BIOBUSINESS BRIEFS

MARKET WATCH

Upcoming market catalysts in Q1 2016

In the first quarter of 2016, there are important market catalysts for potential treatments of rare genetic disorders, including a US FDA advisory committee meeting and approval decision on eteplirsen for Duchenne muscular dystrophy (DMD). Top-line clinical trial data for epidiolex in Dravet syndrome and avoralstat in hereditary angioedema (HAE) are also expected.

The FDA has granted eteplirsen rare paediatric disease and orphan drug designations as well as fast-track status for DMD — a rare, inherited muscle disease caused by the absence of the dystrophin protein. Eteplirsen (developed by Sarepta Therapeutics) is an intravenously administered phosphorodiamidate morpholino oligomer (PMO) designed to induce skipping of exon 51 in the dystrophin gene and increase production of dystrophin protein. The Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee is tentatively scheduled to review the new drug application (NDA) for eteplirsen on 22 January 2016, and a decision on its approval is expected by 26 February 2016. The decision will be based on a Phase IIb multiple-dose, open-label study with published results showing that patients treated with eteplirsen experienced a slower rate of disease progression, a statistically significant improvement in the 6-metre-walk test and a lower incidence of loss of ambulation (16.7% versus 46.2%) compared with untreated matched historical controls at 36 months. In November, a PCNS advisory committee meeting was held to review another exon 51-skipping drug, drisapersen (developed by BioMarin), with a decision on its approval expected by 24 December 2015.

The top-line results for epidiolex (developed by GW Pharmaceuticals) in a Phase III trial known as GWEP1332 for Dravet syndrome are expected in the first quarter of 2016, with results from a second Phase III trial known as GWEP1424 to follow in early 2016. Epidiolex is an oral liquid formulation of plant-derived cannabidiol, and is the first and most advanced treatment to target the cannabinoid system for epilepsy indications. The FDA has granted orphan drug designation to epidiolex as Dravet syndrome is a rare form of epilepsy that is primarily associated with a mutation in the *SCN1A* (sodium channel protein type I subunit alpha) gene. Published results from a Phase III expanded access programme show a greater than 50% reduction in the frequency of seizures over a 12-week period in Dravet syndrome as well as in Lennox–Gastaut syndrome, another form of childhood epilepsy. Phase III data of epidiolex for Lennox–Gastaut syndrome from a Phase III trial known as GWEP1414 are also expected in the first quarter of 2016.

BioCryst Pharmaceuticals will release top-line data from its Phase II/III OPuS-2 study of avoralstat for HAE, an inherited disorder that results in inadequate or non-functioning plasma protease C1 inhibitor (C1INH) protein, a naturally occurring kallikrein inhibitor involved in modulating blood vessel response. Avoralstat is an orally administered kallikrein inhibitor; ecallantide (Kalbitor; Dyax) is an approved kallikrein inhibitor for HAE, but it is indicated for the treatment of acute attacks and is administered subcutaneously. The FDA has granted orphan drug designation to avoralstat for the prevention of acute attacks of angioedema in patients with HAE, as these attacks can cause severe pain and fatal airway obstruction. Previous results from the Phase IIa OPuS-1 study in patients with a high frequency of angioedema attacks reported a significant reduction in attack rate versus a placebo control. Although the reduction of attacks was lower (36% versus 53%) than that observed with a recombinant form of C1INH (Cinryze; Shire), an approved treatment for HAE prophylaxis, the OPuS-2 study of avoralstat included patients with more severe disease. If Phase III results for avoralstat are positive, it could become the first orally administered preventive therapy for HAE patients.

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