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Update 2006 - Treatment of Psychiatric Disorders

(Source: Prous Science Integrity®)

Treatment of Psychiatric Disorders by Condition

Condition	Phase	Drugs under development	Source
Anxiety	III	Vagus nerve stimulation therapy[1]	Cyberonics
	II	AP-521	Asahi Kasei
	II	Casopitant hydrochloride	GlaxoSmithKline
	II	ELB-139	elbion
	II	R-673	Roche
	II	Selank	Russian Academy of Medical Sciences
	II	Vestipitant mesilate/Paroxetine	GlaxoSmithKline
	II	Emapunil	Novartis/Dainippon Sumitomo
	I	163090	GlaxoSmithKline
	I	823296	GlaxoSmithKline
	I	ADX-10059	Addex Pharmaceuticals
	I	AFQ-056	Novartis
	I	BTG-1640	Abiogen
	I	Eglumetad hydrate	Lilly
	I	Itriglumide[2]	Rottapharm
	I	NBI-34041 (876008)	Neurocrine Biosciences/GlaxoSmithKline
	I	ND-7001	Neuro3d
	I	Ono-2333MS	Ono Pharmaceutical
	I	SSR-125543	Sanofi-Aventis
	I	SSR-149415	Sanofi-Aventis
	I	Talaglumetad hydrochloride	Lilly
	I	TS-041 (JNJ-19567470)	Taisho/Janssen (Johnson & Johnson)
	I	WAY-181187	Wyeth
	IND filed	YKP-3089	SK Bio-Pharmaceuticals
Anxiety, generalized	Prereg.	Pregabalin[1,2]	Pfizer
	III	Duloxetine hydrochloride[1,2]	Lilly/Boehringer Ingelheim
	III	PRX-00023	Predix Pharmaceuticals
	III	SR-58611	Sanofi-Aventis
	III	Tiagabine hydrochloride[1]	Cephalon
	II	Osemozotan hydrochloride[2]	MediciNova
	I	WAY-181187	Wyeth
Attention deficit hyperactivity disorder	Prereg.	Lisdexamfetamine	New River Pharmaceuticals/Shire Pharmaceuticals
	Prereg.	Methylphenidate hydrochloride[1], transdermal system	Noven/Shire Pharmaceuticals
	Prereg.	Modafinil[1,2]	Cephalon
	III	SPD-465	Shire Pharmaceuticals
	III	SPD-503	Shire Pharmaceuticals
	II	CX-717	Cortex
	II	NS-2359 (372475)	NeuroSearch/GlaxoSmithKline
	II	SGS-7422	Saegis
Attention deficit hyperactivity disorder, diagnosis	II	Altropane®	Boston Life Sciences
Bipolar disorder	L-2005	Carbamazepine[1], extended-release	Shire Pharmaceuticals
	III	Agomelatine[2]	Servier
	III	Asenapine maleate[2]	Pfizer/Organon
	III	Bifeprunox mesilate[2]	Solvay/Wyeth/Lundbeck

Continuation

Treatment of Psychiatric Disorders by Condition

Condition	Phase	Drugs under development	Source
Bipolar disorder	III	Licarbazapine	Novartis
	III	Vagus nerve stimulation therapy[1]	Cyberonics
	II	Eslicarbazepine acetate	Bial
	II	RG-2417	Repligen
	II	SLV-310	Solvay/Wyeth
	I	DP-VPA2	D-Pharm
	I	RGH-188	Gedeon Richter/Forest
	I	SLV-314	Solvay/Wyeth
Depression	III	Saredutant[2]	Sanofi-Aventis
	III	SR-58611	Sanofi-Aventis
	III	Vilazodone hydrochloride[2]	Genaissance/Merck KgA
	II	Casopitant hydrochloride	GlaxoSmithKline
	II	DOV-216303	DOV Pharmaceutical/Merck & Co.
	II	Emapunil	Dainippon Sumitomo
	II	Mecamylamine hydrochloride[1]	Targacept
	II	Miraxion™	Amarin
	II	NS-2359 (372475)	NeuroSearch/GlaxoSmithKline
	II	Org-34517	Organon
	II	PRX-00023	Predix Pharmaceuticals
	II	R-228060 (YKP-10A)	Janssen (Johnson & Johnson)/SK Bio-Pharmaceuticals
	II	R-673	Roche
	II	Radafaxine hydrochloride	GlaxoSmithKline
	II	SA-4503	M's Science
	II	Vestipitant mesilate/Paroxetine	GlaxoSmithKline
	I	823296	GlaxoSmithKline
	I	DOV-21947	DOV Pharmaceutical/Merck & Co.
	I	Lu-AA-21004	Lundbeck
	I	Lu-AA-24530	Lundbeck
	I	NBI-34041 (876008)	Neurocrine Biosciences/GlaxoSmithKline
	I	ND-7001	Neuro3d
	I	Ono-2333MS	Ono Pharmaceutical
	I	PW-4112	Penwest
	I	SSR-125543	Sanofi-Aventis
	I	SSR-149415	Sanofi-Aventis
	I	TS-041 (JNJ-19567470)	Taisho/Janssen (Johnson & Johnson)
	I	YKP-581	Johnson & Johnson/SK Bio-Pharmaceuticals
Depression, major	R-2006	Selegiline[1,2], transdermal	Somerset/Bristol-Myers Squibb
	Prereg.	Agomelatine[2]	Servier
	Prereg.	Desvenlafaxine succinate	Wyeth
	III	Gepirone[2], extended-release	Fabre-Kramer
	II/III	Nemifitide ditriflutate[2]	Tetragenex
	II	LAX-201	Amarin
	I/II	BMS-562086	Bristol-Myers Squibb
	I	SEP-225289	Sepracor
Depression, psychotic major	III	Mifepristone[1,2]	Corcept Therapeutics
Impulse-control disorder	II/III	Nalmefene[1,2]	BioTie Therapies/Somaxon
Insomnia	L-2005	Eszopiclone[2]	Sepracor
	L-2005	Ramelteon[2]	Takeda
	Prereg.	Indiplon[2]	Neurocrine Biosciences/Pfizer
	III	Doxepin hydrochloride[1]	Somaxon
	III	Gaboxadol[2]	Lundbeck/Merck & Co.
	II	Eplivanserin	Sanofi-Aventis
	II	M-100907[2]	Sanofi-Aventis
	II	NG2-73	Neurogen
	II	OX-22	Orexo
	II	PD-6735	Phase 2 Discovery
	II	Pruvanserin hydrochloride	Lilly
	I	APD-125	Arena
	I	EVT-201	Evotec
	I	MK-0454	Merck & Co.

Continuation

Treatment of Psychiatric Disorders by Condition

Condition	Phase	Drugs under development	Source
Narcolepsy	Prereg.	Armodafinil[2]	Cephalon
Obsessive-compulsive disorder	III	Vagus nerve stimulation therapy[1]	Cyberonics
	II/ III	Escitalopram oxalate[1,2]	Lundbeck/Forest
	II	RG-10681	Repligen
Panic disorder	I	BTG-1640	Abiogen
Phobia, social	R-2005	Fluvoxamine maleate[1,2]	Solvay/Meiji Seika
	II	PH-94B	Pherin
Psychiatric disorders	II	C-9054	Merck & Co.
	II	CP-316311	Pfizer
	II	CP-601932	Pfizer
	II	MK-0364	Merck & Co.
	II	PD-341806	Pfizer
	I	MK-0249	Merck & Co.
Psychosis	II	ACP-103	Acadia
	I	Cannabidiol	GW Pharmaceuticals
	I	Lu-31-130	Lundbeck
Schizophrenia	L-2006	Sertindole[2]	Lundbeck
	Prereg. (JP)	Blonanserin[2]	Almirall Prodesfarma/ Dainippon Sumitomo
	Prereg.	Paliperidone	Johnson & Johnson
	III	Asenapine maleate[2]	Pfizer/Organon
	III	Bifeprunox mesilate[2]	Solvay/Wyeth/Lundbeck
	III	Iloperidone[2]	Titan/Vanda Pharmaceuticals
	III	Paliperidone palmitate	Johnson & Johnson
	II	773812	GlaxoSmithKline
	II	ACP-103	Acadia
	II	ACP-104	Acadia
	II (EU, US)	Blonanserin[2]	Almirall Prodesfarma/ Dainippon Sumitomo
	II	CX-516	Cortex
	II	Farampator	Organon
	II	Lurasidone hydrochloride	Merck & Co./Dainippon Sumitomo
	II	LY-2140023	Lilly
	II	Ocaperidone	Neuro3d/Janssen (Johnson & Johnson)
	II	RG-10681	Repligen
	II	SCA-136	Wyeth
	II	SLV-310	Solvay/Wyeth
	II	SLV-313	Wyeth/Solvay
	II	Talnetant	GlaxoSmithKline
	I	644784	GlaxoSmithKline
	I	742457	GlaxoSmithKline
	I	Abaperidone hydrochloride[2]	Ferrer
	I	ACR-16	Carlsson Research/Astellas Pharma
	I	AVE-1625	Sanofi-Aventis
	I	MEM-3454	Memory Pharmaceuticals/Roche
	I	Neboglamine	Rottapharm/Xytis
	I	ORM-10921	Orion Pharma
	I	PW-4123	Penwest
	I	RGH-188	Gedeon Richter/Forest
	I	SLV-314	Solvay/Wyeth
	I	YKP-1358	SK Bio-Pharmaceuticals
Sleep apnea	II	Esmirtazapine maleate	Organon
	II	(*R*)-Mirtazapine	Cypress Bioscience/Organon
	I/II	BGC-20-0166	BTG
Sleep disorders	Prereg.	Armodafinil[2]	Cephalon
	II	CX-717	Cortex
	II	Ramelteon[2]	Takeda
Stuttering	II	Pagoclone[2]	Indevus

