NEWS IN BRIEF

FDA approves AstraZeneca's anifrolumab for lupus

The FDA has approved AstraZeneca's anifrolumab for adults with moderate to severe systemic lupus erythematosus (SLE) who are receiving standard therapy. This is the first new approval for these patients in 10 years, and just the second in the past 60 years.

Anifrolumab is a first-in-class type I interferon receptor antagonist, blocking the activity of type I interferons including IFNα, IFNβ and IFNκ. Many patients with SLE have elevated levels of these cytokines, and mutations in the interferon-signalling pathway have been linked to disease susceptibility.

The approval was based on results from three trials, in more than 1,000 patients with SLE. The phase II MUSE trial achieved its primary end point, the percentage of patients achieving an SLE Responder Index (SRI4) response at week 24 with sustained reduction of oral corticosteroids. After anifrolumab failed to improve SRI4 scores in the phase III TULIP-1 trial, however, AstraZeneca amended the design of its then-ongoing phase III TULIP-2 trial to instead look at an alternative measure of disease severity, the British Isles Lupus Assessment Group-based composite lupus assessment (BICLA) score. TULIP-2 hit this primary end point: 48% of anifrolumab recipients achieved a BICLA response in this trial, versus 32% of placebo recipients.

In a post-hoc analysis of the MUSE and TULIP-1 trials, 55% and 47% of anifrolumab recipients achieved a BICLA response, respectively, versus 26% and 30% of placebo recipients.

Common side effects of the antibody include nasopharyngitis, upper respiratory tract infection, bronchitis, infusion-related reactions, herpes zoster and cough. Infections associated with use of the immunosuppressant can be serious and fatal, the drug's label warns.

Analysts forecast annual sales of around US$600 million for anifrolumab by 2026.

It will compete with GlaxoSmithKline's belimumab, a B lymphocyte stimulator-targeted antibody approved by the FDA in 2011. Belimumab is forecasted to achieve more than $1 billion in annual sales this year. Last year, belimumab became the first drug to secure FDA approval for lupus nephritis.

Lupus remains a drug development challenge. Progress has been hampered especially by disease heterogeneity, complicating clinical trial design and end point selection.

Asher Mullard

FDA approves first all-oral sleeping sickness drug

The FDA has approved fexinidazole for human African trypanosomiasis, a potentially fatal parasitic disease that is also called sleeping sickness.

Sleeping sickness is endemic in parts of sub-Saharan Africa, and causes fever, headaches, joint pains, abnormal behaviour and debilitating disruptions of sleep patterns. Available, effective treatments helped to reduce case counts to fewer than 1,000 in 2019. But these treatments are injected or infused in hospitals, a challenge for the remote areas where the disease can spread.

Fexinidazole, developed by Sanofi and the Drugs for Neglected Diseases initiative (DNDi), now provides an all-oral option. The drug's approval was based on a phase II/III open-label trial in nearly 400 patients, comparing a 10 day course of oral fexinidazole to nifurtimox-eflornithine combination therapy (NECT), a mixture of oral and injected therapies that was also developed by the DNDi. At 18 months, fexinidazole resulted in cure or probable cure in 91% of participants, compared with 97% in the NECT arm.

"Given the advantages expected of an oral treatment — removal of the need for infusions, and systematic hospitalisation, and the direct and indirect cost advantages — some loss of efficacy versus NECT was considered as acceptable," wrote trial investigators in *The Lancet*. The oral drug's lower efficacy was within the predefined acceptability margin, they added.

"Having a simple all-oral treatment for sleeping sickness is a dream come true for frontline clinicians," said Bernard Pécoul, DNDi's Executive Director.

The antiprotozoal agent was discovered by Hoechst, now Sanofi, but abandoned in the 1980s for strategic reasons. DNDi rebooted the programme in 2005, and subsequently partnered with Sanofi to advance the drug. The drug's discovery and development cost €55 million, says DNDi, demonstrating the potential of low-cost drug repurposing.

Sanofi secured a Priority Review Voucher (PRV) for this approval, under the FDA's Tropical Disease PRV programme. PRVs can be redeemed to secure faster drug reviews, and have been sold for US$67–350 million.

Asher Mullard

Failure of Seres's phase II ulcerative colitis programme renews microbiome concerns

Seres Therapeutics' microbiome-based candidate SER-287 failed to improve outcomes in a phase II trial in ulcerative colitis. This setback has raised questions about the use of consortia of bacteria for indications other than recurrent *Clostridium difficile* infection, casting a shadow over the emerging field.

SER-287 consists of a donor-derived consortia of bacteria that are fractionated and purified from the stool of healthy individuals. A phase Ib trial in 58 adults with mild-to-moderate ulcerative colitis led to high hopes: 18–40% of patients who received SER-287 plus the antibiotic vancomycin achieved clinical remission, compared with 0% in a placebo group, the company reported earlier this year. But newly released phase IIb data from 203 patients paint a grimmer picture. In this larger trial, clinical remission rates were around 10–11% on two different doses of SER-287, and 11% on placebo.

Seres's share price cratered 60% on the news.

The microbiome community has been here before. Seres's SER-109 failed in a phase II trial for *C. difficile* infection in 2016, dimming investor enthusiasm for the field. Seres persevered, however, increasing the dose of SER-109 by tenfold, updating its trial enrolment criteria and advancing the candidate into phase III. That trial hit its primary end point last year: 11% of SER-109 recipients experienced *C. difficile* recurrence, compared with 41% of placebo recipients. Seres is building up the candidate's safety database, in preparation for a regulatory filing. In July, it partnered with Nestle Health Science to co-commercialize SER-109, in a deal worth US$125 million upfront and up to $475 million in milestones.

"As with SER-109, we will again follow the science and the data, conduct a rigorous scientific analysis, and determine the optimal path forward for our [ulcerative colitis] franchise," said Eric Shaff, Chief Executive Officer at Seres.

Results from other companies working in this space — including Vedanta Biosciences, Finch Therapeutics, Rebiotix and NuBiyota — could also turn things around for live, microbiome-based therapeutics. These firms have candidates in clinical trials for *C. difficile* infection, ulcerative colitis, inflammatory bowel disease, cancer and other indications.

Asher Mullard