MediciNova Announces Two Poster Presentations at the 92nd EAS Congress 2024, the Annual Meeting of the European Atherosclerosis Society Regarding the Use of MN-001 (Tipelukast) for Cardiometabolic Conditions

May 28, 2024

LA JOLLA, Calif., May 28, 2024 (GLOBE NEWSWIRE) -- MediciNova, Inc., a biopharmaceutical company traded on the NASDAQ Global Market (NASDAQ: MNOV) and the Standard Market of the Tokyo Stock Exchange (Code Number: 4875), today announced that MediciNova conducted two poster presentations at the 92nd European Atherosclerosis Society (EAS) 2024 Congress held online May 26-29, 2024.

MediciNova's Chief Medical Officer, Kazuko Matsuda, MD PhD MPH presented an update on the Company's ***"STUDY PROTOCOL TO EVALUATE MN-001'S (TIPELUKAST) EFFICACY, SAFETY AND TOLERABILITY IN SUBJECTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) (Abstract # 810) ",*** which included Clinical background, Study objectives, Study design, Inclusion Criteria and Study status of Phase 2 clinical trial ongoing in the US. As of 25 April 2024, 33 patients were enrolled, 19 patients were randomized, 14 patients completed the study. Three subjects reported serious adverse events (SAE) and were all considered "Unlikely related" or "Unrelated" to study drug.

MediciNova's Dr. Huicheng Qi presented ***"MN-002, THE METABOLITE OF MN-001 (TIPELUKAST) PROMOTES MACROPHAGE CHOLESTEROL EFFLUX (Abstract # 856)"***, demonstrating positive data regarding cholesterol efflux capacity by MN-001 (Tipelukast) and MN-002. This is a collaborative effort between MediciNova and Professor Masatsune Ogura at Department of Clinical Laboratory Technology, Juntendo University and Professor Takashi Miida at Department of Clinical Laboratory Medicine, Juntendo University.

Objectives of this study are to evaluate the effects of MN-001 and its major active metabolite MN-002 on cholesterol efflux capacity in THP-1 *1macrophages. ABCA1 *2 and ABCG1 *3 is known to play important roles in the reverse cholesterol transport system. Macrophages derived from THP-1 *3 cells were used to analyze the effect of MN-001 and MN-002 on ABCA1 and ABCG1 mRNA expression was measured by RT-PCR and protein expression was measured by Western blotting. Next, the effects of MN-002 on Apolipoprotein AI (ApoA1) *4 dependent and High-Density Lipoprotein (HDL) dependent cholesterol efflux in THP-1 macrophages were determined, respectively. Finally, analyzed the involvement of Protein Kinase A (PKA) in the mechanism of action of MN-002 using a PKA inhibitor.

The data presented in the abstract demonstrated the following:

- MN-002 enhances ApoA1 and HDL mediated cholesterol efflux.
  - MN-002 increased 44.3% in ApoA1-mediated cholesterol efflux capacity compared to the control group (DMSO).
  - MN-002 increased 15.3% in HDL-mediated cholesterol efflux capacity compared to the control group (DMSO).
- MN-002 increases ABCA1 and ABCG1 protein levels in dose-dependent manner
  - MN-002 increased ABCA1 protein expression in a dose-dependent manner compared to the control group (DMSO); ABCA1 protein increased approximately 2-fold with 10 µM of MN-002.
  - MN-002 increased ABCG1 protein expression in a dose-dependent manner compared to the control group (DMSO); ABCG1 protein increased approximately 2.8-fold with 10 µM of MN-002.
- MN-002 increases ABCA1/ ABCG1/ LXR-alpha mRNA levels.
  - MN-002 increased ABCA1 mRNA expression in a time and dose-dependent manner compared to the control group (DMSO). mRNA expression of ABCA1 increased about 3-fold with 24 hours exposure of 10 µM MN-002.
  - MN-002 increased ABCG1 mRNA expression in a time and dose-dependent manner compared to the control group (DMSO). mRNA expression of ABCA1 by increased 5.4-fold with 24 hours exposure of 10 µM MN-002
  - MN-002 increased LXR-alpha mRNA expression in a time- and dose-dependent manner compared to the control group (DMSO). mRNA expression of ABCA1 increased 2.4-fold with 24 hours exposure of 10 µM MN-002.
- MN-002 increases ABCA1 protein level independent of PKA signaling pathway.
  - MN-002 increased ABCA1 protein expression compared to the control group (DMSO); conditions in which a PKA inhibitor did not cancel the effect of MN-002 to increase ABCA1 protein expression.

Kazuko Matsuda, M.D., Ph.D., M.P.H., Chief Medical Officer, MediciNova, Inc., commented, "We are very pleased to present our clinical trial status and positive research outcomes at the EAS Congress 2024. We have randomized almost half of the randomization goal with our ongoing Phase 2 clinical trial. With the collaborative research with Juntendo University regarding the mechanism of action of MN-001/MN-002 in lipid metabolism, we identified that MN-002, the major metabolite of MN-001 (Tipelukast), had significant positive effects on both ABCA1, ABCG1 expression."

***1 About THP-1**

THP-1 is a human leukemia monocytic cell line, which has been extensively used to study monocyte/macrophage functions, mechanisms, signaling pathways, and nutrient and drug transport.

