop and market the drug candidate in 85 countries throughout Asia, Africa and the Middle East. At the same time, Biocon announced that it had entered into a long-term supply agreement with Bentley which will provide Bentley and its licensees with a competitive supply of insulin for worldwide markets.

Emisphere is developing an oral insulin in phase II clinical trials for the treatment of type 2 diabetes in a tablet formulation using its eligen™ oral drug delivery technology. The formulation contains insulin and the delivery agent sodium *N*-8[-(2-hydroxybenzoyl)amino]-caprylate (SNAC), which allows the activation of insulin after absorption through the gastrointestinal tract.

AT-1391, a daily transdermal insulin patch, is currently undergoing phase I clinical trials at Altea Therapeutics for the treatment of type 2 diabetes.

Flamel Technologies' once-daily injectable insulin product Basulin® is in phase II testing for type 1 and 2 diabetes. The drug candidate incorporates the company's Medusa® nanoparticle technology, "polypeptide-like" amino acid polymers that allow noncovalent capture and subsequent delivery of human insulin. Once injected, the nanoparticles release the captured insulin in a controlled manner.

Insulin Glargine, New Indication

Insulin glargine (Lantus®) is a long-acting recombinant human insulin analogue that was launched in 2000 by sanofi-aventis for the once-daily subcutaneous treatment of diabetes. It is currently in phase III trials for the treatment of diabetic complications.

Insulin Glulisine

Another recombinant human insulin analogue, insulin glulisine (HMR-1964), was introduced as Apidra® in 2005 in Germany and the U.K. by sanofi-aventis for the treatment of hyperglycemia in adult patients with type 1 and type 2 diabetes. The product was subsequently launched in the U.S. in 2006, and phase III trials are ongoing in Japan. Sanofi-aventis is also conducting phase III trials for the treatment of pediatric diabetes. The product has demonstrated a more rapid onset and a shorter duration of action than regular human insulin after subcutaneous administration. It is designed to be injected shortly before or soon after meals and should be given by subcutaneous injection or by continuous subcutaneous pump infusion. In combination with the company's Lantus® (insulin glargine; see above), Apidra® provides a synergistic approach to total glucose control for diabetics.

Original monograph – Drugs Fut 2003, 28(11): 1055.

IoGen™

IoGen™, an iodine technology that generates molecular iodine *in situ* in the stomach of the patient, is currently being evaluated in phase III clinical trials for the treatment of cyclic mastalgia associated with fibrocystic breast disease. Symbollon established an exclusive worldwide license and co-marketing agreement with Bioaccelerate in 2005 for IoGen™.

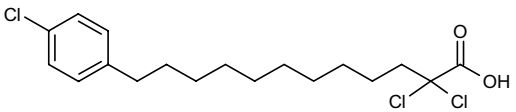
ISIS-113715

The second-generation antisense oligonucleotide ISIS-113715 is being tested in phase II clinical trials at Isis Pharmaceuticals for its potential in the treatment of type 2 diabetes. The compound acts by inhibiting protein-tyrosine-phosphatase 1B (PTP1B), an enzyme that appears to reduce insulin's ability to regulate blood sugar levels. This is accomplished by blocking the expression of the *PTP-N1* gene, which is responsible for PTP1B synthesis. It is hypothesized that PTP1B inhibition could result in prolonged activation of insulin receptors, increasing cellular glucose uptake while lowering glucose levels in the blood. In clinical trials, ISIS-113715 demonstrated a dose-related HbA1c-lowering effect, was not associated with hypoglycemia and was well tolerated.

JTT-551

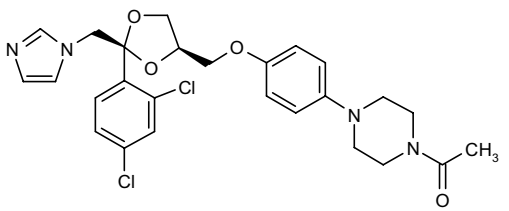
JTT-551 is another PTP1B inhibitor in phase I clinical studies at Japan Tobacco for the oral treatment of type 2 diabetes. The compound decreases blood glucose by enhancing insulin signaling via inhibition of PTP1B.

K-111



The PPARα agonist K-111 is in phase II clinical trials at Kowa for the treatment of type 2 diabetes. The PPAR family of transcription factors plays a key role in regulating dietary fat storage and catabolism. Kowa obtained rights to the drug candidate from Roche (where it was known as BM-17.0744).

Ketoconazole, New Indication



Cortendo is conducting phase II clinical trials of ketoconazole (CORT-001), a cortisol synthesis regulator, for the treatment of type 2 diabetes and metabolic syndrome. Cortendo is developing the compound for this indication on the basis of evidence implicating cortisol hypersecretion in symptoms associated with these disorders. Ketoconazole was launched over 20 years ago in the U.S. by Janssen as Nizoral™ for the topical treatment of cutaneous fungal infections. The product is available for this indication, as well as for the treatment of systemic mycoses, in several countries, including various European countries and Japan. Licensee Connetics filed an NDA with the FDA seeking approval of ketoconazole foam for the treatment of seborrheic dermatitis. However, the company received a nonapprovable letter stating insufficient clinical data. In response to the letter, Connetics will re-commence development by initiating a final phase III trial intended to demonstrate that ketoconazole foam is superior to placebo foam. Licensee Barrier Therapeutics is evaluating ketoconazole topical gel in phase III clinical trials for the treatment of seborrheic dermatitis. Ketoconazole in combination with chemotherapeutic agents is also in early clinical evaluation by the National Cancer Institute (NCI) for the potential treatment of solid tumors, including prostate cancer.

Original monograph – Drugs Fut 1979, 4(7): 496.

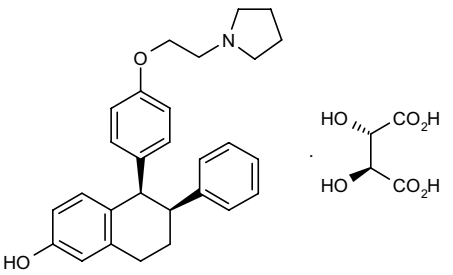
KRP-101

A PPARα agonist from Kyorin, KRP-101 is being tested in phase II clinical trials for the oral treatment of diabetes mellitus.

KRP-104

Kyorin's orally active DPP-IV inhibitor KRP-104 is currently undergoing phase II clinical trials at its wholly owned U.S. subsidiary ActivX for the treatment of type 2 diabetes. The compound is designed to reduce blood glucose through suppression of the degradation of insulin-releasing hormone.

