Innovate Biopharmaceuticals Presents Oral Poster at European Association for the Study of the Liver (EASL) Demonstrating Positive Effect of Larazotide on Reduced Intestinal Permeability in a NASH Preclinical Study

April 11, 2019

Selected for oral poster tour by the scientific committee in the gut microbiota section at the International Liver Congress™ 2019 of EASL

Data presented as a poster showing significant effect on gut epithelial integrity thought to be key for bacterial translocation leading to NAFLD and NASH

RALEIGH, N.C., April 11, 2019 (GLOBE NEWSWIRE) -- Innovate Biopharmaceuticals, Inc. (Nasdaq: INNT), a clinical stage biotechnology company focused on developing novel therapeutics for autoimmune and inflammatory diseases, with its lead drug, larazotide acetate, comprising a new class of medicines based on gut-restricted peptides which re-normalize the gut-epithelial barrier and the gut-liver axis, announced that data demonstrating proof-of-concept in an established model of nonalcoholic steatohepatitis (NASH) will be presented at The International Liver Congress ™, the annual meeting of the European Association for the Study of the Liver (EASL), being held in Vienna, Austria, April 10-14, 2019. There are currently no treatments for nonalcoholic fatty liver disease (NAFLD) or NASH approved by the FDA.

The intestinal epithelium normally forms a tight seal separating the host from gut contents, via a well-regulated physical barrier. Tight junctions, one of the most important physiologic and pathologic structural complexes, regulate the subtle equilibrium among the gut microbiome, epithelial cells, and the intestinal mucosa, helping to maintain a delicate homeostasis. A meta-analysis based on five clinical studies showed that NAFLD and NASH patients are more likely to have altered gut permeability in comparison with healthy controls. This association of increased intestinal permeability was stronger particularly in NASH patients, demonstrating that the inflammatory changes observed in NASH might be caused by the increased intestinal permeability.[1] On a molecular level, NAFLD patients are hypothesized to exhibit dysregulated tight junction molecules, as shown by a genetic model of gut barrier dysfunction which resulted in more severe steatohepatitis vs. control mice, when fed a Western diet.[2]

In the study being presented today, researchers assessed the effects of larazotide in a preclinical model of NASH that develops from consumption of a specified diet, the DIAMOND™ mouse model. The preclinical model recapitulates NAFLD/NASH in response to a high fat, high sugar Western diet, including insulin resistance, obesity, and dyslipidemia, which parallels human disease progression.

The data has been selected as an oral short presentation as part of the *Poster Tour: Gut Microbiota & Liver Disease, Metabolism, Alcohol & Toxicity* section:

Section: Poster Tour - Gut Microbiota and Liver Disease, Metabolism, Alcohol & Toxicity

Poster Tour No. FRI-267: Serial measurement of serum dextran absorption by novel competition ELISA demonstrates larazotide acetate significantly improves "leaky gut" in a Western diet murine model of metabolic liver disease.

- Time: April 12, 2019 at 12:30 pm – 1:00 pm Central European Time (CET)
- Location: Meeting Point 3, Hall B Reed Messe Wien Exhibition & Congress Center
- *Presenter: Rebecca Caffrey, Ph.D.*

The paper poster presentation will be displayed in Reed Messe Wien Exhibition & Congress Center Hall B on Friday, April 12, 2019, from 9:00 am to 5:00 pm, Central European Time (CET). The research will be presented in the Gut Microbiota & Liver Disease poster area as Poster FRI-267.

Arun Sanyal, M.D., Professor of Medicine & Executive Director, Education Core, Clinical Center for Translational Research at the Virginia Commonwealth University (VCU), stated, “The demonstration of reduced gut permeability with larazotide, presented today at the EASL conference, in the setting of diet-induced obesity opens up the possibility of modulating the outcomes of metabolic syndrome, including NASH, via this mechanism and warrants further development for this compound. Increased intestinal permeability has been linked to many aspects of metabolic syndrome including type 2 diabetes and nonalcoholic fatty liver disease.”

