MediciNova Announces Results of Studies under BARDA Contract to Develop MN 166 (ibudilast) as a Medical Countermeasure Against Chlorine Gas-induced Lung Injury

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LA JOLLA, Calif., Sept. 27, 2023 (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 the results of the nonclinical studies conducted under its contract with the Biomedical Advanced Research and Development Authority (BARDA), part of the Administration for Strategic Preparedness and Response (ASPR) in the U.S. Department of Health and Human Services, to repurpose MN-166 (ibudilast) as a potential medical countermeasure (MCM) against chlorine gas-induced lung damage such as acute respiratory distress syndrome (ARDS) and acute lung injury (ALI). Two different nonclinical models were used to investigate the potential clinical utility of MN-166 (ibudilast) for the treatment of chlorine-induced lung damage.

The primary objective of the first nonclinical efficacy study was to determine the safety and pharmacological activity of MN-166 (ibudilast) following ALI induced by chlorine (Cl_2) gas inhalation. In this study, single-dose and multi-dose treatments were evaluated. The primary endpoint was the pulmonary function measure PaO_2/FiO_2, which is the ratio of arterial oxygen partial pressure to fractional inspired oxygen.

After a Cl_2 gas challenge to induce moderate ALI (mean $PaO_2/FiO_2<200$), the test subjects were divided into four different treatment groups - two different doses of MN-166 (ibudilast) (low dose and high dose), a positive control (rolipram), and a negative control (test article vehicle) - which were infused intravenously (IV) over 30 minutes.

In the pilot design single-dose treatment regimen, the test subjects were treated only once after the Cl_2 gas challenge was completed. MN-166 (ibudilast) high dose and the positive control were more efficacious than MN-166 (ibudilast) low dose and the negative control until 12 hours after Cl_2 exposure but this did not yield statistically significant results for overall pulmonary function. MN-166 (ibudilast) was well tolerated and no safety concerns were observed in the single-dose study. A pharmacokinetic (PK) study was conducted to determine the optimal dosing frequency of MN-166 (ibudilast) in the multi-dose study.

In the multi-dose study, based on the PK profile in test subjects, each treatment was given every 12 hours with a total of 4 doses after the Cl_2 gas challenge. Treatment with MN-166 (ibudilast) high dose resulted in greater improvement ($p=0.0001$) in the mean PaO_2/FiO_2 ratio than MN-166 (ibudilast) low dose, rolipram, and negative control. The mean PaO_2/FiO_2 ratio decreased (worsened) by 57% from 518.7 mmHg at baseline (the end of the chlorine gas exposure) to 224.8 mmHg at hour 48 in the negative control group. The mean PaO_2/FiO_2 ratio decreased (worsened) by 36% from 516.0 mmHg at baseline to 327.8 mmHg at hour 48 in the MN-166 (ibudilast) high dose group. At hour 48, the last time point measured in the study, the mean PaO_2/FiO_2 ratio was 46% higher (better) in the MN-166 (ibudilast) high dose group than in the negative control group (327.8 vs. 224.8 mmHg). Since ARDS is defined as a PaO_2/FiO_2 ratio less than 300 mmHg, the mean PaO_2/FiO_2 ratio values indicate that the negative control group was still categorized as having mild ARDS at the end of the 48-hour evaluation period but the MN-166 (ibudilast) high dose group had recovered enough to no longer be defined as having ARDS. MN-166 (ibudilast) was well tolerated and no safety concerns were observed in the multi-dose study.

A preliminary proof-of-concept (POC) study was conducted to determine the feasibility of the second nonclinical model as a tool to evaluate MN-166 (ibudilast) as a MCM for chlorine gas exposure. After multiple attempts by MediciNova's subcontractor to establish the feasibility of the second Cl_2-gas induced lung injury model, it was not deemed to be a feasible model to evaluate a drug candidate and there are no evaluable efficacy results from the second nonclinical model POC study.

Kazuko Matsuda, MD, PhD, MPH, Chief Medical Officer of MediciNova, Inc., commented, "We are very pleased to report the positive results from the multi-dose nonclinical model study in which MN-166 demonstrated a large and significant improvement in pulmonary function and a higher survival rate. We previously reported that MN-166 attenuated histological changes observed in an LPS-induced ARDS nonclinical model, including pulmonary edema in lung tissue, and protected against pulmonary injury by reducing cellular apoptosis in lung tissue. We also previously reported positive and significant outcomes from a clinical trial of MN-166 in hospitalized severe COVID-19 patients at risk of developing ARDS. Combining the positive nonclinical chlorine gas-induced ALI model study results with the positive results from the human clinical trial in severe COVID-19 patients at risk of developing ARDS, we believe MN-166 has potential to treat acute lung disease from various causes. We plan to meet with the FDA to discuss the next steps in this development program. Development of medical countermeasures does not require human clinical trials to establish efficacy when these trials would not be ethical or feasible. There is a great unmet medical need for treatments for chlorine gas exposure as there is no drug approved specifically for this indication. We thank BARDA for their support of this program."

This project has been funded in whole or in part with federal funds from the Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority, under contract number 75A50121C00022.

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 is also in development for glioblastoma, Long COVID, CIPN (chemotherapy-induced peripheral neuropathy), and substance use disorder. In addition, MN-166 (ibudilast) was 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, 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, 2022 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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