MediciNova Announces Publication of MN-166 (ibudilast) Data regarding Prevention of Metastasis in Uveal Melanoma in Molecular Cancer Research

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LA JOLLA, Calif., April 20, 2022 (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 data demonstrating that MN-166 (ibudilast) prevents metastasis in a uveal melanoma (UM) animal model was published in the journal *Molecular Cancer Research.*

The publication entitled "Uveal Melanoma Exosomes Induce a Prometastatic Microenvironment through Macrophage Migration Inhibitory Factor," was co-authored by MediciNova's collaborators Dr. Grazia Ambrosini, Research Scientist at The Herbert Irving Comprehensive Cancer Center (HICCC), Columbia University Medical Center; Alex J. Rai, PhD, Associate Professor of Pathology and Cell Biology, Columbia University Irving Medical Center; Richard D. Carvajal, MD, Associate Professor of Medicine at Columbia Vagelos College of Physicians and Surgeons and co-director of the Precision Oncology and Systems Biology research program at the HICCC; and Gary Schwartz, MD, Professor of Oncology at Vagelos College of Physicians and Surgeons, Division Chief of Hematology/Oncology at Columbia University Irving Medical Center, and Deputy Director at the HICCC.

The publication describes a preclinical study which characterized the proteomic content of uveal melanoma exosomes and identified the presence of markers with metastatic properties. The study included an evaluation of MN-166 (ibudilast) in a metastatic uveal melanoma model.

Key take-aways in the publication include:

- Uveal melanoma exosomes (UM-exo) induce activation of cell signaling pathways and the release of cytokines and growth factors from hepatocytes. These exosome-stimulated liver cells could in turn induce migration of UM cells.
- The proinflammatory cytokine macrophage migration inhibitory factor (MIF) was over expressed in UM exosomes and was a major player in these mechanisms. MIF blockade inhibited UM cell migration in co-cultures with exosome-stimulated hepatocytes and prevented the development of metastases in vivo.
- Most inhibitors of hepatocyte-derived cytokines and growth factors had little or partial effects in blocking UM cell migration toward exosome-stimulated hepatocytes.
- The MIF inhibitor MN-166 (ibudilast) dramatically inhibited UM cell migration ($p<0.001$), suggesting that MIF plays a major role in the cell-to-cell cross-talk.
- In the metastatic UM mouse model study,
    - Quantified bioluminescence signal intensity in the abdominal region was dramatically reduced by MN-166 (ibudilast) treatment ($p<0.05$) in the metastatic UM mouse model at Day 46.
    - Histological analysis of the liver tissues of control mice showed the presence of tumor cell clusters, which were not present in the liver tissues of mice treated with MN-166 (ibudilast).
    - MN-166 (ibudilast) prevented metastasis in the metastatic UM mouse model.
- This study provided the first in vivo evidence that MIF inhibition may serve as a novel adjuvant drug therapy to prevent metastasis in uveal melanoma.
- MIF inhibition with MN-166 (ibudilast) may prevent metastatic spread in uveal melanoma patients and help to address the unmet critical need for novel and effective adjuvant therapies.

Kazuko Matsuda, MD, PhD, MPH, Chief Medical Officer of MediciNova, Inc. commented, "We are very pleased that the details of the research data regarding MN-166 preventing metastasis in the metastatic UM mouse model study has been published. Cancer metastasis is often the major driver of cancer-related death rather than the primary cancer. We previously reported that MN-166 reduced levels of immune suppressive myeloid-derived suppressor cells (MDSCs) and enhanced CD8 T cell activity in the tumor microenvironment. The data from this metastatic UM model study suggested that treatment with MN-166 can potentially address significant unmet medical needs for novel and effective therapies for patients with UM at risk of metastasis. We are optimistic that MN-166 could help patients with UM and other malignancies."

About MN-166 (ibudilast)

MN-166 (ibudilast) is a small molecule compound that inhibits phosphodiesterase type-4 (PDE4) and inflammatory cytokines, including macrophage migration inhibitory factor (MIF). It is in late-stage clinical development for the treatment of neurodegenerative diseases such as ALS (amyotrophic lateral sclerosis), progressive MS (multiple sclerosis), and DCM (degenerative cervical myelopathy); and for glioblastoma, CIPN (chemotherapy-induced peripheral neuropathy), and substance use disorder. In addition, MN-166 (ibudilast) is being evaluated in patients that are at risk for

developing acute respiratory distress syndrome (ARDS).

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 non-alcoholic fatty liver disease (NAFLD). 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, 2021 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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