Evaluate Vantage

May 06, 2016

Upcoming events – Achillion combo data and Agios rare disease play

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Welcome to your weekly digest of approaching regulatory and clinical readouts. Achillion Pharmaceuticals has been nothing if not persistent in trying to find a place in the evolving hepatitis C treatment landscape, and upcoming combination trial results at last could give the group a push over the finish line.

Agios Pharmaceuticals, meanwhile, will use the upcoming European Hematology Association conference as a forum to deliver mid-stage results for AG-348, its candidate for the rare inherited blood disorder pyruvate kinase deficiency.

Hep C's Achillion heel?

Two years ago the prospect of effectively curing hep C in a matter of six weeks would have guaranteed success for any innovator. 48 months on and the number of combination products either launched or in development for hep C mean that even this treatment promise has been greeted with less enthusiasm.

Achillion is set to release phase II data for a triple combination hep C drug with partner Johnson & Johnson before the end of June, and some believe the once-daily pill could cut the treatment duration from the usual 12 weeks of Harvoni to six.

The three arm study includes J&J's Olysio and its NS5B polymerase inhibitor AL-335, and Achillion's NS5A inhibitor, odalasvir, and has seen patients either receive once daily treatment for four, six, or eight weeks. Few in the market are expecting the triple combination to achieve a sustained viral response by four weeks. Even six weeks is seen as ambitious by some after data released at EASL, but if the drug does achieve a six week SVR it would provide crucial differentiation from products already on the market.

There is of course another scenario: that the product is only effective at eight weeks. This would make it a fourth-to-market me-too product in a space with a rapidly shrinking patient population by its launch date. The issue of safety also remains, given the off-target effects of nucs.

If the combo does hit the magic six, as ever with HCV products coming after Gilead and Merck & Co's drugs, the question will be where they fit in the treatment regimen – and more importantly, how commercially successful they will be given the competition in the field.

The commercial question has become even more pointed since the approval of Merck's Zepatier, which was launched at a significant discount to the current market leaders, leading some to forecast that the golden days of HCV pricing are well and truly over.

Achillion and J&J might argue that a six-week treatment schedule could justify a higher price tag. If that argument is persuasive Achillion could see a big uplift in its shares – though in the current climate of austerity payers might instead prefer eight or 12 week scrips with a much lower price.

One-two punch

Meanwhile, Agios is due to report initial data from a phase II study of AG-348 in pyruvate kinase deficiency. The results, from the first 10-15 patients in the Drive-PK trial, will be presented at the European Hematology Association conference in June.

The disorder, which typically presents in early infancy, is caused by mutations in the PKLR gene and is found in around 1 in 20,000 people in the US. It leads to the breakdown of red blood cells, resulting in haemolytic anaemia.

There is no approved therapy to treat the underlying causes of the disease, according to Agios, and '348 is the most-advanced pyruvate kinase R activator in development. Current treatments for severely affected patients include regular blood transfusions or removal of the spleen, which can become enlarged, while milder patients generally receive supportive care.

The Drive-PK trial of 75 transfusion-independent patients has a primary outcome of safety, but will also look at pharmacokinetic parameters and change in levels of biomarkers and haemoglobin.

The results should help determine whether the company takes ’348 forward or opts to focus on its other pyruvate kinase R activator, AG-519, which is in phase I. Data from a dose-finding study of ’519 in healthy volunteers are also due at the EHA meeting.

One potential problem with ’348 is off-target effects, specifically the inhibition of aromatase, which will no doubt be closely watched in phase II. Agios is expected to make a decision between the two molecules later this year as data from the trials accumulate.

EvaluatePharma’s sellside consensus predicts that ’348 will bring in 2022 sales of $250m, while there are currently no forecasts for ’519. This will likely change if Agios ends up plumping for the earlier-stage candidate.

If the company does go with ’519, it should not mean a massive delay. The company has said it would not need to conduct another phase II trial similar to Drive-PK, but could move to an efficacy study immediately, according to Leerink analysts.

The path forward should become clearer this year as data emerge.

Project	**Study**	**Trial ID**
odalasvir	With Olysio and AL-335	NCT02569710
AG-348	Drive-PK	NCT02476916
AG-519	Phase I trial	NCT02630927

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