New Therapeutic for Irritable Bowel Disease

EXECUTIVE SUMMARY

TEAM

Eric Ortlund, PhD
Technical Investigator

Nathan Jui, PhD
Technical Investigator

John Calvert, PhD
Technical Investigator

FUNDING

$155K Biolocity Grant

INTELLECTUAL PROPERTY

1 issued patent, 1 patent pending

Technology available for licensing and partnership

STATUS

Lead Candidate selected, undergoing pharmacokinetic characterization

TECHNOLOGY

This therapeutic is a small molecule that will restore intestinal health for patients with inflammatory bowel disease (IBD). The drug activates Liver Receptor Homolog-1 (LRH-1) with high potency, which in turn increases innate steroid production specifically at the site of inflammation in the gut. Because LRH-1 is expressed primarily in the liver and intestine, agonism of LRH-1 emulates the anti-inflammatory effects of current steroid treatments while minimizing the adverse effects associated with systemic steroid exposure.

LRH-1 has been recognized as an important biological target for the treatment of IBD but was thought to be undruggable with small molecules. Drs. Jui and Ortlund have designed a molecule with greater potency and more favorable pharmacokinetic properties than previously existing LRH-1 agonists for the treatment of IBD.

MARKET NEED

Inflammatory Bowel Disease (IBD) is a progressive chronic disease characterized by flare-ups and remissions. In the US alone IBD effected 1.7M citizens in 2017 and is projected to rise to 2M in 2024. IBD is not curable; treatment goals are to minimize symptoms, improve quality of life, and minimize progression and complications of the disease. The first line of treatment for patients with IBD is aminosalicylates. These nonsteroidal anti-inflammatories are popular due to their tolerability; however, these drugs often fail to sustain disease remission. Further, they work best in the colon and are not particularly effective if the disease is limited to the small intestine. During flare-ups, patients may be prescribed steroids, which are often an effective treatment for IBD; however, serious side effects preclude their sustained use. If steroids are insufficient, patients may be prescribed immunosuppressants or biologic therapies; regrettably, these therapeutics increase risk for serious side effects such as infection, renal and hepatic toxicity, and lymphoma. Most patients require a combination of medications to treat their IBD, and the overall efficacy of current medications is at best, 50%. Patients that do not achieve adequate symptom control from drugs may require surgery. There is a need for a drug that effectively targets inflammation without the detrimental side effects seen with treatments inducing global immunosuppression.

Drug sales for IBD are sizeable: the global market is expected to grow at 4.1% CAGR and reach USD $21.3 Billion by 2026. The U.S. and Europe currently have the largest markets, but the Asia Pacific market is growing rapidly. Prescription treatments are forecasted to be worth $5.9 Billion globally in 2021, representing a CAGR of 8.9%.

STATUS

To date, the team has tested its LRH-1 agonist in two model systems of IBD: 1) A DSS-induced model of colitis in mice with endogenous LRH-1 knockout and human LRH-1 receptor overexpression. And, 2) a T-cell model in mice with endogenous LRH-1 knockout and human LRH-1 receptor overexpression. Additionally, the team has completed lead optimization studies and is evaluating pharmacokinetics of two lead candidate compounds. Currently, target engagement is being assessed after oral administration of the compounds in industry relevant IBD mouse models.

For more information on this technology email biolocity@gatech.edu or contact:
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