Medicenna Updates MDNA11 Clinical Trial Results at the ESMO-IO Congress 2025, Further Bolstering its Anti-Tumor Activity in Advanced Solid Tumors

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MDNA11 demonstrates durable anti-tumor activity in phase-2 eligible expansion cohorts, enriched for immune checkpoint resistant melanoma, MSS endometrial cancer, MSI-H and TMB-H cancers, in each case exceeding objective response rate (ORR) benchmarks in these difficult to treat populations

In the monotherapy expansion cohorts, irrespective of tumor type, patients treated with MDNA11, as the next treatment following progression on immune checkpoint inhibitors (ICI), had an ORR of 42% and a disease control rate (DCR) of 83% underscoring potential of MDNA11 in earlier lines of treatment

Monotherapy expansion cohorts demonstrate ORRs of 38% in melanoma and 22% in MSI-H corresponding to DCR of 75% and 78%, respectively

MDNA11 in combination with KEYTRUDA (pembrolizumab) shows ORR and DCR of 50% and 75%, respectively, for MSS endometrial cancer while MSS TMB-H tumors demonstrated ORR and DCR of 25% and 88%, respectively

Monotherapy and combination treatment achieve durable responses in multiple advanced metastatic tumors, including pancreatic, breast, colorectal, endometrial, bladder, anal cancer and melanoma

Tumor control (responders and those with stable disease) was associated with significantly prolonged median overall survival (mOS) in both monotherapy and combination cohorts

Medicenna will host a webinar with its management team and the presenting Principal Investigator along with commentary from key opinion leaders to discuss the updated data

TORONTO and HOUSTON, Dec. 10, 2025 (GLOBE NEWSWIRE) -- Medicenna Therapeutics Corp. (“Medicenna” or the “Company”) (TSX: MDNA, OTCQX: MDNAF), a clinical-stage immunotherapy company focused on the development of Superkines targeting cancer and autoimmune diseases, today presented updated clinical data from the ongoing Phase 1/2 ABILITY-1 study evaluating MDNA11 in patients with advanced solid tumors at the European Society of Medical Oncology (ESMO) Immuno-Oncology Congress 2025. MDNA11, a long-acting ‘beta-enhanced not-alpha’ interleukin-2 (IL-2) super-agonist, is being evaluated as a monotherapy or in combination with Merck’s (known as MSD outside of the US and Canada) anti-PD-1 therapy, KEYTRUDA® (pembrolizumab).

A live webinar will be hosted this morning with Medicenna’s management team, the presenting investigator, and additional commentary from key opinion leaders. Participants may register at: [Link]. A replay of the webinar will also be available on Medicenna’s website following the event.

“The most important message from today’s data is that they absolutely add to the differentiation of MDNA11’s mechanism relative to other next-generation IL-2s and reinforce the consistency of its anti-tumor activity in late stage cancers refractory to checkpoint inhibitors,” said Fahar Merchant, Ph.D., President and CEO of Medicenna. “With durable responses in multiple late stage metastatic tumors, including pancreatic, breast, colorectal, endometrial, bladder, anal cancer and melanoma, it is difficult for us not to conclude that MDNA11 demonstrates meaningful efficacy. The recent announcement of the NEO-CYT trial sponsored by Fondazione Melanoma, in pre-surgery patients with high-risk melanoma, provides external validation of our approach and adds to our conviction that MDNA11 is potentially a de-risked drug candidate for earlier stage cancer patients harbouring healthier immune systems. We look forward to sharing new and mature data in the coming weeks and months from the ABILITY-1 study, new data from the NEO-CYT study and non-human primate data with MDNA113, our targeted and conditionally activated anti-PD1-IL-2 BiSKIT which is anticipated to enter its first in human study later next year.”

Dr. André Mansinho, Principal Investigator and Presenting Author, commented: “I am encouraged by the durability of responses and the immune activation profile we observed with MDNA11, both as a single agent and combined with pembrolizumab. The clinical activity in checkpoint-resistant cohorts, together with prolonged remissions suggest a meaningful therapeutic signal that merits further evaluation in broader and earlier patient populations.”