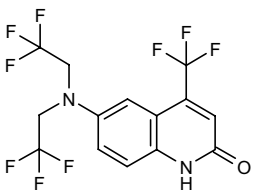
Lasofoxifene Tartrate



The SERM lasofoxifene tartrate (Oporia) was licensed by Pfizer from Ligand for marketing and development. In 2004, Pfizer filed an NDA and an sNDA seeking FDA approval for the prevention of postmenopausal osteoporosis and for the treatment of atrophic vaginitis, respectively. In September 2005, the company received a non-approvable letter for the former indication. An FDA decision regarding the atrophic vaginitis indication is still pending. Like other members of the SERM class, lasofoxifene acts as an estrogen antagonist in breast and uterine tissues and as an estrogen agonist in bone and other tissues. The compound binds to estrogen receptors with comparable affinity to 17β-estradiol and in bone it duplicates many of the effects obtained following administration of estrogen.

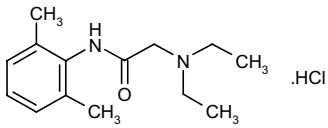
Original monograph – Drugs Fut 1998, 23(10): 1066.

LGD-2941



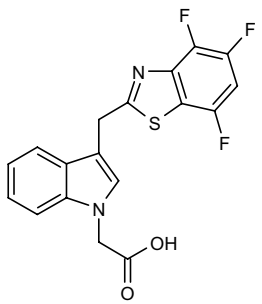
LGD-2941 is an androgen agonist in early clinical development at Ligand and TAP Pharmaceutical for the treatment of osteoporosis, male hypogonadism, female sexual dysfunction and hormone replacement therapy (HRT). The SARMs are a novel class of orally active, non-steroidal molecules that target modulation of the androgen receptor and are designed to enhance the beneficial effects of androgen receptor activation while reducing or eliminating undesired side effects, such as liver toxicity and an increased risk of prostate cancer. They have also been shown to build bone, prevent bone loss and reduce agonist drive on the prostate at doses fully anabolic in bone and muscle. In June 2001, TAP entered into a joint research and development agreement with Ligand relating to SARMs. Pursuant to the agreement, TAP gained exclusive worldwide rights to manufacture and sell any products resulting from the collaboration.

Lidocaine Hydrochloride, New Formulation/Indication



Originally launched more than 60 years ago by Wyeth, lidocaine hydrochloride is a well-known and widely used local anesthetic. In 1999, the compound was launched as a transdermal patch for the treatment of postherpetic neuralgia. An injectable formulation is also available for the treatment of arrhythmias. A phase III clinical trial of a transdermal patch is under way at EpiCept for the treatment of pain following surgery for hernia repair. A solution for inhalation for the treatment of severe asthma is in phase II clinical trials at Corus Pharma. Columbia Laboratories is conducting additional phase I trials with a bioadhesive vaginal gel for the treatment of dysmenorrhea and pelvic pain. Early clinical trials are under way at Endo for osteoarthritis pain. Both EpiCept and Endo are evaluating LidoPAIN® BP in phase II clinical trials for the treatment of low back pain.

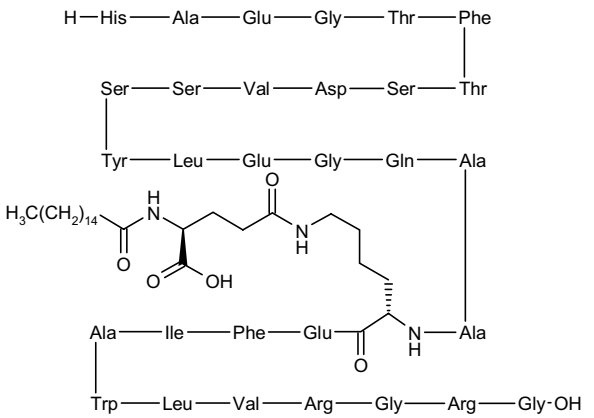
Lidorestat



Phase II clinical trials are under way for lidorestat (ALN-101, IDD-676), an aldose reductase inhibitor, for the treatment of diabetic complications. The compound is

being developed by Alinea Pharmaceuticals under a research collaboration with the Institute for Diabetes Discovery (IDD).

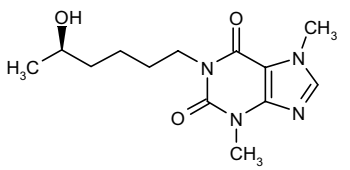
Liraglutide



Novo Nordisk is developing liraglutide (NN-2211), a GLP-1 receptor agonist currently undergoing phase III clinical trials, for the treatment of type 2 diabetes.

Original monograph – Drugs Fut 2001, 26(7): 677.

Lisofylline



Lisofylline, a synthetic small molecule, is in early clinical trials at DiaKine Therapeutics for the treatment of type 1 diabetes. An intravenous formulation is being developed for use following islet cell transplant therapy, and a subcutaneous version is aimed at the treatment of newly diagnosed type 1 diabetes. Lisofylline demonstrates antiinflammatory properties and in preclinical models it was able to effectively prevent type 1 diabetes. Studies further indicate that it improves cellular mitochondrial function, blocks IL-12 signaling and STAT-4 activation in target cells and tissues, and also directly reduces glucose-induced changes in human kidney cells. Cell Therapeutics originally developed the compound for the treatment of cancer and respiratory distress. Pursuant to an agreement between the companies signed in January 2005, DiaKine obtained a license to the patent and other intellectual property related to lisofylline for development in diabetes and related complications.

Original monograph – Drugs Fut 1997, 22(5): 492.

MB-07803

MB-07803, a fructose-1,6-bisphosphatase (FBPase) inhibitor, is currently being evaluated in phase I clinical trials at Metabasis Therapeutics for the treatment of type 2 diabetes. MB-07803 is the second in a new class of drugs discovered by Metabasis that regulate glucose production in the liver by inhibiting FBPase, a key component of the gluconeogenesis pathway. Metabasis retains all development and marketing rights to MB-07803.

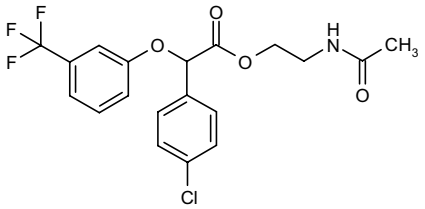
Mecasermin [rDNA origin]

Mecasermin [rDNA origin] for injection (Increlex™), a recombinant human IGF-I therapy, was launched by Tercica in 2006 in the U.S. for the long-term treatment of growth failure in children with severe primary IGF-I deficiency or with GH gene deletion who have developed neutralizing antibodies to growth hormone. Originally discovered by Genentech, the compound was licensed to Tercica in 2002 for development and commercialization, and in 2006 Tercica and Ipsen entered into a strategic cross-licensing agreement whereby Ipsen gained exclusive rights to market the product in all regions of the world except the U.S., Japan, Canada, the Middle East and Taiwan. Also in 2006, orphan drug designation was assigned to the compound in the E.U.

