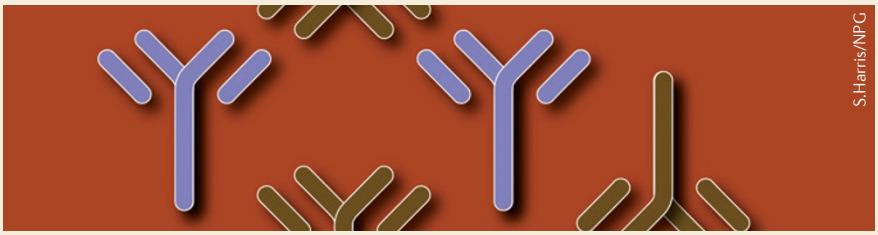
NEWS IN BRIEF



EMA greenlights Novartis' first-in-class IL-17 inhibitor

EU regulators recommended approval for Novartis' secukinumab for first-line treatment of plaque psoriasis, ahead of an anticipated FDA approval.

The lowdown: Interleukin-17 (IL-17) was first identified in 1993, and the cytokine was quickly recognized to have a key role in many inflammatory and autoimmune diseases. Twenty-two years on, the first IL-17 inhibitor is set to hit the market. The European Medicines Agency has given the thumbs up to Novartis' secukinumab for plaque psoriasis, and a final approval from the European Commission will come through shortly. In clinical trials, the drug was significantly superior to Amgen's tumour-necrosis factor (TNF)-targeting etanercept at 12 weeks. In October, an independent US Food and Drug Administration advisory panel voted unanimously that the available data support an approval of secukinumab for plaque psoriasis in the United States as well.

The drug is in Phase III trials for psoriatic arthritis, ankylosing spondylitis and rheumatoid arthritis as well. Analysts expect the drug to hit blockbuster status by 2019, according to the Thomson Reuters Cortellis database.

Two other antibodies targeting the IL-17 pathway are in late-stage development: one against the IL-17 receptor (IL-17R) and the other against IL-17. Amgen and AstraZeneca's brodalumab, which targets IL-17R, is in Phase III trials for psoriasis and psoriatic arthritis. In November, the companies reported the third Phase III psoriasis success for the antibody, with two trials showing superiority over Johnson & Johnson's IL-12- and IL-23-targeting ustekinumab. Eli Lilly's ixekizumab is in Phase III trials for the same two indications. In August, the company presented the first Phase III psoriasis data from the drug, showing that it was superior to etanercept. The sponsors debate the merits of targeting the cytokine itself versus the receptor (*Nature Rev. Drug Discov.* **12**, 815–816; 2013). Regulatory filings for each of the two antibodies are expected in the first half of 2015.

AbbVie's ABT-122 bispecific antibody, which targets IL-17 and TNF, is in Phase II development for rheumatoid arthritis.

FDA approves first bispecific

US regulators approved Amgen's blinatumomab — a CD19- and CD3-targeting bispecific antibody — for acute B-cell lymphoblastic leukaemia, 5 months ahead of schedule.

The lowdown: The US Food and Drug Administration's accelerated approval of Amgen's breakthrough designee blinatumomab marks the first US approval for a bispecific antibody. The bispecific T-cell engager (BiTE) immunotherapy binds CD19 on the surface of B-cell lymphoblasts and CD3 on the surface of T cells, bringing the cell types together and driving an immune response to malignant cells. In clinical trials in 185 adults with acute B-cell lymphoblastic leukaemia (B-ALL), 32% of treated patients had complete remissions for an average of 6.7 months.

Blinatumomab and the BiTE technology were initially developed by Micromet, which was acquired by Amgen in 2012 for US$1.16 billion. Financial analysts expect sales of over $300 million for the bispecific by 2019, according to Thomson Reuters Cortellis. Uptake of blinatumomab may be limited by competition from other exciting drugs in the ALL pipeline, including Pfizer's antibody–drug conjugate inotuzumab ozogamicin and Novartis' Phase II personalized cell therapy CTL019. Blinatumomab's administration route (it is continuously infused with a portable mini-pump for 28 days, and so requires visits to the hospital every 48 hours to change infusion bags) and adverse events (including neurotoxicity and symptoms of cytokine-release syndrome) may also keep sales down.

Blinatumomab leads an explosion of the bispecific antibody pipeline. At least 18 other bispecifics are in clinical development for oncology, autoimmune and infectious-disease indications (*Nature Rev. Drug Discov.* **13**, 799–801; 2014). Trion Pharma secured European approval for a first (rat–mouse hybrid) bispecific in 2009, but the newer bispecific antibody formats that now fill the pipeline are more stable, less immunogenic and easier to manufacture.

Gene therapy pushes the US$1 million price barrier

Chiesi and uniQure have proposed a price tag of roughly US$1.1 million for their alipogene tiparvovec gene therapy.

The lowdown: Gene therapies pose a pricing dilemma for industry. If drugs are only administered once and, in many cases, to small patient populations, how can drug companies recoup development costs and turn a profit? Pricing negotiations for uniQure and Chiesi's alipogene tiparvovec — which is approved in Europe for lipoprotein lipase (LPL) deficiency — provide a first insight into how drug developers and payers are thinking about the problem.

The firms have opened the negotiations for their therapy — an adeno-associated virus (AAV) vector that carries the LPL gene — at around US$1.1 million per dose. The companies reportedly considered pursuing an annuity-pricing model, under which payers would make small upfront payments followed by annual payments for a fixed amount of time or for as long as the treatment continued to provide benefit. But while the firms have shown that their treatment reduces the incidence of pancreatitis in LPL-deficient patients, patients have to be hospitalized for up to 3 days to assess a battery of biomarkers to confirm benefit. Confounding factors such as diabetes and diet also complicate the analysis. Other gene therapies, with simpler disease outcomes, may be better candidates for annuity-pricing models.

A single dose of the gene therapy can provide benefit for at least 6 years, says the company. This brings its annualized cost down to $183,000, which is cheaper than the annual price of many enzyme-replacement therapies that are needed for the lifetime of patients with rare diseases. There are thought to be 150–200 patients in Europe who would be eligible for the gene therapy.

The negotiations are ongoing.