Medicenna Announces Positive Single-Agent Activity of MDNA11 from Dose Expansion Cohort and Encouraging Safety Profile in Combination with KEYTRUDA® (pembrolizumab) at the 39th Annual Meeting of SITC

November 11, 2024

Single-agent MDNA11 shows a 30% objective response rate (3 of 10) in the monotherapy dose expansion cohort among patients with advanced and/or metastatic solid tumors who had disease progression with immune checkpoint inhibitor (ICI) therapy

Among ICI-resistant, high-dose MDNA11, phase 2-eligible patients in the monotherapy escalation and expansion cohorts (N=20), the response rate is 25% (5/20) including 1 complete response (CR) and 4 partial responses (PR)

Treatment responses have been observed in 2 of 3 microsatellite instability-high (MSI-H) patients, both with pancreatic cancer, and in 3 of 11 patients with cutaneous melanoma including one CR

With no dose limiting toxicities (DLTs) or new safety signals observed in combination with Merck's (known as MSD outside of the US and Canada) anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) to date, the combination dose escalation is enrolling patients at the highest dose of MDNA11 evaluated in monotherapy (120 µg/kg)

Among 5 efficacy-evaluable patients in the combination dose escalation arm, tumor control (PR or SD) was observed in 4 patients including a PR in a microsatellite-stable (MSS) colon cancer patient

TORONTO and HOUSTON, Nov. 11, 2024 (GLOBE NEWSWIRE) -- Medicenna Therapeutics Corp. ("Medicenna" or the "Company") (TSX: MDNA, OTCQX: MDNAF), a clinical-stage immunotherapy company focused on the development of Superkines, presented updated clinical results from the ongoing monotherapy dose expansion and combination dose escalation portions of the Phase 1/2 ABILITY-1 (**A B**eta-only **IL**-2 **I**mmunoTherap**Y**) study evaluating MDNA11, a long-acting 'beta-enhanced not-alpha' interleukin-2 (IL-2) super-agonist, as monotherapy or in combination with Merck's (known as MSD outside of the US and Canada) anti-PD-1 therapy, KEYTRUDA® (pembrolizumab), in patients with advanced solid tumors, at the 39th Annual Meeting of the Society for Immunotherapy of Cancer (SITC), held in Houston, Texas, on November 9th, 2024.

"We are thrilled to share promising results from the Phase 1/2 ABILITY-1 study, with MDNA11 continuing to show deep and durable single-agent activity in patients resistant to checkpoint therapy including 2 patients with metastatic, treatment-refractory pancreatic cancer," said Fahar Merchant, Ph.D., President and CEO of Medicenna. "We are especially pleased to see that MDNA11 in combination with KEYTRUDA® is demonstrating a favorable safety profile, robust pharmacodynamics and early signs of anti-tumor activity in heavily pre-treated patients allowing us to bolster the dose of MDNA11 to 120 µg/kg every 2 weeks and begin to evaluate dosing at a more convenient frequency of once every three weeks. We look forward to sharing additional clinical updates from the monotherapy and combination arms at medical conferences in the first half of 2025."

Key findings from the on-going monotherapy and combination dose escalation portions of the ABILITY-1 study at the time of data cut-off (i.e. October 15th, 2024) include:

Monotherapy Tumor Response in Checkpoint Resistant Patients

MDNA11 continues to demonstrate encouraging deep and durable single-agent anti-tumor activity among patients who progressed on prior ICI therapy:

- An objective response rate (ORR) of 30% in the monotherapy dose expansion arm with 3 PRs among 10 patients who had all previously failed ICI therapy and had advanced and/or metastatic melanoma, non-melanoma skin cancer or MSI-H/dMMR tumors irrespective of tumor origin.
- The ORR is 25% (1 CR, 4 PR) from a total of 20 patients when including 10 phase 2 eligible patients from the MDNA11 monotherapy dose escalation arm who received at least 60 µg/kg.
- Objective responses included:
    - 2 PRs among 3 MSI-H patients (ORR of 66.7%) with both responders having pancreatic ductal adenocarcinoma (PDAC). One patient with MSI-H PDAC was initially misclassified as MSI-H small bowel cancer with metastases in the pancreas.
    - 1 CR and 2 PRs among 11 patients with cutaneous melanoma (ORR of 27.3%).
    - SD in 6 patients including 3 with duration > 24 weeks, yielding a clinical benefit rate of 40% (8/20).