Mecasermin Rinfabate [rDNA origin]

Developed by Insmed, mecasermin rinfabate (iPlex™, formerly known as SomatoKine®) for injection is the recombinant protein complex of IGF-I and its principal binding protein IGFBP-3 that was launched in the U.S. in 2006 for the once-daily treatment of growth failure in children with severe primary IGF-I deficiency or with GH gene deletion who have developed neutralizing antibodies to GH, a condition previously referred to as growth hormone insensitivity syndrome (GHIS). The drug candidate has also been evaluated in phase II trials for its potential in the treatment of type 1 and type 2 diabetes, severe burn injury and for the treatment of severe osteoporosis in elderly female patients recovering from hip fractures. The University of Rochester, Insmed and the National Institute of Neurological Disorders and Stroke (NINDS) are evaluating the drug candidate in phase I/II trials for the treatment of myotonic muscular dystrophy. The drug was granted orphan drug designation in the U.S. and in Europe for the treatment of GHIS and extreme insulin resistance.

Metaglidasen



Metaglidasen (formerly MBX-102), a second-generation oral insulin sensitizer and selective PPARγ modulator, is currently being evaluated in phase II/III clinical trials at Metabolex for the treatment of type 2 diabetes. In 2006, Metabolex licensed metaglidasen to Ortho-McNeil for worldwide development and commercialization.

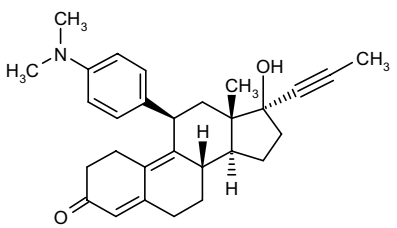
Metreleptin

Amgen's metreleptin, or recombinant human OB protein, is a leptin replacement therapy in phase II clinical trials for the treatment of hypothalamic amenorrhea and congenital lipodystrophy. Low leptin levels have been implicated as a causative factor for both of these indications. Originally developed at the Rockefeller University, an exclusive license to metreleptin was granted to Amgen in 1995.

MF-101

MF-101 is an ERβ-selective agonist that, unlike currently available hormone therapies, does not activate the ERα, known to be implicated in tumor formation. Currently in phase II evaluation, MF-101 is an oral drug designed for the treatment of vasomotor symptoms (hot flushes, night sweats) associated with the menopause. Bionovo believes that, because MF-101 exerts effects on only one of the two known ERs, it will provide ongoing relief from vasomotor symptoms while minimizing side effects. In animal studies, the compound did not adversely alter reproductive hormones or promote tumor formation in the breast or uterus, suggesting that MF-101 will not increase the risk of either breast or uterine cancer.

Mifepristone, New Indication



Mifepristone is an orally active, small-molecule dual glucocorticoid and progesterone receptor antagonist launched in 1989 by what is now sanofi-aventis for the termination of pregnancy. Mifepristone is in phase III trials at Corcept for the treatment of the psychotic features associated with major depression and in phase II clinical trials for the treatment of Alzheimer's-type dementia. The National Institutes of Mental Health (NIMH) and the Université de Poitiers are conducting phase II trials for the treatment of bipolar disorder and symptomatic uterine leiomyoma, respectively. Viral Genomix is also conducting phase II trials of mifepristone for the treatment of hepatitis C based on its ability to inhibit the HCV internal ribosomal entry site (IRES). The drug is thought to exert its effects by modifying the level and release pattern of cortisol in the human body.

Original monograph – Drugs Fut 1984, 9(10): 755.

MK-0533/MK-0893/MK-0941

Merck & Co. is conducting early clinical evaluation of several new agents with potential for the treatment of diabetes: MK-0533, MK-0893 and MK-0941.

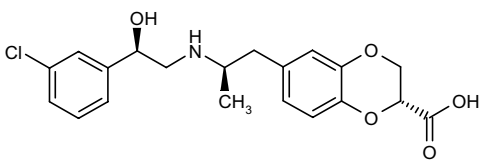
MK-0974

MK-0974 is in phase II clinical trials at Merck & Co. for the treatment of pain, and in early clinical trials for the treatment of endocrine disorders.

MP-513

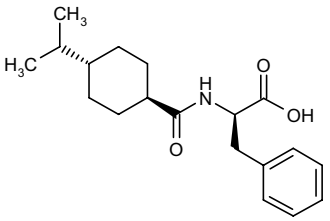
A highly potent and long-acting DPP-IV inhibitor from Mitsubishi Pharma, MP-513 is in phase II clinical trials for the treatment of type 2 diabetes. The compound is reported to have a low risk for hypoglycemia and weight gain.

N-5984 (KRP-204)



N-5984 (KRP-204), a β_3-adrenoceptor agonist, is currently being evaluated in phase II clinical trials for the oral treatment of type 2 diabetes and obesity. Discovered at Nisshin Pharma, the compound is being developed in collaboration with Kyorin.

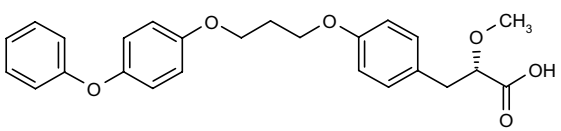
Nateglinide, New Indication



Nateglinide is an insulin secretagogue that was launched in 1999 by Astellas Pharma and the former Sankyo, now Daiichi Sankyo, as an oral therapy for the improvement of postprandial glucose control in patients with non-insulin-dependent type 2 diabetes. The drug is also undergoing phase III clinical trials (NAVIGATOR) in combination with valsartan (Diovan®) at Novartis for the prevention of diabetes and/or cardiovascular events in individuals with impaired glucose tolerance (IGT) who are at high risk for cardiovascular events. Nateglinide is an amino acid derivative that lowers blood glucose levels by stimulating insulin secretion from the pancreas. This action is dependent upon functioning β-cells in the pancreatic islets. The drug interacts with the ATP-sensitive potassium (K^+ ATP) channel on pancreatic β-cells. The subsequent depolarization of the β-cell opens the calcium channel, producing calcium influx and insulin secretion. The extent of insulin release is glucose-dependent and is reduced at low glucose levels. Originally developed at Ajinomoto, nateglinide is manufactured by the company and marketed by Daiichi Sankyo under the trade name Fastic and by Astellas Pharma under the trade name Starsis. The drug was licensed to Novartis worldwide excluding Japan and South Korea, where Ildong Pharmaceuticals markets nateglinide. Nateglinide is sold in more than 70 countries.

Original monograph – Drugs Fut 1993, 18(6): 503.

