Avolynt, Inc. Announces FDA Acceptance of IND to Commence Pivotal Trial of Remogliflozin for NASH

Avolynt, Inc. to Initiate Pivotal REIN Study for NASH

RESEARCH TRIANGLE PARK, N.C., August 22, 2016 – Avolynt, Inc. ("Avolynt"), a privately held biotech company focused on the development of therapeutics for metabolic diseases, announced today that the U.S. Food and Drug Administration ("FDA") has accepted the company's Investigational New Drug Application ("IND") for remogliflozin etabonate ("remogliflozin") to treat nonalcoholic steatohepatitis, or NASH. According to scientific literature, NASH is a chronic disease that affects approxiately12% of the population in United States and in certain European countries and its prevalence is expected to increase in parallel with increased rates of obesity and diabetes. There are currently no approved drugs to treat NASH.

As recently disclosed, Avolynt intends to initiate later this year, a multi-center, randomized, double-blind, placebo-controlled, pivotal adaptive Phase II/Phase III/Phase IV clinical trial of Remogliflozin Etabonate In NASH patients under the FDA's Accelerated Approval Program. The REIN study will evaluate two doses of biphasic remogliflozin, plus placebo, in patients with histologically confirmed NASH. The 48-week Phase II portion of the trial will have a histologically determined composite endpoint of two points or greater reduction in NAS Score and no worsening of fibrosis. Patients completing Phase II will automatically continue into Phase III with additional patients randomized upon successful completion of Phase II. The 96-week Phase III component of the trial will have a composite endpoint of overall histopathologic interpretation of complete resolution of NASH with no worsening of fibrosis based on analysis of liver biopsies. Patients completing the Phase III component of the REIN study will automatically continue into Phase IV, a clinical outcome study. Conditional marketing approval will be sought after successful completion of the Phase III analysis.

"By dually targeting insulin resistance and oxidative stress in the liver, remogliflozin may safely improve the environment leading to fatty liver and ultimately the mechanisms contributing to the progression of NAFLD to NASH and fibrosis," said principal investigator Dr. Manal Abdelmalek. "We have worked closely with our consultants and the FDA to develop a novel and more efficient Phase II/III/IV adaptive clinical approach and look forward to initiating this study very soon."

Remogliflozin is a highly selective SGLT2 inhibitor being developed for NASH. Unlike other SGLT2 inhibitors, remogliflozin has a differentiated chemistry that provides a substantial anti-oxidant effect and reduction in oxidative stress in the liver. In combination with its strong ability to improve insulin sensitivity, remogliflozin is an ideal candidate for the treatment of NASH. Also unlike other SGLT2 inhibitors, remogliflozin allows for the avoidance of overnight inhibition of SGLT2 which is thought to lead to increases in LDL-cholesterol (LDL-c) and increased incidence of urogenital infections (Sykes, et al., Diab Obes Met. 17:94-101, 2015).

Clinical evidence clearly indicates that insulin resistance and hepatic oxidative stress are major risk factors for the development of NASH. Two dose-ranging Phase 2b studies in

subjects with type 2 diabetes showed that treatment with remogliflozin resulted in significant improvements in insulin sensitivity as determined by HOMA, as well as weight loss and improvement in serum levels of ALT after 12 weeks. FIB-4 and NAFLD Fibrosis scores in these subjects were reduced from baseline after remogliflozin dosing whereas placebo and pioglitazone cohorts did not show these reductions. Furthermore, in rodent models of fatty liver disease, remogliflozin significantly reduced hepatic steatosis and markers of both hepatic oxidative stress and inflammation. Remogliflozin also has significant intrinsic anti-oxidant activity (Nakano et al., J Clin Exp Hepatol. 5:190-198, 2015). Taken together, these data show that remogliflozin addresses the known underlying mechanisms involved in the development of fatty liver disease and fibrosis and support its potential as a therapy for NASH. The REIN study described above will evaluate the ability of remogliflozin's insulin sensitization, anti-inflammatory and anti-oxidant properties to address NASH.

"The existing clinical and preclinical data generated to date positions remogliflozin as a very promising candidate for the treatment of NASH," said Avolynt Chief Scientific Officer Dr. William Wilkison. "With its unique combination of insulin sensitizing and anti-oxidant properties, along with its ability to promote weight loss, remogliflozin has significant potential as a first-line therapeutic treatment for NASH."

About Remogliflozin
Remogliflozin is a selective SGLT2 inhibitor and potent anti-oxidant in clinical development for NASH and type 2 diabetes. Remogliflozin has been dosed in over 800 patients in greater than twenty clinical trials. In previous phase 2b clinical studies, remogliflozin demonstrated HbA1c lowering greater than 1% with few adverse events. Low incidence rates of genitourinary infections and little or no increases in LDL-c, common side effects commonly associated with SGLT2 inhibitors, were also observed. Remogliflozin has also demonstrated strong improvements in both insulin sensitivity and beta cell function as well as reductions in liver enzymes and oxidative stress. The REIN study, a global pivotal study of remogliflozin in patients with histologically confirmed NASH, is anticipated to initiate in late 2016.

About Avolynt, Inc.
Avolynt is a privately owned drug development company based in Research Triangle Park, North Carolina. Avolynt's mission is to improve the lives of patients suffering from dysfunctions related to human metabolism. The Avolynt team has significant discovery and development experience across the metabolic syndrome, including diabetes, obesity, and nonalcoholic steatohepatitis (NASH). The Company is developing a novel SGLT2 inhibitor for the treatment of NASH and type 2 diabetes. Avolynt, through its wholly owned subsidiary BHV Pharma, holds an exclusive license to remogliflozin-etabonate for the global territory outside of Japan, Korea, and Taiwan. For more information about Avolynt, visit www.avolynt.com.

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