

## Merck's new sleep drug has soporific effect on markets



[Joanne Fagg](#)

Merck & Co might have been hoping that reporting two sets of positive pivotal data for its new sleep drug suvorexant and dangling the promise of a US filing later on this year would wake up the markets. Instead the news was greeted with barely suppressed yawns. The drug maker's shares hardly moved and observers pointed nervously to the novel orexin antagonist mechanism the drug uses.

But getting investors to get the bunting out about any developmental insomnia drug is always going to be a hard task. Not only does a drug have to get past the high bar set by the regulators there is the herculean task of achieving decent sales once a drug is approved, thanks to the number of generic products in the market. This has meant that there are very few new truly novel sleep treatments currently in development (see tables below).

### **Lack of innovation**

Merck's suvorexant is only one of two new drugs in phase III trials for insomnia and is also the only one of two orexin antagonists in the lab. But the class has not exactly had an illustrious history. In January last year GlaxoSmithKline and Actelion halted their phase III trial of almorexant because of undisclosed safety issues ([Actelion and GSK say rest in peace to almorexant, January 28, 2011](#)).

## Insomnia pipeline

Status	Product	Generic Name	Company	Pharmacological Class	Proprietary Level 2
Phase III	MK-4305	suvorexant	Merck & Co	Orexin receptor antagonist	NME
	Tasimelteon	tasimelteon	Bristol-Myers Squibb/Vanda Pharmaceuticals	Melatonin MT1/MT2 agonist	NME
					NME
Phase II	GSK649868	-	GlaxoSmithKline/Human Genome Sciences	Orexin receptor antagonist	NME
	MK-6096	-	Merck & Co	CNS agent	NME
	MK-3697	-	Merck & Co	CNS agent	NME
	EVT 201	-	Roche	GABA A agonist	NME
	Pruvanserin (EMD 281014)	pruvanserin	Newron Pharmaceuticals/Merck KGaA	5-HT2A (serotonin) antagonist	NME
	Neu-P11	-	Neurim Pharmaceuticals	5-HT1A & 5-HT1D (serotonin) receptor antagonist	NME
	MKC-242	osemozotan	Mitsubishi Tanabe Pharma/MedicNova	5-HT1A (serotonin) agonist	NME
	Temazepam ODT	temazepam	Aptalis Pharma	Benzodiazepine	NDA
	Zaleplon - GR	zaleplon	Intec Pharma	Nonbenzodiazepine	NDA + Proprietary Drug Delivery
	SKP-1041	zaleplon	Somnus Therapeutics/SkyePharma	Non-benzodiazepine hypnotic	NDA
TGAR01H	triazolam	Fabre-Kramer Pharmaceuticals	Benzodiazepine	NDA	

But if Merck can make it work, and that is a big if, it could revolutionise the sleep sector. Originally discovered through studies of dogs with narcolepsy, the neuropeptide orexin is responsible for wakefulness. As such, blocking orexin should help insomniacs to sleep.

This novel approach compares with the older and more prevalent approach to insomnia including benzodiazepines and GABA antagonists like the best selling Ambien, which depress the whole of the central nervous system. These drugs have also shown undesirable side effects including dependency issues and negative withdrawal effects including next day drowsiness.

However, as Merck only released scant details of the trials, waiting for medical conferences later in the year to fully outline the data, it is hard to know how the drug stacks up against older treatments, both in terms of safety and side effect profile.

### New and different or old and different

As for the rest of the novel drugs in the insomnia pipeline, companies appear to have differentiated themselves into those working in niche areas such as Vanda Pharmaceuticals, or those trying to use novel delivery mechanisms for old drugs, such as Intec Pharma and Zaleplon.

Out of the two approaches it is hard to know which will be more successful, but Vanda is almost certain to have its market to itself for a while. The company is currently conducting phase III trials in non-24 hour sleep wake disorder for its drug tasimelteon.

The drug, a circadian regulator, aims to reset the body clock, aligning it to a constant 24 hour day; it has been developed especially for totally blind individuals who cannot use the difference between night and day to regulate their body clock.

In January, Vanda reported positive results from a small patient study and aims to unveil the results of two larger phase III trials by the end of the year.

### Overcoming the old guard

If any of these new drugs outside of niche uses are to be successful they will have to overcome the patient and doctor loyalty attached to the current branded drugs left in the market. Despite losing patent protection in April 2007, Ambien is still clocking up significant sales and is forecast to pull in more than half a billion dollars in 2016. Similarly, Lunesta still managed to report sales of \$561m in 2011.

With these kinds of stats it is not surprising that new entrants to the market have found that it hard to get patients to switch not only from the branded drugs they know and that work for them, but also from the multitude of cheap generic sleep aids available.

Since its approval in March 2010 Silenor has struggled in the market, in the third quarter of 2011 the drug reported sales of just \$4m, down from the \$6m seen in the second quarter ([Somaxon wins approval for Silenor and hunt for partner begins, March 19,2010](#)).

Biggest branded insomnia drugs						
						Annual Sales WW - Sales (\$m)
Status	Product	Generic Name	Company	Pharmacological Class	Proprietary Level 2	2011 Sales
Marketed	Ambien	zolpidem tartrate	Sanofi	Imidazopyridine	NME	675
	Myslee	zolpidem tartrate	Astellas Pharma	Imidazopyridine	NME (ex. USA Only)	443
	Silenor	doxepin hydrochloride	Somaxon Pharmaceuticals	Histamine H1 receptor antagonist	NDA	18
	Lunesta	eszopiclone	Dainippon Sumitomo Pharma	GABA agonist	NME	561
	Meilax	ethyl loflazepate	Meiji Holdings	Anxiolytic	NDA (ex. USA Only)	46
	Rhythmy	rilmazafone	Shionogi	Sedative	NME (ex. USA Only)	25
	Circadin	melatonin	Lundbeck	Hormone	NME (ex. USA Only)	8
Approved	Intermezzo	zolpidem tartrate	Purdue Pharma/Trancept Pharmaceuticals	Imidazopyridine	NDA + Proprietary Drug Delivery	-
					<b>Total available brandedmarket sales**</b>	<b>2,228</b>

\*Forecasts for in-market sales booked by Purdue not available, figure represents royalty forecasts Trancept Pharmaceuticals

\*\*The insomnia market includes many small branded products for which sales figures are not available

Tellingly, Somaxon in December called in advisors to review its 'strategic options'. As such the omens are not

looking good for other newly approved sleep drug, Transcept Pharmaceuticals' Intermezzo.

The product, which has differentiated itself by going for a middle of the night indication, does have the advantage of having a partner, but there were doubts whether Purdue Pharma was going to exercise its rights to market the drug in the US ([\*Intermezzo approval not the end of Transcept thriller\*](#), November 24, 2011).

The group has now committed and pledged to launch Intermezzo in the second quarter of 2012 and to invest approximately \$100 million to support sales and marketing during the first year of commercialization. Transcept will be hoping that this sum will be enough to help Intermezzo, which took three attempts to get approval, crack the market.

But hope may not be lost for the new products both on the market and those in development - analysts at Bernstein believe that some sleep patients are willing to try new and potentially more expensive new medicines as they search for a perfect cure to their symptoms.

This implies that there may after all be a market out there for surovexant, if it gets approval, as well as Transcept's Intermezzo. Creating that market will be hard work.

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[44-\(0\)20-7377-0800](#)

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