

Vertex claims success with its fourth shot at acute pain



Jacob Plieth

Vertex has struck it fourth time lucky in sodium channel blockade, today claiming success in phase 2 trials of VX-548 for treating acute pain in bunionectomy and abdominoplasty. The project represents Vertex's fourth attempt to develop a sodium channel Nav1.8 inhibitor, after VX-128, VX-150 and VX-961 failed to achieve the right mix of efficacy and safety. Pain represents [Vertex's aim to go beyond its cystic fibrosis comfort zone](#), though Stifel analysts today cautioned that the area might not fit into the group's high-margin business. Only the high VX-548 dose hit in both studies, which measured SPID48 as primary endpoint. VX-548's effect versus placebo was more pronounced in the [abdominoplasty](#) (p=0.0097) than in the [bunionectomy](#) (p=0.0251) trial, and one caveat in the latter was lack of dose response, with a mid dose doing numerically worse than placebo and than low-dose VX-548. VX-548 was said to be well tolerated, with less discontinuation than placebo. After canning VX-128 in early 2018 Vertex took VX-150 through three successful phase 2 trials, but paused development while it investigated VX-961; ultimately both molecules were dropped. In the second half VX-548 will enter phase 3, where Vertex will hope that its efficacy does not wane.

Selected pain projects targeting sodium channel blockade

Project	Mechanism	Company	Status
BIIB074 (vixotrigine)	Nav1.7 inhibitor	Biogen	Ph3 in neuropathic pain
VX-548	Nav1.8 inhibitor	Vertex	Positive in ph2 abdominoplasty & bunionectomy surgery
ACP-044	Reactive species decomposition accelerant that inhibits TRPA1 & Nav1.8	Acadia (ex Cersci)	Ph2 bunionectomy data 2022
OLP-1002	Nav1.7 antisense	Olipass	Ph2 in chronic pain
FX301 (funapide)	Topical Nav1.7 inhibitor	Pacira (ex Flexion, licensed from Xenon)	Ph1 bunionectomy data 2022
ST-2427	Nav1.7 inhibitor	Siteone	Ph1 started 2021

Source: Evaluate Pharma & [clinicaltrials.gov](#).

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