BIOBUSINESS BRIEFS

MARKET WATCH

Upcoming market catalysts in Q2 2012

Important drug development events expected in the second quarter of 2012 include decisions by the US Food and Drug Administration (FDA) on the approval of the phentermine/topiramate combination therapy for obesity, and on linaclotide for both irritable bowel syndrome (IBS) and chronic idiopathic constipation (CIC). Mid-stage clinical trial data for several interferon-free treatment regimens for hepatitis C virus (HCV) infection are also expected to be reported at the European Association for the Study of the Liver (EASL) meeting in April 2012.

A second decision by the FDA on the approval of phentermine/topiramate (developed by Vivus) for the treatment of obesity is expected by 17 April 2012 (the Prescription Drug User Fee Act (PDUFA) date). Phentermine/topiramate combines low doses of two approved generic compounds: phentermine, an amphetamine that stimulates noradrenaline release to suppress hunger; and topiramate, an anticonvulsant whose mechanism of action in obesity is unclear. In October 2010, the FDA issued a complete response letter in the first review cycle for phentermine/topiramate, following a 10–6 negative vote from an advisory panel, citing teratogenicity and cardiovascular risks. The current review follows a substantially

more positive advisory panel meeting in February 2012, at which members voted 20–2 in favour of approval. The committee noted that Vivus sufficiently addressed the original teratogenicity risk through retrospective data analyses and expanded on the proposed post-marketing risk evaluation and mitigation strategy in the updated filing. Furthermore, six out of seven members present at both meetings reversed their original negative votes. Phentermine/topiramate is the first of three recently rejected obesity treatments up for second review, and an approval decision could provide a much-needed therapy as well as a boost to the field in general.

The FDA is due to make a decision on the new drug application for linaclotide (developed by Ironwood and Forest Laboratories) for the treatment of IBS and CIC by 8 June 2012. Linaclotide, which is a peptide agonist of the guanylyl cyclase type C receptor, was found to be significantly more effective than placebo in improving bowel movements at both 12 and 26 weeks in four large Phase III studies, two each in IBS and CIC. Of note, long-term safety results have yet to be released, which will prove to be important for this chronic treatment, as both IBS and CIC have had approved treatments removed from the market owing to various safety concerns. Approval of linaclotide would provide a new

treatment in indications with a large unmet patient need.

After a landmark year for the treatment of HCV infection in 2011, with the approval of two oral HCV protease inhibitors, HCV therapy continues to advance through the development of regimens that eliminate the need for interferon injections. Data from several interferon-free regimens are due to be reported at the EASL meeting (18–22 April 2012), including results from Abbott's direct-acting antiviral combinations. These treatments combine various oral small molecules that target multiple next-generation HCV targets: ABT-450 is an oral protease inhibitor; ABT-333 and ABT-072 are non-nucleoside polymerase inhibitors; and ABT-267 is an NS5A inhibitor. Previously reported data from the PILOT and CO-PILOT studies of ABT-450, ritonavir and ABT-333 or ABT-072 showed promising results in a small number of patients. If updated data at the EASL meeting are consistent, there could be another dramatic shift in HCV treatment, not only moving away from interferon but doing so without the use of polymerase inhibitors.

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