About NAFLD/NASH:
Nonalcoholic steatohepatitis (NASH) is a severe disease of the liver caused by inflammation and a buildup of fat in the organ. In the United States, NASH affects up to approximately 2-5% of the population. An additional 10%-30% of Americans have fat in their livers, but no inflammation or liver damage, a condition called NAFLD or “fatty liver.” The underlying cause of NASH is unclear, but it most often occurs in persons who are middle-aged and overweight or obese. It has been shown that chronic liver diseases, including NAFLD/NASH, may cause perturbations in the epithelial lining of the gut, and disrupt barrier integrity, causing a normal intestine to become more permeable. This “leaky gut” could cause passage of unwanted toxins and antigenic components to “cross-talk” to the liver via the blood circulation causing inflammation and damage to hepatocytes. This gut-liver axis is an emerging area of research in chronic liver diseases, such as NAFLD/NASH.

About Larazotide Acetate for Celiac Disease
In celiac disease, larazotide is the only drug which has successfully met its primary endpoint with statistical significance in a Phase 2b efficacy clinical trial (342 patients). Innovate completed the End of Phase 2 Meeting with the FDA and is preparing to launch the Phase 3 registration clinical trials for celiac disease in the second quarter of 2019. Nearly 600 subjects have been exposed to larazotide in clinical trials, and a safety profile comparable to placebo has been demonstrated. Larazotide has received Fast Track designation from the FDA for celiac disease

About Innovate Biopharmaceuticals, Inc. (Nasdaq: INNT)
Innovate is a clinical stage biotechnology company focused on developing novel therapeutics for autoimmune and inflammatory diseases. Innovate's lead drug candidate, larazotide acetate, has a mechanism of action that renormalizes the dysfunctional intestinal barrier by decreasing intestinal permeability and reducing antigen trafficking, such as gliadin fragments in celiac disease, and bacterial toxins and immunogenic antigens in nonalcoholic steatohepatitis (NASH). In several diseases, including celiac disease, NASH, Crohn's disease, ulcerative colitis, irritable bowel syndrome (IBS), type 1 diabetes mellitus (T1DM), chronic kidney disease (CKD), the intestinal barrier is dysfunctional with increased permeability.

Forward Looking Statements
This press release includes forward-looking statements including, but not limited to, statements related to the development of drug candidates, our operations and business strategy, our expected financial results, and corporate updates. The forward-looking statements contained in this press release are based on management's current expectations and are subject to substantial risks, uncertainty and changes in circumstances. Actual results may differ materially from those expressed by these expectations due to risks and uncertainties, including, among others, those related to our ability to obtain additional capital on favorable terms to us, or at all, including, without limitation, to fund our current and future preclinical studies and clinical trials and the success, timing and cost of our drug development program and our ongoing or future preclinical studies and clinical trials, including, without limitation, the possibility of unfavorable new clinical and preclinical data and additional analyses of existing data, as well as the risks that prior clinical and preclinical results may not be replicated. These risks and uncertainties include, but may not be limited to, those described in our Annual Report on Form 10-K filed with the SEC on March 18, 2019, and in any subsequent filings with the SEC. Forward-looking statements speak only as of the date of this press release, and we undertake no obligation to review or update any forward-looking statement except as may be required by applicable law.

SOURCE: Innovate Biopharmaceuticals, Inc.

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1. Luther, J et. al. Hepatic Injury in NASH Contributes to Altered Intestinal Permeability. *CMGH* 2015 Vol. 1, Issue 2, pp. 222-232. (doi: 10.1016/j.cmgh.2015.01.001)

2. Rahman, K et. al. Loss of Junctional Adhesion Molecule A Promotes Severe Steatohepatitis in Mice on a Diet High in Saturated Fat, Fructose, and Cholesterol. Gastroenterology. 2016 Oct; 151(4): 733-746. (doi: 10/1053/j.gastro.2016.06.022)

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