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Zalicus precarious after loss of Synavive

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Zalicus's decision to shutter its rheumatoid arthritis drug Synavive following poor phase II results caused its share price to fall by 43% and has left the firm reliant on its in-house pain programmes as well as prednisporin, a conjunctivitis drug licensed to Sanofi. The drop in the share price wiped $73m off Zalicus's market cap, which is now hovering at just below $100m.

The result will come as a nasty shock to those who had followed the many bullish analyst notes that had festooned the biotech formerly known as CombinatoRx with buys and outperforms. Some analysts cast Synavive as a future blockbuster following its then-predicted launch in 2016.

With that dream kicked firmly into the long grass, what now for Zalicus? In the second quarter of 2012 the company spent $12m of cash, much of which would have gone on relatively cheap mid-stage development programmes, suggesting that it could last for a year or so on its current cash reserves of $51m. It does have a small revenue stream – royalties from its one marketed product, Exalgo, a painkiller licensed to Covidien – but this came to just $4m in 2011, and is unlikely to see Zalicus through to launch of any of its other pipeline projects.

Most advanced

The 12-week Synergy phase IIb trial enrolled 259 patients with moderate to severe RA, all of whom remained on a stable dose of methotrexate. It compared Synavive – a combination of prednisolone, an anti-inflammatory steroid, and the antithrombotic dipyridamole – with each of its separate components, as well the prednisolone prodrug prednisone, and placebo.

Interestingly, Synavive did meet the trial's primary endpoint, significantly improving signs and symptoms of moderate to severe RA compared with placebo. But it missed what the company termed the key secondary, failing to show a meaningful clinical benefit compared with prednisolone.

In the absence of a clinical benefit Zalicus said that it would focus on its other drugs, including the calcium channel blockers it is developing for pain: Z160 is in phase II trials in neuropathic pain and Z944 is expected to hit phase II in the first half of 2013. The phase IIa of Z160 is enrolling 140 patients with lumbosacral radiculopathy, with topline results expected in the second half of next year. It will enter a phase IIa trial for the treatment of postherpetic neuralgia by the end of this year.

Developing calcium channel blockers for pain is a risky strategy. Few calcium channel blockers are in development, and the only marketed drug of this kind, Astellas's Regnite, is a therapy for restless legs syndrome that was abandoned as an analgesic. Moreover, the high placebo effect seen in CNS indications and the FDA's reluctance to approve pain drugs are further reasons for caution.

Zalicus's conjunctivitis project, prednisporin, meanwhile, is not due to reach market until late 2015, and while Zalicus's partner Sanofi is expected to post sales of $31m the following year, Zalicus itself will get a 12% royalty on non-US sales. It will, however, receive $40m on achievement of certain development and regulatory milestones, although it is hard to say whether these will come soon enough to meet the firm's demand for cash.

It is always damaging when a company loses its most advanced product. But with an NPV of $243m and predicted 2018 sales of $320m, Synavive really was important to Zalicus. With no catalyst until the pain trials report in 2013, chances are the company will keep a low profile for a while; if Z160 and Z944 fail too, Zalicus is in real trouble.

Study	Trial ID
Synergy	NCT01369745

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