Disease-Selective Treatment for Rheumatoid Arthritis and Lupus with Anti-IDO2 Antibodies

Technology Readiness Level 6: Demonstrated in Relevant Environment

Lead Investigators

Lisa Laury-Kleintop, PhD
Laura Mandik-Nayak, PhD
Lankenau Institute for Medical Research

Unmet Need

Rheumatoid Arthritis (RA) is a chronic autoimmune disease that occurs when the body's immune system attacks joints, creating debilitating inflammation and pain. Left unchecked, it can permanently damage joints and possibly parts of the cardiovascular and respiratory system. Current treatments ease symptoms or slow disease course, but they do not target the disease itself. Instead, they simply ablate the immune system generally, elevating risks of infection and other immune-based diseases such as cancer.

The market for RA treatment is expected to increase from US $1.7B in 2017 to US $2.3B in 2022 according to the market information resource BCC Research.

Lupus (SLE) is a systemic autoimmune disorder associated with chronic inflammation that can damage any part of the body. An estimated 1.5 million Americans have lupus, with an additional 16,000 new cases reported each year, according to the Lupus Foundation of America. It is believed that about 5 million people throughout the world have lupus. There is no cure for lupus, and as in RA, current treatments are not disease-selective.

The global market for lupus treatment, which includes systemic lupus erythematosus and lupus nephritis, is expected to increase from US $1.2B in 2015 to US $3.2B by 2025, according to research and consulting firm GlobalData.

Opportunity

IDO2 targeting offers a disease-selective approach to treat autoimmune disease that is currently lacking in the field. Present treatments generally blunt inflammatory signals or suppress the native immunity as a whole, producing a host of side-effects including heightened risks of infection and cancer. IDO2-targeting antibodies created at LIMR act selectively within B cells to attenuate pathogenic autoantibody production without affecting normal immune function.

Unique Attributes

The invention is unique in its ability to target a disease-selective mediator of autoimmune disease. It is also technically advanced on the basis of targeting an intracellular antigen, usually considered inaccessible to antibody-based therapies. In preclinical models of RA, systemic administration with the inventors' cell-permeable IDO2 monoclonal antibodies specifically enter and disrupt the function of pathogenic B cells where IDO2 acts to drive autoimmune pathophysiology. Treatment with anti-IDO2 antibodies reduces the levels of autoreactive T and B cells and alleviates pathogenic symptoms in settings of autoimmunity, rather than simply suppressing immune function or inflammatory signaling like presently available biologics or small molecule drugs. In summary, LIMR's innovative approach targets root autoimmune processes that are not generally needed for native immunity or inflammation, with the potential for disease-selective utility with lower side-effects than existing therapies.

Continued on back

Clinical Applications

Beyond treatment of autoimmune arthritis and lupus, clinical development against various orphan autoimmune diseases, e.g., myasthenia gravis, is conceivable as a pathway to proof of concept.

Stage of Development

Technology Readiness Level 6: Demonstrated in Relevant Environment

Preclinical genetic and therapeutic proof of concept in mice is established. The current stage of work is humanization of IDO2-binding antibodies with suitable properties for clinical translation.

Intellectual Property

1. IDO2 nucleic acid sequences:
   US Patent No. 8,058,416 issued 11-15-2011.
   US Patent No. RE49708E1 issued 10-24-2023 (cDNA sequences).
2. IDO2 antibodies:
   US Patent No. 8,436,151 issued 5-7-2013.
   US Patent Application No. 20230242674A1 published on 8-3-2023. Parallel applications pending in JP, EP, CA.
3. IDO2 antibody uses:
   US Patent Application No. 20190062452 published 2-2-2017. Parallel issuances in AU, CA and applications pending in JP, EP.

Collaboration Opportunity

Partners are sought to humanize and develop IDO2 monoclonal antibodies for clinical testing.

References and Publications

- Merlo LM, Pigott E, Duhadaway JB, Grabler S, Metz R, Prendergast GC and Mandik-Nayak L. (2014). IDO2 is a critical mediator of autoantibody production and inflammatory pathogenesis in a mouse model of autoimmune arthritis. J Immunol 92: 2082-90.
- Merlo LM, DuHadaway JB, Grabler S, Prendergast GC, Muller AJ and Mandik-Nayak L. (2016). IDO2 Modulates T Cell-Dependent Autoimmune Responses through a B Cell-Intrinsic Mechanism. J Immunol 196: 4487-97.
- Merlo LM, Grabler S, DuHadaway JB, Pigott E, Manley K, Prendergast GC, Laury-Kleintop, LD and Mandik-Nayak L. (2017). Therapeutic antibody targeting of indoleamine-2,3-dioxygenase (IDO2) inhibits autoimmune arthritis. Clin Immunol 179: 8-16.

INSTITUTIONAL CONTACT

George C. Prendergast, PhD
+1 484.476.8475
prendergast@limr.org

L2C PARTNERS CONTACT

Merle Gilmore, MBA
+1 610.662.0940
gilmore@l2cpartners.com

Alex Toglia, MS
+1 610.937.1067
Toglia@l2cpartners.com