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Sanofi Adds To Immunology Pipeline In Collaboration With Recludix

by Joseph Haas

French pharma gets global rights at the start of Phase II for the US biotech's preclinical program for inhibiting the STAT6 protein in respiratory and dermatologic disorders.

Privately held *Recludix Pharma* debuted in 2021 with a $60m series A financing to back its theory for targeting the SH2 domain of the signal transducer and activator of transcription (STAT) protein family and achieved validation for that approach on 20 July through a partnership with *Sanofi* that will bring the San Diego biotech $125m from an upfront fee and a near-term milestone payment.

In exchange for the money plus up to $1.2bn in future milestone fees, Sanofi gets global clinical development and commercial rights to Recludix's preclinical STAT6 program, which CEO Nancy Whiting said could yield novel small molecule therapies for atopic dermatitis, chronic obstructive pulmonary disease, asthma and allergies. Some of those diseases are indications already treated by Sanofi and *Regeneron Pharmaceuticals, Inc.*'s blockbuster biologic Dupixent (dupilumab).

Recludix will develop the STAT6 program up to the start of Phase II, at which point Sanofi takes over. In addition to the potential for up to $1.2bn in milestone payments, Recludix is also entitled to royalties and has an option to share profits and losses in the US.

Additionally, the deal leaves Recludix with full ownership of its preclinical STAT3 program, which Whiting said is slightly farther along in lead-optimization work. Successfully targeting the SH2 domain in STAT3 proteins could yield new drugs for psoriasis, rheumatoid arthritis, Crohn's disease and ulcerative colitis, she said in an interview. Beyond that, the company has earlier-stage preclinical programs targeting the SH2 domain for cancer and inflammatory diseases, but Recludix's current focus is the STAT3 and STAT6 programs in immunology and inflammation.

Recludix began lab work in 2020, ahead of its November 2021 series A round that brought in $60m. (Also see "*Finance Watch: Venture Capital Drives Record-Breaking Year For Cell And Gene Therapies*" - Scrip, 25 Nov, 2021.) Whiting said the company's scientific founders began discussing the potential of targeting the STAT protein SH2 domain – which multiple companies worked on during the 1990s and 2000s, before determining the pathway was undruggable – with state-of-the-art chemistry and proprietary tools they would build themselves. Recludix's discovery engine stems from DNA-encoded libraries.

"This deal with Sanofi we absolutely see as validating to the approach that we've taken to drug ... these targets and the potential value of unlocking them," Whiting said. "It will really help our company by bringing in some non-dilutive capital and help us continue to move forward our wholly owned programs as well."

STAT Protein Inhibition Factors In Multiple Therapeutic Areas

Targeting the SH2 domain offers therapeutic promise because the STAT6 protein plays a critical role in the IL-4 and IL-13 signaling pathways that modulate Th2-mediated diseases in the respiratory and dermatologic space, the exec explained. Notably, IL-4 and IL-13 are the two cytokines targeted by Sanofi/Regeneron's Dupixent, which is approved for atopic dermatitis, asthma and other inflammatory diseases.

Meanwhile, a STAT3 inhibitor could be critical to addressing when TH17 is in overdrive, which can result in gastrointestinal and autoimmune disorders.

The SH2 domain regulates protein-protein interactions and is similar in each of the seven STAT proteins, Whiting noted, but each has slight differences as well. After STAT proteins interact with a JAK protein and dimerize, they work as transcription factors, producing changes in cells. Inhibiting the SH2 domain of a STAT monomer can block binding and ultimately block gene transcription, she said.

"So, STAT proteins are really great targets," the exec said. "For a long time, companies have wanted to drug the STAT proteins, and the SH2 domain is likely the best place to drug that. The reason why people have failed in the past is because that part of the protein – in fact, the whole STAT protein – is kind of a flat, shallow protein. There aren't any deep pockets or nooks and crannies for a drug to hook into."

"A big challenge for us has been to find a way to very potently bind that flat protein with high affinity to give us high potency and then also to do that with an agent that can be taken orally," Whiting continued.

The STAT6 program is at the tail end of lead optimization, the CEO said, so Recludix anticipates being able to file an investigational new drug (IND) application and enter clinical development in

2025. The wholly owned STAT3 program is farther advanced and could enter the clinic in 2024, she added.

The key to the STAT6 program is finding a candidate with “exquisite selectively,” she noted. “We've shown really great efficacy in multiple animal models of disease and also oral bioavailability,” Whiting said. “That was the other key thing that we needed to demonstrate. So, we are just finishing up lead optimization now and then we'll enter a formal candidate-selection phase.”

The deal with Sanofi should extend Recludix’s cash runway for another year or so, the exec said, but the company still intends to raise a series B round. “We're still going to do a series B,” she said. “This just gives us some more flexibility as to when we want to do that, so we'll be able to choose our time of when to bring in additional capital and additional investors into the syndicate.”

For Sanofi, this is the French pharma’s second significant deal in the immunology space in 2023, following its $2.9bn acquisition of *Provention Bio, Inc.* in March. (Also see "*Sanofi Goes All In For Type 1 Diabetes With Provention Buy*" - Scrip, 13 Mar, 2023.) Gaining full control of type 1 diabetes drug Tzield (teplizumab), for which it already was partnered with Provention on US commercialization, was the driver of that deal.