***2 About ABCA1:**

ATP-binding cassette transporter ABCA1 (member 1 of human transporter sub-family ABCA), also known as the cholesterol efflux regulatory protein (CERP) is a protein which in humans is encoded by the ABCA1 gene. This transporter is a major regulator of cellular cholesterol and phospholipid

homeostasis. ABCA1 is an integral cell membrane protein that protects against cardiovascular disease.

***3 About ABCG1**

The primary function of ATP-binding cassette transporter G1 (ABCG1) is to efflux cholesterol to spherical high-density lipoproteins (HDL). ABCG1 also effluxes cholesterol to low-density lipoproteins (LDL), liposomes and cyclodextrin and it exports sphingomyelin, phosphatidylcholine and oxysterols to HDL and albumin.

***4 About Apolipoprotein AI (ApoA1)**

Apolipoprotein A-I (Apo A-I) is a major protein that has specific roles in the lipid metabolism. It promotes cholesterol efflux by accepting fats from cells to the liver for excretion.

About NAFLD, Type 2 Diabetes Mellitus (T2DM), and Hypertriglyceridemia

NAFLD is considered the hepatic manifestation of metabolic syndrome; studies have reported that 50% of patients with metabolic syndrome also have NAFLD. There is sufficient clinical and epidemiological evidence supporting the assertion that NAFLD is strongly associated with an increased prevalence and incidence of cardiovascular disease, T2DM, chronic kidney disease, and malignancy. The presence of dyslipidemia (hypercholesterolemia, hypertriglyceridemia, or both) is reported in 20 - 80% of NAFLD cases.

About MN-001

MN-001 (tipelukast) is a novel, orally bioavailable, small molecule compound thought to exert its effects through several mechanisms to produce its anti-inflammatory and anti-fibrotic activity in preclinical models, including leukotriene (LT) receptor antagonism, inhibition of phosphodiesterases (PDE) (mainly 3 and 4), and inhibition of 5-lipoxygenase (5-LO). The 5-LO/LT pathway has been postulated as a pathogenic factor in fibrosis development, and MN-001's inhibitory effect on 5-LO and the 5-LO/LT pathway is a novel approach to treat fibrosis. MN-001 has been shown to down-regulate expression of genes that promote fibrosis including LOXL2, Collagen Type 1 and TIMP-1. MN-001 has also been shown to down-regulate expression of genes that promote inflammation including CCR2 and MCP-1. In addition, MN-001 was found to inhibit triglyceride synthesis in hepatocytes by inhibiting arachidonic acid uptake.

About MediciNova

MediciNova, Inc. is a clinical-stage biopharmaceutical company developing a broad late-stage pipeline of novel small molecule therapies for inflammatory, fibrotic, and neurodegenerative diseases. Based on two compounds, MN-166 (ibudilast) and MN-001 (tipelukast), with multiple mechanisms of action and strong safety profiles, MediciNova has 11 programs in clinical development. MediciNova's lead asset, MN-166 (ibudilast), is currently in Phase 3 for amyotrophic lateral sclerosis (ALS) and degenerative cervical myelopathy (DCM) and is Phase 3-ready for progressive multiple sclerosis (MS). MN-166 (ibudilast) is also being evaluated in Phase 2 trials in Long COVID and substance dependence. MN 001 (tipelukast) was evaluated in a Phase 2 trial in idiopathic pulmonary fibrosis (IPF) and a second Phase 2 trial in non-alcoholic fatty liver disease (NAFLD) is ongoing. MediciNova has a strong track record of securing investigator-sponsored clinical trials funded through government grants.

Statements in this press release that are not historical in nature constitute forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include, without limitation, statements regarding the future development and efficacy of MN-166, MN-001, MN-221, and MN-029. These forward-looking statements may be preceded by, followed by, or otherwise include the words "believes," "expects," "anticipates," "intends," "estimates," "projects," "can," "could," "may," "will," "would," "considering," "planning" or similar expressions. These forward-looking statements involve a number of risks and uncertainties that may cause actual results or events to differ materially from those expressed or implied by such forward-looking statements. Factors that may cause actual results or events to differ materially from those expressed or implied by these forward-looking statements include, but are not limited to, risks of obtaining future partner or grant funding for development of MN-166, MN-001, MN-221, and MN-029 and risks of raising sufficient capital when needed to fund MediciNova's operations and contribution to clinical development, risks and uncertainties inherent in clinical trials, including the potential cost, expected timing and risks associated with clinical trials designed to meet FDA guidance and the viability of further development considering these factors, product development and commercialization risks, the uncertainty of whether the results of clinical trials will be predictive of results in later stages of product development, the risk of delays or failure to obtain or maintain regulatory approval, risks associated with the reliance on third parties to sponsor and fund clinical trials, risks regarding intellectual property rights in product candidates and the ability to defend and enforce such intellectual property rights, the risk of failure of the third parties upon whom MediciNova relies to conduct its clinical trials and manufacture its product candidates to perform as expected, the risk of increased cost and delays due to delays in the commencement, enrollment, completion or analysis of clinical trials or significant issues regarding the adequacy of clinical trial designs or the execution of clinical trials, and the timing of expected filings with the regulatory authorities, MediciNova's collaborations with third parties, the availability of funds to complete product development plans and MediciNova's ability to obtain third party funding for programs and raise sufficient capital when needed, and the other risks and uncertainties described in MediciNova's filings with the Securities and Exchange Commission, including its annual report on Form 10-K for the year ended December 31, 2023 and its subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Undue reliance should not be placed on these forward-looking statements, which speak only as of the date hereof. MediciNova disclaims any intent or obligation to revise or update these forward-looking statements.

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