BIOBUSINESS BRIEFS

MARKET WATCH

Upcoming market catalysts in Q3 2021

Upcoming catalysts for the third quarter of 2021 include approval decisions by the US Food and Drug Administration (FDA) on teplizumab for the treatment of type 1 diabetes (T1D), anifrolumab for the treatment of systemic lupus erythematosus (SLE) and oportuzumab monatox for the treatment of bladder cancer.

Teplizumab is a humanized, non-Fc-receptor-binding monoclonal antibody (mAb) directed against the CD3 epsilon chain expressed on mature T lymphocytes. It is thought to attenuate the autoreactive T cells that mediate the destruction of pancreatic β-cells in patients with T1D via effects on regulatory T cells. The drug was originally developed by MacroGenics and Eli Lilly, but was abandoned following a failed phase III trial in patients with newly diagnosed diabetes a decade ago. Provention Bio acquired the rights to teplizumab in 2018, and initiated a new late-stage development programme. Results from the pivotal phase II TN-10 trial suggested a single 14-day infusion course of teplizumab delayed the onset of clinical disease and insulin dependence in individuals at risk of T1D by approximately 3 years (median of 32.5 months).

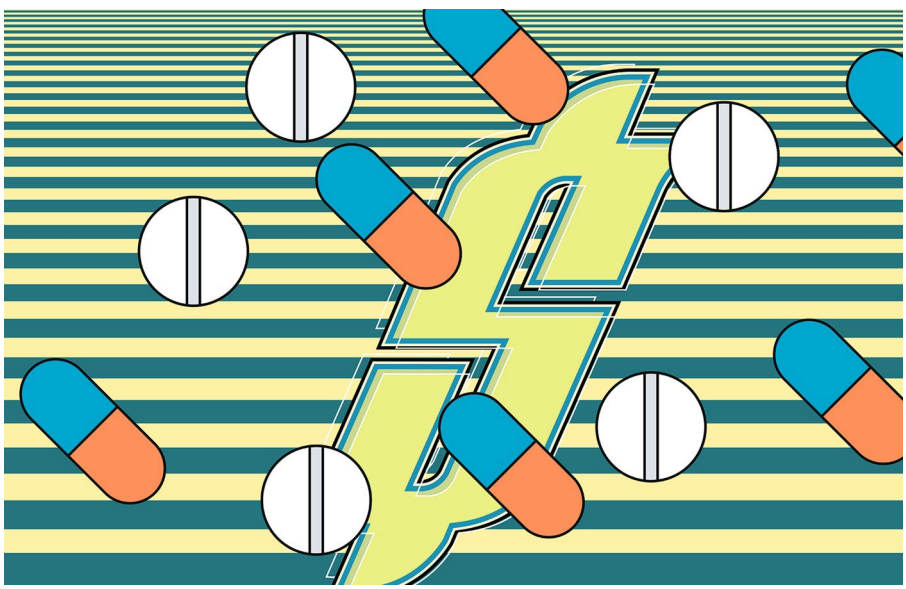
Based on these data, Provention Bio completed a rolling Biologics License Application (BLA) for teplizumab in April 2020 for the delay or prevention of clinical T1D in at-risk individuals, as indicated by the presence of two or more T1D-related autoantibodies. An FDA advisory panel meeting in May 2021 voted 10–7 in favour of approval to delay clinical T1D. Although the pivotal study demonstrated a statistically significant delay in the diagnosis of T1D, the trial was small, with some panellists being uncomfortable with the safety, and data from both the pivotal trial and the trials in patients with T1D. The FDA also had some concerns with regard to the drug substance, as Provention Bio intended to use material manufactured by AGC Biologics, whereas the material used in the TN-10 study submitted for the BLA was from Eli Lilly. Consequently, the agency said that additional data would be required on the pharmacokinetic profile of the drug substance. The Prescription Drug User Fee Act (PDUFA) action date for teplizumab is 2 July 2021. If it were to be approved, not only would this be the first product to be approved for Provention Bio, but also the first mAb-based T1D therapy.

AstraZeneca and Bristol Myers Squibb are developing anifrolumab, a fully human mAb against subunit 1 of the type I interferon receptor (IFNAR1), for the treatment of SLE. The primary end point of a statistically significant reduction in disease activity at 1 year compared with placebo using the SLE Responder Index 4 (SRI4) was not met in the phase III TULIP-1 trial of anifrolumab in patients with moderate-to-severe SLE. However, data for several secondary end points were suggestive of benefit, and, in another phase III trial known as TULIP-2, the same primary end point was met, using the British Isles Lupus Assessment Group based Composite Lupus Assessment (BICLA) instrument instead, with 48% of patients receiving anifrolumab responding compared with 32% of patients that received placebo. Additionally, 49% of patients receiving anifrolumab with moderate-to-severe skin disease experienced improved skin manifestations at week 12, the pre-specified time point, compared with 25% of patients receiving placebo.

A BLA for anifrolumab was submitted to the FDA for the treatment of SLE in November 2020, and the PDUFA action date is 5 July 2021. If approved, anifrolumab would be the first treatment for SLE to be approved by the FDA since its 2011 approval of the BLyS-specific mAb belimumab (Benlysta; GlaxoSmithKline).

Sesen Bio and Qilu Pharmaceuticals are developing oportuzumab monatox, a recombinant protein consisting of a mAb fragment that targets EpCAM with *Pseudomonas aeruginosa* exotoxin A, for the treatment of bladder cancer. It is thought that once bound to EpCAM on the surface of cancer cells, oportuzumab is internalized, whereupon the exotoxin portion of the fusion protein induces apoptosis. In a pivotal phase III trial known as Vista, a complete response rate of 39% after 3 months treatment with oportuzumab was reported, and the drug was well tolerated. Further data suggested that 52% of patients had a complete response for 12 months or longer after starting therapy, and 90% of patients remained progression-free for 2 years or greater.

A BLA submission for oportuzumab monatox to the FDA was completed for the treatment of high-risk, BCG-unresponsive non-muscle invasive bladder cancer in December 2020, with the PDUFA action date set for 18 August 2021. If approved, this would be the first product from Sesen Bio to reach the market.



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https://doi.org/10.1038/d41573-021-00108-5

Competing interests
The author declares no competing interests.