Evaluate Vantage

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Upcoming events – key tests approach for Biogen and Kalvista

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Biogen needs a win with its Tecfidera follow-on, while Kalvista hopes to make HAE where Biocryst failed.

Welcome to your weekly digest of approaching regulatory and clinical readouts. Gastrointestinal issues can be a major problem for patients who take Tecfidera, Biogen's biggest multiple sclerosis drug, and the company hopes to prove that its follow-on asset BIIB098 is markedly more tolerable. Results are due mid-year from a trial pitting the two agents against each other, measuring GI events as its primary endpoint.

Biogen and its partner Alkermes have already sought approval for BIIB098 in the US, and revealed Vumerity as the brand name; an FDA decision is due in the fourth quarter. Because the compound is very similar to Tecfidera – diroximel fumerate versus dimethyl fumarate – the companies have pursued the 505(b)(2) regulatory pathway, which requires less rigorous tests of efficacy.

The groups submitted data from the single-arm Evolve-MS-1 trial, looking at long-term safety, as well as bridging studies demonstrating pharmacokinetic equivalence. Thus the pending head-to-head study, Evolve-MS-2, has been designed with marketing in mind. With Tecfidera's patent due to expire in the next few years, a clear difference in the two agents' tolerability profiles must be demonstrated to give Vumerity a chance of commercial success.

Tecfidera typically causes the most severe GI events in the first month of treatment, so Evolve-MS-2 measures its primary endpoint, the number of days with GI events using an individual GI symptom scale, over five weeks.

Evolve-MS-1 suggests that BIIB098 will have a more tolerable profile. The most common adverse events were flushing (31.7%), pruritus (7.4%) and diarrhoea (6.6%). Compared with the data on Tecfidera's label, the diarrhoea incidence does appear to be lower. In Evolve-MS-1 the rate of discontinuations due to GI events, at 0.5%, was also lower than that described on Tecfidera's label, while no serious GI adverse events were reported with Vumerity.

The head-to-head trial needs to confirm all of this – and the extent of the difference will be crucial. The sellside forecasts Vumerity sales of $239m in 2024, according to *EvaluatePharma*'s consensus, a figure that reflects some scepticism over whether the follow-on agent will look much different from Tecfidera.

Given Biogen's pipeline woes, it needs a win here. Alkermes, which originated the project, is due a $150m approval payment and a mid-teens royalty on sales.

Tecfidera's adverse event profile		
	Tecfidera (N=769)	**Placebo (N=771)**
Flushing	40%	6%
Abdominal pain	18%	10%
Diarrhea	14%	11%
Nausea	12%	9%
Vomiting	9%	5%
Pruritus	8%	4%
Rash	8%	3%
Discontinuations due to GI events	4%	<1%
Serious GI events	1%	-
Source: US drug label.		

Kalvista's chance

Meanwhile, Kalvista will hope to capitalise on a slip-up earlier this week from its hereditary angioedema (HAE) rival Biocryst. The latter crashed on Monday after a phase III trial of its oral HAE candidate BCX7353 showed disappointing efficacy.

BCX7353 was being tested for HAE prevention, while Kalvista's fellow oral kallikrein inhibitor KVD900 is in development for the acute treatment of HAE attacks, which involve severe swelling and can be fatal.

A European phase II trial of the latter is due to report in the second half of the year, and could give early clues on whether subtle differences between the two candidates will work in Kalvista's favour.

KVD900 achieves a higher peak serum concentration than BCX7353, and reaches this faster, at 30 minutes versus two hours, Stifel analysts note. This means that KVD900 could be a more potent drug than Biocryst's contender, although obviously this will need to be proven.

The 50-patient phase II study tests KVD900 versus placebo, given within an hour of an HAE attack. If patients experience a second attack they cross over to the other group, so those previously receiving placebo get KVD900, and vice versa. Attack severity is being monitored over 24 hours.

Patients are allowed to use their normal, on-demand treatments as needed, and time to this rescue therapy will help investors gauge KVD900's chances of becoming a relevant contender.

Here, Kavista's project will need to perform similarly to Takeda's Firazyr, a subcutaneous product approved for treating acute HAE attacks. In a pivotal trial 7% of patients receiving Firazyr also needed additional rescue medication, versus 40% in the placebo group.

If KVD900 can equal this its convenience should give it an edge, but if KVD900 falls short Kalvista could go the way of Biocryst.