Evaluate Vantage

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EP Vantage Interview – BioCryst beefs up hep C holdings with Presidio merger

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While Gilead Sciences leaps ahead in clinical development of an all-oral, interferon-free hepatitis C cure, companies still are making strategic moves to ensure they can find a niche in this increasingly competitive space. The tie-up of BioCryst Pharmaceuticals with privately held Presidio Pharmaceuticals earlier this month was a move to position the merged company as a contender by advancing a combination that works with all genotypes.

The all-stock transaction brings to BioCryst two clinical-stage hep C candidates that will attack via mechanisms different from the North Carolina company's own preclinical compound. The hope is that it can address unmet medical needs outside genotype 1 – the main target of currently marketed direct-acting antivirals, as well as the most advanced R&D candidates. "I think we're absolutely a competitor in this space," Jon Stonehouse, BioCryst's chief executive says. "I'm not sure there are many or any companies that have three direct-acting antivirals that are pan-genotypic that can create an all-oral combination."

"To think that somebody's a winner, while they're in Phase III, and will be able to suck up the whole market, is a big leap."

Outside genotype 1 and western markets

The protease inhibitors Incivek and Victrelis have got off to a fast start and revolutionised the field by improving the effectiveness of mainstay treatments interferon and ribavirin in genotype 1 patients. However, the goal of hep C specialists is to eliminate interferon altogether – the flu-like symptoms and other side effects are a huge barrier to treatment.

Gilead is following closely on the heels of the Vertex and Merck & Co drugs by launching a phase III trial of its single-pill formulation of the compounds GS-7977 and GS-5885. Dosing began two weeks ago – importantly to patients, without an interferon or ribavirin backbone, and importantly to BioCryst, in patients infected with genotype 1 – the most common form of the virus in North America.

Gilead has embarked on late-stage trials of its $11bn GS-7977, also known as sofosbuvir, in genotype 2, 3, 4 and 6 patients – most of those trials are in combination with ribavirin, and the only one that includes 4, 5 and 6 patients is with an interferon-ribavirin regimen. Likewise, Bristol-Myers Squibb is planning a phase III study in genotype 2 and 3 patients on an interferon-ribavirin background.

Although interferon is cited most often as the negative in current therapies, ribavirin carries with it negative side effects, including boxed warnings for birth defects and haemolytic anaemia that can worsen cardiac disease and lead to heart attacks. Thus, current late-stage trials do not so far suggest a more benign therapy is coming anytime soon for the non-genotype 1 patient.

It is thought that many hepatitis C patients are waiting for the interferon-free regimens before seeking a cure, and this patient "warehousing" will mean a major payday for the first to market with such a therapy. In turn, this belief may have doused interest in companies with follow-on compounds (*Signs are growing that the hep C ship is sailing, August 1, 2012*).

Clearly, Mr Stonehouse and the boards of both BioCryst and Presidio disagree with this analysis.

"You look at the size of the market – 170 million people worldwide – the diversity of patients, different genotypes and resistance profiles and then you look at the fact that we could be in combination studies in the second half of next year. So I think we're right in the thick of the race with an attractive set of assets," he says.

Importantly, non-genotype 1 strains represent a significantly larger proportion of patients in both Western and Eastern Europe and emerging markets like China and south and southeast Asia. Thus, global opportunities still await for a drug that addresses single genotypes or all at once.

Opportunity knocks

Presidio's lead candidate is an NS5A inhibitor, PPI-668, which has completed phase I trials and is ready to be advanced into phase II; it is in the same class as Bristol-Myers Squibb's daclatasvir. The merged company then has two NS5B-targeting agents about to start phase I trials, BioCryst's BCX5191, a nucleoside analogue inhibitor like GS-7977, and Presidio's PPI-383, an NS5B non-nucleoside inhibitor like Bristol-Myers' BMS-791325.

Mr Stonehouse says BCX5191 should start trials by the end of 2012, with PPI-383 entering the clinic in the first half of 2013.

The merger with Presidio, which valued the California group at $101m, was the end result of a strategic decision to invest in the hepatitis C pipeline.

"As things progressed through and we started to get over some of the hurdles, the process of getting a drug toward approval and on the market it certainly caused us to get more excited," Mr Stonehouse says.

"For the better part of a year or so we've been looking at strategic moves we could make to accelerate our company and its ability to create value," he adds. "So we looked at other things and nothing was viable or interesting other than Presidio. How often is it that a company like Presidio – a private company with really high-quality assets that complement our BCX5191 very well and with very talented people – comes along in a situation where you have an opportunity to merge at what I believe is a very attractive price?"

The company's investors seem to agree. Shares rose 14% to $4.69 during the three trading sessions following the October 18 announcement of the merger, although they have since retreated, closing at $4.08 on October 26.

With a single transaction, BioCryst has gone from a company with a grab-bag of infectious and inflammatory disease candidates to one that is fully wedded to innovation in hepatitis C. The coming year will be show how much value investors place on pursuing a pan-genotype strategy in treating the disease.

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