Naveglitazar

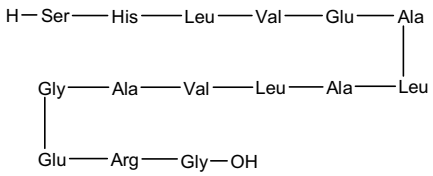


Naveglitazar (LY-818), a PPAR modulator, is currently undergoing phase II clinical trials for the once-daily oral treatment of type 2 diabetes. The compound was discovered through an ongoing research collaboration between Lilly and Ligand.

NBI-42902/NBI-56418

An orally active small-molecule gonadotropin-releasing hormone (GnRH) antagonist, NBI-42902, is in phase II trials at Neurocrine Biosciences for the treatment of endometriosis. NBI-56418 is another orally active small-molecule GnRH antagonist in phase II trials at Neurocrine Biosciences for the treatment of endometriosis, as well as phase I trials for the treatment of BPH.

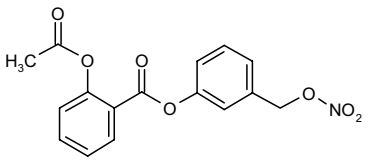
NBI-6024



Neurocrine Bioscience's insulin analogue NBI-6024 is in phase II clinical development for the treatment of type 1 diabetes in newly diagnosed adolescent and adult patients.

Original monograph – Drugs Fut 2002, 27(7): 645.

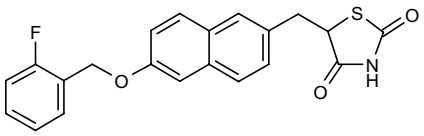
NCX-4016



NCX-4016, a nitric oxide (NO)-donating derivative of acetylsalicylic acid, is in phase II development by NicOx for the treatment of peripheral arterial obstructive disease (PAOD), cardiovascular complications in type 2 diabetic patients and platelet activation inhibition in diabetic patients. In addition to NO donation, NCX-4016 is a nonsteroidal antiinflammatory drug (NSAID) and cyclooxygenase inhibitor. The drug has been shown to reverse endothelial dysfunction and demonstrates anti-inflammatory and antiplatelet activity, acting on multiple targets in the ischemia-reperfusion pathway. Decreases in peripheral vascular resistance have also been noted, an effect that can potentially be explained by the ability of NO to improve arterial compliance (elasticity) and dilate peripheral blood vessels, reducing the strain on the heart and allowing it to pump more efficiently. The compound's inhibition of platelet aggregation and thromboxane matches that of aspirin, while being devoid of the development of hemorrhagic lesions or stomach and duodenal ulcers associated with aspirin.

Original monograph – Drugs Fut 19997, 22(11): 1231.

Netoglitazone



The thiazolidinedione netoglitazone (MCC-555) is in phase II clinical development at Perlegen Sciences for the treatment of type 2 diabetes. The drug acts as an agonist at PPARα and γ receptors and thereby increases the body's sensitivity to insulin. Perlegen obtained exclusive worldwide rights, excluding Asia, to the product from Mitsubishi Pharma in 2005.

Original monograph – Drugs Fut 2002, 27(2): 132.

NN-344/NN-5401/NN-9101

Phase I trials are in progress at Novo Nordisk to evaluate the potential of NN-344 and NN-5401, two human insulin analogues, for the treatment of type 1 and 2 diabetes.

The company is also evaluating a novel compound, NN-9101, which targets a pathway distinct from currently available oral antidiabetic agents, in early clinical trials for type 2 diabetes.

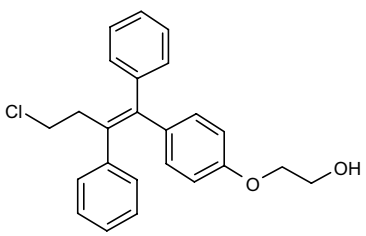
Ono-5129

Ono Pharmaceutical's Ono-5129, a dual PPARα/γ agonist with both hypoglycemic and hypolipidemic effects, is currently undergoing phase I clinical trials in Japan and phase II clinical trials in the U.S. for the treatment of type 2 diabetes.

Org-43228

Org-43228 is an ERα agonist in early clinical trials at Organon for the treatment of postmenopausal syndrome.

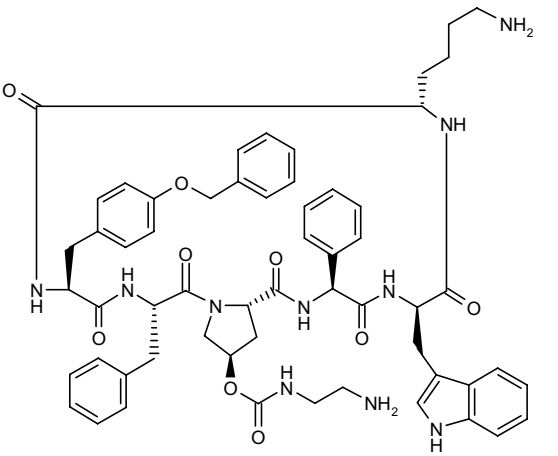
Ospemifene



Ospemifene (Ophena™) is a next-generation SERM in phase III trials at QuatRx for the treatment of urogenital atrophy. Results from completed phase I and II studies have shown the compound to be safe and well tolerated when given orally. Beneficial effects have been demonstrated on vagina, bone, lipids and vasoactive mediators. Findings from preclinical models suggest that ospemifene may offer a more favorable side effect profile than other SERMs. Originally developed by Orion, ospemifene acts as an estrogen agonist on both urogenital and bone tissue and as an estrogen antagonist on the breast, while having no effect on the uterus. In May 2005, QuatRx acquired rights to ospemifene following the acquisition of Hormos, now a wholly owned subsidiary of QuatRx.

Original monograph – Drugs Fut 2004, 29(1): 38.

Pasireotide



Pasireotide is a multiligand somatostatin analogue with high binding affinity for somatostatin sst_1, sst_2, sst_3 and sst_5 receptors, currently in phase II clinical development at Novartis for the treatment of functional gastroenteropancreatic (GEP) endocrine tumors and Cushing's syndrome. The company intends to file for approval in 2007 for these indications.

PC-DAC™:Exendin-4

PC-DAC™:exendin-4 is a GLP-1 analogue and a modified exendin-4 analogue. The drug candidate is currently undergoing early clinical trials at ConjuChem for the treatment of type 2 diabetes. It is believed that exendin-4 may stimulate β-cell proliferation, restore β-cell glucose sensitivity, delay gastric emptying and increase peripheral sensitivity to glucose due to evidence that it decreases glucagon and increases insulin secretion in a glucose-dependent manner. However, the potential of exendin-4 as a drug candidate is limited by its relatively short half-life in plasma (< 1 h). ConjuChem's response to this problem was PC-DAC™:exendin-4, a modified exendin-4 analogue conjugated to recombinant human albumin. The compound is based on the company's Preformed Conjugate-Drug Affinity Complex (PC-DAC™) technology. It has a much longer half-life than the parent compound, while maintaining comparable potency.