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

Treatment of Psychiatric Disorders by Source

Source	Condition	Drugs under development	Phase
Abiogen	Anxiety	BTG-1640	I
	Panic disorder	BTG-1640	I
Acadia	Psychosis	ACP-103	II
	Schizophrenia	ACP-103	II
		ACP-104	II
Addex Pharmaceuticals	Anxiety	ADX-10059	I
Imirall Prodesfarma	Schizophrenia	Blonanserin[2]	Prereg. (JP)
		Blonanserin[2]	II (EU, US)
Amarin	Depression	Miraxion™	II
	Depression, major	LAX-201	II
Arena	Insomnia	APD-125	I
Asahi Kasei	Anxiety	AP-521	II
Astellas Pharma	Schizophrenia	ACR-16	I
Bial	Bipolar disorder	Eslicarbazepine acetate	II
BioTie Therapies	Impulse control disorder	Nalmefene[1,2]	II/III
Boehringer Ingelheim	Anxiety, generalized	Duloxetine hydrochloride[1,2]	III
Boston Life Sciences	Attention deficit hyperactivity disorder, diagnosis	Altropane®	II
Bristol-Myers Squibb	Depression, major	BMS-562086	I/II
		Selegiline[1,2], transdermal	R-2006
BTG	Sleep apnea	BGC-20-0166	I/II
Carlsson Research	Schizophrenia	ACR-16	I
Cephalon	Anxiety, generalized	Tiagabine hydrochloride[1]	III
	Attention deficit hyperactivity disorder	Modafinil[1,2]	Prereg.
	Narcolepsy	Armodafinil[2]	Prereg.
	Sleep disorders	Armodafinil[2]	Prereg.
Corcept Therapeutics	Depression, psychotic major	Mifepristone[1,2]	III
Cortex	Attention deficit hyperactivity disorder	CX-717	II
	Schizophrenia	CX-516	II
	Sleep disorders	CX-717	II
Cyberonics	Anxiety	Vagus nerve stimulation therapy[1]	III
	Bipolar disorder	Vagus nerve stimulation therapy[1]	III
	Obsessive-compulsive disorder	Vagus nerve stimulation therapy[1]	III
Cypress Bioscience	Sleep apnea	(*R*)-Mirtazapine	II
Dainippon Sumitomo	Anxiety	Emapunil	II
	Depression	Emapunil	II
	Schizophrenia	Blonanserin[2]	Prereg. (JP)
		Blonanserin[2]	II (EU, US)
		Lurasidone hydrochloride	II
DOV Pharmaceutical	Depression	DOV-216303	II
		DOV-21947	I
D-Pharm	Bipolar disorder	DP-VPA2	I
elbion	Anxiety	ELB-139	II
Evotec	Insomnia	EVT-201	I
Fabre-Kramer	Depression, major	Gepirone[2], extended-release	III
Ferrer	Schizophrenia	Abaperidone hydrochloride[2]	I
Forest	Bipolar disorder	RGH-188	I
	Obsessive-compulsive disorder	Escitalopram oxalate[1,2]	II/ III
	Schizophrenia	RGH-188	I
Gedeon Richter	Bipolar disorder	RGH-188	I
	Schizophrenia	RGH-188	I
Genaissance	Depression	Vilazodone hydrochloride[2]	III
GlaxoSmithKline	Anxiety	163090	I
		823296	I
		Casopitant hydrochloride	II
		NBI-34041 (876008)	I
		Vestipitant mesilate/Paroxetine	II
	Attention deficit hyperactivity disorder	NS-2359 (372475)	II
	Depression	823296	I
		Casopitant hydrochloride	II
		NBI-34041 (876008)	I
		NS-2359 (372475)	II
		Radafaxine hydrochloride	II
		Vestipitant mesilate/Paroxetine	II

Continuation

Treatment of Psychiatric Disorders by Source

Source	Condition	Drugs under development	Phase
GlaxoSmithKline	Schizophrenia	644784	I
		742457	I
		773812	II
		Talnetant	II
GW Pharmaceuticals	Psychosis	Cannabidiol	I
Indevus	Stuttering	Pagoclone[2]	II
Janssen (Johnson & Johnson)	Anxiety	TS-041 (JNJ-19567470)	I
	Depression	R-228060 (YKP-10A)	II
		TS-041 (JNJ-19567470)	I
	Schizophrenia	Ocaperidone	II
Johnson & Johnson	Depression	YKP-581	I
	Schizophrenia	Paliperidone	Prereg.
		Paliperidone palmitate	III
Lilly	Anxiety	Eglumetad hydrate	I
		Talaglumetad hydrochloride	I
	Anxiety, generalized	Duloxetine hydrochloride[1,2]	III
	Insomnia	Pruvanserin hydrochloride	II
	Schizophrenia	LY-2140023	II
Lundbeck	Bipolar disorder	Bifeprunox mesilate[2]	III
	Depression	Lu-AA-21004	I
		Lu-AA-24530	I
	Insomnia	Gaboxadol[2]	III
	Obsessive-compulsive disorder	Escitalopram oxalate[1,2]	II/ III
	Psychosis	Lu-31-130	I
	Schizophrenia	Bifeprunox mesilate[2]	III
		Sertindole[2]	L-2006
MediciNova	Anxiety, generalized	Osemozotan hydrochloride[2]	II
Meiji Seika	Phobia, social	Fluvoxamine maleate[1,2]	R-2005
Memory Pharmaceuticals	Schizophrenia	MEM-3454	I
Merck & Co.	Depression	DOV-216303	II
		DOV-21947	I
	Insomnia	Gaboxadol[2]	III
		MK-0454	I
	Psychiatric disorders	C-9054	II
		MK-0249	I
		MK-0364	II
	Schizophrenia	Lurasidone hydrochloride	II
Merck KgA	Depression	Vilazodone hydrochloride[2]	III
M's Science	Depression	SA-4503	II
Neuro3d	Anxiety	ND-7001	I
	Depression	ND-7001	I
	Schizophrenia	Ocaperidone	II
Neurocrine Biosciences	Anxiety	NBI-34041 (876008)	I
	Depression	NBI-34041 (876008)	I
	Insomnia	Indiplon[2]	Prereg.
Neurogen	Insomnia	NG2-73	II
NeuroSearch	Attention deficit hyperactivity disorder	NS-2359 (372475)	II
	Depression	NS-2359 (372475)	II
New River Pharmaceuticals	Attention deficit hyperactivity disorder	Lisdexamfetamine	Prereg.
Novartis	Anxiety	AFQ-056	I
		Emapunil	II
	Bipolar disorder	Licarbazapine	III
Noven	Attention deficit hyperactivity disorder	Methylphenidate hydrochloride[1], transdermal system	Prereg.
Ono Pharmaceutical	Anxiety	Ono-2333MS	I
	Depression	Ono-2333MS	I
Orexo	Insomnia	OX-22	II
Organon	Bipolar disorder	Asenapine maleate[2]	III
	Depression	Org-34517	II
	Schizophrenia	Asenapine maleate[2]	III
		Farampator	II
	Sleep apnea	Esmirtazapine maleate	II
		(*R*)-Mirtazapine	II
Orion Pharma	Schizophrenia	ORM-10921	I

Continuation

Treatment of Psychiatric Disorders by Source

Source	Condition	Drugs under development	Phase
Penwest	Depression	PW-4112	I
	Schizophrenia	PW-4123	I
Pfizer	Anxiety, generalized	Pregabalin[1,2]	Prereg.
	Bipolar disorder	Asenapine maleate[2]	III
	Insomnia	Indiplon[2]	Prereg.
	Psychiatric disorders	CP-316311	II
		CP-601932	II
		PD-341806	II
	Schizophrenia	Asenapine maleate[2]	III
Phase 2 Discovery	Insomnia	PD-6735	II
Pherin	Phobia, social	PH-94B	II
Predix Pharmaceuticals	Anxiety, generalized	PRX-00023	III
	Depression	PRX-00023	II
Repligen	Bipolar disorder	RG-2417	II
	Obsessive-compulsive disorder	RG-10681	II
	Schizophrenia	RG-10681	II
Roche	Anxiety	R-673	II
	Depression	R-673	II
	Schizophrenia	MEM-3454	I
Rottapharm	Anxiety	Itriglumide[2]	I
	Schizophrenia	Neboglamine	I
Russian Academy of Medical Sciences	Anxiety	Selank	II
Saegis	Attention deficit hyperactivity disorder	SGS-7422	II
Sanofi-Aventis	Anxiety	SSR-125543	I
		SSR-149415	I
	Anxiety, generalized	SR-58611	III
	Depression	Saredutant[2]	III
		SR-58611	III
		SSR-125543	I
		SSR-149415	I
	Insomnia	Eplivanserin	II
		M-100907[2]	II
	Schizophrenia	AVE-1625	I
Sepracor	Depression, major	SEP-225289	I
	Insomnia	Eszopiclone[2]	L-2005
Servier	Bipolar disorder	Agomelatine[2]	III
	Depression, major	Agomelatine[2]	Prereg.
Shire Pharmaceuticals	Attention deficit hyperactivity disorder	Lisdexamfetamine	Prereg.
		Methylphenidate hydrochloride[1], transdermal system	Prereg.
		SPD-465	III
		SPD-503	III
	Bipolar disorder	Carbamazepine[1], extended-release	L-2005
SK Bio-Pharmaceuticals	Anxiety	YKP-3089	IND filed
	Depression	R-228060 (YKP-10A)	II
		YKP-581	I
	Schizophrenia	YKP-1358	I
Solvay	Bipolar disorder	Bifeprunox mesilate[2]	III
		SLV-310	II
		SLV-314	I
	Phobia, social	Fluvoxamine maleate[1,2]	R-2005
	Schizophrenia	Bifeprunox mesilate[2]	III
		SLV-310	II
		SLV-313	II
		SLV-314	I
Somaxon	Impulse control disorder	Nalmefene[1,2]	II/III
	Insomnia	Doxepin hydrochloride[1]	III
Somerset	Depression, major	Selegiline[1,2], transdermal	R-2006
Taisho	Anxiety	TS-041 (JNJ-19567470)	I
	Depression	TS-041 (JNJ-19567470)	I
Takeda	Insomnia	Ramelteon[2]	L-2005
	Sleep disorders	Ramelteon[2]	II
Targacept	Depression	Mecamylamine hydrochloride[1]	II

Continuation

Treatment of Psychiatric Disorders by Source

Source	Condition	Drugs under development	Phase
Tetragenex	Depression, major	Nemifitide ditriflutate[2]	II/III
Titan	Schizophrenia	Iloperidone[2]	III
Vanda Pharmaceuticals	Schizophrenia	Iloperidone[2]	III
Wyeth	Anxiety	WAY-181187	I
	Anxiety, generalized	WAY-181187	I
	Bipolar disorder	Bifeprunox mesilate[2]	III
		SLV-310	II
		SLV-314	I
	Depression, major	Desvenlafaxine succinate	Prereg.
	Schizophrenia	Bifeprunox mesilate[2]	III
		SCA-136	II
		SLV-310	II
		SLV-313	II
		SLV-314	I
Xytis	Schizophrenia	Neboglamine	I

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

Drugs Under Development for the Treatment of Psychiatric Disorders

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644784

Compound 644784 is a cyclooxygenase type 2 (COX-2) inhibitor in phase I development at GlaxoSmithKline for the treatment of acute and chronic pain conditions including neuropathic pain. In addition, to explore the utility of COX-2 inhibitors in the treatment of psychiatric disorders, GlaxoSmithKline is conducting early clinical trials for the treatment of schizophrenia.

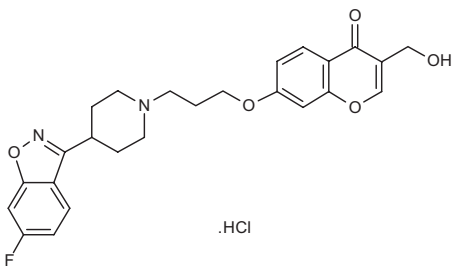
773812

GlaxoSmithKline is conducting phase II clinical trials with compound 773812, a mixed 5-HT/dopamine antagonist, for the treatment of schizophrenia.

823296

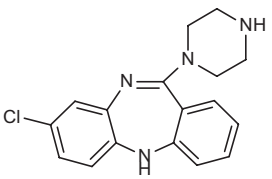
Compound 823296 is a tachykinin NK_1 receptor antagonist in early clinical evaluation at GlaxoSmithKline for the treatment of depression and anxiety.

Abaperidone Hydrochloride



Ferrer's abaperidone hydrochloride, a 5-HT_{2A} and dopamine D2 antagonist, is currently undergoing phase I trials as an atypical antipsychotic for the treatment of schizophrenia.

ACP-103/ACP-104



ACP-104

Phase II trials are under way at Acadia with ACP-103, a 5-HT_{2A} receptor inverse agonist with potential as adjunctive therapy for schizophrenia and psychosis induced by Parkinson's disease therapy. When combined with available antipsychotic agents, ACP-103 may reduce the side effects associated with these drugs, as well as expand their range of efficacy. Recently reported phase II clinical results demonstrated that ACP-103 reduced both the motor disturbances and hyperprolactinemia caused by haloperidol in healthy volunteers.

