BIOBUSINESS BRIEFS

MARKET WATCH

Upcoming market catalysts in Q4 2019

Important catalysts expected to occur during the fourth quarter of 2019 include US approval decisions for brolucizumab in wet age-related macular degeneration (AMD) and for a long-acting cabotegravir and rilpivirine combination, CARLA, to treat HIV-1 infection, as well as top-line results from a phase III study of SAGE-217 in major depressive disorder (MDD).

Novartis is developing brolucizumab, a humanized single-chain antibody fragment that targets vascular endothelial growth factor A (VEGF-A), for the treatment of wet AMD. The FDA accepted the biologics license application for brolucizumab in April 2019, and as Novartis used a priority review voucher to expedite its review, the estimated Prescription Drug User Fee Act (PDUFA) date is in November 2019.

The application is based on data from two phase III studies, HAWK and HARRIER, which evaluated brolucizumab versus Regeneron's Eylea (aflibercept) with a primary end point of mean change in best-corrected visual acuity (BCVA) from baseline to week 48. The mean change in BCVA was 6.6 letters in the brolucizumab group versus 6.8 letters for aflibercept in HAWK and 6.9 letters versus 7.6 letters, respectively, in HARRIER. It is important to mention that after a 3-month loading phase, patients in the brolucizumab arm were dosed every 12 weeks with an option to adjust to an 8-week dosing interval based on masked disease activity assessments while patients in the aflibercept arm were dosed every 8 weeks.

Novartis is seeking approval for brolucizumab dosed once every 12 weeks.

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Aflibercept is approved for dosing every 4 or 8 weeks after the first 3-monthly treatments and received an additional approval in August 2018 for dosing every 12 weeks after the first year of treatment, with the caveat that treatment may not be as effective compared with dosing every 8 weeks.

If approved, brolucizumab has the potential to be a serious contender in the AMD treatment space. The data indicating that brolucizumab is as effective to aflibercept, but at a less frequent dosing schedule could be a major selling point for most patients because the intravitreal injections associated with these drugs can be uncomfortable.

ViiV Healthcare is developing CARLA, a monthly, injectable, two-drug regimen of ViiV Healthcare's investigational integrase inhibitor cabotegravir and Janssen's approved non-nucleoside reverse transcriptase inhibitor rilpivirine to treat HIV-1 infection in adults whose viral load is suppressed and who are not resistant to cabotegravir or rilpivirine. The new drug application has been granted priority review by the FDA, with a PDUFA date in late December.

The application is based on two phase III studies, ATLAS and FLAIR. In the ATLAS study, once-monthly injections of long-acting cabotegravir and rilpivirine were shown to maintain non-inferior rates of virological suppression compared with standard three-drug regimens at week 48 based on the proportion of participants with plasma HIV-1 RNA ≥50 copies per millilitre. The FLAIR study, which compared switching to once-monthly CARLA injections versus remaining on Triumeq (dolutegravir–abacavir–lamivudine), confirmed the results from ATLAS.

Between these two trials and additional studies conducted for ViiV's other two-drug regimens — Dovato (dolutegravir–lamivudine) in the treatment-naive and maintenance settings and Juluca (dolutegravir–rilpivirine) in the maintenance setting only — there is now substantial evidence that two-drug regimens containing a potent integrase inhibitor with a high barrier to resistance have comparable efficacy to standard three-drug regimens. This should provide physicians with the confidence to prescribe a simplified treatment plan to patients who have already achieved virological suppression, although some are expected to remain cautious regarding the use of two-drug regimens until long-term (≥144 weeks) virological suppression data are available showing minimal resistance generation. The monthly injections should also appeal to patients who struggle to adhere to once-daily pills, as well as those who would prefer not to have a daily reminder of their disease.

Finally, Sage Therapeutics is developing SAGE-217 (zuranolone), a positive allosteric modulator of $GABA_A$ receptors, for the treatment of MDD and postpartum depression (PPD). During a meeting with the FDA in June 2018, Sage finalized an expedited development plan intended to support the potential filing for approval in both indications, which includes a phase III study known as ROBIN in PPD and a phase III study known as MOUNTAIN in MDD.

In January 2019, Sage announced results from the ROBIN study, which evaluated short-course treatment with SAGE-217 in women with severe PPD. The primary end point was the change from baseline in the 17-item Hamilton Rating Scale for Depression (HAMD-17) total score at day 15. After 2 weeks, treatment with SAGE-217 showed a significant improvement in HAMD-17 over placebo, with a reduction of 17.8 points compared with 13.6 points, respectively. Reductions in HAMD-17 were first observed at day 3, and maintained through the end of the 4-week follow-up. The drug's rapid-acting effects and durable efficacy are attractive features that could maximize SAGE-217's commercial potential, considering that current standard-of-care drugs may take 6–8 weeks to confer clinically meaningful effects.

The MOUNTAIN study is evaluating SAGE-217 in adult patients with MDD and has the same primary end point as the ROBIN study. Demonstration of similar efficacy and safety in this patient population would provide Sage Therapeutics with a robust data set across multiple depression types to file for FDA approval for both PPD and MDD. If approved, SAGE-217 would be Sage's second marketed drug, joining Zulresso (brexanolone), an intravenous therapy for PPD that was approved by the FDA in March 2019.

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Competing interests
The author declares no competing financial interests.