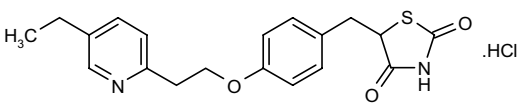
PEG-Encapsulated Human Islets

Novocell is currently conducting a phase I/II study to determine the safety and efficacy of human pancreatic islets encapsulated with polyethylene glycol (PEG) and implanted into patients with type 1 diabetes. The islets are protected from immune destruction after implantation by the PEG coating. These encapsulated islets release human insulin via natural mechanisms in response to the recipient's blood glucose concentration. The islet cells used in this study are isolated from pancreata procured from human cadaver donors who meet a specific human donor profile. The implant procedure is performed under local anesthesia and the encapsulated islets are injected into a surgically formed micropocket in the subcutaneous tissues of the thigh or lower abdomen of the recipient.

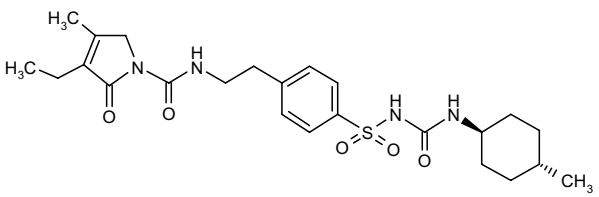
PHX-1149

PHX-1149 is a DPP-IV (CD26) inhibitor in phase II clinical trials at Phenomix for the oral, once-daily treatment of type 2 diabetes. Inhibition of DPP-IV, a serine protease, increases the cellular concentration of regulatory peptides made by the body that are critical for the control of blood glucose.

Pioglitazone Hydrochloride/ Glimepiride



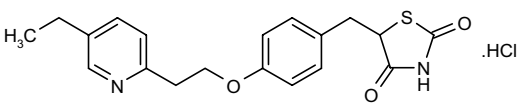
Pioglitazone Hydrochloride



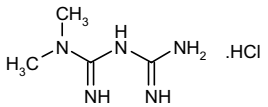
Glimepiride

The combination of pioglitazone hydrochloride/glimepiride was approved in the U.S. in 2006 for the oral treatment of type 2 diabetes. It has also been filed for approval in the E.U. Pioglitazone hydrochloride, an insulin sensitizer belonging to the thiazolidinedione class of oral antidiabetic medications, directly targets insulin resistance, while the sulfonylurea glimepiride acts primarily by increasing the amount of insulin produced by the pancreas. The two agents work in combination to help patients with type 2 diabetes manage their blood glucose levels. The drug candidate was discovered and developed by Takeda.

Pioglitazone Hydrochloride/ Metformin Hydrochloride



Pioglitazone Hydrochloride



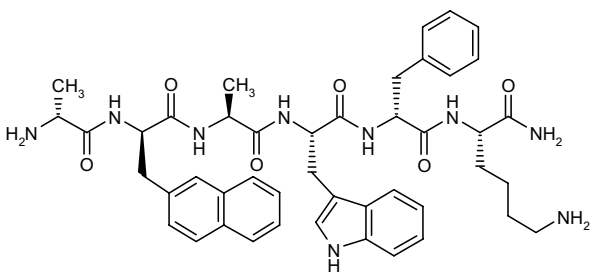
Metformin Hydrochloride

Pioglitazone hydrochloride/metformin hydrochloride is a combination therapy that was launched by Takeda in the U.S. in 2005 as ACTO*plus* met™ as an adjunct to diet and exercise for the improvement of glycemic control in type 2 diabetes patients. The drug combines two antihyperglycemic agents with different mechanisms of action: pioglitazone hydrochloride, a member of the thiazolidinedione class, and metformin hydrochloride, a member of the biguanide class. The combination was just recently approved in the E.U., where it will be known as Competact™.

PN-2034

The PPAR modulator PN-2034 is undergoing phase II clinical evaluation at Wellstat Therapeutics for type 2 diabetes.

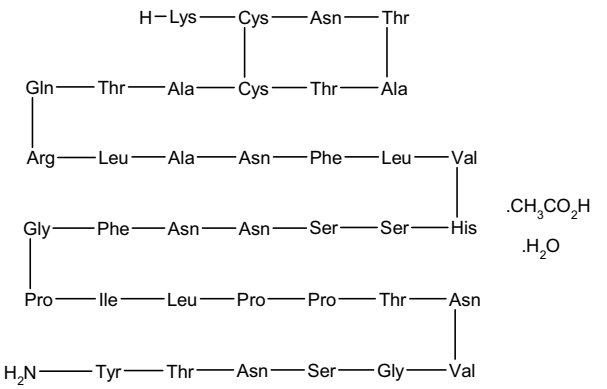
Pralmorelin, New Indication/ Formulation



Pralmorelin (KP-102) was initially launched in Japan as GHRP Kaken 100 in 2005 as a diagnostic agent for GH deficiency. The agent, which was discovered at Tulane University and developed by Kaken, is a novel GH-releasing peptide (GHRP) that induces GH release through a receptor distinct from that of GH-releasing hormone (GHRH). A nasal drop formulation is in phase II development at Kaken for the treatment of short stature.

Original monograph – Drugs Fut 2005, 30(2): 124.

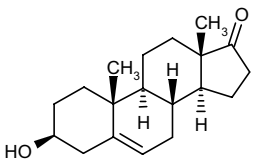
Pramlintide Acetate



Pramlintide acetate (Symlin®), a synthetic analogue of human amylin, was launched by Amylin in 2005 for the treatment of type 1 and 2 diabetes. The product is used in conjunction with insulin in patients who have failed to achieve desired glucose control despite optimal insulin therapy. Pramlintide (AC-137) has also been evaluated in phase II trials for the treatment of obesity.

Original monograph – Drugs 2001, 26(5): 444.

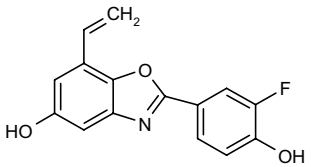
Prasterone



Prasterone, a synthetic form of the human hormone dehydroepiandrosterone (DHEA), is the active ingredient in a number of products under development by several pharmaceutical companies. Paladin, which acquired the development and marketing rights to DHEA in 1999 following its acquisition of Neuroscience Pharma, has completed phase II trials with prasterone (Fidelin™) for the treatment of Addison's disease. Genelabs is currently designing an additional clinical trial for its prasterone product, Prestara™, for the treatment of systemic lupus erythematosus (SLE) utilizing the FDA guidance document published in 2005, but due to lack of sufficient funds for additional clinical evaluation, the company would need to secure a development partner for this trial. Alternatively, development of the product will be delayed or possibly discontinued. A separate phase III trial, not regulated by an FDA IND, is under way in Taiwan by Genovate Biotechnology, Genelabs' licensee in Australia, New Zealand and most Asian countries. In June 2004, Genelabs withdrew its European marketing authorization application (MAA) for prasterone following the receipt of a list of questions issued by the EMEA to be addressed by the company. Inflabloc has completed phase I trials with its prasterone product and expects to begin phase II trials for the treatment of Crohn's disease. The Université de Versailles is conducting phase II/III trials for the treatment of myotonic dystrophy. In 2003, prasterone was assigned orphan drug designation as replacement therapy for the treatment of Addison's disease (adrenal insufficiency) by both the FDA and the EMEA.