ACP-104, the major metabolite of clozapine with potent muscarinic M_1 receptor-agonist activity, is also in phase II clinical trials at Acadia for the treatment of schizophrenia. The compound appears to have additional beneficial cognitive effects.

ACR-16

A dopaminergic stabilizer, ACR-16 has completed early clinical studies at Carlsson Research for the treatment of Parkinson's disease, Huntington's disease and schizophrenia. Pursuant to a license agreement signed in February 2005, Astellas Pharma obtained rights to further develop, manufacture and market ACR-16 for the treatment of schizophrenia, while Carlsson Research retained full and exclusive rights for development, sales and marketing of the compound for Huntington's disease in Europe and North America. Results from the clinical trials demonstrated a good safety and pharmacokinetic profile,

as well as efficacy in the treatment of schizophrenia and Parkinson's disease, with beneficial effects on psychotic symptoms, cognitive, emotional and motor functions, and sleep. Preclinical studies indicate its utility in treating the full range of symptoms of schizophrenia, including both positive and negative symptoms and impaired cognitive and social functions, coupled with a low likelihood for extrapyramidal symptoms.

The drug holds orphan drug designation in the U.S. for the treatment of Huntington's disease.

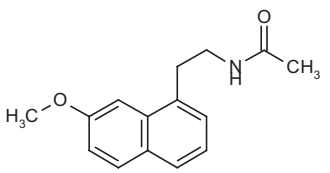
ADX-10059

The first compound from Addex Pharmaceuticals' allosteric modulator discovery platform, ADX-10059 is a negative allosteric modulator of the metabotropic glutamate receptor subtype 5 ($mGluR_5$) currently undergoing phase I trials to evaluate its potential for use in the treatment of migraine and anxiety.

AFQ-056

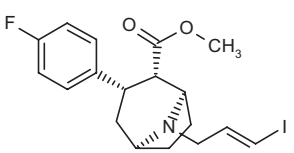
AFQ-056 is in early clinical studies at Novartis for the treatment of anxiety.

Agomelatine



Agomelatine, a dual melatonergic agonist and serotonergic antagonist discovered and developed by Servier, is currently awaiting registration for the treatment of major depression. The drug candidate is also being evaluated in phase III clinical trials for the treatment of bipolar disorder.

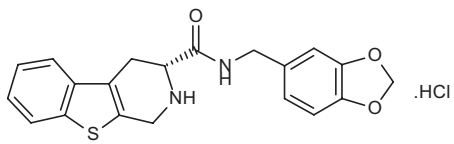
Altropane®



The diagnostic agent Altropane® is undergoing phase III trials at Boston Life Sciences for the diagnosis of Parkinson's disease (PD) and phase II trials for the diagnosis of attention deficit hyperactivity disorder (ADHD).

The agent binds with extremely high affinity and specificity to the dopamine transporter (DAT). Consequently, the amount of Altropane® taken up by the brain is directly proportional to the number of DATs that are present in any given area of the brain. In patients with PD, there is a marked decrease in the number of DATs in the striatal region (caudate and putamen). As a result, scientists can use SPECT imaging in combination with the Altropane® marker to determine the binding potential number for each patient. This number is directly proportional to the number of DATs in the striatal region, and is calculated using a simple computer algorithm. Binding potential numbers differ significantly between PD and healthy patients. Conversely, ADHD appears to be associated with an excess number of DATs in this same region in the brain, and thus diagnosis can also be achieved for this indication by the procedure outlined above. Altropane® was invented by researchers at Harvard and its affiliates, including Massachusetts General Hospital. It was licensed to Boston Life Sciences, which signed an agreement in August 2000 with MDS Nordion. Pursuant to this agreement, MDS Nordion is responsible for supplying the drug for Boston Life Sciences' regulatory filing and for manufacturing the drug for market if the product is approved.

AP-521

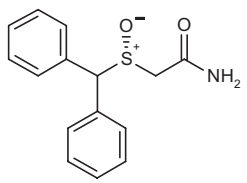


Developed by Asahi Kasei, AP-521 is a benzothienopyridine derivative with 5-HT_{1A} receptor-antagonist activity in phase II clinical trials for the treatment of anxiety.

APD-125

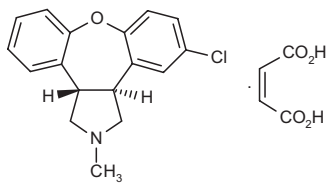
APD-125 is a highly selective 5-HT_{2A} inverse agonist in early clinical evaluation at Arena for the treatment of insomnia.

Armodafinil



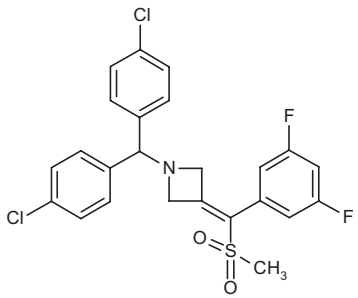
Armodafinil (Nuvigil™), an α_1-adrenoceptor agonist, is currently awaiting registration in the U.S. for the treatment of excessive sleepiness associated with narcolepsy, shift work sleep disorder (SWSD) and obstructive sleep apnea/hypopnea syndrome (OSA/HS). Discovered and developed at Cephalon, the compound is a single-isomer formulation of modafinil, currently marketed as Provigil®.

Asenapine Maleate



The dual 5-HT/dopamine antagonist asenapine maleate is a potential new medication for the treatment of a variety of neurological/psychiatric disorders that is in phase III trials for schizophrenia and bipolar disorder under a global agreement between Organon and Pfizer.

AVE-1625

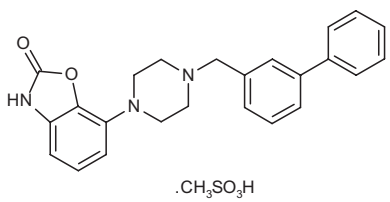


AVE-1625 is a cannabinoid CB_1 antagonist in early clinical development at Sanofi-Aventis for the treatment of Alzheimer's-type dementia, obesity and schizophrenia.

BGC-20-0166

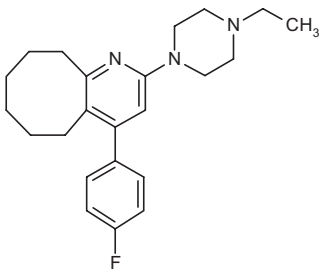
BGC-20-0166 is in early clinical trials at BTG for the treatment of obstructive sleep apnea. The drug is thought to work by targeting two distinct mechanisms of 5-HT signaling.

Bifeprunox Mesilate



A putative new antipsychotic compound, bifeprunox mesilate, a partial dopamine D2 agonist and $5\text{-}HT_{1A}$ receptor agonist, is being developed jointly by Lundbeck, Solvay and Wyeth in phase III trials for the treatment of schizophrenia and bipolar disorder. In addition to efficacy against both the positive and negative symptoms of schizophrenia, bifeprunox is expected to provide an improved safety profile, with the advantages of no weight gain, increase in prolactin, glucose dysregulation or $Q\text{-}T_c$ prolongation. In addition, the drug is expected to have a favorable lipid profile and extrapyramidal symptoms comparable to placebo. Submissions are planned in a number of markets in 2006, with expected market launch in 2007. Lundbeck has marketing rights to bifeprunox in Europe and a number of other markets, while Lundbeck and Solvay will jointly market the product in Brazil and Argentina. Solvay and Wyeth established a development and marketing agreement for the U.S., Canada, Japan and Mexico in 2004.

Blonanserin



Blonanserin (AD-5423) is a chemically novel antipsychotic agent being co-developed by Dainippon Sumitomo and Almirall Prodesfarma for the treatment of schizophrenia. A dopamine $D2/5\text{-}HT_2$ receptor antagonist, blonanserin is under regulatory review in Japan and is in phase II trials in Europe and the U.S. In 2001, Almirall Prodesfarma was granted a license to blonanserin for worldwide development with the exception of Japan, China, Taiwan and South Korea, where Dainippon Sumitomo retains rights to the compound.

BMS-562086

A phase I/II clinical trial of Bristol-Myers Squibb's BMS-562086 for the treatment of major depressive disorder is recruiting patients.

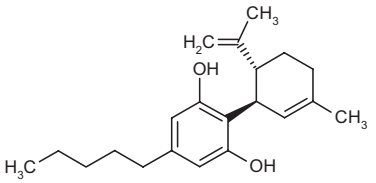
BTG-1640

A member of a new class of nonsedating, nonaddictive drugs that BTG licensed to Abiogen, BTG-1640 recently entered phase I clinical trials for the treatment of anxiety and panic disorder. The precise mechanism of action of BTG-1640 has not yet been established but is thought to be different from established anxiolytics.

C-9054

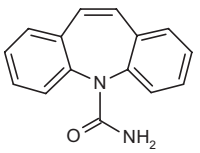
Merck & Co. is evaluating C-9054 in phase II clinical trials as a potential new agent for the treatment of psychiatric disorders.

Cannabidiol



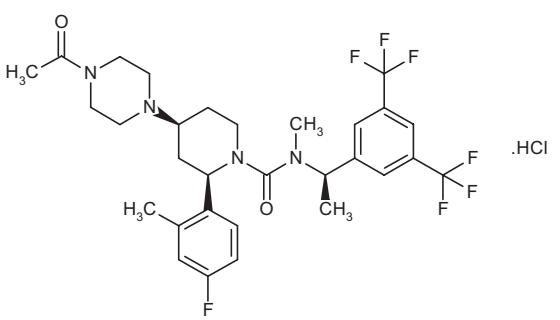
The cannabinoid receptor agonist cannabidiol (Nabidiolex) is currently undergoing phase II clinical evaluation at GW Pharmaceuticals for various indications, including the treatment of neuropathic pain, rheumatoid arthritis and inflammatory bowel disease (IBD). Early clinical trials and preclinical studies are under way for the treatment of psychotic disorders and epilepsy, respectively.

Carbamazepine, *Extended-Release*



Carbamazepine (Tegretol®), a sodium channel blocker, was launched over 40 years ago by Novartis for the prophylactic management of epilepsy in adults and children, the symptomatic treatment of pain associated with trigeminal neuralgia and the treatment of psychosis, including the prophylaxis of manic-depressive psychosis unresponsive to lithium and as an adjunct to antipsychotic therapy for the symptomatic treatment of acute schizophrenia. In 2005, Shire Pharmaceuticals launched an extended-release capsule formulation (SPD-417) as Equetro™ in the U.S. for the treatment of acute manic and mixed episodes associated with bipolar disorder. The extended-release capsule uses Shire's Microtrol™ technology to permit administration of a twice-daily dosing regimen, marking an improvement over the 3 or 4 doses required daily for immediate-release tablets.

Casopitant Hydrochloride



A tachykinin NK_1 receptor antagonist, casopitant hydrochloride is in phase II clinical evaluation at GlaxoSmithKline for the treatment of depression and anxiety. It is also in phase II development for the prophylaxis of nausea and vomiting induced by chemotherapy or surgery, and in phase I clinical trials for the treatment of urinary incontinence.

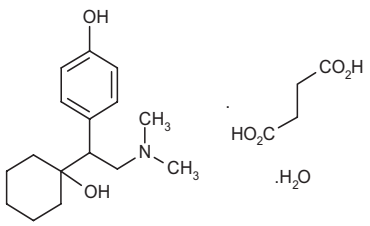
CP-316311/CP-601932/PD-341806 –

Pfizer is evaluating three compounds –CP-316311 (a CRF receptor antagonist), CP-601932 (a nicotinic acetylcholine receptor partial agonist) and PD-341806 (a calcium channel activator)– in phase II clinical trials as potential therapeutics for psychiatric disorders and other neurological disorders.

