Evaluate Vantage

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Data in 14 has Regulus joining ranks of hep C high flyers

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The doubling of Regulus Therapeutics' market capitalisation yesterday on phase I data for its hepatitis C project looks overdone in the context of the swift evolution of the space.

The fact that the 14 infected patients, after a single injection, saw a viral load reduction that exceeded company expectations is a positive signal, as is six of them having undetectable hep C levels a month later. How RG-101 fits into a market that is likely to have five or more well-established therapies by the time it might premiere is a key question, but a pan-genotypic benefit along with once-monthly administration probably has some bulls viewing it as the next Sovaldi.

The results are part of a four-arm study of RG-101 that tests safety and activity of the anti-microRNA candidate in healthy candidates and proof of concept in infected patients. The efficacy portion comprised 14 patients injecting the agent and two who took a placebo.

After 29 days, patients taking RG-101 saw the number of copies of hep C viral RNA drop to a mean of 0.01% of their baseline levels, a sign of significant and sustained response to the single injection. Of the six who had undetectable RNA at 29 days, three have reached a 57-day follow-up and have not seen their viral loads rise. Regulus said the study protocols had now been amended to allow follow-up through six months.

Another arm of the study dosed healthy patients with both RG-101 and Johnson & Johnson and Medivir's protease inhibitor Olysio, and found no drug-drug interactions, paving the way for further tests in combination with established products. Regulus said it planned to start a phase II trial with a direct-acting antiviral in the second quarter of 2015, although it did not specify Olysio.

Shares more than doubled Wednesday to $13.75 and climbed a further 10% in early trade today, valuing the company at $662m.

Shrinking warehouse?

As with approved oral agents Olysio and Gilead Sciences' Sovaldi and Harvoni, RG-101 seeks to eliminate the virus by inhibiting replication. The difference is inhibition of microRNA as opposed to the polymerase with Sovaldi or protease with Olysio.

Much of the discussion in hepatitis C medicine has centred on the "warehousing" of patients – that is, patients waiting to seek treatment until interferon-free regimens were available because of the hope for better cure rates and elimination of interferon's flu-like side effects.

With Sovaldi having been on the market since late 2013 and Harvoni now launched, many of these patients have now sought treatment – Gilead's hep C franchise is forecast to sell more than $12bn this year. It is not clear how many patients will be left after the current surge; non-genotype 1 patients will be less well served, as well as patients who do not live in wealthy industrialised nations.

A 2018 launch is reckoned for the Regulus agent, and the space will be much more competitive by then with therapies from AbbVie, Merck & Co and Bristol-Myers Squibb entering in coming months as well as follow-on agents. On the one hand, if RG-101 proves to be a pan-genotypic cure after a single injection, it could represent a significant advance; on the other hand, if the markets in the US, Europe and Japan have been saturated, microRNA will probably not be the lower-cost option that will suit the less-well-off health systems of developing nations.

Of course, the rush to buy shares yesterday could be driven as much by speculation of a takeout as it was by RG-101's commercial outlook; after all, when Gilead paid $11bn for Pharmasset to obtain the active ingredient at the heart of Sovaldi and Harvoni this had been tested in scarcely more patients than Regulus's. In the hep C game every developer is seen as a ripe target.

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