EMERGING COMPANY PROFILE

GOBBLING GLOBULINS

BY EMILY CUKIER-MEISNER, SENIOR WRITER

Syntimmune Inc. is targeting a receptor that mediates the life span and activity of immunoglobulin G to control autoimmune disease more precisely and potentially more safely than broadly acting agents. The company aims to differentiate its lead program from more advanced ones by optimizing the compounds to block multiple functions of the receptor-IgG interaction.

Many autoimmune diseases are held at bay with effective yet toxic agents with broad activity on the immune system. For example, immunosuppressants, B cell-depleting agents and high-dose steroids all increase the risk of infection, and intravenous immunoglobulin (IVIG) carries risks of renal failure and hemolytic complications.

Syntimmune is targeting the Fc fragment of IgG receptor transporter alpha (FCRN; FCGRT) to tamp down only the immune pathways activated by IgG antibodies to treat diseases associated with high levels of IgG. These include myasthenia gravis, heparin-induced thrombocytopenia (HIT), immune thrombocytopenia purpura (ITP), inflammatory bowel disease (IBD) and rheumatoid arthritis.

While most proteins are recycled naturally via lysosomal degradation, FCRN rescues IgGs by binding to them in endosomes and returning them to the bloodstream to maintain the high IgG levels needed for immunity.

Syntimmune's lead program, SYNT001, is a mAb that blocks the FCRN-IgG interaction. Preventing IgG from binding to FCRN leads to decreased serum IgG levels, which in IgG-driven pathologies could mean reduced levels of autoantibodies.

COO Laurence Blumberg said FCRN also plays roles in the early steps of innate and adaptive immunity, such as facilitating inflammatory cytokine secretion and antigen presentation.

"The ability to drive innate and adaptive immunity is significantly diminished when you block the FCRN-IgG interaction," he said.

SYNTIMMUNE INC.
New York, N.Y.

Technology: Blockers of FCRN interactions with its ligands

Disease focus: Autoimmune, cancer

Clinical status: Phase I

Founded: 2013 by Richard Blumberg and Laurence Blumberg

University collaborators: University of Pennsylvania, The Jackson Laboratory, Brigham and Women's Hospital, University of Oslo

Corporate partners: Undisclosed

Number of employees: 5

Funds raised: $28 million

Investors: Apple Tree Partners, Baxalta Ventures, Partners Innovation Fund

CEO: David De Graaf

Patents: Undisclosed

President and CEO David De Graaf added that blocking that interaction with an anti-FCRN agent should be "relatively reversible," and spares non-IgG antibodies as well as the B cells needed to generate antibodies, which could reduce the risk of infection, compared to non-specific therapies.

"It specifically dismantles the IgG machinery while preserving other immunoglobulins and immune cell populations," said De Graaf.

Syntimmune has unpublished data from a Phase Ia study in healthy volunteers showing that SYNT001 reduced IgG levels to below a clinically meaningful threshold within five days. Blumberg said the response lasted for "weeks," and that the only notable adverse events were headaches. Syntimmune declined to give a timeline for publishing the data.

At least four other companies are developing anti-FCRN agents. UCB Group's UCB7665 is in Phase II testing to treat primary immune thrombocytopenia. argenx N.V.'s ARGX-113 is in Phase II testing to treat myasthenia gravis. Momenta Pharmaceuticals Inc.'s M281 is in Phase I testing in healthy volunteers. And HanAll Biopharma Co. Ltd. plans to begin clinical testing of HL161 early this year.

Blumberg said SYNT001 was optimized to bind FCRN at both neutral and endosomal pH, and to block FCRN's three functions in recycling IgG and driving innate and adaptive immunity. He said Syntimmune believes its optimization strategy could make the molecule best in class, though he declined to give details.

"We engineered what we think are ideal binding characteristics at both of those pHs," said Blumberg.

Spokesperson Minjae Shin said HanAll thinks all the anti-FCRN programs will have similar effects on innate and adaptive immunity, and that differentiation will instead come from immunogenicity and potency.

argenx spokesperson Joke Comijn declined to compare the programs directly but said ARGX-113 is unique because it uses an Fc-fragment rather than a full-length antibody and incorporates argenx's proprietary mutations to increase Fc/FCRN binding. Momenta declined to comment, and UCB was unable to comment in time for publication.

Syntimmune plans to conduct and report data from Phase Ib/IIa studies of SYNT001 this year to treat two undisclosed Orphan diseases.

Syntimmune expects its funding to last through the studies; it is raising a series B round of undisclosed size to bring SYNT001 through registrational studies.

Behind SYNT001, Syntimmune has preclinical programs that block FCRN's interactions with other ligands, including albumin. bc

COMPANIES AND INSTITUTIONS MENTIONED

argenx N.V. (Euronext:ARGX), Breda, the Netherlands

HanAll Biopharma Co. Ltd. (KOSDAQ:009420), Seoul, South Korea

Momenta Pharmaceuticals Inc. (NASDAQ:MNTA), Cambridge, Mass.

Syntimmune Inc., New York, N.Y.

UCB Group (Euronext:UCB), Brussels, Belgium