CX-717

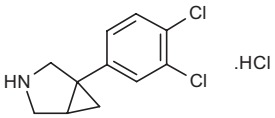
CX-717 is an AMPA receptor modulator (Ampakine®) in phase II clinical trials at Cortex for the treatment of sleep disorders, attention deficit hyperactivity disorder (ADHD) and Alzheimer's-type dementia.

Desvenlavaxine Succinate



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

DOV-21947/DOV-216303



DOV-21947

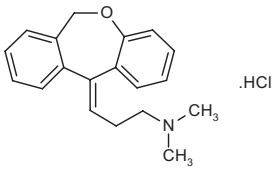
DOV Pharmaceutical has two triple dopamine, norepinephrine and 5-HT reuptake inhibitors in clinical development for various psychopharmacological disorders.

DOV-21947 ([+]-isomer) is currently undergoing phase I clinical trials for the treatment of depression. The compound is being advanced in collaboration with Merck & Co. under a licensing agreement established in 2004,

giving the latter exclusive worldwide rights to the novel triple uptake inhibitor for all therapeutic indications.

DOV-216303 (racemic) is in phase II trials for the treatment of depression. Originally developed at Wyeth, the compound was subsequently licensed to DOV, which established an agreement in 2004 with Merck & Co., giving the latter exclusive worldwide rights for the treatment of depression, anxiety and addiction.

Doxepin Hydrochloride, *New Indication*

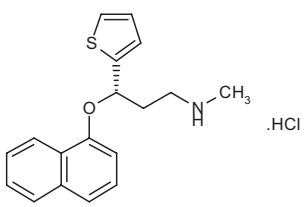


Doxepin hydrochloride is a histamine H_1 and H_2 receptor antagonist that was launched over 35 years ago by Pfizer for the treatment of depression and anxiety and by Bioglan in 1998 for the treatment of eczema-associated pruritus. Somaxon holds a license to doxepin (Silenor™) for the U.S. market and is currently conducting phase III trials for the treatment of chronic primary insomnia in adults and elderly patients. Silenor™ is an oral formulation of doxepin in strengths of 1-6 mg as compared to the marketed formulation dosed at 75-300 mg/day for anxiety and depression.

DP-VPA

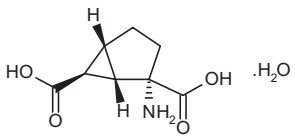
DP-VPA is a unique phosphatidylcholine conjugate of valproic acid currently in phase II clinical trials at D-Pharm for the treatment of epilepsy and in phase I clinical trials for the treatment of bipolar disorder and for the prevention of migraine. The activity of DP-VPA is triggered by an enzyme that has supranormal activity at the site of excitatory or seizure activity in the brain. In unaffected tissues, where the enzyme levels are normal, the drug remains as an inert prodrug. DV-VPA was designed using D-Pharm's Regulated Activation of Prodrugs (D-RAP™) technology that allows precise control of drug action at the site of pathology.

Duloxetine Hydrochloride, *New Indication*



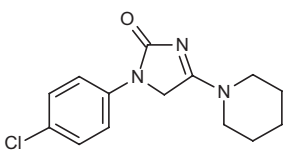
Duloxetine hydrochloride is an inhibitor of 5-HT and norepinephrine reuptake that was launched in 2004 by Lilly and partner Boehringer Ingelheim for the treatment of major depression, urinary incontinence and pain caused by diabetic peripheral neuropathy. The drug is also undergoing phase III clinical trials for the treatment of generalized anxiety disorder and fibromyalgia. The December 2002 worldwide commercialization agreement with Boehringer Ingelheim excluded Japan, where Shionogi holds development rights.

Eglumetad Hydrate



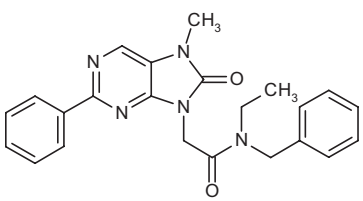
Phase I clinical trials are in progress at Lilly with eglumetad hydrate (LY-354740), a metabotropic glutamate II receptor agonist for the treatment of anxiety.

ELB-139



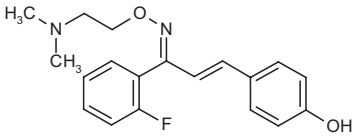
ELB-139 is a low-affinity α3-selective partial benzodiazepine agonist with potential as an anxiolytic, exhibiting many of the favorable effects of benzodiazepines without their potential for the development of tolerance or low-dose dependency. Phase II trials are under way at elbion.

Emapunil



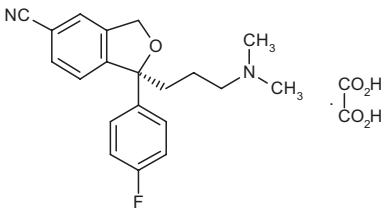
Emapunil (XBD-173 at Novartis; AC-5216 at Dainippon Sumitomo), a mitochondrial benzodiazepine receptor agonist discovered by the former Dainippon Pharmaceutical (now Dainippon Sumitomo), is a potential new anxiolytic presently in phase II clinical testing at Dainippon Sumitomo and Novartis. Dainippon is also evaluating the compound in phase II trials as an antidepressant. The product was licensed worldwide (except for Japan, South Korea Taiwan and China) to Novartis.

Eplivanserin



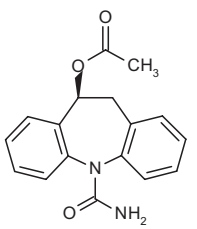
Sanofi-Aventis is evaluating eplivanserin (SR-46349), a 5-HT_{2A} receptor antagonist, in phase II clinical trials for the treatment of chronic insomnia and fibromyalgia.

Escitalopram Oxalate



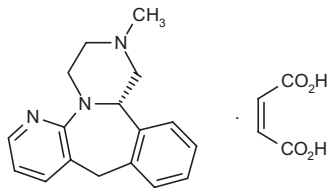
Escitalopram oxalate is a selective serotonin reuptake inhibitor (SSRI) and the active (*S*)-isomer of the antidepressant citalopram that was first introduced by Lundbeck in Europe in 2002 under the tradename Cipralex® for the treatment of major depressive disorder and panic disorder. In late 2003, the product was approved in several European countries for social anxiety disorder (SAD), and is now available in major European markets. The compound was approved in the E.U. for the treatment of generalized anxiety disorder (GAD) in September 2005. Licensee Forest received FDA approval for the drug, known as Lexapro™, in August 2002 for the treatment of major depressive disorder in adults and in December 2003 for the treatment of GAD in adults. In March 2005, Forest received nonapprovable letters from the FDA for sNDAs submitted for the treatment of panic disorder and SAD. Lundbeck is also assessing escitalopram in advanced clinical trials for the treatment of obsessive-compulsive disorder. Escitalopram is licensed to Mochida for development in Japan, where phase I trials for depression have been completed. The company plans to seek approval of escitalopram for use in pediatric patients with major depressive disorder. Forest had been studying escitalopram for the treatment of kleptomania, but no recent development for this indication has been reported.

Eslicarbazepine Acetate



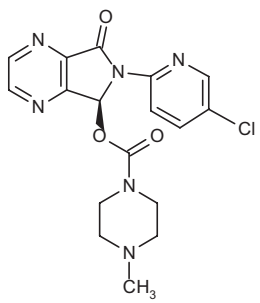
Bial's sodium channel blocker eslicarbazepine acetate is currently undergoing phase III clinical evaluation for the treatment of epilepsy and phase II trials for bipolar disorder.

Esmirtazapine Maleate



In addition to phase III clinical development for the treatment of hot flashes and night sweats, esmirtazapine maleate (Org-50081), the (+)-enantiomer of mirtazapine and a 5-HT_2 antagonist, is also in phase II clinical trials at Organon for the treatment of obstructive sleep apnea.

Eszopiclone

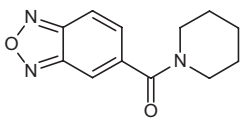


Eszopiclone (Lunesta™, formerly referred to as Estorra) is a nonbenzodiazepine hypnotic launched in the U.S. in 2005 by Sepracor for the treatment of transient and chronic insomnia. To further expand the compound's clinical applications, Sepracor is conducting phase III trials for the treatment of secondary insomnia in patients suffering from depression, rheumatoid arthritis and in women who experience symptoms of perimenopause. Postmarketing clinical evaluation is under way at Sepracor for the treatment of insomnia associated with GAD and at Massachusetts General Hospital (MGH) for the treatment of sleep disturbances and nightmares in post-traumatic stress disorder (PTSD). The National Institute of Mental Health (NIMH) is conducting an additional phase IV trial to evaluate eszopiclone's potential to improve sleep and psychological functioning in patients with depression and insomnia. Eszopiclone's hypnotic effect is believed to result from its interaction with GABA receptor complexes at binding domains located close to or allosterically coupled to benzodiazepine receptors. The drug was discovered by the former Aventis Pharma (Sanofi-Aventis) and licensed exclusively in the U.S. to Sepracor in 1999.

EVT-201

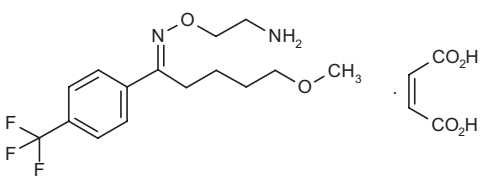
A drug candidate that acts on $GABA_A$ receptors, EVT-201 is in early clinical trials at Evotec for the treatment of insomnia. In clinical trials, the compound was well tolerated and effective in improving the time to sleep onset, duration of sleep, as well as quality of sleep, with minimal residual effects the following morning. Evotec holds exclusive commercial rights to EVT-201 pursuant to a licensing agreement with originator Roche.

Farampator



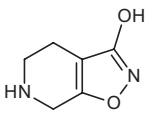
Farampator (Org-24448) belongs to the family of AMPA receptor modulators, or Ampakine® compounds, originally discovered by Dr. Gary Linch at the University of California, Irvine. The Ampakine® technology, licensed to Cortex, is based on small synthetic molecules that have good to excellent bioavailability and rapidly cross the blood-brain barrier. The drug acts by stimulating the glutamatergic system. Pursuant to a license agreement, Organon is conducting a phase II trial of farampator as a potential treatment for schizophrenia following favorable results from phase I trials. The National Institute of Mental Health (NIMH) is also conducting phase II trials with the compound for the treatment of depression.

Fluvoxamine Maleate, *New Indication*



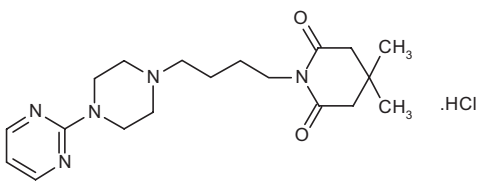
Fluvoxamine maleate, a selective serotonin reuptake inhibitor (SSRI), was launched over 20 years ago by Duphar for the treatment of depression and by Solvay for obsessive-compulsive disorder (OCD). In 2005, Meiji Seika and Solvay received additional approval in Japan (Depromel) for the treatment of social phobia. Solvay is developing a controlled-release formulation in phase III clinical trials. Fluvoxamine is specifically designed to increase 5-HT concentrations through reuptake inhibition. Pursuant to agreements signed in 1996 and 1997, the drug is marketed in Japan by Meiji Seika and Astellas Pharma, respectively, under different brand names. Duphar has maintained distribution rights in Germany and Switzerland for the treatment of depression. Originally discovered and developed by Solvay and Duphar, the product is marketed in more than 70 countries worldwide.

