Medicenna Presents Updated Preclinical Data on MDNA113, a First-in-Class, Targeted and Masked Bi-functional anti-PD1-IL2 Superkine, at the 2024 Annual Meeting of the American Association for Cancer Research (AACR)

April 9, 2024

MDNA113 is targeted to the tumor site where it is activated to simultaneously deliver two immunotherapies, an IL-2 superkine and anti-PD1 antibody, to the same cancer fighting immune cells in the tumor micro-environment (TME) to maximize efficacy and minimize systemic toxicity

MDNA113 is our most advanced pre-clinical candidate that targets IL-13Rα2, a tumor associated antigen, which is overexpressed by immunologically "cold" tumors with high unmet needs in pancreatic, prostate, ovarian, breast and brain cancer affecting over two million patients every year

TORONTO and HOUSTON, April 09, 2024 (GLOBE NEWSWIRE) -- Medicenna Therapeutics Corp. ("Medicenna" or the "Company") (TSX: MDNA), a clinical-stage immunotherapy company focused on the development of Superkines, today announced new preclinical data on MDNA113, the Company's novel T-MASK (**T**argeted **M**etallo/protease **A**ctivated **S**uper**K**ine) candidate, an IL-13Rα2 (Interleukin-13 receptor alpha2) specific superkine featuring unique masking and tumor targeting characteristics, were presented at the 2024 Annual Meeting of the American Association for Cancer Research (AACR) held in San Diego, CA, on April 9th, 2024.

"We are pleased to show preclinical data demonstrating the ability of Medicenna's first T-MASK candidate, MDNA113 to enhance tumor accumulation and tolerability of our potent bi-functional immune modulator, anti-PD1-IL-2^{SK}," said Fahar Merchant, Ph.D., President and Chief Executive Officer of Medicenna. "MDNA113 has novel features, including the tunable blockade of the IL-2R agonism to reduce peripheral immune stimulation for enhanced tolerability, and tumor targeting to IL-13Rα2 which is linked to aggressive cancers that annually affect over 2 million patients world-wide. The cleavage and release of the IL-13 tumor-targeting/masking domain by matrix metalloproteases restores IL-2R signaling within the tumor microenvironment, thereby benefiting from the simultaneous and synergistic activity of IL-2R agonism and immune checkpoint blockade at the tumor site."

The Company selected MDNA113, a novel, first-in-class tumor-targeted and tumor-activated bi-functional anti-PD1-IL-2 superkine with high selectivity and affinity for IL-13Rα2, a tumor associated antigen expressed in many aggressive solid tumors. The IL-13 Superkine (MDNA213) is a highly specific tumor-targeting/masking domain which is fused via a protease sensitive linker to a bi-functional immunotherapy domain (MDNA223) containing an IL-2 Superkine fused to an anti-PD1 antibody.

Key findings presented at the conference include:

- When not activated, MDNA113 shows reduced IL-2R agonism with no change to PD-1/PDL-1 blockade activity.
- Cleavage and activation of MDNA113 by cancer specific enzymes (metalloproteases) releases the T-MASK domain (MDNA213), restoring activity of the IL-2 Superkine at the tumor site.
- MDNA113 shows attenuated systemic lymphocyte expansion compared to non-masked version (MDNA223), consistent with design of MDNA113.
- MDNA113 is better tolerated than non-masked counterpart (MDNA223), supporting higher and more efficacious dosing schedule.
- MDNA113 selectively binds IL-13Rα2 positive tumor cells *in vitro,* and durably accumulates (>7 days) in IL-13Rα2 positive tumors in mice.
- Cleavable MDNA113 shows similar efficacy as non-masked MDNA223 in mouse tumor models by either localized (intra-tumoral) or systemic (intra-peritoneal) delivery, consistent with proteolytic activation within TME.
- Single neoadjuvant treatment with MDNA113 in a highly invasive orthotopic 4T1.2 breast cancer model significantly increases survival by preventing metastasis.
- In summary, the T-MASK platform exemplified by MDNA113, facilitates tumor targeting and minimizes systemic toxicity while maximizing therapeutic activity at the tumor site.

The poster, "Characterization of MDNA113, a Tumor-Targeting Anti-PD1-IL-2 ^{SK} Immunocytokine with Conditional Activation to Increase Tolerability and Maximize Efficacy" can be found on the AACR website for conference registrants. It will be also available on the Scientific Presentations page of Medicenna's website following the conclusion of the 2024 Annual Meeting of AACR.

About the T-MASK Platform

Medicenna's novel T-MASK (**T**argeted **M**etallo/protease **A**ctivated **S**uper**K**ine) platform involves fusion of a dual tumor-targeting/masking domain to an immune modulator (such as a Superkine or a BiSKIT) via a matrix metalloprotease (MMP) sensitive linker to (i) reduce and fine-tune the potency of the immune modulator, (ii) increase its systemic tolerability (iii) prolong its retention in the TME and (iv) to maximize and restore full potency at the intended target site. The T-MASK platform offers opportunity to target and fine-tune immune cell stimulation in the TME to improve the therapeutic index of Medicenna's Superkine and BiSKIT platforms.

About MDNA113

MDNA113 is a novel, first-in-class tumor-targeted and tumor-activated bi-functional anti-PD1-IL-2 Superkine with high affinity for IL-13Rα2 without

binding to the functional IL-13Rα1. IL-13Rα2 is overexpressed in a wide range of solid tumors, including cold tumors. IL-13Rα2 is a tumor-associated antigen with minimal to no expression in normal tissues but is highly expressed by a wide range of tumors including “cold” tumors. IL-13Rα2 expressing tumors also have abundant MMPs in the TME that may efficiently activate MDNA113. IL-13Rα2 expression is associated with poor clinical outcome in multiple tumor types with an annual world-wide incidence of over 2 million in different tumor types including prostate cancer, pancreatic cancer, ovarian cancer, liver cancer, breast cancer and brain cancer, and among others.

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 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™ (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.

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 Company’s cash runway, preclinical and clinical development activities and the potential benefits of its Superkine platform, clinical trial designs and results, clinical potential, expectations and beliefs around safety profiles and upcoming milestones and data reporting, including with respect to MDNA11, the ABILITY study and its expansion, bizaxofusp (MDNA55), MDNA113 and MDNA223. 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 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. 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 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.

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 news release.

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