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Allysta Pharmaceuticals, Inc. Announces Positive Preclinical Data in a NASH Model Demonstrating its Adiponectin Analogue ALY688 Reduces Liver Fat, Inflammation, and Fibrosis

BELLEVUE, WA (ACCESSWIRE). Allysta Pharmaceuticals, Inc. ("Allysta") today announced results from a study of its adiponectin analogue peptide, ALY688, in a mouse model of nonalcoholic steatohepatitis (NASH) conducted in collaboration with the laboratory of Professor Aimin Xu, Chair of Metabolic Medicine in the Department of Medicine at the University of Hong Kong. Professor Xu is a recognized authority on the biology of NASH.

In the study, mice were fed a choline-deficient high fat diet designed to induce fatty liver resulting in an accelerated progression to inflammation and fibrosis that resembles the human disease. The mice were randomized to receive vehicle, ALY688 (3 mg/kg sc daily), ALY688 (15 mg/kg sc daily), or obeticholic acid (30 mg/kg oral daily) for 9 weeks while continuing to receive the high fat diet.

At the end of treatment, animals fed the diet and receiving vehicle developed the typical picture of fatty liver with increases in serum alanine aminotransferase and accumulation of triglycerides in the liver accompanied by hepatic inflammation and marked fibrosis on histology.

In contrast, animals treated with ALY688 showed a significant reduction in the ALT and AST compared with vehicle. Significant dose-related reductions in liver fat (by histology and liver triglyceride content) and inflammation together with a significant decrease in the overall NASH Activity Score was seen in ALY688 treated groups. There was a marked reduction in the degree of fibrosis, both on histology and biochemical measurements. The improvement seen with ALY688 15 mg/kg was greater than that seen with obeticholic acid 30 mg/kg on all these measures. The reduction in inflammation and fibrosis was further supported by significant decreases in pro-inflammatory gene expression in the liver (TNFα, IL-1β, MCP-1, IL-6) and decreases in pro-fibrotic markers (αSMA, TGF-β, TIMP1, Col.1). ALY688-treated animals showed a shift in body composition (assessed by nuclear magnetic resonance) with decreased total fat and increased lean percent body mass.

“These data, supported by other studies showing that adiponectin and ALY688 reduces inflammation and fibrosis while improving metabolic parameters, provides a unique opportunity to address the major factors driving NASH with a single agent,” said Henry Hsu MD, CEO. “The effects on fibrosis are particularly striking and we believe ALY688 has great potential in other inflammatory and fibrotic diseases.”

Allysta plans to initiate a Phase 1 clinical study of ALY688 in the second quarter of 2021. The study will evaluate safety, pharmacokinetics, and biomarkers of activity for a range of doses in both single and multiple dose cohorts.

About Nonalcoholic Steatohepatitis (NASH)

Nonalcoholic fatty liver disease (NAFLD) is a condition in which fat builds up in the liver (steatosis), most often related to obesity and Type II diabetes. NASH is a more advanced form of NAFLD in which inflammation and liver cell damage accompany the fat build-up in the liver. Advanced NASH can cause scarring or fibrosis of the liver, which leads to cirrhosis. NAFLD is the most common chronic liver condition in the US. It is estimated that about 25 percent of adults in the U.S. have NAFLD. Of those, about 20 percent have NASH (5% of adults in the US). NASH prevalence is expected to increase by 63% between 2015 and 2030 and is expected to become the leading cause of liver transplantation in the US between 2020 and 2025. Current treatment for NAFLD/NASH relies on lifestyle modification, particularly long-term weight loss. There are no drugs in the US approved specifically to treat NASH.

About ALY688

ALY688 peptide is a potent specific analogue of adiponectin and activates multiple beneficial adiponectin signaling pathways. Adiponectin is a major hormone produced by adipose tissue and plays important roles in regulating a range of cellular process in many organs. Adiponectin is considered a unique “protective” cytokine due to its broad beneficial actions including reduction of inflammation and fibrosis, improvement in insulin sensitivity and lipid oxidation, and enhancement of cellular regeneration. This provides opportunities to develop ALY688 in multiple disease indications.

About Allysta

Allysta is a venture-backed clinical stage biopharmaceutical company developing first-in-class peptide therapeutics with a focus in inflammatory and fibrotic diseases. Allysta’s lead candidates are in clinical and late preclinical stages, supported by compelling science and pharmacology. Allysta is advancing next-generation treatments for dry eye disease and NASH. Visit www.allysta.com.

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