DEAL WATCH

Biogen acquires Stromedix to pursue novel fibrosis therapy

Biogen Idec has agreed to buy Stromedix for an upfront fee of US$75 million and up to $487.5 million in milestone payments. Stromedix is a privately held biotechnology company focused on innovative therapies for fibrosis and organ failure. Its lead compound, STX-100 (which it licensed from Biogen in 2007), is a humanized monoclonal antibody against αVβ6 integrin, which is currently in a Phase II trial to treat idiopathic pulmonary fibrosis (IPF).

Fibrosis is the excessive and persistent accumulation of connective tissue matrix (scar tissue) following injury, which disrupts normal tissue architecture and function, ultimately causing organ failure. "In some fibrotic diseases (for example, alcoholic cirrhosis), the initiating injury is clear, but in many others (for example, IPF) the initial insult is unknown," notes Dean Sheppard, Lung Biology Center, University of California, San Francisco, USA, whose laboratory collaborated with Biogen in the original development of STX-100. "Although pathological fibrosis is a major cause of organ dysfunction in a number of chronic diseases, there are essentially no currently available effective treatments targeting the fibrotic process directly," he adds.

The development of therapies for fibrosing lung diseases, such as IPF, represents a particular challenge. Luca Richeldi, Centre for Rare Lung Diseases, University Hospital of Modena, Italy, explains: "Given the relatively low prevalence of each of these entities, trials with survival as the primary end point require considerable logistic and financial support. We need to identify robust surrogate end points and non-invasive prognostic biomarkers in order to make randomized trials more feasible." IPF is characterized by the irreversible loss of pulmonary function, progressive dyspnoea and cough. Treatment is largely palliative, as there are no drugs approved specifically for IPF by the US Food and Drug Administration. However, several novel agents are currently being investigated (*Nature Rev. Drug Discov.* **9**, 129–140; 2010).

STX-100 selectively targets transforming growth factor-β (TGFβ) — a cytokine that drives the profibrotic response of fibroblasts following injury — through inhibition of αVβ6 integrin. "TGFβ is a major player in experimental lung fibrosis models, and has a crucial role in human disease. However, as a critical molecule in normal pulmonary homeostasis, its inhibition might result in unwanted effects. For this reason, targeting a specific component of the pathway, such as integrin αVβ6, might lead to safer and more specific TGFβ inhibition," says Richeldi. Sheppard explains further: "Although TGFβ is stored in the extracellular matrix of most organs, it is in a latent form that needs to be 'activated' to have any biological effect. In the lung, kidney and biliary tract, the αVβ6 integrin appears to have a major role in pathological TGFβ activation, as inhibition of this integrin dramatically inhibits pathological fibrosis at these sites. However, this integrin is not needed for all TGFβ activation."

Integrins have diverse biological roles and are attractive drug targets in several diseases, but the clinical development of integrin inhibitors has proved to be challenging. However, "unlike other integrins, the αVβ6 integrin appears to have one major ligand (latent TGFβ) and a relatively restricted tissue distribution (the most dramatic expression is on epithelial cells in injured or inflamed organs), which both increase its value as a drug target", says Sheppard.

STX-100 has exhibited significant antifibrotic activity in preclinical animal models of fibrotic disease, and a favourable safety and tolerability profile in a Phase I trial. "Thus far, the most convincing evidence for the utility of targeting this integrin comes from mouse models. The results of the ongoing clinical trials will be critical for determining whether it is also effective in treating fibrotic diseases in people," concludes Sheppard.

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