Gaboxadol



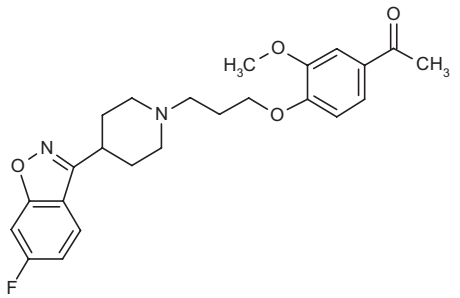
The $GABA_A$ receptor modulator gaboxadol is in phase III development at Merck & Co. and Lundbeck for the treatment of insomnia. The drug interacts directly with the GABA receptor recognition site and mediates its effects via a GABA receptor population that is different from that modulated by benzodiazepine ligands. This mechanism causes increased time in NREM sleep without suppression of REM sleep. Gaboxadol was licensed by Lundbeck from Garching Innovation on behalf of the Max Planck Institute in 1999. In 2004, gaboxadol was licensed to Merck when the two companies signed an agreement for co-development and commercialization in the U.S. Pursuant to the agreement, Merck and Lundbeck will jointly complete the ongoing phase III program, with Merck funding the majority of the remaining development activities. Following FDA approval, the companies intend to co-promote gaboxadol in the U.S.

Gepirone Hydrochloride, *Extended-Release*



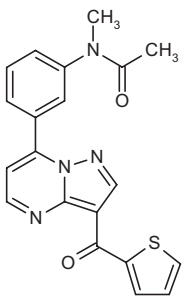
Gepirone hydrochloride is a $5\text{-}HT_{1A}$ partial agonist under development in an extended-release formulation for the treatment of major depression. Former licensee Organon filed an NDA with the FDA in 2001, but in 2004, the application was considered not approvable. In June 2005, Organon returned to Fabre-Kramer all rights to gepirone ER in exchange for a milestone payment and royalties in the event of commercialization. Fabre-Kramer plans to submit an amended NDA to the FDA based on an improved set of data from additional clinical studies. The antidepressant effects of gepirone are attributed to an agonist effect on postsynaptic 5-HT receptors. Originally developed by Bristol-Myers Squibb, gepirone is a first-in-class direct 5-HT agonist. If approved, gepirone ER would be the first effective extended-release formulation of a $5\text{-}HT_{1A}$ partial agonist.

Iloperidone



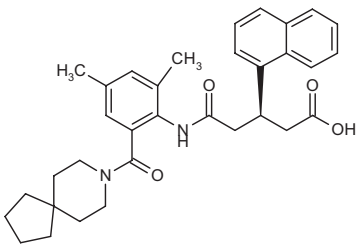
An antipsychotic 5-HT/dopamine receptor antagonist developed by Titan Pharmaceuticals, iloperidone is currently in phase III development at Vanda Pharmaceuticals for the treatment of schizophrenia and related disorders. Titan originally granted rights to iloperidone to Novartis in 1997, and in 2004, Novartis in turn licensed the drug to Vanda.

Indiplon



Indiplon is a $GABA_A$ receptor modulator that is currently awaiting registration for the treatment of primary chronic insomnia in an immediate-release capsule and a modified-release tablet formulation. The drug candidate is also being evaluated for the treatment of insomnia in early clinical trials in patients with mild to moderate chronic obstructive pulmonary disease (COPD). Originally discovered by Wyeth, the compound was licensed to DOV Pharmaceutical in 1998 for further development. DOV subsequently licensed indiplon to Neurocrine Biosciences, which established an exclusive worldwide development and commercialization agreement with Pfizer in 2002. Indiplon binds preferentially to the specific subtype of $GABA_A$ receptors within the brain believed to be responsible for promoting sleep. This receptor specificity is thought to minimize the unwanted side effects associated with benzodiazepine compounds. The immediate-release capsule has the advantage of rapid clearance, resulting in rapid sleep onset and a reduced risk of next-day impairment. The modified-release formulation delivers two doses, one at bedtime and one in the middle of the night, achieving rapid sleep initiation and maintenance throughout the night.

Itriglumide

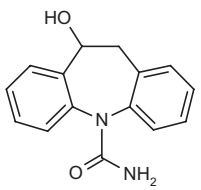


Rottapharm is conducting phase I trials with itriglumide (CR-2945), an anthranilic acid derivative with potent and selective cholecystokinin CCK_2 receptor-antagonist activity and potential for the treatment of anxiety, peptic ulcers, gastroesophageal reflux disease (GERD) and dyspepsia. The compound proved to be safe and well tolerated following single oral doses to healthy volunteers.

LAX-201

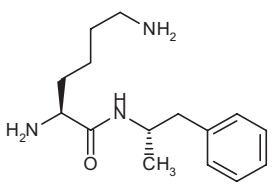
LAX-201, a combination of folic acid and an SSRI/selective norepinephrine reuptake inhibitor (SNRI), is in phase II clinical development by Amarin for the treatment of major depression in women.

Licarbazapine



Phase III clinical trials are in progress at Novartis for licarbazepine (LIC-477), a sodium channel blocker with potential for the treatment of bipolar disorder.

Lisdexamfetamine



Lisdexamfetamine (NRP-104), a conditionally bioreversible derivative of amphetamine, is awaiting registration for the treatment of ADHD in the U.S. Lisdexamfetamine is intended to provide better overdose protection and a reduced potential for addiction compared to currently available amphetamine drugs. Originally discovered and developed by New River Pharmaceuticals, the company entered into a collaborative agreement with

Shire Pharmaceuticals in 2005 for global commercialization of the drug candidate.

LU-31-130

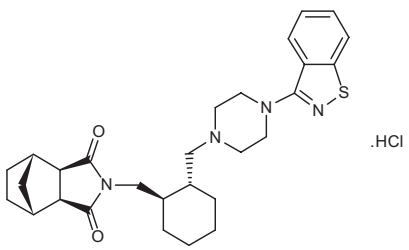
Lundbeck has an atypical antipsychotic, Lu-31-130, in early clinical trials for the treatment of psychosis.

LU-AA-21004/LU-AA-24530

A 5-HT reuptake inhibitor, Lu-AA-21004 is currently undergoing phase I clinical trials at Lundbeck for the treatment of depression. The drug is believed to have multiple targets.

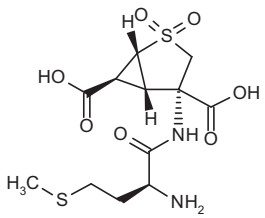
Another potential antidepressant with multiple targets and a rapid onset of action, Lu-AA-24530 is also in phase I clinical trials at Lundbeck.

Lurasidone Hydrochloride



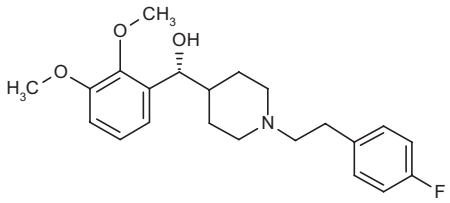
Lurasidone hydrochloride (SMP-13496, formerly SM-13496) is an atypical antipsychotic agent with 5-HT/dopamine-antagonist activity in phase II development in Japan by Dainippon Sumitomo and in other markets by Merck & Co. for the treatment of schizophrenia. The former Sumitomo granted Merck & Co. an exclusive worldwide license, with the exception of Japan, China, Korea and Taiwan, for the development of lurasidone as a schizophrenia therapy last year.

LY-2140023



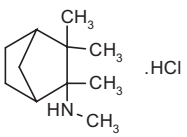
LY-2140023 is a potent and systemically active metabotropic glutamate $mGluR_{2/3}$ receptor agonist from Lilly undergoing testing in phase II clinical trials for the treatment of schizophrenia.

M-100907



The selective 5-HT_{2A} receptor antagonist M-100907 (MDL-100907) is in phase II clinical trials at Sanofi-Aventis as a potential new treatment for insomnia.

Mecamylamine Hydrochloride, *New Indication*

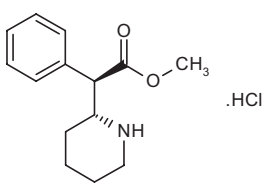


Mecamylamine hydrochloride is a nicotinic acetylcholine receptor antagonist that was first launched by Merck & Co. for the oral treatment of moderately severe to severe hypertension over 50 years ago. The drug is presently undergoing phase II clinical trials at Targacept for the treatment of depression as add-on therapy to citalopram hydrobromide.

MEM-3454

MEM-3454, a nicotinic acetylcholine $\alpha 7$ receptor partial agonist, is in early clinical trials at Memory Pharmaceuticals for the treatment of Alzheimer's-type dementia and schizophrenia. Pursuant to a collaboration agreement established between Memory Pharmaceuticals and Roche in 2003, Roche has the right to obtain an exclusive license to MEM-3454 following the completion of phase IIa clinical trials.

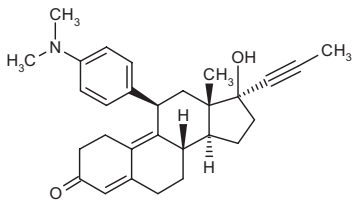
Methylphenidate Hydrochloride, *Transdermal*



A controlled-release, once-daily transdermal patch containing methylphenidate hydrochloride (Daytrana™), which uses Noven's DOT-Matrix™ patch technology, received an approvable letter from the FDA late last year

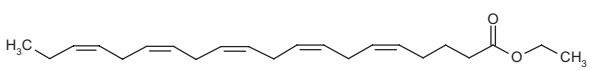
for use in the treatment of ADHD. The formulation is licensed globally to Shire Pharmaceuticals. Methylphenidate is a dopamine transporter (DAT) inhibitor launched more than 50 years ago by Novartis for the treatment of ADHD. The product, widely known as Ritalin®, is available in several formulations, including tablets and capsules.

Mifepristone, *New Indication*



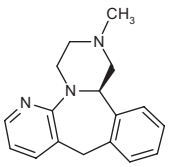
Mifepristone is an orally active, small-molecule, organic dual glucocorticoid and progesterone receptor antagonist launched in 1989 by the former Roussel-Uclaf (now Sanofi-Aventis) for the termination of pregnancy. Mifepristone (Corlux®) is now in phase III trials at Corcept Therapeutics for the treatment of psychotic major depression (PMD) and in phase II clinical trials for the treatment of Alzheimer's-type dementia. The drug is thought to exert its effects by modifying the level and release pattern of cortisol in the human body. Mifepristone was assigned fast track designation in the U.S. for the treatment of PMD, as well as orphan drug designation for the treatment of Cushing's syndrome secondary to ectopic adrenocorticotropic hormone (ACTH) secretion. Viral Genomix has discovered that mifepristone (VGX-410, Pictovir™) represents the first drug in a novel class of hepatitis C virus internal ribosomal entry site (IRES) inhibitors and is conducting phase II trials for the treatment of hepatitis C.

Miraxion™



Miraxion™ (formerly referred to as LAX-101) is a semisynthetic, highly purified derivative of eicosapentaenoate (EPA), an n-3 fatty acid, launched by Mochida over 15 years ago for the treatment of atherosclerosis obliterans and dyslipidemia. The drug is in phase II and III development at Amarin for the treatment of depression and Huntington's disease, respectively. The company is also evaluating its potential as therapy for Parkinson's disease, while Mochida is conducting phase II trials for the potential treatment of Alzheimer's-type dementia. The mechanism of action of Miraxion™ is believed to involve stabilization of mitochondrial integrity of suffering neurons, thereby preventing or slowing progression from neuronal dysfunction to apoptosis. In 2000, Amarin licensed exclusive U.S. rights to Miraxion™ from Laxdale, a company subsequently acquired by Amarin. Fast track status has been granted in the U.S. for the treatment of Huntington's disease and orphan drug designation was granted for this indication in both the U.S. and the E.U.