Monotherapy Safety Profile

Key findings from the monotherapy dose escalation and ongoing monotherapy expansion arms of the ABILITY-1 study demonstrate MDNA11's favorable safety profile:

As previously reported, DLT or vascular leak syndrome were not observed during monotherapy dose escalation with a majority (94%) of treatment-related adverse events (TRAEs) being either grade 1 or 2 and resolving within 48 hours; grade 3 TRAEs mainly constituted asymptomatic transient LFT elevations; one isolated grade 4 TRAE was observed with asymptomatic transient LFT elevation in the monotherapy dose expansion arm which

resolved within 72 hours without intervention. Repeat administration of MDNA11 at the target doses continues to improve tolerability.

Monotherapy Pharmacodynamics

Pharmacodynamic analyses showed potent and durable systemic immune responses following MDNA11 administration with clear evidence of immune activation in the tumor microenvironment:

- MDNA11 showed significant increases in markers of stemness, central and effector memory and enhanced effector function in circulating $CD8^+$ T and NK cells.
- Analysis of paired biopsies showed increased tumor infiltration of $CD25^+$ activated $CD8^+$ T cells and NK cells post-MDNA11 treatment.

Combination Dose Escalation Safety Profile

No DLTs, grade 4 or 5 TRAEs were observed in combination dose escalation cohorts 1 or 2 (60 µg/kg Q2W or 90 µg/kg Q2W MDNA11 with 400 mg Q6W KEYTRUDA®) during the DLT observation period. The Safety Review Committee approved enrollment of the next higher-dose cohorts as follows:

Cohort 3: 120 µg/kg Q2W MDNA11 and 400 mg Q6W KEYTRUDA®
Cohort 4: 120 µg/kg Q3W MDNA11 and 400 mg Q6W KEYTRUDA®

Combination Dose Escalation Pharmacodynamics

Early pharmacodynamic analyses demonstrated robust lymphocyte expansion which was sustained with repeat dosing at both 60 µg/kg and 90 µg/kg Q2W MDNA11 in combination with 400 mg Q6W KEYTRUDA®.

Combination Dose Escalation Tumor Response

Encouraging preliminary signs of anti-tumor activity were observed with MDNA11 in combination with KEYTRUDA® (400 mg Q6W) in dose escalation cohorts 1 (60 µg/kg Q2W MDNA11) and 2 (90 µg/kg Q2W MDNA11). Among 5 heavily pre-treated efficacy-evaluable patients, tumor control (PR or SD) was observed in 4 patients including a PR in a microsatellite-stable (MSS) colon cancer patient.

A copy of the poster and a related slide deck have been posted on the "Scientific Presentations" page of Medicenna's website.

About MDNA11

MDNA11 is an intravenously administered, long-acting 'beta-enhanced not-alpha' IL-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 monotherapy and in combination with 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 KEYTRUDA®. In the combination dose escalation portion of the Phase 2 study, approximately 6-12 patients are expected to be enrolled and administered ascending doses of MDNA11 intravenously in combination with KEYTRUDA®. 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 Therapeutics

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 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. MDNA11 is being evaluated in the Phase 1/2 ABILITY-1 Study (NCT05086692) as a monotherapy and in combination with pembrolizumab. 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 high-affinity IL-2β biased IL-2/IL-15 Super-antagonists, from its MDNA209 platform, are being evaluated as potential therapies for autoimmune and graft-versus host diseases. Medicenna's early-stage BiSKITs ™ (Bifunctional SuperKine ImmunoTherapies) and the T-MASK™ (Targeted Metalloprotease Activated SuperKine) programs are designed to enhance the ability of Superkines to treat immunologically "cold" tumors.

For more information, please visit www.medicenna.com, and follow us on Twitter and LinkedIn.

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. Forward-looking statements include, but are not limited to, express or implied statements regarding the future operations of the Company, estimates, plans, strategic ambitions, partnership

activities and opportunities, objectives, expectations, opinions, forecasts, projections, guidance, outlook or other statements that are not historical facts, such as statements on the therapeutic potential and safety profile of MDNA11 (both as monotherapy and in combination with KEYTRUDA®), and the timing and/or release of any additional clinical updates. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage pre-clinical or clinical studies may not be indicative of full results or results from later stage or larger scale clinical studies and do not ensure regulatory approval. You should not place undue reliance on these statements, or the scientific data presented.

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 information form of the Company and in other filings made by the Company with the applicable securities regulators from time to time in Canada.

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.

This news release contains hyperlinks to information that is not deemed to be incorporated by reference in this new release.

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