Alaunos Therapeutics Announces Positive Preclinical Proof-of-Concept Data for ALN1003, a Differentiated Non-Hormonal Oral Treatment for Obesity and Related Metabolic Disorders

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- *The lead drug candidate, ALN1003, showed dose-related body weight loss and favorable body composition changes in the DIO mouse model*
- *ALN1003 also demonstrated reductions in liver weight and improvements in select biomarkers associated with liver injury compared to untreated mice*
- *Efforts to conduct additional preclinical studies, pursue optimized formulations and refine manufacturing processes are ongoing*

FORT LAUDERDALE, Fla., March 02, 2026 (GLOBE NEWSWIRE) -- **Alaunos Therapeutics, Inc. (Nasdaq: TCRT)**, an early-stage biotechnology company, today announced early data from two non-Good Laboratory Practice (non-GLP) diet-induced obesity (DIO) mouse studies evaluating **ALN1003**, the Company's lead small-molecule drug candidate for treating obesity and related conditions, such as metabolic dysfunction-associated steatotic liver disease (MASLD, a type of fatty liver disease). ALN1003 is an oral small-molecule drug being developed for a non-hormonal, non-incretin approach, unlike hormone-based treatments like GLP-1 drugs. We conducted two separate studies using a standard diet-induced obesity (DIO) mouse model in male C57BL/6 mice maintained on a high-fat diet (60% of calories from fat). Highlights from these studies include dose-dependent body weight loss with favorable body composition changes, reductions in liver weight, decreases in liver injury enzymes (ALT, AST and ALP) and other liver-related biomarker, and improvement in metabolic biomarkers (e.g., glucose and total cholesterol). Collectively, these findings suggest encouraging metabolic effects of ALN1003 in the DIO model.

These studies provide early signs of how the drug works and its potential safety profile that will help guide the Company's ongoing preclinical work and chemistry, manufacturing, and controls (CMC) initiatives. Key findings from these studies are summarized below (nominal reported p-values are unadjusted for multiple comparisons):

DIO Study 1

The purpose of the first study was to evaluate the pharmacokinetics (PK) and tolerability of ALN1003 and to assess early proof-of-concept anti-obesity efficacy including changes in weight, metabolic biomarkers, and adipose remodeling. Mice received low, controlled oral doses of ALN1003, split into two doses each day. Measurements included daily body weight, food and water consumption at the cage level, and metabolic markers (blood collection after a 4-6 hour fast at end of study). All animals were observed prior to and after each dose administration. There were 12 mice in each group, with mice housed 3 per cage.

Relative to DIO controls, mean percent change in body weight for ALN1003-treated mice peaked at -12.9% ($p<0.0001$) on Day 34 and was -10.3% ($p<0.0001$) after 48 days of treatment. Peak reductions in absolute weight loss were observed by Day 13 and remained lower than DIO controls through Day 48 ($p<0.0001$ at selected timepoints).

Food and water consumption: ALN1003 reduced cumulative food consumption versus DIO control (347.5 g/cage vs 425.0 g/cage; nominal $p<0.05$). ALN1003 reduced water consumption (445.8 mL/cage vs 494.5 mL/cage; not statistically significant).

Liver and Fat Tissue: In this study, ALN1003 reduced liver weight compared to untreated mice by 43% ($p<0.0001$) and by 39% when expressed as a percentage of body weight ($p<0.0001$). Long-term administration of ALN1003 was associated with lower ALT (alanine aminotransferase; $p<0.0001$), AST (aspartate aminotransferase; nominal $p<0.0001$) and ALP (alkaline phosphatase; $p<0.0001$), with a trend toward lower total bilirubin (nominal $p=0.058$) compared to untreated mice.

An unblinded macroscopic visual review of organ morphology was conducted comparing the liver and adipose tissues of the DIO control to the ALN1003 treatment group. Relative to DIO controls, ALN1003-treated animals exhibited smaller, deep reddish-brown livers; reduced epididymal white adipose tissue (eWAT) and inguinal white adipose tissue (iWAT) depots consistent with decreased adiposity; and darker interscapular BAT with appearance consistent with reduced "whitening" of BAT.

Tolerability: ALN1003 was generally well tolerated throughout the study. Mild, short-term, reversible hypolocomotion was observed after dosing in approximately one-half of dose administrations. There were no similar observations in DIO control animals.

