Medicenna Announces Peer-Reviewed Publication of Preclinical Data on MDNA11 in the Journal for ImmunoTherapy of Cancer

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-- MDNA11 demonstrates a 30-fold increase in affinity for IL-2 receptor beta without binding to IL-2 receptor alpha when compared to recombinant human IL-2

-- MDNA11 was well-tolerated and induced durable proliferation and expansion of anti-cancer immune cells with limited stimulation of pro-tumor Treg cells in non-human primates

-- MDNA11 alone or in combination with a checkpoint inhibitor generated durable complete responses and provided long-term protection against tumor re-challenge in murine cancer models

TORONTO and HOUSTON, Jan. 26, 2022 (GLOBE NEWSWIRE) -- Medicenna Therapeutics Corp. ("Medicenna" or "the Company") (NASDAQ: MDNA TSX: MDNA), a clinical stage immuno-oncology company, today announced the peer-reviewed publication of preclinical data on MDNA11, the Company's selective, long-acting and novel IL-2 super-agonist. The paper, which was published in the *Journal for ImmunoTherapy of Cancer*, is entitled, "Fine-tuned Long-Acting Interleukin-2 Superkine Potentiates Durable Immune Responses in Mice and Non-Human Primate."

"We believe that this prestigious peer-reviewed publication provides important external validation for MDNA11's preclinical dataset, which demonstrates the advantages of the Superkine's differentiated 'beta-only' approach to targeting the IL-2 receptor," said Fahar Merchant, Ph.D., President and Chief Executive Officer of Medicenna. "MDNA11 showed potent and long-lasting anti-cancer activity in mice, as well as a pharmacokinetic profile that was vastly superior to recombinant human IL-2. In non-human primates, the long-acting Superkine selectively induced durable proliferation and expansion of anti-cancer immune cells without safety issues typically associated with IL-2. These preclinical findings are notably consistent with preliminary safety and pharmacodynamic data from our Phase 1/2 ABILITY study, which we believe provides early clinical evidence of MDNA11's potential."

Data presented in the paper are from *in vitro,* murine, and non-human primate (NHP) studies evaluating MDNA11's anti-cancer activity as well as its selective IL-2 receptor (IL-2R) binding, pharmacokinetic, pharmacodynamic, and safety profiles. While recombinant human IL-2 (rhIL-2) has been approved for the treatment of metastatic melanoma and kidney cancer, its use is limited by its short half-life and superior binding to the trimeric high-affinity receptor comprising the IL-2R alpha (IL-2Rα), which leads to preferential activation of pro-tumor Treg cells and toxicity. MDNA11 was engineered to overcome these shortcomings by virtue of its vastly superior selectivity and activation of cancer fighting immune cells, via IL-2R beta (IL-2Rβ), unlike "not-alpha" IL-2 variants, which to-date have shown sub-optimal single-agent activity.

Key data and conclusions from the paper include:

In vitro studies:

- MDNA11 demonstrated a 30-fold increase in binding affinity for IL-2Rβ compared to rhIL-2 (MDNA11 K_D = 6.6 ± 0.1 nM; rhIL-2 K_D = 210 ± 30 nM).
- MDNA11 showed no affinity for IL-2Rα at concentrations up to 2,000 nM MDNA11.
- MDNA11 showed enhanced signaling in anti-cancer T and NK cells and reduced activation of pro-tumor Treg cells when compared to rhIL-2 as shown by 231-fold and 124-fold enhancements in $CD8^+$/Treg and NK/Treg pSTAT EC_{50} ratios, respectively.

Murine studies:

- The terminal half-life of MDNA11 in mice was 25 times greater than that of rhIL-2.
- Cell depletion studies showed that both, $CD8^+$ T cells and NK cells are important for MDNA11 mediated anti-tumor efficacy.
- There was enhanced activation of $CD8^+$ T cells within the tumors as demonstrated by significant increase in expression of intracellular interferon γ.
- MDNA11 alone or in combination with checkpoint inhibitors generated durable complete responses and provided long-term protection against tumor re-challenge in murine cancer models.

NHP studies:

- MDNA11 preferentially induced durable proliferation and expansion of anti-cancer immune effector cells ($CD8^+$ T-cells, NK cells and non-Treg $CD4^+$ T-cells), with limited stimulation of pro-tumor Treg cells.
- Proliferation of anti-cancer immune effector cells remained elevated for at least 7 days following treatment with MDNA11.
- MDNA11 was well tolerated. The main safety observations of reduced activity and diarrhea were primarily observed at the highest dose level following the first dose and were generally transient in nature.

