Medicenna Provides Clinical Update and Announces First Complete Responder in MDNA11 in Combination with KEYTRUDA® (pembrolizumab) Combination Dose Escalation Arm of the ABILITY-1 Study

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70-year-old patient with advanced chemo-refractory anal cancer achieves complete response (CR) in 8 weeks when treated with MDNA11 in combination with Merck's (known as MSD outside of the US and Canada) anti-PD-1 therapy, KEYTRUDA ® (pembrolizumab)

Complete regression of all tumors in two CPI-resistant patients in monotherapy arms continue to show durability with a patient with melanoma remaining tumor free at week 63 while a patient with pancreatic cancer remains off all anti-cancer therapy for 11 months after completing the study

A patient with advanced MSS colorectal cancer with a previously announced partial response (PR) continues treatment in the combination escalation arm as of week 32 with a confirmed PR

Both objective responses (1 CR and 1PR) among evaluable patients in the combination dose escalation arm (N=9) are in tumor types with high unmet need and where checkpoint inhibitors (CPI) have not been approved

The ABILITY-1 study is showing promising disease control rates (DCR = CR+PR+SD) of 55% (1 CR, 4 PRs, and 6 SDs) and 78% (1 CR, 1 PR and 5 SDs) in the monotherapy and combination arms, respectfully

Additional monotherapy and combination clinical data from the ABILITY-1 study will be presented at medical conferences in Q1 and Q2 of 2025

TORONTO and HOUSTON, Dec. 05, 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, announced that updated clinical data from the ongoing Phase 1/2 ABILITY-1 study were presented today at the 2024 Immunotherapy Bridge held in Naples, Italy.

The oral presentation by Dr Arash Yavari, MB BS, DPhil, included new data highlighting the first complete response (CR) in the combination dose escalation phase of the study in a 70-year-old patient with advanced anal squamous cell carcinoma (anal SCC), in addition to follow up safety and efficacy results from the monotherapy and combination arms of the ABILITY-1 study. The anal SCC patient previously progressed on two prior lines of treatment comprising of chemotherapy combination and chemo-radiation treatments. The patient achieved a 100% reduction of all measurable target and non-target lesions by Week 8, highlighting MDNA11's potential to enhance checkpoint inhibitor efficacy in advanced solid tumor types traditionally considered less sensitive to immunotherapy.

"These remarkable results from our monotherapy and early data from the combination dose escalation highlights the transformative potential of MDNA11 as a combination therapy with checkpoint inhibitors like KEYTRUDA®, while demonstrating an acceptable safety profile as dose escalation continues," said Fahar Merchant, PhD, President and CEO of Medicenna. "Achieving a complete response in a patient with anal squamous cell carcinoma, a cancer with historically low immunotherapy response rates, demonstrates MDNA11's ability to reinvigorate the immune system and tackle difficult-to-treat tumors. We look forward to sharing additional clinical data at medical conferences in Q1 and Q2 of 2025 as we advance MDNA11 as a potent and safe immunotherapy to dramatically improve current immunotherapies and deliver life-changing outcomes for patients."

Key findings from the on-going ABILITY-1 study (data cut-off as of November 18th, 2024) include:

Safety Profile

- MDNA11 has a favorable safety profile both as a monotherapy and in combination with KEYTRUDA®. Over 90% of treatment-related adverse events (TRAEs) were Grade 1-2 and transient, with no DLTs or new safety signals observed in combination dose escalation cohorts. MDNA11 at doses of 120 µg /kg (Q3W monotherapy; Q2W and Q3W in combination with KEYTRUDA (400 mg Q6W) are currently being evaluated.

Immunodynamics

- MDNA11 preferentially expands immune effector cells, including activated ($CD25^+$) and "stemness-like" ($TCF\text{-}1^+$) $CD8^+$ T cells, which are critical for sustained anti-tumor responses.
- Robust, dose-dependent lymphocyte expansion in combination with KEYTRUDA, sustained with repeat MDNA11 dosing.

Monotherapy Tumor Response in Immune Checkpoint Inhibitor-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. The ORR is 25% 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 MDNA11 and were ICI-resistant.

- Overall, objective responses in ICI-resistant patients include 1 CR and 4 PRs
    - 2 PRs among 3 MSI-H patients (ORR of 66.7%) with both responders having metastatic pancreatic ductal adenocarcinoma (PDAC).
    - 1 CR and 2 PRs among 11 patients with cutaneous melanoma (ORR of 27.3%).
- Complete resolution of all target and non-target lesions in two patients:
    - 1 confirmed CR in a melanoma patient continues on treatment as of week 63.
    - Pancreatic cancer patient (MSI-H) achieved complete resolution of target and non-target metastatic lesions in the liver including a new lesion treated with MDNA11 following a single cycle of radiation, achieved durable response for 20 months during the study and continues to remain off anti-cancer therapy for 11 months.
- SD in 6 patients for a disease control rate (DCR = CR+PR+SD) of 55% including 3 with duration > 6 months, yielding a clinical benefit rate of 40% (8/20).

MDNA11 in Combination with KEYTRUDA Tumor Response

The objective of the combination dose escalation/evaluation portion of the ABILITY-1 study is to assess the safety, pharmacokinetics and immunodynamics of MDNA11 at various doses and dosing regimens in combination with KEYTRUDA (400mg, Q6W), and to determine the recommended dose and schedule for the combination dose expansion portion of the study.

Encouraging preliminary signs of anti-tumor activity have been observed with MDNA11 in combination with KEYTRUDA® to date in dose escalation cohorts 1 (60 µg/kg Q2W MDNA11) and 2 (90 µg/kg Q2W MDNA11). Among 9 heavily pre-treated, efficacy-evaluable patients, tumor control was observed in 7 patients for a DCR of 78% including a CR in an anal squamous cell carcinoma patient and PR in a microsatellite-stable (MSS) colorectal cancer patient (overall response rate, ORR, 2 /9 22%).

- **CR in a 70-year-old male with anal squamous cell carcinoma**
    - Patient progressed on 2 prior lines of chemotherapy (1L capecitabine/mitomycin plus radiation therapy; 2L carboplatin/paclitaxel)
    - CR achieved on first study evaluable imaging scan at Week 8; patient continues on combination treatment
- **Confirmed PR in 52-year-old female with MSS colorectal cancer**
    - Patient progressed on 2 prior lines of chemotherapy (1L folinate/fluorouracil/oxaliplatin; 2L capecitabine)
    - Continues on combination treatment as of week 32

A copy of the presentation has 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 20 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 combination dose expansion.

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 KEYTRUDA®. 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 may contain 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 treatment 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. Forward-looking statements are based on a number of assumptions believed by the Company to be reasonable at the date of this news release. Although the Company believes that the expectations reflected in such forward-looking statements are reasonable, there can be no assurance that such statements will prove to be accurate. These statements are subject to certain risks and uncertainties and may be based on assumptions that could cause actual results and future events to differ materially from those anticipated or implied 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 or implied in forward-looking statements. 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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