Medicenna To Present Evidence of Durable Single Agent Activity and Potent Immune Effector Response with MDNA11 in the Dose Escalation Portion of Phase 1/2 ABILITY-1 Study at the 10th Annual Oncology Innovation Forum

May 31, 2024

MDNA11 demonstrates durable response in pancreatic cancer patient with 100% regression of target and non-target lesions for over 104 weeks and continues to show remission 4 months after stopping treatment

Melanoma patient continues to show sustained 100% regression of target lesions

Dose escalation in combination with KEYTRUDA® is now enrolling at the next higher dose of 90g/kg following absence of any dose limiting toxicities at 60g/kg

MDNA11 shows significant increases in stemness, central and effector memory and markers of enhanced effector function in circulating CD8+ T and NK cells, all of which are critical for achieving meaningful and durable anti-cancer response.

Analysis of gene expression signatures from pretreatment and on-treatment paired biopsies show that cancer promoting pathways were degraded while immune-related pathways against cancer cells were enhanced following MDNA11 treatment.

TORONTO and HOUSTON, May 31, 2024 (GLOBE NEWSWIRE) -- Medicenna Therapeutics Corp. (“Medicenna” or the “Company”) (TSX: MDNA, OTCQB: MDNAF), a clinical-stage immunotherapy company focused on the development of Superkines, today announced that comprehensive clinical results from the monotherapy dose escalation portion of the Phase 1/2 ABILITY-1 (A Beta-only IL-2 ImmunoTherapY) study evaluating MDNA11, in patients with advanced solid tumors, will be presented today at the 10th Annual Oncology Innovation Forum being held in Chicago.

“We are encouraged by four partial responses observed in the study to date, especially 2 patients from the dose-escalation cohort where a pancreatic cancer patient is in remission following complete regression of all target and non-target lesions in addition to a melanoma patient that continues to show durable complete response of the target lesions,” said Fahar Merchant, Ph.D., President and CEO of Medicenna. “We are particularly pleased to see good tolerability of MDNA11 in combination with Keytruda allowing us to increase its dose to the next higher level which is identical to the MDNA11 dose used in the monotherapy expansion arm. These advances, together with the first ever observation of increases in unique biomarker specific cancer fighting immune cells in the tumor micro-environment, differentiates MDNA11’s mechanism relative to other competing IL-2 programs and its potential to be a best-in-class next-generation IL-2 super-agonist for treatment of advanced solid tumors. We look forward to reporting additional data from the ongoing monotherapy expansion and combination arms of the ABILITY-1 study at medical conferences in the second half of 2024.”

Tumor Response:

As reported last month (AACR PR), key findings from the monotherapy dose escalation and expansion portions of the ABILITY-1 study showed a response rate of nearly 29% in Phase 2 eligible patients with aggressive tumor types who had progressed on prior checkpoint inhibitors and treated with MDNA11 at doses of ≥ 60 µg/kg (N=14). Specifically, in the monotherapy dose escalation cohort:

o A pancreatic ductal adenocarcinoma (PDAC; MSI-H) patient with primary resistance to pembrolizumab was treated with 60 µg/kg MDNA11 and showed 100% resolution of all baseline target and non-target lesions at week 66. A new lymph node lesion that developed while patient was on a 8-week treatment break during vacation was treated with a single course of radiotherapy prior to resumption on MDNA11. At week 88, all baseline lesions remained completely resolved and the new lymph node lesion was reduced to <10 mm in size (considered physiological per RECIST v1.1), at which time MDNA11 treatment ended. The patient continues to be in complete remission at follow-up on week 104, nearly 4 months after ending treatment. Off-study follow-up is continuing.

o A patient with cutaneous melanoma, progressed on a prior line of dual checkpoint inhibitors, was treated with MDNA11 (90 µg/kg) and showed deepening tumor shrinkage on successive scans at weeks 12 and 20. Subsequent scans at week 28, 36 and 44 all showed 100% resolution of target lesions. Non-target lesions continue to regress, and the patient remains on MDNA11 treatment.

Monotherapy Safety:

Key findings from the monotherapy dose escalation portion of the ABILITY-1 study are consistent with a favorable safety profile. Specifically:

No dose limiting toxicity (DLT) was reported with no evidence of vascular leak syndrome (VLS). Vast majority (95 %) of treatment-related adverse events (TRAEs) were of grade 1-2 and resolved within 48 hours; grade 3 TRAEs mainly constituted asymptomatic transient LFT elevations; no grade 4 or 5 events were reported. Repeat administration of MDNA11 at the target doses showed further improvement in tolerability.

Pharmacodynamics

In depth pharmacodynamic analyses showed potent and durable systemic immune response following MDNA11 administration with clear evidence of immune activation in the tumor microenvironment (TME). Key findings were as follows:

- Durable expansion of circulating CD8+ T and NK cells but not immune suppressive Tregs with each repeat dose of MDNA11.
- Expanding populations of CD8+ T and NK cells expressing TCF-1, a key regulator of ‘stemness’ responsible for

maintaining self-renewal capacity, high proliferative potential and diverse immune effector characteristics.

