Medicenna Presents Preclinical Results from its IL-2 Super-Antagonist and Anti-PD1-IL-2 BiSKIT Programs at The Promise of Interleukin-2 Therapy Conference

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MDNA209 is a first-in-class "beta-enhanced" IL-2 Super-antagonist being developed for the potential treatment of autoimmune diseases, a disorder attributed to an imbalance of the immune system and affecting 5 to 10% of the global population

MDNA209 restores immune balance by selectively blocking IL-2Rβγ_C, a receptor highly expressed by effector CD8 T cells which are known to promote tissue damage in autoimmune diseases

In an aggressive animal model of graft versus host disease (GvHD) MDNA209 was able to extend overall survival by 400 percent, reduce weight loss and improve clinical scores, highlighting its therapeutic potential for treating GvHD and autoimmune diseases

MDNA113 is an IL-13Rα2 tumor-targeted BiSKIT (Bifunctional SuperKine for ImmunoTherapy) which delivers an anti-PD1-IL-2 Superkine (anti-PD1-IL-2^{SK}) directly to the tumor microenvironment (TME) where it is conditionally activated by tumor-associated proteases

MDNA113's efficacy was significantly enhanced in mice harboring tumors engineered to overexpress IL-13Rα2, highlighting its potential to treat immunologically "cold tumors" such as pancreatic, prostate, ovarian, and breast cancers that globally affect over two million patients every year

TORONTO and HOUSTON, Sept. 09, 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, announced today that, as planned and previously announced, new data from two of its preclinical programs were presented orally at the Promise of Interleukin-2 Conference held in Paris, France from September 4-7, 2024.

"Inspired by the promising Phase 1/2 clinical results from the ABILITY-1 clinical trial of MDNA11, we are leveraging the same IL-2 Superkine platform to advance our pipeline of transformative medicines to treat not only cancer but also autoimmune diseases," said Fahar Merchant, Ph.D., President and CEO of Medicenna. "We are encouraged by these preclinical data, which validates the versatility of our IL-2 Superkines beyond cancer as we further evaluate MDNA209 in GvHD and other disease models. Additionally, our IL-13 Superkines enable us to precisely deliver and localize BiSKITs to the tumor site which could potentially benefit patients with cancers that have not responded to currently approved checkpoint inhibitors, thereby addressing a huge unmet need."

MDNA209 and MDNA113 are preclinical assets based on the MDNA109 platform also used to develop MDNA11, a long-acting IL-2 Super-agonist, currently being evaluated in the Phase 1/2 ABILITY-1 clinical trial for the treatment of solid tumors.

- The first presentation outlined the potential of MDNA209 to treat autoimmune diseases, including high grade GvHD which has a 1-year survival rate of only 40%. Transplant patients with GvHD experience significant morbidity and mortality with limited therapeutic options to prolong survival. The initial preclinical data presented on the MDNA209 platform highlight the potential of the Company's long-acting, high-affinity IL-2β biased IL-2/IL-15 Super-antagonists to downregulate the immune system, with therapeutic potential for GvHD and autoimmune diseases.
- The second presentation focused on MDNA113, which is being developed as a novel, targeted and bifunctional version (anti-PD1-IL-2 Superkine fusion) of a class of blockbuster anti-PD1 therapies, with current annual sales of over $30 billion but lose patent protection from 2028 onwards. Although Anti-PD-1 checkpoint blockade has improved survival outcomes in many types of solid tumors, approximately 70% of cancer patients do not benefit. To further improve patient outcomes, Medicenna has designed an anti-PD1-IL-2^{SK} BiSKIT that uses an IL-13 Superkine to simultaneously target and localize the BiSKIT to the TME while masking the IL-2 domain during peripheral circulation and reducing its toxicity. At the TME, tumor specific proteases cleave the IL-13 component, releasing the BiSKIT to engage with T-cells thereby stimulating T-cell activity via the IL-2 domain and preventing T-cell exhaustion via the anti-PD1 domain.

Key highlights from the presentations are:

MDNA209, a High Affinity IL-2β Biased IL-2/IL-15 Super-antagonist, for the Treatment of Autoimmune Diseases

- MDNA209 is an IL-2 Super-antagonist with enhanced affinity for IL-2Rβ but does not engage with the γ_c subunit, therefore acting as a receptor clamp to exclude native IL-2 as well as native IL-15.
- MDNA209 is fused to an Fc scaffold (MDNA209-Fc) to extend its in vivo half-life, reducing the need for frequent dosing.
- MDNA209-Fc inhibits both, IL-2 and IL-15 induced p-STAT5 signaling, reduces IFNγ release and slows immune cell proliferation without reducing Treg population.
- In an aggressive animal model of acute GvHD, MDNA209 was able to extend overall survival by 400 percent, reduce weight loss and improve clinical scores.

MDNA113, an IL-13Rα2 Tumor Targeting and Conditionally Activatable anti-PD1-IL-2^{SK} BiSKIT Shows Enhanced Safety and Potent Therapeutic

Efficacy

- MDNA113 (masked version) showed reduced capacity to induce IL-2R mediated pSTAT5 signaling compared to anti-PD1-IL-2^{SK} (non-mask version) in cell-based assay and human CD8+ T cells without impacting PD1/PDL1 blockade.
- Proteolytic cleavage of MDNA113 releases anti-PD1-IL-2^{SK} and fully restores its capacity to activate IL-2R signaling.
- Mice treated with MDNA113 showed reduced peripheral lymphocyte expansion compared to anti-PD1-IL-2^{SK} due to masking by the IL-13 Superkine.
- MDNA113 showed greater tolerability than anti-PD1-IL-2^{SK} following repeat dose administration in mice.
- MDNA113, but not a non-cleavable version, demonstrated similar efficacy as anti-PD1-IL-2^{SK} in MC38 colon tumor model despite these tumors lacking IL-13Rα2 expression.
- Efficacy of MDNA113 is substantially enhanced when tested in mice harboring MC38 tumors that have been engineered to overexpress IL-13Rα2, resulting in complete tumor regression in most animals.
- Variants of MDNA113 have also been designed with tunable masking of the IL-2 Superkine underscoring the versatility of the platform.

Copies of the two presentations are available on the "Scientific Presentations" page of Medicenna's website.

About MDNA209

The Company's MDNA209 platform consists of IL-2 muteins with targeted mutations enabling high-affinity IL-2 receptor antagonism. MDNA209 blocks the formation of the IL-2Rβγ_C complex, preventing downstream signaling and blocking effector T-cell functions. MDNA209 outcompetes IL-2 for IL-2Rβ and impedes γ_C engagement, blocking downstream signaling and restraining reactive effector immune cells, thereby offering therapeutic potential for treating inflammatory and autoimmune diseases.

About MDNA113

MDNA113 is a novel, first-in-class tumor-targeted and tumor-activated bi-functional anti-PD1-IL2 Superkine with exceptionally 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 with minimal to no expression in normal tissues. IL-13Rα2 expressing tumors also have abundant matrix metalloprotease in the tumor microenvironment that may efficiently activate MDNA113. IL-13Rα2 expression is associated with poor clinical outcome in multiple tumor types including prostate cancer, pancreatic cancer, ovarian cancer, liver cancer, breast cancer and brain cancer, with an annual world-wide incidence of over 2 million.

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 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.

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 MDNA209 and MDNA113. 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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