Innovate Biopharmaceuticals Announces Positive Effect of Larazotide Acetate on Reducing Intestinal Permeability in a NASH Preclinical Study

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Top line results showed larazotide having a significant effect on intestinal permeability, a mechanism thought to be key for bacterial translocation leading to NAFLD/NASH

Further preclinical data in combination with approved drugs in development for NASH liraglutide (VICTOZA®) and obeticholic acid (OCALIVA®) expected in early 2019

Company plans to launch clinical development program in NASH in 2019, based on larazotide's mechanism as an intestinal permeability re-normalizing agent

RALEIGH, N.C., Oct. 29, 2018 (GLOBE NEWSWIRE) -- Innovate Biopharmaceuticals, Inc. (Nasdaq: INNT), a clinical stage biotechnology company focused on developing novel therapeutics for autoimmune and inflammatory diseases, announced today a potential expanded use for its lead agent, larazotide acetate, with topline preclinical data demonstrating proof-of-concept in an established model of nonalcoholic steatohepatitis (NASH). Innovate intends to launch a clinical program in NASH with a phase 2 trial in 2019. There are currently no treatments for nonalcoholic fatty liver disease (NAFLD) or NASH approved by the FDA.

In the study, 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, including histopathology. Researchers aimed to assess the effects of multiple doses of larazotide on various markers of NASH. In addition, researchers sought to gauge the effects of larazotide on gut integrity, using a highly specific technique measuring epithelial barrier normalization and intestinal permeability. This measure demonstrated with statistically high significance that larazotide at the doses tested had a clear benefit in reducing gut barrier permeability, a known pathological abnormality in chronic liver diseases, specifically NASH. Agents which may prevent this "leaky" barrier to worsen through the progression of NASH are thought to provide a potential advantage in treating this disease. Innovate plans to submit the complete NASH preclinical results for publication at a major upcoming conference in 2019.

We believe that studies investigating the potential for synergy between larazotide and drugs in development for NASH, which are already approved for other indications, should help facilitate a pathway for finding a drug combination that is effective for treating NASH. Innovate is studying Novo Nordisk A/S's VICTOZA ® (liraglutide) approved for type 2 Diabetes and Intercept Pharmaceuticals Inc.'s OCALIVA ® (obeticholic acid) approved for primary biliary cholangitis (PBC) in combination with larazotide in preclinical models with the goal of determining the optimal synergistic drug combination with different mechanisms of action.

"We are excited about looking at how larazotide could synergistically work with drugs in late-stage clinical trials for NASH, which are already approved in other indications. We believe that larazotide's more upstream mechanism of blocking the inflammatory cascade without impacting the liver directly may support its potential therapeutic effect in NAFLD and NASH," said Dr. Christopher Prior, Chief Executive Officer of Innovate Biopharmaceuticals, Inc.

Dr. Arun Sanyal, Professor and Chair, Division of Gastroenterology, Hepatology and Nutrition at the Virginia Commonwealth University (VCU) School of Medicine added, "Increased intestinal permeability has been linked to many aspects of metabolic syndrome including type 2 diabetes and nonalcoholic fatty liver disease. The demonstration of reduced gut permeability with larazotide 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 these indications."

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 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 NASH. In several diseases, including celiac disease, NASH, Crohn's disease, ulcerative colitis, and irritable bowel syndrome (IBS) the intestinal barrier is dysfunctional with increased permeability.

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 in 2017 and is preparing to begin Phase 3 registration clinical trials for celiac disease, targeted to commence in the first half 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.

Forward Looking Statements
This press release includes forward-looking statements including, but not limited to, statements related to our operations and business strategy. 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; 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; the lengthy and unpredictable nature of the drug approval process; and our ability to commercialize our product candidates if approved. These risks and uncertainties include, but may not be limited to, those described in our Quarterly Report on Form 10-Q filed with the SEC on August 14, 2018, 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.

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