Evaluate Vantage

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Upcoming events: AstraZeneca and Actelion at ACC, panels for Bridion and Breo

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Welcome to your weekly digest of approaching regulatory and clinical readouts. The American College of Cardiology's annual meeting kicks off on March 14, promising a swathe of data on cardiovascular projects. Keenly awaited presentations include AstraZenenca's Pegasus trial of Brilinta and Actelion's Griphon study, conducted with the latest drug in the group's pulmonary arterial hypertension franchise.

Elsewhere, Merck & Co and GlaxoSmithKline are facing FDA advisory committee hearings. The US group's long-troubled anaesthesia project Bridion is set for review on March 18, seven years after its first non-approvable letter. The next day Glaxo's respiratory drug Breo will be discussed, specifically over whether larger safety studies are needed before approval can be granted in asthmatic patients aged 12 and over.

Brilinta: AstraZeneca

On March 14 AstraZeneca will present further data from the Pegasus study of Brilinta plus aspirin in secondary prevention. The trial represents a major plank in the company's strategy to reinvigorate sales of the blood thinner, as it could support the use of dual anti-platelet therapy for longer than currently recommended in these patients.

In January Astra said the primary endpoint had been met at both doses tested, with Brilinta significantly reducing major cardiovascular thrombotic events in patients with a history of heart attack. No unexpected safety issues were reported.

Confirmation of these findings will come in the full presentation, and readings on secondary endpoints are also keenly awaited. Measures looking at cardiovascular death and all-cause mortality could provide the differentiation from generic clopidogrel that Brilinta really needs.

The full commercial impact of the study is likely to remain hard to assess, however, given criticisms including the lack of a clopidogrel comparator arm. And a strong readout might ultimately still be interpreted as an endorsement of extended dual-antiplatelet therapy rather than explicit backing for Brilinta itself (*Pegasus finds its wings but will it help Brilinta get off the ground?, January 14, 2015*).

Uptravi: Actelion

Actelion will unveil full results on March 15 from the Griphon study of Uptravi (selexipag) in PAH. Hopes are high that the strong efficacy signal seen in topline data will be confirmed, and that an improved safety profile versus competitors will emerge.

Last year the Swiss group disclosed that the pill had shown significant benefit on a tantalising "morbidity/mortality" endpoint, and convincingly hit the primary endpoint of the study with a 39% reduction in the risk of death or complication (*Event – Proving survival the hope for Actelion's next act, February 17, 2015*).

Eagerly awaited are details on safety, including drug interaction data, and a reading on the key secondary endpoint of mortality. Showing a survival benefit would be a first for any agent in this disease, with obvious implications for Uptravi's commercial prospects.

Bridion: Merck

Bridion (sugammadex) is a selective relaxant binder for reversing neuromuscular blockade agents in intensive care settings. Back in 2008 it had been unanimously endorsed by a US advisory panel, but the FDA refused to grant approval, citing issues related to hypersensitivity reactions and bleeding.

A complete response letter followed in September 2013 (*Time for Merck to rethink niche hospital strategy, September 24, 2013*). Last October Merck said it had submitted new studies designed to examine hypersensitivity reactions, as well as an updated review of pharmacovigilance.

Bridion was first launched in Europe in 2008 and in Japan two years later; worldwide it sold $340m last year,

and consensus forecasts from *EvaluatePharma* have 2020 sales hitting $795m, with $375m of that expected in the US. Convening another panel could signal that the FDA remains open minded. A final decision is due by July.

GlaxoSmithKline/Theravance: Breo Ellipta

Breo Ellipta has been on the market in the US since 2013, but only for COPD. In Europe it has been on the market for both COPD and asthma, since last year.

It is a combination of fluticasone and vilanterol; US regulators have been very reluctant to endorse this type of combination for asthma owing to a link to increased risk of asthma-related deaths, and in 2011 the FDA required companies to conduct large post-marketing safety trials comparing the combination products to steroids used alone. At the time it was said that results would be expected in 2017.

The FDA has said that while efficacy data will be discussed the focus of the Breo meeting will be on safety.

In phase III Breo generated a statistically significant improvement in lung function in moderate to severe persistent asthma versus a steroid alone. It also significantly increased the time to severe exacerbation, and decreased the annual rate of severe exacerbations, with no differences in the number of asthma-related hospitalisations and no asthma-related deaths.

Last year it sold $110m. *EvaluatePharma* consensus data forecast 2020 sales of $1.1bn, with about half of that coming from asthma. After the panel a final FDA decision is expected by April 30. Bank of America Merrill Lynch analysts assume an 85% likelihood of an asthma approval this year; any request for a pre-approval study would hit estimates hard.

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Merck announced on March 13 that the advisory panel for Bridion had been cancelled. The FDA advised Merck that it plans to conduct additional site inspections related to a hypersensitivity study (Protocol 101). Due to the timing of the additional inspections, Merck expects to receive a CRL by April 22, 2015.

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