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Signs are growing that the hep C ship is sailing

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A day after Vertex surprised Wall Street with disappointing quarterly earnings, hit by softer-than-expected sales of the hepatitis C antiviral Incivek, Novartis handed back rights to hepatitis C candidates being developing by its partner Idenix. Warning signs are flashing for this booming area of drug development, and Novartis seems to have taken notice.

Shareholders need also take note, as Novartis's decision to abandon ship effectively forces the funding of any further development of these now more risky assets on to investors. Only hours after announcing the return of the Swiss pharma giant's options Idenix revealed plans for a substantial $150m share sale.

Declining market?

Last week, Merck seemed nonplussed with second-quarter sales of the other most recently launched hepatitis C antiviral, Victrelis, which posted global sales of $126m. This was up 14% on the previous quarter but was a weaker performance than many were expecting.

On a conference call, Merck said it was already seeing a contraction in new patient starts in the US, the first market it launched in less than a year ago. While Vertex's Incivek saw more healthy second-quarter sales of $328m, this was still about $50m below consensus estimates.

Since the advent of highly sensitive blood screening for hepatitis C in the early 1990s the incidence, or rate of new infections, has dropped dramatically. New patients are now largely confined to high-risk groups like intravenous drug abusers. Estimates of the total number of people infected with the disease have varied widely and in the light of Merck's and Vertex's recent financial results may have to be revised downwards.

Furthermore, as the diminishing pool of easily accessible patients complete treatment, it leaves those who have failed the current best standard of care owing to mutations the virus develops. These relapsed or refractory patients present a much higher bar for the new agents to treat, and are less likely to be enrolled in the first clinical trials of a new antiviral.

Reasons to jump

All of these factors are likely to have contributed to Novartis's decision to walk away from the Idenix partnership. But the clincher might not have been the existing competition, but future rivals.

Only last week, alongside second-quarter earnings Gilead Sciences said it would be accelerating development of a formulation of two novel antivirals, GS-7977 and GS-5885, combined into a single pill (*Gilead pushes forward on short but risky path to hep C validation, July 27, 2012*), Even Merck's and Vertex's highly active direct protease inhibitors have to be administered with intravenous interferons and oral ribavirin.

So while Novartis's decision is understandable in the light of recent events surrounding the prevalence of patients, it makes even more sense when considering the far more advanced, all-oral combinations already in late-stage clinical development.

Big headache

For Idenix, and other companies like Achillion with earlier-stage unpartnered hepatitis C assets, Novartis's withdrawal presents a big headache.

With the future of hepatitis C lying in combinations of therapies, and one big pharma participant showing signs of reticence, these unencumbered compounds could struggle to find air time with the cadre of pharmaceutical business development and licensing managers.

IDX184 is a nucleotide polymerase inhibitor which Idenix is developing in combination with IDX719, an NS5A inhibitor. Although companies including Bristol-Myers Squibb are likely to be on the lookout for assets to test in combination with their own in-house candidates, Novartis's rejection is hardly a vote of confidence.

Paradoxically, it is the prospect of another big pharmaceutical partner like Bristol-Myers licensing IDX184 that will be used to entice investors to foot the $150m bill for the development of Idenix's pipeline. In a similar vein, when Achillion was on its IPO roadshow in 2006 it held out the possibility of its shareholder Gilead licensing the lead product for HIV, elvucitabine. Investors are still waiting.

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