Original monograph – Drugs Fut 1995, 20(6): 575.

Prinaberel



Prinaberel (ERB-041) is a potent and selective ERβ agonist in phase II clinical development at Wyeth for the treatment of rheumatoid arthritis and endometriosis.

Original monograph – Drugs Fut 2005, 30(4): 333.

PSN-010

PSN-010, an oral glucokinase activator, is currently undergoing phase I clinical trials at Prosidion, a wholly owned subsidiary of OSI Pharmaceuticals, for the treatment of type 2 diabetes. Glucokinase activators improve insulin sensitivity, increase glucose uptake in the liver and increase insulin secretion from the pancreas.

PSN-357

PSN-357 is a glycogen phosphorylase inhibitor (GPI) in phase II trials at Prosidion for the oral treatment of type 2 diabetes. The drug rapidly lowers blood glucose levels *in vivo* by preventing glycogen breakdown to glucose in the liver. Late-stage type 2 diabetics usually have increased overnight liver glucose output and PSN-357 will be positioned for overnight reduction of blood glucose levels. The compound has been shown to induce glucose-lowering effects in both single- and multiple-dose studies in diabetic animal models, most significantly in the fasting state when glycogenolysis is increased compared to the fed state.

PSN-9301

PSN-9301, a DPP-IV inhibitor, is currently being evaluated in phase II clinical trials for the oral treatment of type 2 diabetes. Originally discovered by Probiodrug, the compound was acquired in 2004 by Prosidion.

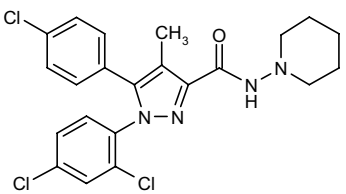
R-1438/R-1440/R-1439/R-1499

Roche has several compounds in phase I or II clinical evaluation for their potential in the treatment of type 2 diabetes. Phase II trials are under way for R-1438, an enzyme inhibitor, and R-1440, and phase I studies are in progress with R-1439 and R-1499, another enzyme inhibitor.

rhGAD65

rhGAD65 (Dyamid™) is a recombinant human DNA vaccine in phase II/III clinical trials at Diamyd Medical for the subcutaneous injection treatment of type 2 diabetes in adults, and phase II trials are also under way for the treatment of children and adolescents with type 1 diabetes. An oral formulation is in preclinical investigation. Glutamic acid decarboxylase (GAD) is an autoantigen in pancreatic β-cells that regulates the autoreactive $CD4^+$ and $CD8^+$ T-cells involved in the autoimmune destruction of β-cells. Preclinical studies have demonstrated that the vaccine prevents insulitis, β-cell apoptosis and diabetes onset in nonobese diabetic (NOD) mice. Originally developed at the University of California at Los Angeles (UCLA), rhGAD65 was subsequently licensed to Diamyd.

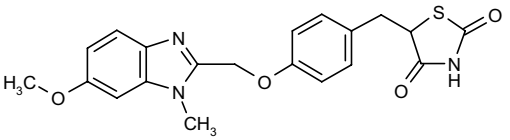
Rimonabant, New Indication



Rimonabant, a cannabinoid CB_1 antagonist, was launched by sanofi-aventis in the U.K. in mid-2006 as an adjunct to diet and exercise for the oral treatment of obesity. Approval in the U.S. for this indication is pending. Approval of rimonabant is also pending in the U.S. and Europe as an oral aid in smoking cessation and phase III trials are under way for the treatment of atherosclerosis, type 2 diabetes and dyslipidemia. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) is conducting a phase II trial for the treatment of alcoholism. CB_1 receptor blockade acts to decrease the overactivity of the endocannabinoid system that has been shown to play an important role in regulating body weight and controlling energy balance, as well as glucose and lipid metabolism. Moreover, studies of rimonabant and other CB_1 antagonists demonstrate attenuation of drug and alcohol consumption in murine models.

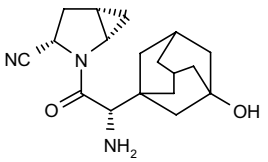
Original monograph – Drugs Fut 2005, 30(2): 128.

Rivoglitazone



Rivoglitazone (CS-011), a PPARγ agonist, is currently undergoing phase II/III clinical trials at Daiichi Sankyo for the oral treatment of type 2 diabetes. The drug candidate is also being evaluated at Santen for the treatment of corneal and conjunctival epithelial disorders, including dry eye. Under a 2005 agreement, Santen will develop, manufacture and market the drug for eye disorders, while Daiichi Sankyo retains an option to co-promote the drug in Japan.

Saxagliptin

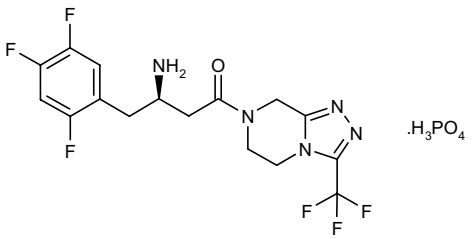


Saxagliptin is a long-acting, orally active DPP-IV inhibitor in phase III clinical trials at Bristol-Myers Squibb for the treatment of type 2 diabetes. The drug acts by preventing the degradation of GLP-1, resulting in higher levels of endogenous insulin and lower levels of plasma glucose.

Sipoglitazar

Sipoglitazar (TAK-654) is an insulin sensitizer that had reached phase II clinical testing at Takeda for the oral treatment of type 2 diabetes, but development was just recently discontinued.

Sitagliptin Phosphate

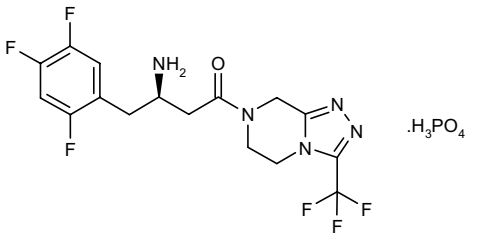


The DPP-IV inhibitor sitagliptin phosphate (MK-0431, Ono-543, Januvia™), developed at Merck & Co., recently received its first approval in Mexico for the once-daily oral treatment of type 2 diabetes; it has also been submitted for approval in the U.S. Sitagliptin boasts a much lower risk of hypoglycemia than currently available

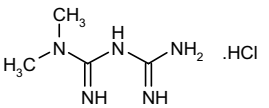
insulin-inducing products due to its novel mechanism of action. Banyu, a subsidiary of Merck & Co., is developing the drug candidate in Japan in collaboration with Ono Pharmaceutical, with phase III trials in progress.

