

Adipo Therapeutics, LLC Announces Positive Results of Human Adipose Tissue Explants Study at the American Diabetes Association 84th Scientific Sessions

Notch Signaling Inhibitor, ADPO-002, Promotes Expression of Key Browning Biomarkers in Human White Adipose Tissue Supporting the Translation of this Novel Mechanism of Action in Humans

INDIANAPOLIS, Indiana – June 24, 2024 – Adipo Therapeutics, LLC

Adipo Therapeutics, LLC (Adipo), a late pre-clinical biopharmaceutical company developing treatments for obesity and related metabolic disorders, announced the positive results for a key study demonstrating that ADPO-002, a Notch inhibitor, promotes the expression of two key browning biomarkers in a study using adult human white adipose tissues obtained from obese patients undergoing bariatric surgery. Compared to the median expression values of the control group treatment, ADPO-002 30- μ M dose showed a 7-fold increase in PRDM16 (p value = 0.0001) and an 8-fold increase in PGC1 α (p value = 0.0537) in subcutaneous adipose tissue samples. ADPO-002 30- μ M dose also showed a 20-fold increase in PRDM16 (p value = 0.0002) and a 3-fold increase in PGC1 α (p value = 0.0061) in omental adipose tissue samples. The statistical significance values reflect the paired comparison (control vs ADPO-002) of at least 13 human patient's adipose tissue samples. PRDM16 and PGC1 α are two master regulators that are important in mitochondrial biogenesis and browning of white adipose tissue. “This is the first study to demonstrate the browning of human adult white adipose tissue through Notch inhibition and provides strong evidence that this novel mechanism of action translates to humans,” said Robert Considine, PhD, Professor at the Indiana University School of Medicine.

Excess energy-storing white adipose tissue is associated with obesity, type 2 diabetes mellitus, and cardiovascular disease; whereas energy-burning brown adipose tissue plays a beneficial role in overall metabolic health. Brown adipose tissue has a high number of mitochondria, increases energy expenditure, and is associated with improved insulin sensitivity and decreased risks for type 2 diabetes and cardiovascular disease according to a 2021 published article in Nature Medicine entitled Brown Adipose Tissue is Associated with Cardiometabolic Health.

The human adipose tissue explants study was conducted by the scientists at Adipo Therapeutics in collaboration with the Division of Endocrinology, Indiana University School of Medicine in Indianapolis, Indiana and Ascension St. Vincent Hospital in Carmel, Indiana. This research was partially funded by the State of Indiana through an Indiana Innovation Voucher Grant. The scientific founder of Adipo is Meng Deng, PhD. Dr. Deng is an associate professor in Purdue University's Department of Agricultural and Biological Engineering, Weldon School of Biomedical Engineering and School of Materials Engineering.

To conduct this study patients undergoing bariatric surgery consented to have their harvested subcutaneous and omental white adipose tissue donated to the study through informed consent.

A total of 21 patient-donated tissue samples were treated. The average age was 46 years +/- 11.6 years, and the average BMI was 45.9 +/- 9.2. The tissue samples for each patient were cut into small pieces (5-10 mg) using surgical scissors. The pieces of adipose tissue were transferred into a well plate, cultured in medium M199 supplemented with 0.7 nM insulin and 10 nM dexamethasone. The treatment groups were DMSO (negative control), 50 µM forskolin (positive control), and 3, 10 and 30 µM ADPO-002. After 7-days treatment, total RNA was isolated, and cDNA synthesis and RT-qPCR were performed for the browning marker genes PRDM16 and PGC1α. Statistical significance was determined using Wilcoxon non-parametric paired t-test. “This study is an important milestone in the development of ADPO-002NP as future treatment for obesity and supports the understanding that Notch inhibition is a well-preserved pathway in the animal kingdom,” said Dr. Deng.

According to the National Institutes of Health, by 2030 in the US, there will be 140 million people with obesity and 41 million people with type 2 diabetes. Obesity is a global health crisis that affects over 40% of U.S. adults. People who are overweight or suffer from obesity are at increased risk for many other serious diseases and health conditions including T2D, fatty liver and gallbladder diseases, high blood pressure, dyslipidemia, cardiovascular diseases, sleep apnea, breathing disorders, osteoarthritis, mental illness, and some cancers. ADPO-002NP has a unique mechanism of action that has the potential to be a complementary product to existing weight loss and diabetes drugs given its ability to increase energy expenditure and improve insulin resistance.

“While weight loss can be achieved through decreasing calorie intake and/or increasing energy expenditure, the newer therapies on the market today are focused primarily on appetite suppression to reduce a person’s daily caloric intake,” said Karen Wurster CEO of Adipo. “There is a need for new products that work to increase energy expenditure to lose weight without limiting calorie intake. Adipo’s treatment increases energy expenditure by converting energy-storing white fat into energy-burning, metabolically beneficial brown fat.”

The Adipo team is currently raising \$35M in Series A funding to move this breakthrough product to the first human dose to demonstrate safety and efficacy in people. The Series A capital will enable the team to continue its efficient execution to advance ADPO-002NP including GMP manufacturing, IND enabling studies, IND approval and completion of Phase 1 clinical development.

About Adipo Therapeutics, LLC

Adipo is a privately held, late pre-clinical biopharmaceutical company developing a first-in-class breakthrough approach to treat the obesity epidemic and related metabolic disorders. Adipo's lead asset (ADPO-002NP), combines a Notch inhibitor with novel PLGA (poly(lactic-*co*-glycolic) Acid) nano-particle technology. ADPO-002NP is being developed as a once weekly treatment to increase brown fat through localized conversion of white fat. Studies in animals have shown that when treated weekly with the active ingredient, local fat browning leads to weight loss, improved blood glucose control and a decrease in lipids with no change in calorie intake. Human adipose tissue *ex vivo* explants study results demonstrates that ADPO-002 promotes the expression of two key browning biomarkers and provides strong evidence that Notch inhibition, as a novel browning mechanism, translates to human adipose tissue.

To learn more about the company and its technology, please visit www.adipotherapeutics.com

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