- Increased expression of DNAM-1 (aka CD226), a potent regulator of anti-tumor immunity necessary for maintaining immune effector cell function.
- Increased central and effector memory CD8+ T cells provide a reliable reservoir of educated immune cells that can continually expand to enable durable anti-tumor immunity.
- Immune suppressive Tregs showed limited increase in number and were further functionally compromised based on increased OX-40, TCF-1 and DNAM-1 that repress the expression of FoxP3, a key master regulator of Tregs.
- Analysis of paired tumor biopsies by multiplex immunofluorescence (mIF) showed higher number of CD8+ T and NK cells within the TME following MDNA11 treatment, including increased activated CD8+ T cells
- Gene expression analysis captured signature of enhanced immune effector function in on-treatment biopsies vs pre-treatment biopsies, characterized by increased cytotoxic activity of CD8+ T and NK cell populations (i.e., elevated Granzyme gene family members) responsible for tumor cell killing.

Combination Safety:

The first dose level in the combination escalation portion of the study was as follows:

MDNA11: Step-up dosing at 30 and 30g/kg followed by target dose of 60g/kg every 2 weeks by IV infusion
Pembrolizumab (Keytruda): 400 mg every 6 weeks by IV infusion

No dose limiting toxicities were observed in any of the 3 patients during the observation period. The Safety Review Committee approved enrolment of 3 patients in the next higher dose as follows:

MDNA11: Step-up dosing at 30 and 60g/kg followed by target dose of 90g/kg every 2 weeks by IV infusion
Pembrolizumab (Keytruda): 400 mg every 6 weeks by IV infusion

Enrollment:

Monotherapy expansion part of ABILITY-1 is enrolling patients with metastatic melanoma, non-melanoma skin cancers (CSCC, MCC, and BCC) and MSI-H/dMMR tumors. Combination escalation part of the ABILITY-1 study is enrolling patients with advanced solid tumors who progressed following earlier lines of treatment.

A copy of the related slide deck will be posted to the “Events” page of Medicenna’s website following the presentation.

About MDNA11

MDNA11 is an intravenously administered, long-acting ‘beta-enhanced not-alpha’ interleukin-2 (rIL-2) Superkine specifically engineered to overcome the shortcomings of aldesleukin and other next generation IL-2 variants by preferentially activating immune effector cells ($CD8^+$ T and NK cells) responsible for killing cancer cells, with minimal or no stimulation of immunosuppressive Tregs. These unique proprietary features of the IL-2 Superkine have been achieved by incorporating seven specific mutations and genetically fusing it to a recombinant human albumin scaffold to improve the pharmacokinetic (PK) profile and pharmacological activity of MDNA11 due to albumin’s natural propensity to accumulate in highly vascularized sites, in particular tumor and tumor draining lymph nodes. MDNA11 is currently being evaluated in the Phase 1/2 ABILITY-1 study as both a monotherapy and in combination with pembrolizumab (Keytruda®).

About the ABILITY-1 Study

The ABILITY-1 study (NCT05086692) is a global, multi-center, open-label study that assesses the safety, tolerability, pharmacokinetics, pharmacodynamics and anti-tumor activity of MDNA11 as monotherapy or in combination with pembrolizumab (KEYTRUDA®). In the combination dose escalation of the Phase 2 study, approximately 6-12 patients are expected to be enrolled and administered ascending doses of MDNA11 intravenously once every two weeks in combination with pembrolizumab. This portion of the study includes patients with a wide range of solid tumors with the potential for susceptibility to immune modulating therapeutics. Upon identification of an appropriate dose regimen for combination, the study will proceed to a combination dose expansion cohort.

About Medicenna

Medicenna is a clinical-stage immunotherapy company focused on developing novel, highly selective versions of IL-2, IL-4 and IL-13 Superkines and first in class class-empowered superkines. Medicenna’s long-acting IL-2 Superkine, MDNA11, is a next-generation IL-2 with superior affinity toward CD122 (IL-2 receptor beta) and no CD25 (IL-2 receptor alpha) binding, 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 enrolling over 130 patients, 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 (Bifunctional SuperKine ImmunoTherapies) is designed to enhance the ability of Superkines to treat immunologically “cold” tumors.

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

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 that are not historical facts, including, without limitation, statements on the clinical development and potential and safety profile of MDNA11, additional data and reporting thereof. Forward-looking statements are often identified by terms such as “will”, “may”, “should”, “anticipate”, “expect”, “believe”, “seek”, “potentially” 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 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.

Investor and Media Contact:

Christina Cameron
Investor Relations, Medicenna Therapeutics
ir@medicenna.com
(647) 953-0673

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