Medicenna Presents Preclinical Data from its Anti-PD1-IL-2 BiSKIT and IL-2 Super Agonist Programs at the 39th Annual Meeting of the Society for Immunotherapy of Cancer (SITC)

November 8, 2024

MDNA113 is a novel IL-13Rα2 tumor-targeted and "masked" BiSKIT (Bifunctional SuperKine for ImmunoTherapy), engineered to deliver an anti-PD1-IL-2 Superkine (anti-PD1-IL-2^{SK}) to the tumor microenvironment (TME), where it is conditionally activated by tumor-associated proteases

MDNA113 treatment achieved complete tumor regression of IL-13Rα2 expressing tumors, highlighting its potential to treat a vast range of malignancies, including immunologically "cold tumors" that annually affect over two million cancer patients worldwide

Internationally recognized academic teams in the UK showed promising pre-clinical results with a long-acting IL-2^{SK} (MDNA11) and anti-PD1-IL-2^{SK} BiSKIT, in mouse models of glioblastoma (GBM) and patient-derived GBM explants

Updated MDNA11 clinical results from the ABILITY-1 study will be presented tomorrow at SITC

TORONTO and HOUSTON, Nov. 08, 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 new preclinical data from its BiSKIT (MDNA113) and IL-2 super agonist (MDNA11) programs will be presented today at the 39th Annual Meeting of SITC being held in Houston, Texas. In addition, as announced previously, updated clinical results from the MDNA11 Phase 1/2 ABILITY-1 study will be presented tomorrow, Saturday November 9, 2024 at SITC.

"We are excited to demonstrate our ability to generate novel therapeutics such as MDNA113, to address unmet needs in oncology, by smartly leveraging both our IL-2 and IL-13 Superkine platforms in one molecule," said Fahar Merchant, Ph.D., President and CEO of Medicenna. "Today's data demonstrates the effectiveness of MDNA113 to inhibit tumor growth, particularly in IL-13Rα2 positive tumors, and showcase its potential to completely protect and prevent metastasis in an aggressive breast cancer model when administered just once prior to surgery. In a separate presentation, independent work from our academic collaborator in the UK demonstrated the capacity of MDNA11 and anti-PD1-IL-2SK BiSKIT to significantly extend overall survival in an aggressive GBM mouse model and stimulate activity of resident effector immune cells in fresh human GBM explants."

MDNA113 is based on the Company's IL-2 and IL-13 Superkine Platforms, the former being used to develop MDNA11, a long-acting IL-2 super agonist, currently being evaluated in the Phase 1/2 ABILITY-1 study for the treatment of advanced and/or metastatic solid tumors.

Key highlights from the presentations are:

MDNA113 is a conditionally activatable anti-PD1-IL-2^{SK} with a cleavable IL-13^{SK} dual masking/tumor-targeting domain to limit systemic immune stimulation while maximizing anti-tumor response

- Mice treated with MDNA113 showed reduced peripheral lymphocyte expansion without impacting anti-PD1/PDL1 blockade, and better tolerability when compared to unmasked anti-PD1-IL-2^{SK}.
- Cleavage by tumor-specific proteases removes the IL-13^{SK} targeting and masking domain of MDNA113, restoring the synergy between IL-2R agonism and anti-PD1 blockade
- Efficacy of MDNA113 is substantially enhanced in mice harboring MC38 tumors that have been engineered to overexpress IL-13Rα2, resulting in complete tumor regression in a vast majority of animals
- Single neoadjuvant treatment (pre-surgery) with MDNA113 in a highly invasive orthotopic 4T1.2 model of triple negative breast cancer resulted in 100% survival by preventing metastasis and enrichment of cytotoxic GrzB-positive CD8^{+}T cells within the tumor microenvironment.

Stimulation of IL-2 signaling with highly selective IL-2R super-agonists enhances immune effector cell response in mouse and patient-derived glioblastomas

- Long-acting IL-2^{SK} (i.e., MDNA11) and anti-PD1-IL-2^{SK} (i.e., therapeutic core of MDNA113) significantly extended the survival of mice bearing aggressive orthotopic GBMs when compared to control mice or mice treated with native IL-2 or anti-PD1.
- GBMs from anti-PD1-IL-2^{SK} treated mice showed higher frequency of infiltrating CD8^{+}T and NK cells with no change in immune suppressive Tregs.
- Ex-vivo primary patient-derived fresh GBM explants treated with IL-2^{SK} or anti-PD1-IL-2^{SK} showed increased CD8^{+} T and NK cell populations concomitant with reduced tumor cell burden.

Copies of the two presentations will be available on the "Scientific Presentations" page of Medicenna's website after the conference.

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 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 (NCT05086692) as both monotherapy and in combination with pembrolizumab.

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 MDNA11 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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