Hepatitis C (HCV) is big in the news this week with the continued success of Vertex's telaprevir and the clinical suspension for two of Idenix Pharmaceuticals' early stage candidates. But on the front page has to be Bristol-Myers Squibb's tactical $735m purchase of ZymoGenetics, mainly for the Seattle company's pegylated interferon lambda for HCV that BMS had already licensed (Bristol-Myers, Zymo deal shows interest in hep C remains high, January 13, 2009).

BMS' play for full ownership of the "gentler and kinder" interferon strategy, as one analyst describes it, firms up its place in the growing HCV space. However, as a variant of the dominant first-line treatment protocol, PEG-IFN-lambda will need to show either fewer side effects or superior efficacy, or both, to find a place in an increasingly competitive space.

Another interferon?

The HCV candidates getting the most attention have been the above-mentioned telaprevir and its fellow protease inhibitor, boceprevir, owned by Merck & Co, both of which are queueing up for FDA registration in the near future. It is unclear, however, how such issues as cost and insurance coverage will influence commercial uptake of the new class of protease inhibitors, given that they would presumably come onto the market at a premium compared to the current standard of care, PEG-IFN-alpha in combination with ribavirin.

As such, the gamble is that Zymo's PEG-IFN-lambda will show fewer side effects, such as flu-like symptoms and hematopoietic effects, making it a more tolerable treatment protocol than its alpha counterpart, and find a place in the market. The results of phase I trials found antiviral activity with some side effects, although given the sample size in those trials it is not clear how those findings will be reflected in larger populations.

It is not a gamble that has inspired much confidence from analysts. According to consensus estimates at EvaluatePharma, PEG-IFN-lamda is forecast to sell just $19m in 2016, although with a 2014 launch that may not be too surprising. Phase II trials just completed enrolment. A more bullish estimate not included in the consensus comes from Canaccord Genuity, which in an initiation note August 10 suggests sales of $91.6m in 2015 – along with a 12-month price target of $7 a share.

Still, in the scheme of HCV, the estimates for PEG-IFN-lambda look like small potatoes: Roche's Pegasys is still forecast to be pulling down $1.59bn in 2016, in the shadow of telaprevir's mega-blockbuster $4.39bn.

Bonus for investors

BMS' offer of $9.75 a share amounts to $885m, or $735m net of ZymoGenetics' current cash, an 84% premium on Tuesday's closing price of $5.30. The total price is in the ballpark of the total $932m in milestones remaining as part of BMS' January 2009 deal for worldwide rights to PEG-IFN-lambda.

This deal was the ninth-biggest deal of 2009 ranked by upfront fees, which amounted to $105m for ZymoGenetics (AstraZeneca tops the product deal charts in 2009, February 16, 2010).

In announcing the offer, BMS says it has already agreed transactions with shareholders representing 37% of ZymoGenetics' common shares, and in addition, Novo Nordisk, which spun out ZymoGenetics in 2000, has agreed to sell its 26% stake in the company.

With the purchase of the Seattle biotech BMS also secured rights to surgical bleeding product Recothrom and melanoma candidate IL-21. Only Recothrom and the HCV candidate have estimated sales in 2016.

Whilst Recothrom is already on the market and was close to making ZymoGenetics a profit-making company, investor confidence in the firm appears to have been sagging since December. In those nine months, shares were off by more than a quarter, following the news that the European Medicines Agency had rejected Recothrom and that Bayer had handed back virtually all its worldwide marketing rights.

This setback was the cap on a challenging 15-month period that saw the company lay off one-third of its workers and out-license eight non-core early-stage candidates, whilst Recothrom itself fizzled on the launchpad (ZymoGenetics' Recothrom...
In its offer of marriage rather than cohabitation, the hope must be that BMS will get more for its dollar than the previous licensing deal was promising. Should PEG-IFN-lambda beat analysts’ expectations, it will turn out to be a smart purchase. However, with the protease inhibitors forecast to become such huge products in the HCV market, the role that interferons will play in the future remains unclear.