Original monograph – Drugs Fut 2005, 30(4): 337.

Sitagliptin Phosphate/Metformin Hydrochloride



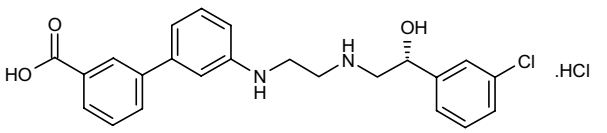
Sitagliptin Phosphate



Metformin Hydrochloride

The combination of sitagliptin phosphate and metformin hydrochloride (MK-0431A), also developed by Merck & Co., is undergoing regulatory review for the treatment of type 2 diabetes.

Solabegron Hydrochloride

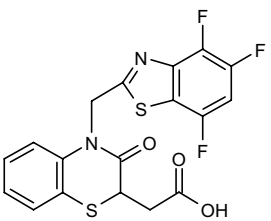


Solabegron hydrochloride (427353) is a β_3-adrenoceptor agonist developed at GlaxoSmithKline and presently in phase II trials for the treatment of type 2 diabetes and in early clinical trials for the treatment of overactive bladder (OAB).

Somatropin [rDNA Origin], New Formulation

Recombinant human growth hormone (rhGH, somatropin [rDNA origin]) was initially launched by Lilly in 1987 as Humatrope®, an injectable formulation, and is now available for several indications in pediatric patients, including the long-term treatment of patients who have growth failure due to an inadequate secretion of normal endogenous GH, the treatment of short stature associated with Turner syndrome and the long-term treatment of idiopathic short stature. In adults, Humatrope® is indicated for replacement of endogenous GH in either childhood- or adult-onset GH deficiency. Pfizer commercializes the product as Genotropin®, also for injection, for the long-term treatment of pediatric patients who have growth failure due to an inadequate secretion of endogenous GH, growth failure in children due to Prader-Willi syndrome (PWS) and growth failure in children born small for gestational age (SGA) who fail to manifest catch-up growth by age 2. The product is also available for the long-term treatment of adults with GH deficiency of either childhood- or adult-onset etiology. Pfizer has filed a regulatory application in the U.S. seeking approval of Genotropin® for the treatment of short stature and growth problems resulting from Turner syndrome. In collaboration with Novartis, Emisphere is developing an oral formulation of recombinant human somatropin for the treatment of GH deficiency using its eligen® technology, which is in phase I clinical evaluation.

SPR-210



Early clinical trials are under way for SPR-210, an aldose reductase inhibitor for the treatment of complications associated with diabetes. Originally developed at Sapporo Breweries, the drug candidate was subsequently licensed to Senju.

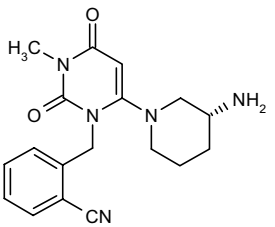
SRT-501

SRT-501 is a histone deacetylase SIRT1 activator in early clinical development at Sirtris Pharmaceuticals for the once-daily oral treatment of metabolic diseases, such as diabetes and obesity. The first small molecule targeting SIRT1 to be evaluated clinically, SRT-501 acts by increasing mitochondrial activity. SIRT1 is one of seven human sirtuins, a family of enzymes that promote the body's natural defense against disease.

SUN-E7001 (CS-872)

The GLP-1 analogue SUN-E7001 (CS-872) is undergoing phase I development at Daiichi Sankyo as an intranasal treatment for type 2 diabetes.

SYR-322

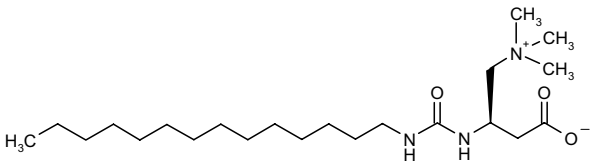


SYR-322 is a DPP-IV inhibitor from Takeda in phase III clinical evaluation in the U.S. and the E.U. and phase I evaluation in Japan for the oral treatment of type 2 diabetes. By blocking the degradation of GLP-1, DPP-IV inhibitors assist in maintaining the concentration of GLP-1 in the blood and therefore stimulate pancreatic β-cells to increase the secretion of insulin.

TA-6666

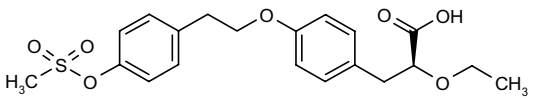
Tanabe Seiyaku is evaluating TA-6666, a DPP-IV inhibitor, in phase II clinical trials for the treatment of diabetes.

Teglicar



Sigma-Tau's centrally acting carnitine *O*-palmitoyltransferase I (CPT-I) inhibitor teglicar, potentially useful for the treatment of type 2 diabetes, is presently in phase II clinical evaluation in Europe.

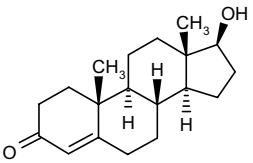
Tesaglitazar



A balanced PPARα/γ agonist, tesaglitazar (Galida™) had reached phase III clinical development at AstraZeneca for the treatment of type 2 diabetes. However, based on analysis of phase II and phase III clinical trial results, the company discontinued development of the drug candidate. Results suggest that the overall benefit/risk profile of tesaglitazar shows no significant advantage over currently marketed therapies.

Original monograph – Drugs Fut 2003, 28(10): 959.

Testosterone, Transdermal Cream



Opterone is a SEPA®-enhanced testosterone cream that is currently being evaluated in phase I clinical trials at MacroChem for the topical treatment of male hypogonadism. SEPA® is MacroChem's family of patented compounds that can enhance the transport, penetration and controlled delivery of a wide range of drugs through the skin.

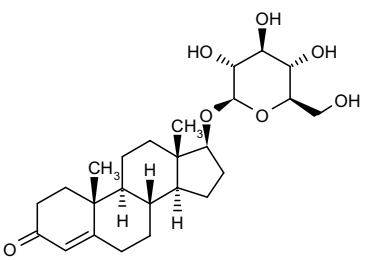
Ardana Bioscience is also developing a testosterone cream formulation in phase II clinical trials for the topical treatment of hypogonadism.