(*R*)-Mirtazapine



Organon and Cypress Bioscience are collaborating on the development of (*R*)-mirtazapine (Org-4419) for the treatment of obstructive sleep apnea. Phase II trials are under way. Mirtazapine exerts its effects by increasing levels of both 5-HT and norepinephrine, while also blocking certain 5-HT receptors. The racemate was approved in the U.S. 10 years ago for the treatment of major depressive disorder.

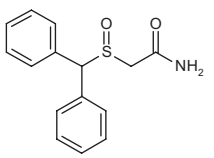
MK-0249/MK-0364

Merck & Co. has several compounds in the clinical pipeline for use in psychiatric disorders, among them MK-0249 in phase I and MK-0364 in phase II. The latter compound is also being evaluated for its potential in the treatment of obesity.

MK-0454

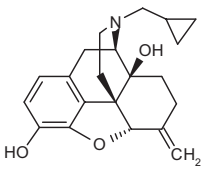
MK-0454 is in early clinical development at Merck & Co. for the treatment of insomnia.

Modafinil, *New Indication*



Modafini (Provigil®) was initially launched in 1994 by Cephalon for the treatment of narcolepsy, and subsequently for the treatment of moderate to severe chronic shift work sleep disorder with excessive sleepiness in patients working night shifts. The drug (Sparlon™) is currently awaiting registration for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents. An α_1-adrenoceptor agonist, modafinil is marketed in more than 20 countries worldwide in collaboration with several companies, including Shire, Dompé, Ortho-McNeil and Novartis.

Nalmefene, *New Indication/ Formulation*



BioTie Therapies' nalmefene is a kappa opioid receptor antagonist derived from naltrexone that is being developed for the oral treatment of impulse-control disorders (ICDs), including pathological gambling, and for the treatment of alcoholism and alcohol abuse, for which it is in phase II/III and III clinical trials, respectively. BioTie Therapies granted North American rights to Somaxon to develop, manufacture and commercialize oral nalmefene for the treatment of ICDs in 2004. In February 2005, Somaxon obtained rights from the University of Miami to the use of oral nalmefene for the treatment of nicotine dependence and phase II trials are also under way for smoking cessation. An i.v. formulation of the drug has been available for several years as Revex™ from Baker Norton for use in reversing opioid effects and for opioid overdose.

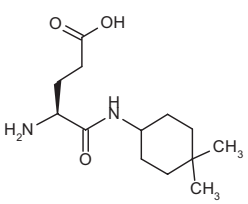
NBI-34041 (876008)

A CRF_1 receptor antagonist known as NBI-34041 at Neurocrine Biosciences and as compound 876008 at GlaxoSmithKline is in early clinical development for the treatment of anxiety and depression, as well as irritable bowel syndrome (IBS). In 2001, Neurocrine entered into a worldwide research, development and commercialization agreement with GSK for corticotropin-releasing factor (CRF) receptor antagonists, under the terms of which the companies agreed to conduct a collaborative research program for up to 5 years to identify and develop CRF receptor antagonists.

ND-7001

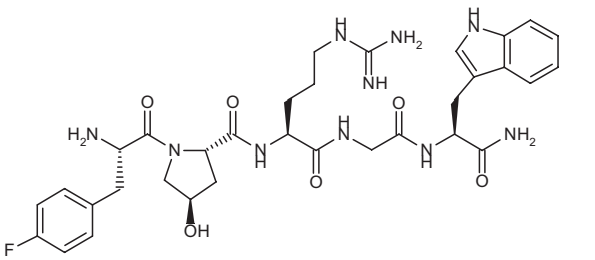
ND-7001 is a selective phosphodiesterase type 2 (PDE2) inhibitor in early clinical development at Neuro3d for the treatment of anxiety and depression.

Neboglamine



Neboglamine (CR-2249, XY-2401), a positive allosteric glycine site-specific modulator of the glutamate NMDA receptor complex developed by Rottapharm as a potential new agent for schizophrenia, is currently being evaluated by licensee Xytis in a phase I clinical trial in healthy volunteers. To a significant extent, the underlying pathophysiology of schizophrenia is believed to be a result of endogenous dysfunction or dysregulation of neurotransmission mediated at the NMDA glutamate receptor complex. For this reason, NMDA glycine-site modulators hold potential for the treatment of the negative symptomatology and cognitive impairment associated with the disease. In March 2005, Rottapharm granted Xytis a license to develop and market neboglamine in the U.S., Canada, Japan, Australia and New Zealand. Rottapharm retained rights for the rest of the world.

Nemifitide Ditriflutate



$.2CF_3CO_2H$

Tetragenex, the former Innapharma, is reportedly continuing the development of nemifitide ditriflutate (INN-00835), a novel pentapeptide compound administered by subcutaneous or needleless injection, in phase II/III clinical trials for the treatment of major depression. Results from a series of clinical studies involving over 400 subjects suggest that nemifitide has clinical advantages over other antidepressants, including a rapid onset of action, a short period of administration, a relatively long duration of treatment effect and an excellent safety profile. Furthermore, some of the significant side effects commonly associated with other antidepressants were not observed with nemifitide. Nemifitide has demonstrated clinical efficacy in both major depression and refractory depression. A subcutaneous injection is the lead formulation under development; however, the company has data that show that needle-free (Bioject™) administration is also effective. Tetragenex also intends to investigate other forms of delivery, including a transdermal patch and sublingual administration. In addition to treating major depression, the company has preliminary data that nemifitide may have potential in the treatment of anxiety disorders and plans to study other CNS disorders such as anorexia, bulimia, panic disorder and post-traumatic stress disorder.

NG2-73

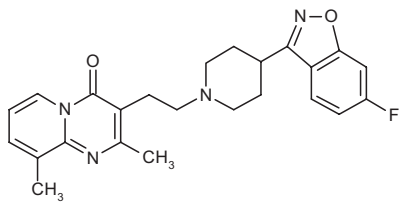
NG2-73, a selective GABA receptor partial agonist, is in phase II clinical studies at Neurogen for the treatment of insomnia. The drug candidate may hold an advantage

over first-generation GABA hypnotic agents as preclinical data demonstrate reduced activity at the GABA subunit receptor believed to be associated with certain adverse effects. Additional data show increased activity at the $\alpha 3$ subunit, which promotes sleep-inducing hypnotic effects.

NS-2359 (372475)

NeuroSearch and GlaxoSmithKline are jointly developing a new triple monoamine reuptake inhibitor, known respectively as NS-2359 and 372475, which is currently undergoing phase II clinical trials for the treatment of attention deficit hyperactivity disorder (ADHD) and depression. The drug acts by increasing the concentrations of dopamine, norepinephrine and 5-HT in the areas of the brain where attention, concentration and memory are based. It has also been shown to increase acetylcholine concentrations in the prefrontal cortex. Originally discovered by NeuroSearch, the product is being developed under a joint venture established in 2003 between NeuroSearch and GlaxoSmithKline.

Ocaperidone

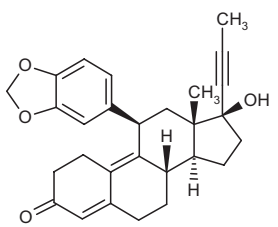


Ocaperidone is an atypical antipsychotic agent with mixed 5-HT_2/dopamine D2 receptor-antagonist activity. Neuro 3d licensed ocaperidone from Janssen in 2002 and is currently conducting phase II clinical studies in schizophrenia. Janssen retains an option to repurchase rights to the compound following phase II trials.

Ono-2333MS

Ono Pharmaceutical's CRF_1 antagonist Ono-2333MS is in early clinical trials in the U.S. for the oral treatment of anxiety and depression.

Org-34517

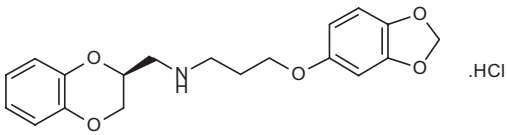


Org-34517, a glucocorticoid receptor (GR) antagonist, is currently undergoing phase II trials at Organon for the treatment of depression. The drug acts by normalizing hyperactivity in the hypothalamus-pituitary-adrenal (HPA) axis, which has been implicated in the pathogenesis of depression.

ORM-10921

Phase I clinical trials are being conducted at Orion Pharma with ORM-10921, the company's α_{2C}-adrenoceptor antagonist with potential for the treatment of schizophrenia.

Osemozotan Hydrochloride

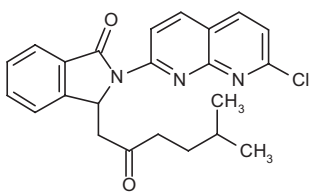


Osemozotan hydrochloride (MN-305) is a 5-HT_{1A} receptor agonist, a potentially rapid-acting and orally bioavailable agent specific for anxiety disorders that appears to lack the sedation characteristic of benzodiazepines or the side effects of SSRIs and SNRIs. The compound was originally discovered and developed by Mitsubishi Pharma (referred to as MKC-242) and has been evaluated in phase II testing as a potential treatment for anxiety disorders and depression. In June 2004, MediciNova acquired exclusive worldwide rights to osemozotan (designated MN-305), except for an ophthalmic solution and excluding Japan, China and other Southeast Asian countries. MediciNova is conducting a phase II clinical trial in patients with generalized anxiety disorder.

OX-22

Based on Orexo's sublingual technology and comprising a well-documented active substance, OX-22 is in phase II clinical development at Orexo for the treatment of transient insomnia, including sleep induction and sleep maintenance.

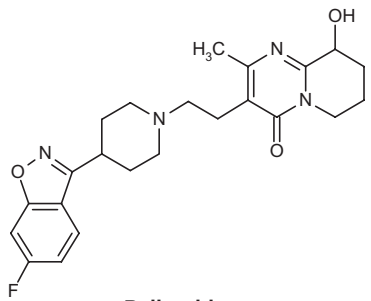
Pagoclone



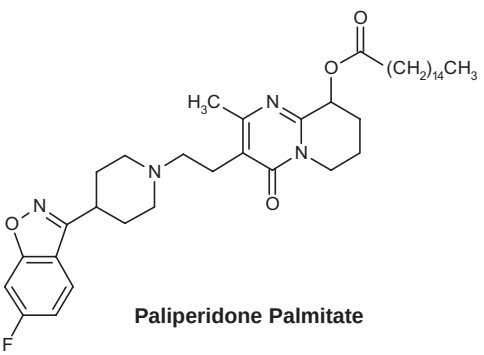
Pagoclone is a novel member of the cyclopyrrolone class that acts as a GABA receptor modulator and is

thought to increase the action of GABA, thereby reducing excess neuronal activity and alleviating the symptoms of anxiety and panic. The compound is in phase II clinical development at Indevus for the treatment of persistent developmental stuttering. Indevus obtained an exclusive worldwide license from the former Rhône-Poulenc Rorer (now Sanofi-Aventis) for the manufacture, use and sale of pagoclone, with an option for marketing rights in France reverting back to Sanofi-Aventis. After extensive clinical and regulatory development activities, Indevus entered into an exclusive worldwide license with the former Warner-Lambert (now Pfizer) in 1999 for the manufacture, use and sale of pagoclone. Following reacquisition of the worldwide rights to the product from Pfizer in June 2002, where it had reached phase III clinical trials, Indevus is currently pursuing new partnerships for the development of pagoclone.