DIO Study 2

The second study conducted was a pilot study to evaluate palatability, tolerability, anti-obesity effects, body composition and PK of ALN1003 administered orally in drinking water at three dose levels in DIO mice. The study comprised a treatment period of 14 days and a PK period of 4 days. ALN1003 was administered at three dose levels: low, medium and high. The middle and highest planned doses were 3 and 9 times higher than the low dose, respectively. Measurements included daily body weight, food and water consumption at the cage level, and metabolic parameters (blood

collection after a 4-6 hour fast at end of study). All animals were observed each day. There were 6 mice in each group (2 mice per cage).

Food and water consumption: ALN1003 reduced cumulative food intake in a dose-dependent manner over the 14-day treatment period. Cumulative food consumption in grams per cage was 84.5g, 80.8g, 76.7g and 56.7g (nominal $p<0.05$) for the DIO control, low, medium and high doses, respectively. Cumulative food consumption when normalized to body weight per cage was 87.9g, 85.6g, 86.7g and 73.6g for the DIO control, low, medium and high doses, respectively. ALN1003 reduced water intake significantly over the 14-day treatment period. Cumulative water consumption in milliliters per cage was 112.8 mL, 80.1 mL (nominal $p<0.05$), 71.1 mL ($p<0.0001$) and 63.5 mL ($p<0.0001$) for the DIO control, low, medium and high doses, respectively. Cumulative water consumption when normalized to body weight per cage was 116.9 mL, 84.9 mL, 80.5 mL and 80.3 mL for the DIO control, low, medium and high doses, respectively. Actual dose consumed is dependent on how much water mice drink. Actual doses consumed during the 14-day treatment period were consistent with planned doses, with variances to planned doses of +7.3%, -0.3% and -6.9% in the low, medium and high dose groups, respectively.

Body composition was assessed using a Bruker Minispec^{TM} LF90II Body Composition Analyzer (Bruker BioSpin, Billerica, MA, USA) and demonstrated dose-related changes that were driven primarily by fat loss but also included the loss of lean and fluid mass. The table below summarizes the mean percentage change from baseline through Day 17 in fat, lean and fluid as a % of body weight (BW) and mass in grams:

Mean % Change:	Control	Low	Medium	High
D17 Fat% of BW	+2.4%	-1.5%	-5.4%	-21.9%[c]
D17 Lean% of BW	-1.3%	+2.4%	+4.6%	+17.2%[c]
D17 Fluid% of BW	+0.4%	-9.3%	-12.0%	-25.7%[b]
D17 Fat in grams	+4.7% (+0.9g)	-1.8% (-0.4g)	-12.3% (-2.5g)[b]	-44.6% (-8.9g)[c]
D17 Lean grams	+1.9% (+0.5g)	+2.2% (+0.6g)	-4.1% (-1.1g)[a]	-18.8% (-5.0g)[c]
D17 Fluid grams	+2.7% (+0.1g)	-9.6% (-0.4g)	-18.8% (-0.7g)[a]	-47.3% (-1.8g)[c]

Significance of comparison to Control group: a: nominal $p<0.05$; b: nominal $p<0.001$; c: $p<0.0001$

Liver and Fat Tissue: At end of study Day 18, including the 14-day treatment period plus the PK period, dose-related reductions in liver weights compared to DIO control were -6.8%, -20.5% and -55.0% (nominal $p<0.01$) in the low, medium and high dose groups, respectively. Reductions in liver weights expressed as a percentage of body weight relative to DIO control were -2.6%, -12.0% and -32.6% (nominal $p<0.05$). Liver enzymes showed no statistically significant change after 18 days; gross liver appearance suggested reduced fat accumulation. Histological analyses of liver and adipose tissues are planned.

An unblinded macroscopic visual review of organ morphology was conducted comparing the liver and adipose tissues of the DIO control to the high dose group. This analysis showed reductions in white fat depots (such as epididymal white adipose tissue, or eWAT, and inguinal white adipose tissue, or iWAT) and an interscapular BAT appearance consistent with reduced “whitening” in the ALN1003 tissues vs DIO control. Review of liver images suggested less visible fat accumulation and smaller, deep red-brown livers compared to DIO control.

Metabolic parameters: In this study, the highest-dose group showed lower blood sugar (glucose; 197 mg/dL in high dose vs 320 mg/dL in DIO control; $p<0.0001$) and lower total cholesterol (162 mg/dL in high dose vs 209 mg/dL in DIO control; nominal $p<0.05$). HDL-C (high-density lipoprotein cholesterol), the dominant lipoprotein in DIO mice, also decreased to 130 mg/dL in high dose vs 165 mg/dL in DIO control; nominal $p<0.05$.

