BIOBUSINESS BRIEFS

MARKET WATCH

Upcoming market catalysts in Q4 2020

Catalysts expected during the fourth quarter of 2020 include FDA approval decisions on the complement pathway inhibitor sutimlimab, the chimeric antigen receptor (CAR) T cell therapy lisocabtagene maraleucel and the RNAi-based therapy lumasiran.

Sanofi's sutimlimab is a monoclonal antibody inhibitor of C1s in the classical complement pathway of the immune system. It is currently under priority review by the FDA as a treatment for C1-activated haemolysis in patients with cold agglutinin disease (CAD) — a chronic rare blood disease that affects approximately 5,000 people in the USA alone — and it has been granted orphan and breakthrough therapy designation.

Clinical data from a single-arm phase III trial known as CARDINAL showed that sutimlimab met the primary composite efficacy end point, with 54% of patients having an increase from baseline in haemoglobin levels, 62% of patients achieving normalization of haemoglobin levels ≥12 g dl^{-1} at week 26 and 71% remaining transfusion-free after week 5. If approved, sutimlimab will be the first marketed treatment for patients with CAD. The Prescription Drug User Fee Act (PDUFA) target action date is 13 November 2020.

Bristol-Myers Squibb's lisocabtagene maraleucel (expected to be marketed as Breyanzi) is a CAR-T cell therapy that targets CD19, a protein that is expressed on the surface of B cells. The therapy, which was gained through the US$74 billion acquisition of Celgene in 2019, is under regulatory review in the USA, EU and Japan as a treatment for third-line or later relapsed or refractory large B cell lymphoma. If approved, Breyanzi will compete with two other CD19-targeted CAR-T therapies, Gilead's axicabtagene ciloleucel (Yescarta) and Novartis' tisagenlecleucel (Kymriah). A point of differentiation for Breyanzi is the combination of purified $CD4^+$ and $CD8^+$ cells in a defined ratio; although this complicates manufacturing, it has been proposed to reduce product variability and improve safety.

The TRANSCEND clinical trial evaluating Breyanzi, which involved 269 patients with relapsed/refractory large B cell lymphoma, demonstrated an overall response rate (ORR) of 73% and a complete response (CR) rate of 53% in the efficacy-evaluable population. These results compare well with historical data from Yescarta's ZUMA-1 trial and Kymriah's JULIET trial, which reported CR rates of 51% and 32%, respectively, in patients with relapsed/refractory large B cell lymphoma. Regarding safety, only six patients (2%) experienced grade 3/4 cytokine release syndrome with Breyanzi, compared with 13% with Yescarta and 23% with Kymriah. The US regulatory review for Breyanzi was delayed when Bristol-Myers Squibb submitted additional information to the FDA, which was deemed to constitute a major amendment to the application, and the new PDUFA target action date is 16 November 2020.

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Lumasiran is an siRNA therapeutic developed by Alnylam that targets hydroxyacid oxidase 1 (HAO1). It has been granted breakthrough designation and is currently under priority review as a treatment for primary hyperoxaluria type 1 (PH1), an ultra-rare disease that is estimated to have a prevalence of approximately 3,000–5,000 patients across the USA and the EU. The disease is characterized by overproduction of liver oxalate, causing progressive decline in kidney function and typically culminating in kidney failure. By depleting glycolate oxidase, the enzyme encoded by *HAO1*, lumasiran inhibits production of oxalate.

Results from a phase III trial known as ILLUMINATE-A demonstrated that at 6 months, lumasiran lowered patients' urinary oxalate levels by 65% compared with baseline and by 54% compared with placebo. In addition, approximately 52% of lumasiran-treated patients achieved urinary oxalate levels within normal range and 84% achieved near normal levels, whereas none of the patients on placebo achieved normal or near-normal levels. Although a clinical benefit was not seen, the trial may have been too short, and with longer follow-up, the strong reduction in oxalate is hoped to have a favourable impact on kidney function and disease progression. If approved, lumasiran will be the first marketed therapy for PH1, and the third RNAi therapy to be approved, following Alnylam's pioneering success with patisiran in 2018. The PDUFA target action date is 3 December 2020.

Luis Pablos
Sagient Research Systems, San Diego, CA, USA.
e-mail: Luis.Pablos@informa.com

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Competing interests
The author declares no competing interests.