In summary, MDNA11's durable and potent memory response as a single agent together with a favorable safety profile positions the Superkine as a potential long-acting next generation IL-2 for cancer immunotherapy. Being independent of chemical conjugation, pegylation, or complex stearic hindrance techniques to modulate IL-2 activity, MDNA11 provides a versatile framework for a wide range of applications including arming CAR-based cellular therapies, oncolytic viruses, fusion to therapeutic antibodies or development of **Bi**functional **S**uper**K**ine **I**mmuno**T**herapie**s** (BiSKITs ™) to simultaneously target multiple cytokine pathways.

MDNA11 is currently being evaluated in patients with advanced, relapsed or refractory solid tumors in the Phase 1/2 ABILITY (**A B**eta-only **IL**-2 **I**mmuno**T**herap**Y**) study. Medicenna expects to provide an update on safety, pharmacokinetic, and pharmacodynamic data from the ABILITY study in the first quarter of 2022. An initial efficacy data update from the study is expected in mid-2022.

About the Phase 1/2 ABILITY Study
The ABILITY (**A B**eta-only **IL**-2 **I**mmuno**T**herap**Y**) study is designed to assess the safety, pharmacokinetics, pharmacodynamics, and anti-tumor activity of various doses of intravenously administered MDNA11 in patients with advanced, relapsed, or refractory solid tumors. The trial includes an MDNA11 monotherapy arm, as well as a combination arm designed to evaluate MDNA11 with a checkpoint inhibitor. Approximately 80 patients are expected to be enrolled into the ABILITY study. Following establishment of the recommended Phase 2 dose (RP2D) and optimal treatment schedule in the study's dose escalation phase, Medicenna plans to conduct a dose expansion phase that will enroll patients with renal cell carcinoma, melanoma, and other solid tumors in monotherapy and combination settings. For more information on the ABILITY study, see ClinicalTrials.gov Identifier: NCT05086692.

About Medicenna
Medicenna is a clinical stage immunotherapy company focused on the development of novel, highly selective versions of IL-2, IL-4 and IL-13 Superkines and first in class Empowered Superkines. Medicenna's long-acting IL-2 Superkine, MDNA11, is a next-generation IL-2 with superior CD122 (IL-2 receptor beta) binding without CD25 (IL-2 receptor alpha) affinity thereby preferentially stimulating cancer killing effector T cells and NK cells. Medicenna's early-stage BiSKITs™ program, (**Bi**functional **S**uper**K**ine **I**mmuno**T**herapie**s**) is designed to enhance the ability of Superkines to treat immunologically "cold" tumors. Medicenna's IL-4 Empowered Superkine, MDNA55, has been studied in 5 clinical trials including a Phase 2b trial for recurrent GBM, the most common and uniformly fatal form of brain cancer. MDNA55 has obtained Fast-Track and Orphan Drug status from the FDA and FDA/EMA, respectively.

Forward-Looking Statement
This news release contains forward-looking statements within the meaning of applicable securities laws that relate to the future operations of the Company and other statements that are not historical facts including, but not limited to, statements related to the clinical potential, safety profile and development of MDNA11 and the timing for additional results and data for such MDNA11 clinical study. Forward-looking statements are often identified by terms such as "will", "may", "should", "anticipate", "expect", "believe", "seek" and similar expressions. All statements other than statements of historical fact, included in this release, including statements on the future plans and objectives of the Company, are forward-looking statements that are subject to risks and uncertainties. There can be no assurance that such statements will prove to be accurate and actual results and future events could differ materially from those anticipated in such statements. Important factors that could cause actual results to differ materially from the Company's expectations include the risks detailed in the annual information form for the year ended March 31, 2021, which is available on SEDAR at www.sedar.com, and Form 40-F of the Company filed with the United States Securities and Exchange Commission and in other filings made by the Company with the applicable securities regulators from time to time in Canada and the United States.

The reader is cautioned that assumptions used in the preparation of any forward-looking information may prove to be incorrect. Events or circumstances may cause actual results to differ materially from those predicted, as a result of numerous known and unknown risks, uncertainties, and other factors, many of which are beyond the control of the Company. The reader is cautioned not to place undue reliance on any forward-looking information. Such information, although considered reasonable by management, may prove to be incorrect and actual results may differ materially from those anticipated. Forward-looking statements contained in this news release are expressly qualified by this cautionary statement. The forward-looking statements contained in this news release are made as of the date hereof and except as required by law, we do not intend and do not assume any obligation to update or revise publicly any of the included forward-looking statements.

Further Information

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