Medicenna Completes MDNA11 Dose Escalation and Commences Monotherapy Dose Expansion in the Phase 1/2 ABILITY Study

August 9, 2023

- Durable anti-cancer activity was observed during monotherapy dose escalation without dose-limiting toxicities

- Late-stage pancreatic cancer patient achieved 80% tumor shrinkage with complete regression observed in two of three metastatic lesions in the liver in response to single-agent MDNA11

- Immune pharmacodynamic data continues to support a differentiated mechanism with preferential expansion of potent cancer-fighting immune cells

- The monotherapy Recommended Dose for Expansion was established at 90ug/kg administered every 2 weeks

TORONTO and HOUSTON, Aug. 09, 2023 (GLOBE NEWSWIRE) -- Medicenna Therapeutics Corp. (“Medicenna” or “the Company”) (NASDAQ: MDNA TSX: MDNA), a clinical-stage immunotherapy company, today announced a clinical update on the monotherapy dose escalation portion of the first-in-human, Phase 1/2 ABILITY Study in patients with advanced solid tumors, as its drug candidate MDNA11, a beta-only, long-acting IL-2 super-agonist, advances to the monotherapy dose expansion phase.

“We are pleased to see that MDNA11 continues to demonstrate durable single-agent activity in patients with advanced, treatment-refractory cancer, together with a manageable safety profile, and preserving its differentiated pharmacodynamic (PD) qualities, even though the Phase 1 ABILITY Study was not specifically designed to demonstrate efficacy,” said Fahar Merchant, Ph.D., President and CEO of Medicenna. “The promising therapeutic activity observed in patients who have progressed on multiple prior anti-cancer therapies, including a patient with a particularly aggressive form of cancer – pancreatic ductal adenocarcinoma - fuels our enthusiasm for initiating the dose expansion phase of the study. The PD data supports 90ug/kg dose as the Recommended Dose for Expansion (RDE), which will be evaluated in selected cancers that are most likely to benefit from MDNA11 monotherapy. We look forward to the upcoming readouts from the monotherapy dose expansion phase later this year and commencing the combination portion of the trial, where MDNA11 will be evaluated with KEYTRUDA®, as part of our clinical collaboration with Merck.”

The main objectives of the dose escalation stage of the Phase 1/2 ABILITY study were to evaluate MDNA11’s safety, tolerability, pharmacokinetics and pharmacodynamics (PK/PD), and preliminary anti-tumor activity to inform RDE selection in patients with advanced cancers that were refractory to up to 4 different lines of systemic therapy. A total of six dose escalation cohorts (MDNA11 dose ranging from 3ug/Kg to 120 ug/Kg) constituting 20 patients were evaluated, with the majority (75%) having also received at least one line of immunotherapy.

Key findings from the dose escalation portion of the study include:

1. **Favorable safety profile:** MDNA11 was generally well tolerated across cohorts, with the majority of adverse events (AEs) being grade 1 or 2, with no grade 4 or 5 AEs.

2. **Promising single-agent activity and durable tumor control:** Several patients exhibited encouraging evidence of single-agent activity with tumor control observed in 7 of 19 evaluable patients (37%).
    a. **Confirmed partial response to single-agent MDNA11 in a highly aggressive tumor type:** A patient in cohort 4 (60ug/kg dose) with metastatic pancreatic ductal adenocarcinoma (PDAC), who had failed to respond to multiple prior systemic therapies, continues to show tumor shrinkage of all metastatic lesions in the liver after each successive scan. The most recent scan, showed an 80% decrease in total tumor size (sum of tumor diameters of the target lesions) with complete regression of 2 out of 3 lesions. This patient continues on study treatment with MDNA11.
    b. **Prolonged stable disease in metastatic melanoma progressed on prior immune checkpoint inhibition:** A patient in cohort 2 (commenced on 10 ug/kg dose and subsequently increased to 30, 60 and 90 ug/kg), having failed prior immunotherapy, experienced stable disease for 84 weeks.

3. **Pharmacodynamic data on effector anti-tumor immune cells continue to support the mechanistic rationale for MDNA11’s promising anti-tumor activity** , with MDNA11 inducing robust expansion of a population of potent activated $CD8^{+}$T cells and increasing NK cells, but with limited expansion of Tregs which can suppress anti-tumor immunity. More details are described in today’s call and the presentation available on Medicenna’s website .

4. Based on the totality of the dose escalation data, a **RDE of 90 ug/kg given every other week by IV infusion has been chosen for the monotherapy expansion phase of the trial.**

5. Selection of specific cancers for evaluation in the monotherapy dose expansion phase was determined based on clinical data available from the ABILITY Study, discussions with Medicenna’s Clinical Advisory Board and other expert KOLs, and an understanding of the immunobiology of the selected tumor types and the potential for MDNA11 monotherapy in the post-checkpoint inhibitor setting. **The following tumor types will be recruited in the dose expansion phase of the study**:
    a. **Melanoma**

b. **Non-Melanoma Skin Cancers**
c. **Microsatellite Instability-High (MSI-H) or deficient DNA mismatch repair (dMMR) cancers**. This population was selected to determine if the response achieved in the PDAC patient may have been due to the MSI-H profile. The PDAC patient unequivocally progressed on Keytruda, which is approved for MSI-H cancers.

Medicenna expects to report initial results from ABILITY's monotherapy dose expansion in the fourth quarter of 2023. Plans are to commence the combination phase of the trial evaluating MDNA11 with Keytruda in the fourth quarter of 2023, with initial results expected in early 2024.

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, treatment-refractory solid tumors. The trial includes an MDNA11 monotherapy phase, as well as a combination phase designed to evaluate MDNA11 with KEYTRUDA® (pembrolizumab). Approximately 104 patients are expected to be enrolled into the ABILITY Study. Following establishment of the RDE in the study's monotherapy dose escalation phase, Medicenna plans to conduct a dose expansion phase that will enroll patients with melanoma and other selected solid tumor types in the monotherapy and combination settings. For more information, see ClinicalTrials.gov Identifier: NCT05086692.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

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 IL-4 Empowered Superkine, bizaxofusp (formerly 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. Bizaxofusp has obtained FastTrack and Orphan Drug status from the FDA and FDA/EMA, respectively. Medicenna's early-stage BiSKITs ™ program, (**Bi**functional **S**uper**K**ine **I**mmuno**T**herapies) is designed to enhance the ability of Superkines to treat immunologically "cold" tumors.

Forward Looking Statements
This news release contains forward-looking statements within the meaning of applicable securities laws that relate to the future operations of the Company, plans and projections and other statements, including statements on the clinical development and potential of MDNA11 and the report of additional data that are not historical facts. Forward-looking statements are often identified by terms such as "will", "may", "should", "anticipate", "expect", "believe", "seek", "potentially", "equivocally," and similar expressions. and 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 latest Annual Information Form and Annual Report on Form 20-F of the Company 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

For further information about the Company please contact:

Elizabeth Williams, Chief Financial Officer, ewilliams@medicenna.com
Delphine Davan, Vice President, Investor Relations and Corporate Communications, ddavan@medicenna.com

Investor Contact

For more investor information, please contact:

Dan Ferry, Managing Director, LifeSci Advisors, 617-430-7576, daniel@lifesciadvisors.com

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Source: Medicenna Therapeutics Corp.