Key findings from the ABILITY-1 study (data cut-off as of December 1, 2025) include:

Safety Profile

- MDNA11 continues to demonstrate a manageable safety profile both as a single agent and in combination with KEYTRUDA. Over 90% of treatment-related adverse events (TRAEs) were Grade 1-2 and transient, typically resolving within 48 hours. No dose-limiting toxicities (DLTs) were observed with MDNA11 at doses up to 120 µg/kg in monotherapy or in combination with KEYTRUDA and Grade 3-4 events were mainly laboratory abnormalities without clinical sequelae.

Biological Effective Dose Range (BEDR)

- The preliminary recommended dose for expansion for both monotherapy and combination arms was established at 90 µg/kg Q2W with the BEDR set at 60 to 120 µg/kg (Q2W and Q3W).

Monotherapy Tumor Response in Immune Checkpoint Inhibitor (ICI) Resistant Patients

Amongst Phase-2 Eligible Patients treated at the BEDR (60 to 120 µg/kg) with Single-Agent MDNA11 (N=22):

- ORR of 42% (5 of 12) and DCR of 83% (1 CR, 4 PR, 5 SD) amongst patients who were treated with MDNA11 as the next treatment line following progression on a checkpoint inhibitor, highlighting the potential of MDNA11 in earlier treatment settings.
- ORR in 2° checkpoint-resistant cutaneous melanoma was 38% (3 of 8) with a disease control rate of 75% (1 CR, 2 PR, 3 SD).
- ORR in MSI-H tumors was 22% (2 of 9) with a disease control rate of 78% (2 PR, 5 SD).
- Two monotherapy patients with long-term remission include a pancreatic MSI-H patient (>21 months off-treatment) and a melanoma patient (>7 months off-treatment).

Clinical Activity of MDNA11 in Combination with KEYTRUDA

Encouraging anti-tumor activity was also observed with MDNA11 in combination with KEYTRUDA in patients who either progressed on checkpoint therapy or were ineligible for ICI therapy.

Amongst phase-2 eligible patients treated at the BEDR with MDNA11 (60 to 120 µg/kg) and KEYTRUDA (400 mg Q6W) (N=30):

- In microsatellite stable (MSS) endometrial cancers with secondary resistance to immune checkpoint inhibition, the ORR was 50% (2 of 4) with a DCR of 75% (2 PR, 1 SD)
- In TMB-H tumors, the ORR was 25% (2 of 8) with a DCR of 88% (2 PR, 5 SD) and tumor regression observed in 6 of 8 patients (75%)
- In addition, a patient with cutaneous melanoma and primary resistance to a standard of care combination of two immune checkpoint inhibitors (nivolumab + ipilimumab), including hepatic tumor involvement, achieved a PR with MDNA11 + KEYTRUDA at the first on-study scan.

Significant Improvements to Overall Survival Amongst Those with Disease Control

MDNA11 demonstrated a significant association between disease control (CR, PR and SD) and overall survival (OS) in both monotherapy and combination cohorts among patients treated within the BEDR of MDNA11 with or without KEYTRUDA:

- In the monotherapy cohorts, patients with disease control (N=24) had a median OS of 120.2 weeks compared with 28.6 weeks in those without disease control (N=24) (p=0.002; HR 0.29 [95% CI: 0.13-0.66]).
- In the combination cohorts, patients with disease control (N=27) had a median OS that was not yet reached compared with 26 weeks in those without disease control (N=18) (p=0.014, HR 0.28 [95% CI: 0.02-0.85]).

Although these survival data are exploratory, they provide additional support for the clinical relevance of MDNA11-mediated disease control.

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

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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 Merck's anti-PD-1 therapy, KEYTRUDA

(pembrolizumab). In the combination dose escalation portion of the Phase 2 study, patients have been 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. The combination Recommended Dose for Expansion (cRDE) has been established and the study has commenced 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. Medicenna's first-in-class targeted PD-1 x IL-2 bispecific, MDNA113, is in development for solid tumors and was designed using the Company's proprietary BiSKITs ™ (Bifunctional SuperKine ImmunoTherapies) and T-MASK™ (Targeted Metalloprotease Activated SuperKine) platforms 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.

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

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 Merck's anti-PD-1 therapy, KEYTRUDA [pembrolizumab]) 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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