Sanyal Biotechnology and Innovate Biopharmaceuticals Present Data at AASLD Validating a Proprietary “Leaky Gut” Assay Demonstrating Reduced Intestinal Permeability with Larazotide Acetate Treatment in a NASH Preclinical Study

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- Significant effect on gut epithelial integrity, a mechanism thought to be key for bacterial translocation leading to NAFLD and NASH. Innovate plans to launch a clinical development program for NASH in 2019
- Data presented for a proprietary in vivo blood test that measures gut epithelial integrity and intestinal permeability with a competition ELISA technique
- In vivo utility of the proprietary assay validated with larazotide, an intestinal permeability, gut-restricted re-normalizing agent

RALEIGH, N.C. and NORFOLK, Va., Nov. 12, 2018 (GLOBE NEWSWIRE) -- Innovate Biopharmaceuticals, Inc. (Nasdaq: INNT), a clinical stage biotechnology company focused on developing novel therapeutics for autoimmune and inflammatory diseases and Sanyal Biotechnology Inc, a contract research organization built to serve the needs of clients seeking preclinical research into liver disease and metabolic syndrome, showed data to assess the effects of multiple doses of larazotide on various markers of non-alcoholic steatohepatitis (NASH). The companies also announced a proprietary methodology utilizing a modified competition ELISA enabling serial serum dextran measurements in small volumes of serum to measure gut integrity. These data were reported in a poster presentation at The Liver Meeting® 2018, the annual meeting of the American Association for the Study of Liver Diseases (AASLD), in San Francisco. Researchers sought to gauge the effects of larazotide on gut integrity, using this highly specific technique measuring dextran absorption. Western diet-fed DIAMOND^{TM} animals dosed with larazotide (low-dose gavage) had significantly less intestinal permeability via dextran serum measurements at 16 weeks when compared to negative control, vehicle gavage or pioglitazone, a known NASH positive control which has been used in multiple animal models and clinical trials ($p = 0.049$ and $p = 0.04$, respectively; $n = 8$ per arm). Furthermore, pair-wise analysis showed that the administration of larazotide over time was able to maintain gut integrity at close to baseline levels, in effect preventing the barrier from deteriorating. Agents which may prevent this “leaky” barrier from worsening through the progression of NASH are thought to provide a potential advantage in treating non-alcoholic fatty liver disease (NAFLD) and NASH. Innovate intends to submit more complete NASH preclinical results for publication at a major upcoming conference and plans to commence a clinical trial for NASH in 2019.

Dr. Arun Sanyal, Professor and Chair, Division of Gastroenterology, Hepatology and Nutrition at the Virginia Commonwealth University (VCU) School of Medicine commented, “It is clear that compromised gut integrity is a contributing factor that drives development of NASH and other inflammatory diseases. As measured by our new method, larazotide was effective in maintaining gut integrity in this pilot study. These results support the rationale for advancement to clinical trials of drugs such as larazotide that improve gut integrity. We look forward to continuing to work with Innovate Biopharmaceuticals as they move larazotide to the clinic and continue to develop their pipeline.”

“The data not only underscore the use of dextran as a plausible marker to detect gut epithelial integrity in a diet only model of NASH, but further validate that the effects of larazotide, our gut-specific lead clinical peptide, can affect the important pathologic process of intestinal epithelial permeability. We plan to further larazotide’s clinical development in 2019 for this unmet need in gastroenterology and hepatology.” said Dr. Christopher Prior, Chief Executive Officer of Innovate Biopharmaceuticals, Inc.

In the study, researchers assessed the effect of larazotide on gut integrity and intestinal permeability *in vivo* using a proprietary model of NASH, which develops NASH solely due to a high-fat, high-sugar “Western diet.” The development of NASH in this model closely parallels human disease progression, including the development of insulin resistance, obesity, dyslipidemia, changes in the gut microbiome, and increased intestinal permeability. Current methods for assessing gut integrity *in vivo* require dosing with fluorescein isothiocyanate-dextran (FITC-dextran) and then measuring the FITC fluorescence in animal serum as a surrogate marker to gauge intestinal permeability or “leaky-gut.” The new method developed by Sanyal Biotechnology can be used in any mammal, has a broad dynamic range, and because it does not harm the animal, allows for repeat measurements so that response to drug therapies can be measured pair-wise in individual animals rather than just groups. DIAMOND™ animals on a Western diet have significantly higher levels of serum dextran than those on normal diet beginning as early as eight weeks, when the first signs of NASH develop in this strain, than those on a normal diet. Researchers found that as NASH got progressively worse, the animal’s guts became progressively leakier, suggesting that this plays a role in driving the NASH pathology.

About NAFLD/NASH:
Non-alcoholic 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 non-alcoholic fatty liver disease (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 and 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 and NASH.

About Sanyal Biotechnology, Inc.:
Sanyal Biotechnology, Inc. is a contract research organization built to serve the needs of clients who seek a more physiologically relevant small animal model for their preclinical research into liver diseases and other comorbidities resulting from the metabolic syndrome. The company develops customized studies to screen compounds of interest based on customized end-points, while providing expert interpretation of data. SBI offers a flexible menu of core services beyond histopathology carried out in an Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC)

accredited and GLP environment. Sanyal Biotechnology also offers PK and toxicology work on the DIAMOND™ model and have successfully induced autoimmune hepatitis (AIH). The company offers other models including PK, toxicology and a variety of diets for NASH, fibrosis, and hepatocellular carcinoma studies including ELISA, PCR, blot work, and a propriety “leaky gut” assay.

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 the development of drug candidates, 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.

Sanyal Biotechnology, Inc.
Rebecca Caffrey, Ph.D., MBA
Chief Executive Officer
Email: rebecca@sanyalbio.com
www.sanyalbio.com

Innovate Biopharmaceuticals, Inc.
Jennifer K. Zimmons, Ph.D.
Investor Relations
Tel: +1-917-214-3514
Email: jzimmons@innovatebiopharma.com
www.innovatebiopharma.com

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