MARKET WATCH

Upcoming market catalysts in Q2 2016

Important market catalysts expected in the second quarter of 2016 include regulatory decisions by the US Food and Drug Administration (FDA) on pimavanserin (developed by Acadia) for the treatment of Parkinson disease and deutetrabenazine (developed by Teva) for the treatment of Huntington disease, as well as top-line Phase III data for vepoloxamer (developed by Mast Therapeutics) for the treatment of sickle-cell anaemia.

Acadia is seeking approval for pimavanserin, a small-molecule serotonin 5-HT_{2A} receptor inverse agonist, for the treatment of psychosis associated with Parkinson disease. The FDA granted breakthrough designation to pimavanserin in this indication in September 2014, and a decision for this new drug application (NDA) is expected by the Prescription Drug User Fee Act (PDUFA) action date of 1 May 2016, following priority review. The NDA is supported by results from the pivotal Phase III -020 study, which met its primary endpoint of antipsychotic efficacy as measured by SAPS-PD, a 9-item scale adapted from the hallucinations and delusions domains of the Scale for the Assessment of Positive Symptoms (SAPS), as well as key secondary endpoints including clinical global improvement (CGI) by the investigator using the CGI-I scale. Subsequent data released by Acadia demonstrated further improvement in night-time sleep and daytime wakefulness, in addition to a consistently safe tolerability profile. In previous Phase III studies (-012 and -014), pimavanserin failed to meet the primary endpoint owing to a much higher placebo response outcome. In addition, the resignation of Acadia's CEO in March 2015 altered the timing of submission for approval. Despite these setbacks, study -020 demonstrates steady efficacy and tolerability in an area of high unmet medical need.

Teva has been assigned a PDUFA date in May 2016 for deutetrabenazine for the treatment of chorea associated with Huntington disease. Deutetrabenazine is a deuterium-substituted analogue of tetrabenazine (Xenazine), a small-molecule inhibitor of vesicular monoamine 2 transporter (VMAT2) that is currently the only approved drug for this indication; deuteration is intended to prolong the drug's half-life without affecting its activity. The NDA filing is based on results from two Phase III studies (FIRST-HD and ARC-HD), both of which demonstrated reductions in chorea in patients dosed with deutetrabenazine. Data from the FIRST-HD study demonstrated statistically significant improvements versus placebo in the primary and secondary endpoints, including change in total maximal chorea (TMC) score (4.4 points versus 1.9 points, P <0.0001). Deutetrabenazine was well tolerated, and the side-effect profile was favourable in regards to the incidence of akathisia and somnolence. In addition, data from the ARC-HD study showed that patients receiving tetrabenazine could switch to deutetrabenazine and maintain control of chorea, an important discovery for patients prone to akathisia and somnolence who are already taking tetrabenazine.

Finally, top-line data from the saline-controlled Phase III EPIC study of vepoloxamer for the treatment of sickle-cell anaemia in 388 participants are expected in the second quarter of 2016. There are no approved treatments for sickle-cell anaemia in either the United States or Europe, and Mast Therapeutics has received orphan and fast-track designations from the FDA for vepoloxamer, a non-ionic block copolymer surfactant believed to adhere to hydrophobic surfaces that develop when cells are damaged. The primary endpoint of the EPIC study is the reduction of the duration of vaso-occlusive crisis. Of note, a September 2015 Data Monitoring Board Analysis (DMBA) concluded that no safety concerns were present in the study and that an additional DMBA meeting was unnecessary. Notable safety issues separate from the EPIC study included nephrotoxicity and impaired renal function. According to Mast, a new purified formulation largely addresses these concerns, and an additional Phase III study evaluating the pharmacokinetics in patients with varying renal insufficiencies is underway. Data from the EPIC study will provide an additional source of safety data on these issues. Overall, results from the EPIC study will have a key role in regulatory filings for vepoloxamer, in addition to an impact on the competitive drug landscape for sickle-cell anaemia.

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doi:10.1038/nrd.2016.49
Published online 1 Apr 2016

The author declares no competing interests.