Paliperidone/Paliperidone Palmitate



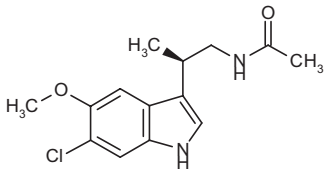
Paliperidone



Paliperidone Palmitate

The active metabolite of the known atypical antipsychotic risperidone, paliperidone has been filed for approval in the U.S. by Johnson & Johnson for the treatment of schizophrenia. The company is seeking approval for an extended-release formulation of paliperidone, developed with Alza's OROS® oral drug delivery system and designed to deliver drug over a 24-h period. Paliperidone palmitate is in phase III trials as a long-acting injectable formulation using Elan's proprietary NanoCrystal® technology, also for schizophrenia.

PD-6735

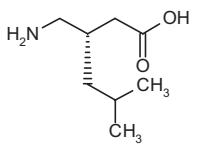


PD-6735 is in phase II development at Phase 2 Discovery for reducing sleep latency in patients with primary insomnia. The melatonin MT_1 and MT_2 agonist exhibits high selectivity and provides a novel mode of action different from that of benzodiazepine receptor ligands currently on the market. Furthermore, the drug candidate is believed to be nonaddicting, therefore offering an advantage over marketed sleep medications. Originally discovered by Lilly, PD-6735 was licensed to Phase 2 Discovery in 2002 for further development. In 2001, the compound was assigned orphan drug designation for the treatment of circadian rhythm sleep disorders in blind people with no light perception.

PH-94B

Pherin was last reported to be evaluating the vomeropherin PH-94B in phase II clinical trials for the treatment of acute social phobia in female patients. Vomeropherins are a unique family of pharmaceuticals that act directly on the human vomeronasal organ (VNO) to send electrical signals to the hypothalamic center of the brain. Vomeropherins act rapidly and directly on the end organ, eliminating the need for systemic exposure, and produce discrete responses in the hypothalamus in picogram quantities.

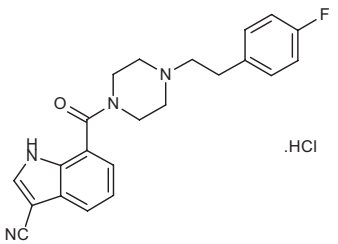
Pregabalin, *New Indication*



Pregabalin is a GABA analogue with a newly defined mechanism of action, launched in the U.K. and Germany in 2004 and in Italy in 2005 as Lyrica™ by Pfizer for the treatment of peripheral neuropathic pain and as adjunctive therapy for partial seizures resulting from epilepsy, following E.U. approval in July 2004. Also in 2004, the drug received FDA approval for the treatment of postherpetic neuralgia (PHN) and for neuropathic pain associated with diabetic peripheral neuropathy, the first FDA-approved treatment for both of these neuropathic pain states. In 2005, a revised label was approved by the FDA for the add-on indication of partial seizures due to epilepsy. Pregabalin was launched for these indications in the U.S. in September 2005. At the beginning of 2006, pre-

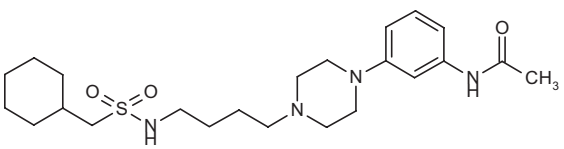
gabalin received a positive opinion in the E.U. for the treatment of generalized anxiety disorder (GAD), although a nonapprovable letter was issued by the FDA for this indication in 2004. Pfizer is also studying pregabalin in phase III trials in patients with neuropathic pain associated with spinal cord injury and for the treatment of fibromyalgia. Pregabalin acts as a voltage-dependent calcium channel $\alpha 2$-δ subunit ligand and possesses analgesic, anticonvulsant and anxiolytic properties.

Pruvanserin Hydrochloride



Lilly obtained worldwide development and marketing rights to pruvanserin hydrochloride, a 5-HT_{2A} antagonist, under license from Merck KGaA in 2004. Phase II trials are under way for the treatment of insomnia.

PRX-00023



PRX-00023 is a 5-HT_{1A} receptor agonist currently undergoing phase III trials at Predix Pharmaceuticals for the treatment of moderate to severe GAD. Phase II trials are also under way for the treatment of depression. Discovered using PREDICT, the company's proprietary G-protein-coupled receptor (GPCR) modeling, screening and optimization technology, the drug is intended to treat a variety of neuropsychiatric disorders.

PW-4112/PW-4123

Penwest is developing two compounds using the company's proprietary drug delivery technologies for psychopharmacological disorders in early clinical trials: PW-4112 for the treatment of depression and PW-4123 for the oral treatment of schizophrenia.

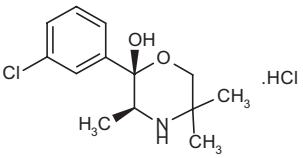
R-673

Discovered and developed by Roche, the NK_1 receptor antagonist R-673 is in phase II clinical evaluation for the treatment of anxiety and depression.

R-228060 (YKP-10A)

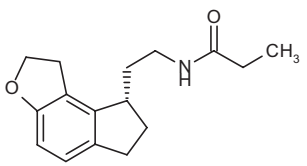
R-228060 (YKP-10A) is being assessed in phase II clinical trials for the treatment of depression. This compound is structurally different from the tricyclics and currently marketed 5-HT reuptake inhibitors. Originally developed at SK Bio-Pharmaceuticals, it was licensed to Janssen Pharmaceuticals, a subsidiary of Johnson & Johnson, in December 2000 for further development.

Radafaxine Hydrochloride



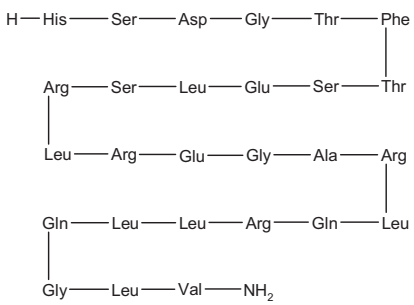
GlaxoSmithKline's radafaxine hydrochloride is a dopamine and norepinephrine reuptake inhibitor that is currently in phase II trials for the treatment of depression and in phase I trials for the treatment of obesity, fibromyalgia and neuropathic pain. The drug is a potent metabolite of bupropion.

Ramelteon



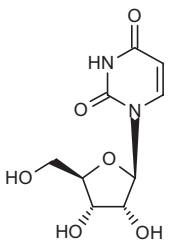
Takeda launched ramelteon (Rozerem™), a specific melatonin MT_1 and MT_2 agonist reportedly devoid of affinity for GABA or opiate receptors, in the U.S. in 2005 for the treatment of primary insomnia characterized by difficulty with sleep onset. Phase III trials are being conducted in Japan and the E.U. for its use in insomnia, and phase II trials are under way for the treatment of circadian rhythm sleep disorders.

RG-1068



RG-1068 is a synthetic human secretin being tested at Repligen in phase II clinical trials for schizophrenia and obsessive-compulsive disorder.

RG-2417

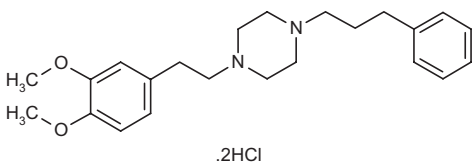


Repligen's proprietary oral formulation of uridine, RG-2417, has entered a phase II clinical trial for the treatment of bipolar disorder. The application of uridine as a therapy for neuropsychiatric disorders is supported by preclinical and clinical research, which indicates that certain genes that encode for mitochondrial proteins are significantly downregulated in the brains of bipolar patients, suggesting that the symptoms of bipolar disorder may be linked to dysregulation of energy metabolism in the brain.

RGH-188

A novel, orally active, potent dual dopamine D2 and D3 antagonist synthesized at Gedeon Richter, RGH-188 is in early clinical development for the oral treatment of schizophrenia and bipolar mania. The compound is licensed to Forest in the U.S. and Canada.

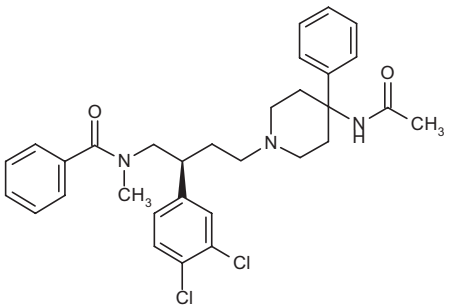
SA-4503



.2HCl

SA-4503 (Msc1) is an acetylcholine release enhancer and sigma receptor agonist in phase II trials at M's Science for the treatment of depression and in phase I/I trials at AGY Therapeutics (AGY-94806) for use in enhancing functional recovery from stroke. SA-4503 functions by inhibiting glutamate-induced delayed neuronal cell death. The product was originally developed at Santen and licensed to M's Science in 2000. In July 2004, AGY Therapeutics signed an agreement with M's Science to acquire exclusive development and commercialization rights for the enhancement of functional recovery after stroke.

Saredutant

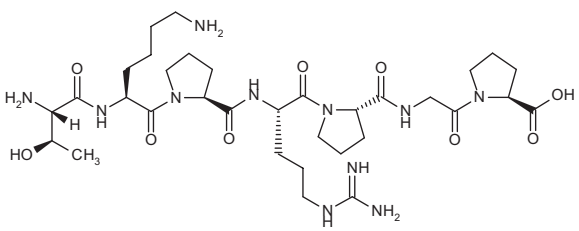


A tachykinin NK_2 receptor antagonist from Sanofi-Aventis, saredutant (SR-48968) is being evaluated in phase III clinical trials for the treatment of depression.

SCA-136

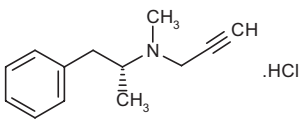
SCA-136, a novel 5-HT_{2C} agonist, is about to enter phase II clinical trials at Wyeth for the treatment of schizophrenia.

Selank



The tuftsin derivative Selank is in phase II clinical trials at the Russian Academy of Medical Sciences as a novel anxiolytic.

Selegiline, *Transdermal*



.HCl

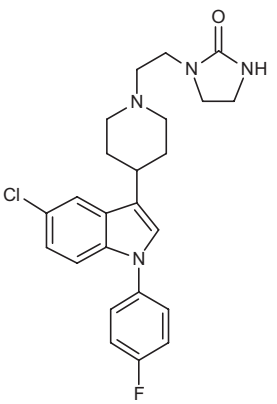
Early this year, the FDA approved Emsam® (transdermal selegiline) as the first skin patch for the treatment of major depression. Selegiline is a MAO-B inhibitor that was formulated with Somerset's transdermal patch system. The drug candidate is also in phase III trials at Somerset for the treatment of Alzheimer's-type dementia and Parkinson's disease. In December 2004, Bristol-Myers Squibb and Somerset, a joint venture between Mylan Laboratories and Watson, signed a commercialization and distribution agreement for the drug. Pursuant

to the agreement, Bristol-Myers Squibb receives exclusive distribution rights to commercialize the product in the U.S. and Canada, with an opportunity to negotiate, within a specified time frame, rights in any or all of the rest of the world. Somerset will supply the product to Bristol-Myers Squibb and receive royalties. Selegiline was initially approved in capsule form for the treatment of Parkinson's disease.