Testosterone, Transdermal Gel

Testosterone transdermal gel (Tostrex™) was launched in 2005 in Sweden for the topical treatment of male hypogonadism. In 2006, the product was approved for this indication in the E.U. It is currently being evaluated in phase III trials for the treatment of female sexual dysfunction. Developed by Cellegy, the product was licensed to ProStrakan in 2004 for commercialization in Europe.

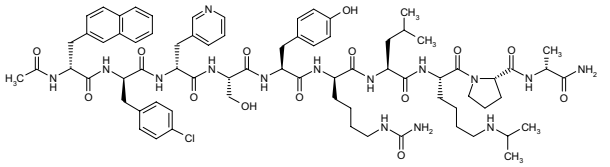
Another testosterone transdermal gel, Bio-T Gel™, is currently in phase II and III clinical development at BioSante for the treatment of female sexual dysfunction in postmenopausal women and hypogonadism, respectively. The once-daily gel is designed to be quickly absorbed through the skin after application on the arms, shoulders or abdomen. It incorporates Antares Pharma's patented ATD™ technology, allowing delivery of testosterone to the bloodstream evenly over time in a noninvasive system. This represents a viable alternative to injected testosterone, which is rapidly absorbed and degraded, making maintenance of physiological levels in plasma difficult.

Testosterone Glucoside



Testosterone glucoside is currently undergoing early clinical trials at ProStrakan for the treatment of hypogonadism.

Teverelix



Phase II trials are under way at Ardana Bioscience with a long-acting formulatin of teverelix, a GnRH (or LHRH) antagonist that produces a rapid and complete suppression of testosterone levels, for the treatment of prostate cancer and BPH. Phase I trials are also under way at Ardana with a long-acting formulation for the treatment of endometriosis and uterine fibroids. In 2004, Ardana acquired full global rights to teverelix, as well as the intellectual property, from originator AEterna Zentaris.

Thyrotropin Alfa, Recombinant, New Indication

Thyrotropin alfa (Thyrogen®), a highly purified recombinant form of human thyroid-stimulating hormone (TSH), was initially launched in 1998 for use as an adjunctive diagnostic tool for the follow-up of patients with well-differentiated thyroid cancer. It has since been launched in combination with radioiodine for the ablation of remnant thyroid tissue, the most common approach to treating thyroid cancer. Early clinical studies are also under way for the treatment of goiter. Developed by Genzyme General, the product has been approved in more than 40 countries worldwide.

TRX4

A humanized anti-CD3 monoclonal antibody, TRX4 is in phase II clinical development at TolerRx for the treatment of new-onset type 1 diabetes and in early clinical trials for the treatment of moderate to severe psoriasis. The drug is designed to block the function of effector T-cells that attack the body and cause autoimmune disease. Because effector T-cells and regulatory T-cells utilize different signaling pathways for activation, TRX4 is expected to suppress autoreactive T-cells while promoting regulatory T-cell activity, resulting in a state of immunological tolerance. In diabetes, TRX4 has been shown to preserve the function of insulin-producing β-cells in the pancreas and reduce the amount of administered insulin needed to control blood glucose levels. In November 2005, TolerRx entered into an agreement with Abbott for the manufacture of TRX4 pursuant to which Abbott will perform scale-up and GMP manufacturing of the antibody for use in clinical trials, as well as supply commercial-grade material to support regulatory submissions and potential commercial launch. In 2006, orphan drug designation was assigned to the antibody in the U.S. for the treatment of new-onset type 1 diabetes.

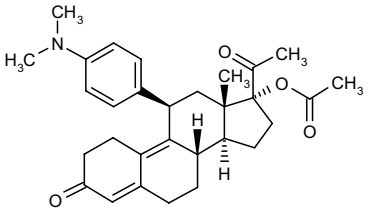
TS-021

TS-021, an oral DPP-IV inhibitor, is currently being evaluated in phase I clinical trials for the treatment of type 2 diabetes. Originally developed by Taisho, the company granted exclusive rights to Lilly in 2005 for the development and commercialization of TS-021 worldwide, except Japan and China.

TS-033

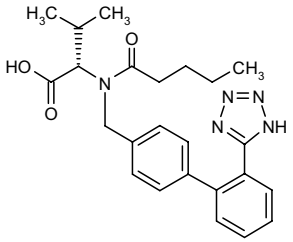
Taisho is conducting phase II trials with TS-033, a sodium-glucose co-transporter inhibitor with potential for the treatment of type 1 and 2 diabetes.

Uliprisnil Acetate



Uliprisnil acetate (CDB-2914), originally developed at the Research Triangle Institute, is an SPRM in phase II clinical trials at the National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH) for the treatment of uterine fibroids and premenstrual syndrome (PMS), respectively. Uliprisnil acetate is a well-known steroid chemically related to mifepristone that possesses antiprogestational and antiglucocorticoid activity. In preclinical studies, the growth of lead follicles exposed to a midfollicular dose of the compound was delayed in a dose-related fashion, indicating that it may have an additional mechanism of action involving progesterone or estrogen antagonism.

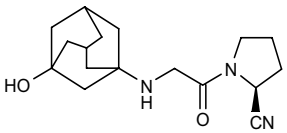
Valsartan, New Indication



The angiotensin AT_1 receptor antagonist valsartan was initially launched in 1996 by Novartis for the oral treatment of hypertension and is available in several countries for this indication, including the U.S., Canada, the U.K. and certain E.U. countries. The drug was launched by Novartis in 2002 for the treatment of CHF in patients intolerant to angiotensin-converting enzyme (ACE) inhibitors and it was approved in 2004 for the treat-

ment of pre- and post-myocardial infarction to improve survival and reduce cardiovascular events in patients at high risk after surviving a heart attack. In 2005, valsartan was approved in the E.U. and the U.S. as life-saving therapy for symptomatic heart failure when an ACE inhibitor can not be used or as add-on therapy to ACE inhibitors when β-blockers can not be used. Valsartan is approved in more than 80 countries and Novartis has alliances with Esteve, Ipsen, Lacer, Menarini and Schwarz for worldwide marketing of the drug. In addition, a phase III clinical trial (NAVIGATOR) is under way to evaluate the potential of valsartan in combination with nateglinide to reduce or delay the development of type 2 diabetes and cardiovascular disease in people with impaired glucose tolerance.

Vildagliptin



Novartis's vildagliptin (Galvus®) is a potent, highly selective, orally active DPP-IV inhibitor which has been filed for regulatory approval in the U.S. as monotherapy or in combination with other agents for the treatment of type 2 diabetes.

Original monograph – Drugs Fut 2004, 29(9): 887.

XP-12-B

XP-12-B is in phase III clinical trials at Xanodyne for the treatment of heavy menstrual bleeding associated with menorrhagia.

ZYH-2

Phase I clinical trials are under way at Zydus Cadila with ZYH-2 for the treatment of type 2 diabetes.