

## Jazz overture rekindles hopes for orexin agonism



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After Takeda stopped trials of TAK-994 last year the future for treating narcolepsy with orexin-2 agonists looked bleak. But hopes were rekindled yesterday when Jazz endorsed the approach with a \$50m up-front payment to Sumitomo Pharma to license the latter's DSP-0187. The companies describe DSP-0187, which recently entered phase 1 in Japan, as a highly selective oral agent, and perhaps the hope is that selectivity will circumvent the [toxicity signal that appeared to trip up TAK-994 in phase 2](#). While antagonising orexin receptors to develop sedative drugs is the subject of much clinical work the pipeline for agonists, which cause the opposite effect, is barren. The most advanced asset is NLS Pharmaceuticals' Quilience, an extended-release formulation of mazindol, a drug that had been sold for decades for weight loss under the brand name Sanorex, but which is no longer marketed. Despite Takeda's termination of TAK-994 studies the Japanese group has two other orexin-2 receptor agonists in clinical trials. And perhaps the most heavily invested company is the Centessa subsidiary Orexia, set up specifically to develop oral and intranasal orexin receptor agonists, which [last October struck a discovery deal with Schrödinger](#).

### Orexin agonists in development

Project	Company	Mechanism	Status
Quilience (mazindol)	NLS Pharmaceuticals	Pan-monoamine reuptake inhibitor & orexin 2 receptor agonist	<a href="#">Ph2</a>
TAK-994	Takeda	Orexin 2 receptor agonist	<a href="#">Ph2 terminated</a>
TAK-925	Takeda	Orexin 2 receptor agonist	<a href="#">Ph1 completed</a>
TAK-861	Takeda	Orexin 2 receptor agonist	<a href="#">Ph1</a>
DSP-0187/ JZP441	Jazz/ Sumitomo	Orexin 2 receptor agonist	<a href="#">Ph1</a>
Centessa-Schrödinger Research Project	Orexia (Centessa)/ Schrödinger	Orexin 2 receptor agonist	Preclinical

Source: Evaluate Pharma, [clinicaltrials.gov](#) & [Japan Registry of Clinical Trials](#).

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