MediciNova Announces MN-001 (tipelukast) Data regarding Lipid Metabolism in NASH/NAFLD to be Presented at The Liver Meeting® 2021, the Annual Meeting of the American Association for the Study of Liver Diseases

November 11, 2021

LA JOLLA, Calif., Nov. 11, 2021 (GLOBE NEWSWIRE) -- MediciNova, Inc., a biopharmaceutical company traded on the NASDAQ Global Market (NASDAQ:MNOV) and the JASDAQ Market of the Tokyo Stock Exchange (Code Number: 4875), today announced that MediciNova's research collaborator Masatsune Ogura, M.D., Ph.D., Associate Professor at the Department of General Medical Science, Chiba University Graduate School of Medicine, is presenting results and findings of a study that investigated the mechanism by which MN-001 (tipelukast) alters triglyceride (TG) metabolism in hepatocytes at The Liver Meeting® 2021, the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) to be held online from November 12th to 15th. In this study, HepG2 cells derived from human hepatocellular carcinoma samples were incubated for 48 hours with arachidonic acid (AA), LXR agonist T0901317, and MN-001 (tipelukast) each alone or in various combinations. The amount of TG synthesis in the HepG2 cells was calculated by extracting lipids from the HepG2 cells before and after treatment. As a result, it was found that MN-001 had an inhibitory effect on TG synthesis in HepG2 cells.

To further clarify part of the mechanism, mRNA was extracted from cell samples and the mRNA expression of molecules related to TG metabolism was measured using real-time PCR. As a result, the expression of CD36, one of the fatty acid transporters involved in the uptake of AA into liver cells, was suppressed in the samples by adding MN-001. This suggests that MN-001 reduces TG synthesis by inhibiting the AA uptake into hepatocytes. CD36 enhances cellular fatty acid uptake in the liver and is known to be involved in the pathogenesis of fatty liver.

The highlights of the presentation entitled "Improvement of Intracellular Lipid Metabolism by Tipelukast in the Pathogenesis of NASH/NAFLD" (Poster Publication # 1793) are as follows:

- TG synthesis (μg/mg protein) in HepG2 cells
  - Compared to the vehicle, T0901317 alone increased TG synthesis by 3.8-fold, AA alone increased TG synthesis by 15.3-fold, and the combination of T0901317 + AA increased TG synthesis by 24.3-fold.
  - Compared to MN-001 alone, the combination of T0901317 + MN-001 increased TG synthesis by 1.7-fold, the combination of AA + MN-001 increased TG synthesis by 3.7-fold, and the combination of T0901317 + AA + MN-001 increased TG synthesis by 3.7-fold.
- CD36 mRNA expression was downregulated in all 4 groups (vehicle, T0901317 alone, AA alone, T0901317 + AA) by adding MN-001.
- It was suggested that downregulation of CD36 expression is an important mechanism of MN-001. CD36 is one of the molecules responsible for fatty acid uptake into hepatocytes. MN-001 inhibits AA uptake into hepatocytes and suppresses TG synthesis, which is expected to reduce TG accumulation in hepatocytes.

Kazuko Matsuda, M.D. Ph.D, MPH., Chief Medical Officer, MediciNova, Inc., commented, "We are very pleased to present new results and findings from our collaboration with Dr. Ogura which elucidate MN-001's ability to improve lipid metabolism. In particular, its ability to suppress CD36 expression and reduce intracellular triglyceride synthesis may account for the role of MN-001 in NASH/NAFLD pathogenesis in addition to the significant lowering of serum triglyceride levels which was observed in multiple clinical trials."

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 considered to be 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, histopathological data shows that MN-001 reduces fibrosis in multiple animal models.

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 glioblastoma, patients at risk of developing acute respiratory distress syndrome (ARDS), and substance dependence. MN-001 (tipelukast) was evaluated in a Phase 2 trial in idiopathic pulmonary fibrosis (IPF) and is in preparation for a second Phase 2 trial in nonalcoholic steatohepatitis (NASH). 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, 2020 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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