Tolerability: ALN1003 was generally well tolerated throughout the study; however, on Day 16 (during the PK portion of the study), two mice in the high-dose group were noted to be slightly dehydrated for the remainder of the study, although they otherwise appeared normal.

Important Context and Model Limitations

- Behavior-coupled dosing in unrestricted (ad libitum) drinking-water studies: In this paradigm, ALN1003 caused dose-related loss of appetite and thirst (anorexia/hypodipsia), leading to avoidance of medicated water. Despite actual doses consumed approximating planned doses in this study, reductions in drinking may confound attribution of weight loss solely to drug exposure in this model.

“These early non-GLP data support ALN1003’s potential as a non-hormonal treatment to achieve meaningful body weight loss with favorable body composition changes and select liver-related findings,” said Holger Weis, CEO of Alaunos. “We are focused on additional preclinical studies, optimizing formulations and refining manufacturing processes as we advance toward studies to enable an Investigational New Drug (IND) application. ALN1003 has the potential to offer a new option for patients seeking alternatives to hormone-based obesity drugs.”

Development Roadmap

The findings from these two studies support the Company’s strategy to focus on additional preclinical studies and CMC activities to optimize formulations while maintaining effective overall drug levels. We are also planning to conduct studies to better understand mechanisms of ALN1003, including measuring liver fat levels and scoring MASLD severity of the liver in a blinded manner. We are planning to further refine manufacturing processes and to run a small-scale production run based on these improvements. Thereafter, a larger scale production run is planned. In parallel, the Company has initiated a computational chemistry program to design, make, and test ALN1003 variations to strengthen the Company’s intellectual property and assess next-generation compounds. These initiatives, including large animal pharmacokinetic studies, will inform plans to conduct IND enabling studies.

As of September 30, 2025, the Company had cash and cash equivalents of approximately $1.9 million. The Company’s current cash runway extends into the second quarter of 2026. The Company intends to pursue additional financing to support continued operations and advancement of its preclinical obesity and metabolic program.

About Alaunos Therapeutics, Inc.
Alaunos Therapeutics is a biotechnology company focused on developing novel therapeutics. The Company's obesity and metabolic disorders program is advancing ALN1003, an oral small-molecule candidate designed to offer a differentiated, non-hormonal approach compared with currently available therapies.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements. Forward-looking statements are statements that are not historical facts, and in some cases can be identified by terms such as "may," "will," "could," "expects," "plans," "anticipates," "believes" or other words or terms of similar meaning. These statements include, but are not limited to, statements regarding the Alaunos Therapeutics, Inc.'s ("Alaunos" or "the Company") business and strategic plans, the timing of the Company's research and development programs, including potential data read out dates as well as any potential patent filings for the Company's obesity program.

These forward-looking statements are based on current expectations and assumptions that are subject to risks and uncertainties, which could cause actual results to differ materially. Important factors that could cause actual results to differ materially include, but are not limited to: changes in the Company's operating plans that may impact its cash expenditures; uncertainties built into research and development such as preclinical mouse data not translating to human trials, or challenges in scaling up formulations, including the risk that early non-GLP study results may not be replicated in confirmatory studies or pose safety concerns in IND-enabling studies; delays or failures in future studies; whether Alaunos' product candidates will advance further in the clinical trial process, including getting approval by the U.S. Food and Drug Administration (FDA) or other foreign health authority to conduct clinical trials and whether and when, if at all, they will receive final approval from the FDA or equivalent foreign regulatory agencies and for which uses; challenges to the strength and enforceability of Alaunos' intellectual property rights (such as patent disputes); competition from other pharmaceutical and biotechnology companies (including in the crowded obesity treatment market); funding shortages or market changes affecting our cash needs; tolerability issues from drug administration; the inherent uncertainties in drug development, including potential failures optimizing formulations, mechanistic studies, or large-animal pharmacokinetics that could delay IND-enabling activities; manufacturing and supply chain disruptions related to CMC work; and other factors discussed in our latest Form 10-Q and Form 10-K filed with the Securities and Exchange Commission (SEC). Forward-looking statements may also be protected if they are immaterial.

We caution you not to place undue reliance on these forward-looking statements, which speak only as of the date of this press release. Except as required by law, Alaunos undertakes no obligation to update these statements to reflect events that occur or circumstances that exist after the date hereof.

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