Evaluate Vantage

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Merck’s Idenix write-off another bad sign in hep C

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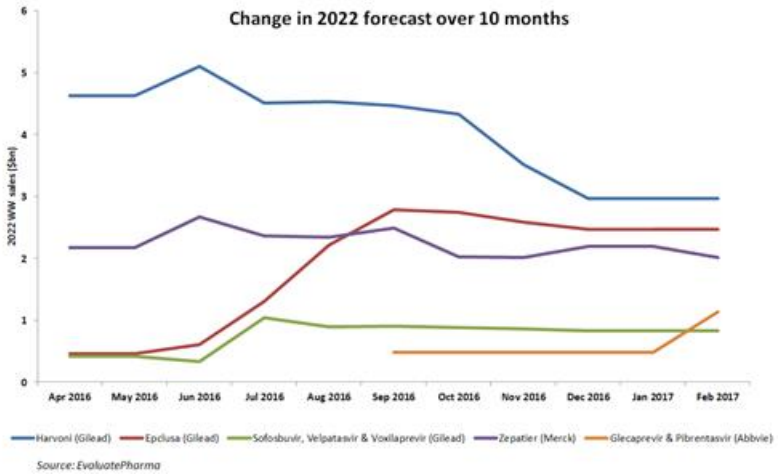
Merck’s $2.9bn impairment charge on uprifosbuvir proves what many have long suspected: that the company overpaid for Idenix, effectively spending $3.9bn on an asset it now estimates is worth just $240m.

The bigger issue is what this means for the broader market, being another blow after Gilead was recently forced to slash its hepatitis C forecasts in the face of dwindling patient numbers. With new products and combinations approaching approval, an increasing number of players look set to be fighting for a piece of an ever-smaller hep C pie (see tables below).

Nevertheless, some believe that the news of Merck’s write-down is positive for others in the space. Leerink analysts estimate that Gilead and Abbvie would gain $400m in annual sales between them from Merck’s loss of market share – but this assumes that other market dynamics stay the same.

And this seems far from certain: forecasts for Gilead’s juggernaut Harvoni have fallen dramatically over the past year. Its newest doublet, Epclusa, should make up some of the shortfall, but the group’s February guidance suggests that things could be even worse than expected for its overall hep C franchise (*Buying growth is a tricky choice for Gilead, February 8, 2017*).



Until now, issues in the market do not seem to have had much of an impact on hep C R&D, with *EvaluatePharma* listing 17 projects that are filed or in phase III. But, with many of the more easily treatable patients already having been cured, the focus is shifting to hep C strains other than genotype 1, as well as shorter treatment cycles, which could make it harder for new therapies to find a market.

Some unapproved assets are still forecast to become big sellers: Abbvie’s glecaprevir/pibrentasvir – previously known as ABT-493/ABT-530 – and Gilead’s triplet of sofosbuvir, velpatasvir and voxilaprevir are set to be among the top-five bestsellers in 2022, according to consensus forecasts.

Hepatitis C combos in development			
Project	**Company**	**Status**	**2022e sales ($m)**
Glecaprevir/pibrentasvir	Abbvie	Filed	1,137
Sofosbuvir/velpatasvir/ voxilaprevir	Gilead	Filed	829
Grazoprevir/elbasvir/ uprifosbuvir	Merck & Co	Phase II	100
AL-335/odalasvir/simeprevir	Johnson & Johnson/Achillion	Phase II	19
Ruzasvir/uprifosbuvir	Merck & Co	Phase II	-
Grazoprevir/ruzasvir/ uprifosbuvir	Merck & Co	Phase II	-
Source: EvaluatePharma			

Combinations are also the way forward for uprifosbuvir, also known as MK-3682. Merck is testing the project as part of various combinations, including a doublet with ruzasvir, as well as two triplets: alongside Zepatier – elbasvir and grazoprevir – in one, and grazoprevir and ruzasvir in the other.

The group has already reported results from three phase II trials of grazoprevir/ruzasvir/uprifosbuvir, but according to the Leerink analysts it has now been told by regulators that it will need to show an added benefit with the triplet over the uprifosbuvir/ruzasvir doublet.

This suggests that Merck will have to wait for data with the doublet, expected later this year, before starting phase III studies with the triple, and the analysts believe that the delay is the main reason for the impairment charge. Merck's stated reason is changes to the product profile, and changes to its expectations for pricing and the market opportunity.

The other assets that Merck gained through the Idenix acquisition will not pick up the slack either: the group appears to have already discontinued development of a second nucleotide polymerase inhibitor, IDX21459, and samatasvir, an NS5a inhibitor.

The proceeds from a lawsuit against Gilead, if the decision is upheld in an appeals court, could mean that the takeover of Idenix is not a dead loss. But, as far as products go, the deal is even more disappointing than previously thought.

Study detail	**Trial ID**	**Primary completion**
Phase II trial of grazoprevir + uprifosbuvir with elbasvir or ruzasvir in genotypes 3-6	NCT02332720	Feb 2017
Phase II trial of uprifosbuvir + ruzasvir in genotypes 1-6	NCT02759315	Jul 2017
Phase II trial of uprifosbuvir + ruzasvir in genotypes 1-6	NCT02956629	Dec 2017
Phase II trial of uprifosbuvir + grazoprevir + ruzasvir in genotype 1 or 3 patients who have failed a direct-acting antiviral regimen	NCT02613403	Apr 2018

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