SEP-225289

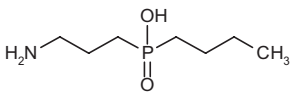
SEP-225289 is an antidepressant in early clinical trials at Sepracor for the treatment of major depressive disorder. In preclinical studies, the drug has been shown to be a potent and balanced triple serotonin, norepinephrine and dopamine reuptake inhibitor (SNDRI), with the potential for providing a broader spectrum of activity than currently marketed antidepressants.

Sertindole



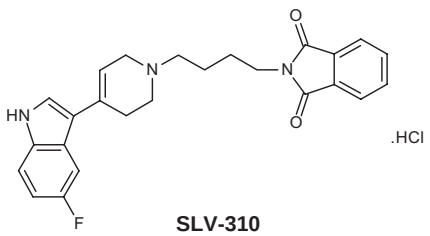
Sertindole (Serdolect®), a dual dopamine D2 and 5-HT_{2A} antagonist discovered by Lundbeck, was first launched in the U.K. in 1996 for the treatment of schizophrenia. In late 1998, following the observation of serious cardiac problems in patients treated with the drug, marketing authorization for the product was suspended in The Netherlands and soon thereafter several other European countries followed suit. In November 1998, Lundbeck decided to voluntarily withdraw Serdolect® in all countries where it was marketed in order to permit analysis of data by health authorities. Shionogi, the licensee in Japan, also discontinued its own development efforts with the compound. Abbott had been developing sertindole in phase III trials in the U.S. Following the temporary suspension of the marketing authorization in 1998, Lundbeck included an additional 5,000 patients in a study confirming that the product could be prescribed safely. In April 2005, the European Committee for Medicinal Products for Human Use (CHMP) recommended that the marketing restrictions be lifted, allowing the product to be launched. In January, it was approved in the E.U. for the treatment of schizophrenia and launched in Estonia. Sertindole is an effective antipsychotic drug for the treatment of schizophrenia, without sedative effects and with extrapyramidal symptoms similar to placebo. In addition to its inhibitory effect on central dopamine D2 and 5-HT_2 receptors, the compound also acts on α-adrenoceptors. Through testing in more than 17,000 patients. sertindole's clinical and pharmacological profile indicates that the drug may increase the likelihood of patients remaining on therapy, thereby improving their daily functioning, increasing their quality of life and reducing the relapse rate.

SGS-742



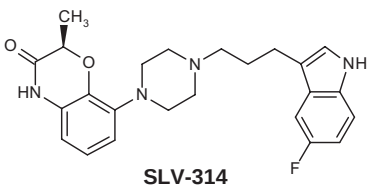
SGS-742 is a selective, orally active $GABA_B$ antagonist in phase II clinical development by Saegis for the treatment of mild to moderate Alzheimer's dementia, as well as mild cognitive impairment (MCI) and age-related cognitive decline (ARCD), and for the treatment of attention deficit hyperactivity disorder in adults. SGS-742, discovered by Novartis and licensed to Saegis in 2001, is a phosphoamino acid derivative that is highly water-soluble and readily crosses the blood-brain barrier.

SLV-310/SLV-313/SLV-314



SLV-310

SLV-313

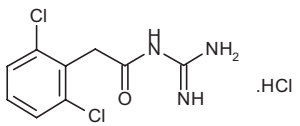


SLV-314

Solvay and Wyeth are co-developing several putative antipsychotic agents. SLV-310 combines potent dopamine D2 receptor antagonism and 5-HT reuptake inhibition and is presently undergoing phase II clinical tri-

als for the treatment of schizophrenia and bipolar disorder. Another agent with a similar mechanism of action is SLV-314, which is in early clinical evaluation for its utility in schizophrenia and bipolar disorder. SLV-313 is a dual-acting dopamine D2 receptor antagonist and 5-HT_{1A} receptor agonist in phase II clinical evaluation for schizophrenia.

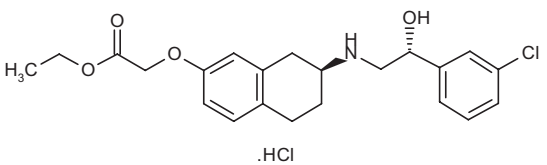
SPD-465/SPD-503



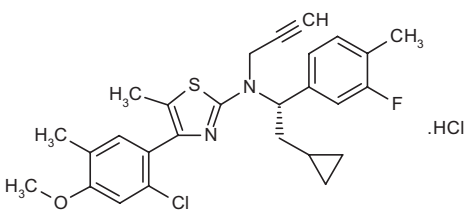
SPD-503

Shire Pharmaceuticals has two compounds in late-stage clinical testing for use in ADHD: SPD-465 and SPD-503. SPD-503 is an extended-release formulation of the α_2-adrenoceptor agonist guanfacine hydrochloride, launched over 30 years ago by Novartis for the treatment of hypertension.

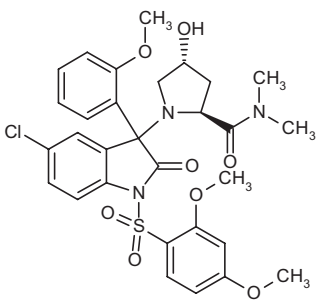
SR-58611/SSR-125543/ SSR-149415



SR-58611



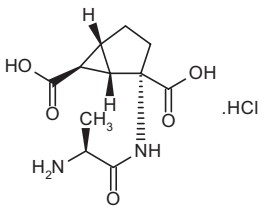
SSR-125543



SSR-149415

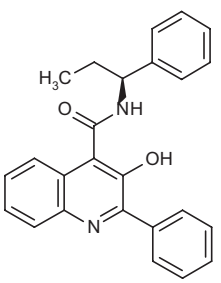
Sanofi-Aventis has three compounds with different mechanisms of action in clinical trials for use in depression and anxiety. The most advanced compound is SR-58611, a β_3-adrenoceptor agonist, which is currently undergoing phase III clinical trials. In phase I clinical evaluation are SSR-125543, a CRF_1 antagonist, and SSR-149415, a selective, orally active, nonpeptide vasopressin V_{1b} receptor antagonist.

Talaglumetad Hydrochloride



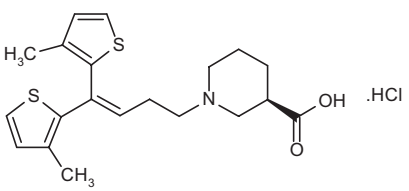
Talaglumetad hydrochloride (LY-544344), a prodrug of the type II metabotropic glutamate receptor agonist eglumetad (see above), is currently undergoing phase I trials at Lilly for the treatment of anxiety.

Talnetant



The tachykinin NK_3 receptor antagonist talnetant is in phase II clinical development at GlaxoSmithKline for the treatment of schizophrenia.

Tiagabine Hydrochloride, *New Indication*



Tiagabine hydrochloride, a GABA reuptake inhibitor that acts by binding to the GAT-1 transporter, was initially launched in 1996 by Novo Nordisk as adjunctive therapy for the treatment of epilepsy. The compound was sub-

sequently licensed to Cephalon for worldwide marketing and sales, except in Canada, Latin America and Japan, where Novo Nordisk retains these rights. At present, Cephalon is conducting phase III trials evaluating its potential for the treatment of generalized anxiety disorder (GAD).

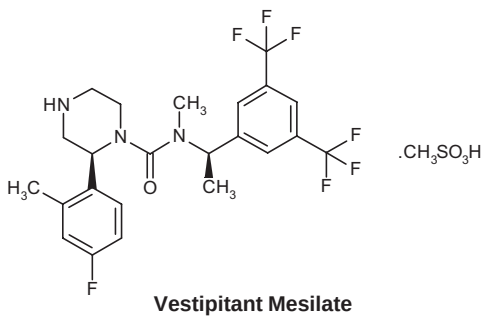
TS-041 (JNJ-19567470)

Phase I clinical trials are under way overseas for TS-041 (JNJ-19567470), a CRF_1 receptor antagonist synthesized at Taisho and licensed to Janssen. The compound has potential for the treatment of anxiety and depression.

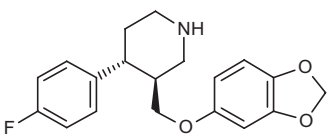
Vagus Nerve Stimulation Therapy, *New Indication*

The Vagus Nerve Stimulation (VNS) therapy system, an implantable VNS device, was initially launched in the late 1990s by Cyberonics for the treatment of epilepsy. Since then, the system has been marketed as therapy for treatment-resistant or -intolerant depression. Cyberonics is currently conducting phase II clinical trials for the treatment of Alzheimer's-type dementia and chronic headache/migraine, as well as phase III trials for anxiety, bipolar disorder and obsessive-compulsive disorder. The device uses the NeuroCybernetic Prosthesis (NCP) that transmits electrical pulses from a generator which is implanted under the collar bone, like a pacemaker, connected by a wire to the vagus nerve in the neck, and delivers preprogrammed, intermittent, mild electrical pulses to the vagus nerve.

Vestipitant Mesilate/Paroxetine



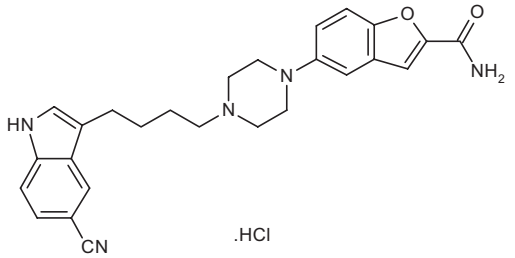
Vestipitant Mesilate



Paroxetine

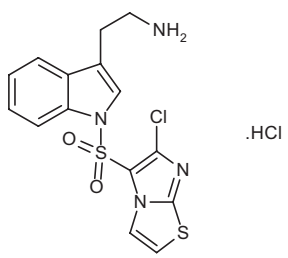
GlaxoSmithKline is investigating the combination of vestipitant mesilate, a tachykinin NK_1 receptor antagonist, and the SSRI paroxetine in patients with depression and anxiety. Phase II trials are under way. Vestipitant alone is also in phase II evaluation for postoperative nausea & vomiting.

Vilazodone Hydrochloride



A dual SSRI and 5-HT_{1A} partial agonist, vilazodone hydrochloride is currently undergoing phase III clinical trials for the treatment of depression. Originally developed by Merck KGaA, the compound was licensed on an exclusive worldwide basis to Genaissance in 2004 for development and commercialization.

WAY-181187



WAY-181187 is a 5-HT_6 agonist in early clinical trials at Wyeth for the treatment of acute anxiety and generalized anxiety disorder (GAD). WAY-181187 is the first potent, selective and high-affinity 5-HT_6 receptor agonist reported.

YKP-581

YKP-581 is currently in phase I trials at Johnson & Johnson and SK Bio-Pharmaceuticals for the treatment of depression. The drug was originally developed at SK Bio-Pharmaceuticals, but has since become part of a collaboration agreement between the two companies to identify and characterize CNS-active drugs with potential therapeutic application in psychiatric disorders.

YKP-1358

YKP-1358 is a novel compound discovered and developed by SK Bio-Pharmaceuticals that has demonstrated potent activity in animals that relates to both positive and negative symptoms of schizophrenia. Its pharmacological profile suggests a very low potential for extrapyramidal side effects. YKP-1358 is in phase I clinical trials for the treatment of schizophrenia.

YKP-3089

YKP-3089 is an orally active nonbenzodiazepine small molecule poised to enter phase I clinical development at SK Bio-Pharmaceuticals. In September 2005, the FDA approved the company's IND to commence clinical evaluation of the drug candidate for the treatment of anxiety. The mechanism of action is unknown at present.