BIOBUSINESS BRIEFS

MARKET WATCH

Upcoming market catalysts in Q4 2018

Potential market catalysts in the fourth quarter of 2018 include top-line clinical trial results for SAGE-217 (developed by Sage Therapeutics) for postpartum depression (PPD) and LentiGlobin (developed by Bluebird bio) for transfusion-dependent β-thalassaemia (TDT), as well as a US approval decision for larotrectinib (developed by Loxo Oncology) for solid tumours harbouring a neurotrophic tyrosine receptor kinase (NTRK) gene fusion.

Sage expects top-line data from a pivotal phase II trial of SAGE-217 in severe PPD during the fourth quarter. SAGE-217 is a next-generation $GABA_A$ receptor positive allosteric modulator with a similar pharmacology profile to Sage's lead product, brexanolone, which is currently under FDA review for approval in PPD. Robust results in an initial phase II study of SAGE-217 in major depressive disorder (MDD) were comparable to the early efficacy results of brexanolone, providing the basis for SAGE-217's FDA fast-track and breakthrough therapy designations. Importantly, SAGE-217 has the added convenience of once-daily oral administration over intravenously infused brexanolone. The outcome of the decision on brexanolone, for which the Prescription Drug User Fee Act (PDUFA) date is 19 December, alongside an advisory panel review, will have major implications for SAGE-217. A successful outcome coupled with positive pivotal trial results could help advance SAGE-217 as the first short-course oral treatment for MDD and PPD.

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Results from the phase III Northstar-3 trial of LentiGlobin for TDT are expected in December during the 2018 American Society of Hematology (ASH) meeting. The gene therapy uses a lentiviral vector to insert a human β-globin gene into a patient's own haematopoietic stem cells ex vivo. These modified cells are then transplanted into the patient's blood stream through autologous stem cell transplantation. LentiGlobin has been granted fast-track, orphan drug and breakthrough therapy designations by the FDA. In the phase III Northstar-2 trial for non-β^0/β^0 TDT patients, both vector copy number and the proportion of transduced $CD34^+$ cells increased when the refined process was utilized. Current supportive care for TDT patients involves regular blood transfusions. This can pose a life-threatening risk owing to lifelong iron buildup, although this can be managed to some extent by iron chelation therapy. If approved, LentiGlobin is anticipated to have a strong market impact as the first treatment with the potential to target the underlying genetic deficiency in TDT.

Larotrectinib, a small-molecule tropomyosin receptor kinase (TRK) inhibitor, is under FDA priority review with a PDUFA date of 26 November. Rather than being developed based on the site of origin of the tumour, larotrectinib has been developed based on the tumour genetics, and is intended to treat locally advanced or metastatic solid tumours harbouring an NTRK gene fusion. In an analysis of the phase II NAVIGATE and SCOUT trials evaluating adult and paediatric patients with NTRK gene fusions, larotrectinib demonstrated a 75% centrally-assessed confirmed overall response rate (ORR) and an 80% investigator-assessed confirmed ORR. Larotrectinib displayed antitumour activity in patients with TRK fusion mutations regardless of tumour type or previous therapies. If approved, larotrectinib would be the first drug successfully developed primarily for a tissue-agnostic indication, as well as a new treatment option for patients with TRK fusions.

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Competing interests
The authors declare no competing interests.