BIOBUSINESS BRIEFS

MARKET WATCH

Upcoming market catalysts in Q4 2010

Several important US Food and Drug Administration (FDA) approval decisions are expected in the fourth quarter of 2010. First, the Prescription Drug User Fee Act (PDUFA) date for a decision on the approvability of sodium oxybate (Rekinla; developed by Jazz Pharmaceuticals) for the treatment of fibromyalgia is 11 October.

Fibromyalgia is a relatively newly defined rheumatic disease with an array of pain symptoms and it is only in the past few years that drugs have been specifically approved for its management. In 2007, pregabalin (Lyrica; Pfizer) became the first such drug to be approved in the United States, followed by duloxetine (Cymbalta; Eli Lilly and Company) and milnacipran (Savella; Forest & Cypress) in 2008 and 2009, respectively.

Sodium oxybate has been marketed by Jazz Pharmaceuticals in the United States for several years for the treatment of narcolepsy under the trade name Xyrem. In studies involving patients with fibromyalgia, it showed strong efficacy and a relatively clean safety profile. However, an FDA advisory panel in August voted overwhelmingly against its approval for this indication. A key issue for further study was safety in the broad fibromyalgia population because in the Phase III trial, patients with important comorbidities were excluded and other medications were washed out.

Another substantial concern was the abuse potential of the drug. Sodium oxybate, which is also known as γ-hydroxybutyric acid (GHB), can be used recreationally or to facilitate sexual assault and most panellists considered that its approval in an indication as large as fibromyalgia would require a more restrictive risk evaluation and mitigation strategy (REMS). This issue did not preclude sodium oxybate's prior approval, as narcolepsy is considered to be a much rarer and more severe disorder than fibromyalgia.

October could also see the approval of AVP-923, a product that combines dextromethorphan and quinidine (developed by Avanir), which would be the first drug specifically approved in the United States to treat pseudobulbar affect (PBA). The PDUFA date for a decision on AVP-923 is 29 October.

PBA is a fairly common neurological disorder for which the defining characteristic is emotional lability (laughing or crying excessively or at inappropriate times). It often manifests secondary to other neurological diseases, such as multiple sclerosis. AVP-923 was originally reviewed by the FDA in October 2006 but was rejected, mainly owing to findings of increased QTc intervals (a risk factor for arrhythmias). Avanir and the FDA agreed that lowering the dose of quinidine in the co-formulation would probably resolve the QTc issue. However, before approval, Avanir was required to conduct another Phase III study of AVP-923 in patients with PBA, which was initiated in 2007.

Results for this trial were released in 2009. AVP-923's efficacy was still strong, even with the lower dose of quinidine. However, although this study showed no clinically meaningful changes in the QTc interval, a numerically higher percent of patients died in both AVP-923 groups than in the placebo group (2.8% and 2.9% versus 0.9%). The FDA will have to balance these potential safety issues with the lack of other treatments for this indication and the poor prognosis for patients.

Finally, by 9 December the FDA is expected to decide on perhaps the most anticipated potential drug approval of the quarter: belimumab (Benlysta; developed by Human Genome Sciences and GlaxoSmithKline) for the treatment of systemic lupus erythematosus. In both of its pivotal Phase III studies, belimumab, a human monoclonal antibody that is specific for the cytokine B-lymphocyte stimulator (BLyS; also known as BAFF), showed statistically significant improvements in disease activity versus placebo. There is particular interest in this decision as no new drugs have been specifically approved to treat systemic lupus erythematosus in over 50 years in the United States. The FDA is convening an advisory panel to discuss belimumab on 16 November. Should the drug reach the market, it is predicted to have annual global sales in the multi-billion dollar range.

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