BIOBUSINESS BRIEFS

MARKET WATCH

Upcoming market catalysts in Q4 2011

Key market catalysts in the fourth quarter of 2011 include top-line results from a Phase III trial of alemtuzumab in relapsing–remitting multiple sclerosis (RRMS), and decisions by the US Food and Drug Administration (FDA) on the approval of dapagliflozin for the treatment of type 2 diabetes and on the approval of ruxolitinib for the treatment of myelofibrosis.

Alemtuzumab (developed by Genzyme, a Sanofi company) is a humanized monoclonal antibody specific for CD52 that is in development for the treatment of RRMS. In a 3-year Phase II trial, alemtuzumab provided a substantial 74% reduction in the risk of relapse and a 71% reduction in the risk of disability progression relative to the active control interferon-β1a (IFN-β1a). In a Phase III trial reported in July, involving previously untreated patients with RRMS, relapses were reduced by 55% relative to IFN-β1a. However, the co-primary end point of reduction of disability progression was missed, apparently owing to an unexpectedly low rate of disability progression in the control group. Top-line results from a second Phase III trial comparing alemtuzumab to IFN-β1a in the treatment of patients with more aggressive or advanced disease are expected in the fourth quarter of 2011.

Dapagliflozin (developed by Bristol-Myers Squibb and AstraZeneca) is the most advanced of a new class of anti-diabetes agents targeting the renal sodium-dependent glucose cotransporter 2 (SGLT2). Dapagliflozin and other investigational SGLT2 inhibitors reduce hyperglycaemia by increasing the excretion of glucose into the urine. The dapagliflozin clinical development programme consisted of 26 pharmacology trials, 3 Phase IIb trials and 11 Phase III trials, with a cumulative exposure of 4,009 patient-years in Phases IIb and III. The FDA Endocrinologic and Metabolic Drugs Advisory Committee voted 9 to 6 against the approval of dapagliflozin in July 2011 (*Nature Rev. Drug Discov.* **10**, 645–646; 2011). Six of the nine members who voted against approval expressed concerns about small numerical increases in the incidence of breast cancer and bladder cancer that were observed in dapagliflozin-treated subjects relative to controls. Panel members supporting approval questioned the relevance of these numerical increases and the feasibility of performing a pre-approval safety trial that was powered to exclude risk on the order of 0.2%. One panellist estimated that a meaningful answer to this question would require a new trial involving more than 30,000 patients. The Prescription Drug User Fee Act (PDUFA) decision date for dapagliflozin is 28 October 2011. The FDA's decision will provide insight into the agency's future expectations for demonstrating the safety of new drugs.

Ruxolitinib (developed by Incyte Corporation) is the most advanced of several Janus kinase 2 (JAK2) inhibitors currently in development for the treatment of myelofibrosis, a blood cancer that is characterized by the loss of bone marrow function, dysregulated blood cell counts, increased extramedullary haematopoiesis and enlargement of the spleen. There are currently no disease-modifying therapies available for treating myelofibrosis. Approximately half of the patients with the disease have a specific activating mutation (V617F) in JAK2, which is a key enzyme in certain signalling cascades, including those downstream of erythropoietin and thrombopoietin. In Phase III trials in patients with myelofibrosis, ruxolitinib reduced spleen enlargement and overall symptoms such as night sweats, itching and pain. Efficacy was observed in both carriers and non-carriers of the V617F mutation. Thrombocytopaenia and anaemia were the most important adverse events occurring with a higher frequency in ruxolitinib-treated patients than in placebo-treated patients. The PDUFA decision date for ruxolitinib, for the treatment of myelofibrosis, is 3 December 2011.

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