

## Centrexion still has work to do after pain Triumph



[Madeleine Armstrong](#)

Centrexion Therapeutics is celebrating phase IIb success with its chronic pain candidate CNTX-4975, but there are reasons to be cautious about the project's future. One red flag is the fate of an earlier fellow capsaicin-based pain asset, Neurogesx's Qutenza.

That earlier patch got the go-ahead for neuropathic pain due to postherpetic neuralgia in 2009 but has made little impact commercially; it is forecast to sell just \$73m in 2022, according to *EvaluatePharma* consensus forecasts. Centrexion will need CNTX-4975, its lead asset, to do better.

It will hope that CNTX-4975's novel injectable formulation will help: Centrexion says its project is the first and only patented capsaicin designed to be administered via injection into the site of pain, which means that it manages pain without disrupting other nerve functions.

Here it could have the edge over Qutenza, a patch containing synthetic capsaicin, and other gel and cream formulations. Presumably these struggle to achieve a high concentration of the active ingredient at the site of pain.

Of course, first Centrexion needs to prove CNTX-4975's efficacy in phase III - not an easy task in pain, where a high placebo response has scuppered other contenders.

Qutenza has struggled to prove itself outside postherpetic neuralgia, producing mixed results in HIV-related neuropathy amid reports of cases of pain from the patch itself. Astellas licensed the product in Europe in 2009, but earlier this month offloaded rights to Grünenthal.

### Triumph

Centrexion has focused on different indications, choosing to test CNTX-4975 in knee osteoarthritis and Morton's neuroma, a rare nerve disorder in the foot, where it is also in phase II.

The dose-ranging phase IIb Triumph trial in knee osteoarthritis pain met its primary endpoint, a reduction in the pain with walking WOMAC score at week 12. This was numerically better than placebo at both doses tested, 0.5mg and 1.0mg, Centrexion said, with the 1.0mg dose meeting statistical significance, although it did not give specific figures.

The group added that the trial had shown the largest clinically relevant reductions in knee osteoarthritis pain reported for any drug treatment, marketed or in development. It plans to present the full data at an upcoming medical conference.

Emphasis of the 1.0mg dose suggests that this will be taken forward into phase III development this year.

In the 1.0mg group, 22% of patients achieved a 90% or greater reduction in pain and 67% percent of patients achieved 50% or greater reduction in pain at 12 weeks. Centrexion also noted that 1.0mg of CNTX-4975 was numerically better than placebo on the secondary outcome measures of stiffness, function and patient global impression of change at every time point studied.

### Pain pipeline

Centrexion does not seem to be daunted by the difficulty of developing pain treatments as these make up its entire pipeline. It acquired three of its assets - CNTX-6970, CNTX-6016 and CNTX-0290 - from Boehringer Ingelheim in March for an undisclosed sum.

## Centrexion's pipeline

	Project	Mechanism	Indication
Phase II	CNTX-4975	TRPV1 agonist	Osteoarthritis/Morton's neuroma pain
Phase I	CNTX-2022	Local anaesthetic (topical lidocaine)	Superficial pain
	CNTX-6970	CCR2 antagonist	Inflammatory pain
Preclinical	CNTX-6016	CB2 agonist	Neuropathic pain
	CNTX-0290	SSTR4 agonist	Mixed pain

Notably, Centrexion is homing in on non-opioid medications for pain that, if successful, could do well in the current climate.

But, with most of its compounds at an early stage, it has a long road ahead.

Its chief executive, Jeffrey Kindler, should be well equipped to spot the potholes: he was at the helm of Pfizer during the development of tanezumab, which was put on hold in 2010 after reports of osteonecrosis. The compound only resumed phase III development last year ([Tanezumab's return shows pharma has held its nerve](#), March 24, 2015).

Just because he has been here before, however, will not make proving CNTX-4975's worth in phase III any easier.

Study	Trial ID
Triumph	NCT02558439
Phase II in Morton's neuroma	NCT02678793

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