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Spotlight on Achillion as post-Sovaldi world takes shape

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The lesson of Merck & Co's takeout of Idenix Pharmaceuticals is that nobody is out of the hepatitis C race just yet. This has been brought home in the case of another company once thought to be an also-ran, Achillion Pharmaceuticals, which saw its shares jump 83% yesterday on news that the FDA had lifted a clinical hold on its lead project, sovaprevir.

While Gilead's Sovaldi has been mopping up billions of dollars of sales just a few months into launch, hepatologists have been pointing to the possibility of achieving Sovaldi-like outcomes with shorter treatment durations. Thus, interest remains strong in newer molecules, keeping the acquisition thesis alive for smaller developers like Achillion.

New optimism

The news Monday that Merck was willing to gamble $3.9bn on Achillion's peer Idenix had already provided a boost, but the clinical hold lift ignited a fire under shares in the Connecticut-based company. The stock has more than doubled in two days, and stood at $7.79 at yesterday's close. In context, this is still well down on the group's record high of $19.61 in February 2007, however, a mark that has never been matched since one of its early hep C protease inhibitors showed a kidney safety signal.

Similarly, sovaprevir was stalled in phase II because of liver safety, but these concerns appear to have been addressed with the lifting of the FDA hold (*Pessimism infects Achillion as FDA sustains clinical hold, September 30, 2013).* What is surprising about the reaction to the news is how much focus has now turned to earlier-stage projects like ACH-3102 and ACH-3422 as potential candidates for combination therapies that could shorten the duration of treatment.

Such an approach represents an evolution in hep C care as 90% cure rates are now the benchmark for 12-week treatments like Sovaldi and Johnson & Johnson/Medivir's Olysio – both of which are administered on a backbone of ribavirin and/or interferon. The next immediate milestone in treatment is eliminating ribavirin and interferon – Gilead's once-daily pill that combines Sovaldi with ledipasvir, if approved in October, would achieve this.

What the Gilead combination has been unable to do in the clinic is shorten the treatment duration to less than 12 weeks for the most part, although an eight-week regimen has cured more than 90% of patients with genotype 1 who have never been treated before.

Moreover, a six-week regimen of the Gilead combo pill did not achieve satisfactory cure rates. Hepatologists, however, are hoping for a four-week regimen as this would require them to write only a single prescription to achieve a cure (*EASL – Pace of hep C innovation tests pricing choices, April 11, 2014*).

The shape of pills to come

The search for a shorter regimen was the justification that Merck used in its Idenix transaction this week (*Biotech bull market charges with Merck's Idenix takeout, June 9, 2014*).

Achillion's ACH-3102 is an NS5A inhibitor like ledipasvir, Bristol-Myers Squibb's daclatasvir, AbbVie's ABT-267 and Idenix's samatasvir; ACH-2684 is a protease inhbitor like Olysio, AbbVie's ABT-450 and Merck's MK-5172.

Along with news on the clinical hold, Achillion said it had begun dosing on a phase II trial of ACH-3422, a nucleotide NS5B inhibitor like Sovaldi and Idenix's IDX21437.

Nucleotide inhibitors are among the scarcer hep C assets, and are thus more valuable. This might be among the factors driving Achillion's latest surge, on top of the company's position as one of the last hep C plays left standing, not to mention the fact that it has candidates in all three of the major hep C drug classes.

Combining three different targets in a single regimen should help prevent the virus from using the usual mechanisms to develop resistance, which in theory should enable shorter regimens.

This remains to be proven, however, and a high bar has been set for the next generation of hep C drugs. The takeout scenario now driving Achillion's market valuation relies on a company willing to bet that in its four clinical stage compounds is a product that can close in on the four-week cure.

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