Emerging Company Profile

Innovimmune: Structuring immunotherapies

By Chris Cain
Senior Writer

Innovimmune Biotherapeutics Inc. is using structure-based drug design to develop small molecules that precisely modulate the activity of autoimmune targets that other companies are also targeting, but for which there are not yet marketed drugs.

The company is focusing its discovery efforts against proteins that could be targeted in a variety of inflammatory and autoimmune indications.

President and CEO Anderson Gaweco cited **Pfizer Inc.**'s tofacitinib as an example of the types of compound Innovimmune hopes to develop. The oral pan-Janus kinase (JAK) inhibitor is under FDA review to treat rheumatoid arthritis and is in seven Phase II or III trials in additional indications.

Gaweco had worked on the tofacitinib program at Pfizer and was most recently CMO at **Veloxis Pharmaceuticals A/S**, which is developing the immunosuppressant LCP-Tacro tacrolimus to prevent transplant rejection.

Innovimmune is using its structure-based approach to take a new look at familiar autoimmune targets. The company's lead programs target RAR-related orphan receptor C thymus-specific isoform (RORgamma2; RORgammaT) and macrophage migration inhibitory factor (MIF).

RORgammaT is a nuclear hormone receptor that is a key regulator of T helper type 17 (Th17) cell differentiation. Th17 cells are normally produced in response to infection, but have been linked to the development of autoimmune diseases.

Th17 cells produce multiple pro-inflammatory cytokines including IL-17. There are a number of anti-IL-17 mAbs in development, including **Eli Lilly and Co.**'s ixekizumab and **Novartis AG**'s secukinumab. Both biologics are in Phase III testing for autoimmune conditions.

Gaweco said small molecule RORgammaT inhibitors could offer both delivery and safety advantages over mAbs because the former can be designed to fine tune the amount of IL-17 produced without completely blocking the target. Side effects seen in Phase II trials of IL-17 mAbs include an increased rate of infection and cases of neutropenia.

Innovimmune Biotherapeutics Inc.

New York, N.Y.
Technology: Structure-based design of oral anti-inflammatory compounds
Disease focus: Autoimmune, inflammation
Clinical status: Preclinical
Founded: 2010 by Anderson Gaweco
University collaborators: None
Corporate partners: None
Number of employees: 9
Funds raised: Not disclosed
Investors: Not disclosed
CEO: Anderson Gaweco
Patents: None issued

Innovimmune's IL-17 program, INV-17, is in lead optimization. Gaweco said the company has identified compounds that inhibit the target in functional assays.

"We don't have the resources of pharma to screen libraries of millions of compounds. We use the more rational approaches of structure-based drug design and fragment-based drug design," he said.

The company is deciding among eight autoimmune indications to pursue for this program, including RA and multiple sclerosis (MS).

At least three other companies have small molecule RORgammaT inhibitors in preclinical development. In March 2011, **Lycera Corp.** partnered with **Merck & Co. Inc.** to develop compounds against the target. Last December, **Karo Bio AB** partnered with Pfizer to develop RORgammaT modulators. **Visionary Pharmaceuticals Inc.** also has a RORgammaT program.

Innovimmune's second program in lead optimization, INV-88, targets the proinflammatory cytokine MIF.

The company initially is focused on inhibiting MIF to treat RA, but said there are at least 10 potential therapeutic areas of interest.

Previous efforts to target MIF have focused on inhibiting its enzymatic tautomerase activity, which did not completely block the protein's proinflammatory function. However, a team of European researchers showed in a 2007 *Nature Medicine* paper that MIF is a ligand of CXC chemokine receptor 2 (CXCR2) and CXCR4, suggesting that blocking this interaction could provide another means to target MIF activity.

According to Gaweco, the company has developed potent MIF inhibitors that target several important enzymatic, allosteric and receptor pharmacophoric sites and therefore offer more complete functional inhibition of the target.

Carolus Therapeutics Inc. also is developing MIF inhibitors that disrupt the interaction between the protein and its receptors. The company's peptide inhibitors are in preclinical development for a variety of inflammatory-related diseases.

Baxter International Inc. has a humanized anti-MIF mAb in Phase I to treat solid tumors and lupus nephritis.

In June, the company received a $600,000 Small Business Innovation Research (SBIR) award to fund the MIF program.

The company is not fundraising at this time. "Early on we had interest in venture capital backing, but because of our data, we think early partnering with a big pharma for autoimmune would be the best fit," said Gaweco. In the meantime, "we are advancing into IND-enabling studies."

The company hopes to partner one program as soon as possible, and retain control of the other program for in-house development through at least Phase I.

Innovimmune has filed several composition of matter patents on its small molecule portfolio.

COMPANIES AND INSTITUTIONS MENTIONED

Baxter International Inc. (NYSE:BAX), Deerfield, Ill.
Carolus Therapeutics Inc., San Diego, Calif.
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Innovimmune Biotherapeutics Inc., New York, N.Y.
Karo Bio AB (SSE:KARO), Stockholm, Sweden
Lycera Corp., Ann Arbor, Mich.
Merck & Co. Inc. (NYSE:MRK), Whitehouse Station, N.J.
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
Pfizer Inc. (NYSE:PFE), New York, N.Y.
Veloxis Pharmaceuticals A/S (CSE:VELO), Horsholm, Denmark
Visionary Pharmaceuticals Inc., San Diego, Calif.