Innovative approaches to treat immuno-inflammatory diseases

Companies are investing in a range of pioneering strategies in the search for the next therapeutic advances for immuno-inflammatory diseases.

Biopharma Dealmakers

For several years, Humira (adalimumab; AbbVie), a monoclonal antibody (mAb) that inhibits the pro-inflammatory cytokine tumor necrosis factor, has been the top-selling drug globally, based on its use to treat multiple immuno-inflammatory disorders such as rheumatoid arthritis and inflammatory bowel disease (IBD). Although successful, a substantial proportion of patients do not respond to established drugs such as Humira, and the search continues for new approaches that might be effective for these individuals. Targeting signaling by other pro-inflammatory cytokines is one approach, as exemplified in Horizon Therapeutics' May deal with Q32 Bio (see below) to develop its mAb targeting interleukin-7 receptor subunit alpha (IL-7Rα). Ion channels on immune cells are another class of promising targets, such as Kv1.3, which is the focus of a June deal between Lilly and D. E. Shaw Research. There is also growing interest in the potential to harness immune cells themselves as therapeutics, which is highlighted by Bristol Myers Squibb's August deal with GentiBio to develop engineered regulatory T cells to re-establish immune tolerance in IBD.

Horizon Therapeutics signs deal with Q32 Bio to develop its IL-7Rα-targeted antibody for the treatment of autoimmune diseases

Deal announced: 15 May 2022

Potential deal value: $700 million

Deal overview

- Q32 Bio is a clinical-stage company developing biologics that target immune-system regulators including interleukin-7 (IL-7) and thymic stromal lymphopoietin (TSLP) to treat severe autoimmune and inflammatory diseases.
- The deal focuses on Q32 Bio's most advanced clinical candidate, ADX-914, a fully human mAb that binds to IL-7Rα, one of the components of the IL-7 receptor. ADX-914 thereby blocks signaling mediated by IL-7 and TSLP, which has been implicated in driving T cell-mediated pathological processes in autoimmune diseases (*Front. Immunol.* **11**, 1557; 2020). At the time the deal was signed, Q32 had completed a biomarker-enabled phase 1 study showing pharmacological effects of ADX-914 on T cells in healthy volunteers.
- Under the terms of the deal signed in May, Horizon will pay $55 million to Q32 to conduct two phase 2 trials of ADX-914, one in atopic dermatitis (in which the first patient was dosed in October 2022) and one in another autoimmune disease to be determined. Horizon has an option to acquire the ADX-914 program following completion of the phase 2 trials, and if it exercises the option, Q32 may be eligible to receive up to a further $645 million in closing and milestone payments, as well as royalties on sales.

Lilly licenses Kv1.3 ion-channel inhibitor for the treatment of immunological and inflammatory diseases from D. E. Shaw Research

Deal announced: 13 June 2022

Potential deal value: $535 million

Deal overview

- D. E. Shaw Research applies computational methods such as molecular-dynamics simulations and machine learning to design drug candidates to be tested by contract research organizations or external partners. Four of its candidates have entered into clinical trials so far, three of which are targeted cancer drugs developed through a partnership with Relay Therapeutics, a separate company that D. E. Shaw Research co-founded in 2016.
- The company's first independently developed drug candidate, DES-7114, is an orally administered selective inhibitor of the ion-channel protein Kv1.3, which is involved in T cell proliferation and inflammatory cytokine production (*J. Transl. Autoimmun.* **5**, 100146; 2022). DES-7114 has been reported to have efficacy in preclinical models of inflammatory and autoimmune diseases, including ulcerative colitis, Crohn's disease and atopic dermatitis, and a phase 1 trial in healthy volunteers was successfully completed in 2022.
- In June, Lilly and Company signed a deal to exclusively license D.E. Shaw Research's Kv1.3 targeted therapeutics for immunological and inflammatory diseases, including DES-7114. Lilly agreed to pay $60 million upfront and up to $475 million in potential development and commercial milestone payments, as well as royalties on sales.

GentiBio enters collaboration with Bristol Myers Squibb to develop engineered regulatory T cell therapies for inflammatory bowel diseases

Deal announced: 10 August 2022

Potential deal value: $1.9 billion

Deal overview

- GentiBio is a preclinical-stage company developing engineered regulatory T cells (T_{reg}s) to treat patients with immuno-inflammatory and allergic diseases by providing tissue-specific immune suppression. It launched in August 2020 with $20 million of seed funding, and closed a $157 million Series A financing round in August 2021.
- T_{reg}s are a subset of immune cells that have a key role in maintaining immune system homeostasis by dampening excessive inflammation, and deficiencies in their function can lead to a wide range of immune disorders (*Nat. Rev. Drug Discov.* **18**, 749–769; 2019). As the use of endogenous T_{reg}s is limited by factors including their rarity and heterogeneity, GentiBio has developed engineering approaches to produce T_{reg}s from more abundant cell sources and guide the engineered cells to the desired tissue. Its lead candidate is GNTI-122, an autologous engineered T_{reg} product for treating type 1 diabetes that is in IND-enabling studies.
- In August, Bristol Myers Squibb entered a partnership with GentiBio to work on up to three programs applying genetically modified T_{reg}s to treat inflammatory bowel diseases. The deal could involve payments of up to $1.9 billion to GentiBio by Bristol Myers Squibb, including an undisclosed upfront payment.