



Medicenna Presents Clinical Validation of the IL4 Receptor as a Biomarker for MDNA55 in Recurrent Glioblastoma

June 3, 2019

TORONTO and HOUSTON, TX, June 3, 2019 /CNW/ - Medicenna Therapeutics Corp. ("**Medicenna**" or "the **Company**") (TSX: MDNA, OTCQB: MDNAF), a clinical stage immunotherapy company developing first-in-class Superkines and Empowered Cytokines, presented a poster entitled "*MDNA55: A Locally Administered IL4 Guided Toxin as a Targeted Treatment for Recurrent Glioblastoma*" at the 55th Annual Meeting of the American Society of Clinical Oncology (ASCO) being held in Chicago, IL.

The presentation by Dr. Dina Randazzo of Duke University School of Medicine and a Principal Investigator in the Phase 2b clinical trial MDNA55-05, which recently completed its enrollment (N=46), focused on the development of a new biomarker test for the interleukin-4 receptor (IL4R) that may enable better selection and superior treatment outcomes for patients with recurrent glioblastoma ("rGBM"), a highly aggressive and uniformly fatal form of brain cancer.

Highlights from the presentation, encompassing 18 of 21 subjects enrolled in the low dose cohort of the trial and with IL4R results, are summarized below:

- 75% (6 of 8) of subjects with moderate to high IL4R (**IL4R⁺**) expression show disease control (tumor shrinkage or tumor stabilization from baseline) without clinical decline on assessment of imaging data within 90 days following a single treatment with MDNA55. This is compared to 25% (2 of 8) in subjects with no/low IL4R (**IL4R⁻**) expression. Sixteen of 18 subjects were evaluable for tumor response.
- 100% (8 of 8) of **IL4R⁺** subjects show disease control compared to 38% (3 of 8) of **IL4R⁻** subjects, following initial pseudoprogression in some subjects.
- IL4R expression appears to be predictive of a more aggressive form of GBM. Patients with **IL4R⁺** GBM at initial diagnosis had a shorter time to relapse (10.5 months) when compared to subjects with **IL4R⁻** GBM (18.1 months).
- Significantly longer survival ($p = 0.0147$) was seen in **IL4R⁺** subjects (mOS = 15.2 months) compared to **IL4R⁻** subjects (mOS = 8.1 months) after one treatment with MDNA55, despite their more aggressive form of the disease.
- Survival rates at 6, 9, and 12 months were 100%, 88% and 60% versus 70%, 30%, and 20%, for **IL4R⁺** vs. **IL4R⁻** subjects, respectively.
- IL4R is over-expressed in nearly 75% of Central Nervous System ("CNS") tumors, including GBM, but not in normal brain.
- IL4R expression levels at initial diagnosis of GBM is retained or increased at recurrence.

"Treatment options for recurrent GBM are very limited and the survival of rGBM patients currently is dismal at 6-9 months¹⁻³. Treatment with targeted therapies such as MDNA55 may provide new hope for this under-served population and can help determine a role for IL4R as a biomarker for more aggressive forms of GBM," states Dr. Dina Randazzo, Assistant Professor of Neurosurgery at Duke University School of Medicine.

"Developing an IL4R companion diagnostic for use alongside MDNA55 could help us determine which patients will receive optimal therapeutic benefit from MDNA55 treatment," states Dr. Martin Bexon, Head of Clinical Development at Medicenna. "These early validation data appear to show an impressive prolongation of survival and tumor control in subjects with IL4R expressing tumors. They are certainly encouraging results and offer promise for patients with aggressive forms of rGBM."

One of the aims of the study was to determine whether expression of the IL4R on the surface of GBM cells would be a suitable biomarker and target for treatment with MDNA55, an IL4R-directed toxin. In addition to the results summarized above, the poster highlighted the development and qualification of an immunohistochemistry (IHC)-based assay for IL4R. For clinical validation, the assay was used to retrospectively test subjects for IL4R expression levels in the Phase 2b clinical trial, MDNA55-05. Biopsy samples are categorized into four groups based on H-Score (representing no/low to very high expression of IL4R). The poster also described the validation of the assay and explored the relevance of IL4R expression levels to patient outcomes using preserved tumor tissue collected at first diagnosis of GBM.

Enrolment into the Phase 2b MDNA55-05 trial has been completed. Preliminary top-line response data will be presented at a conference this month.

About the Interleukin-4 Receptor (IL4R)

The IL4R target for MDNA55 is an ideal but under-exploited drug target for central nervous system ("CNS") tumors, including glioblastoma ("GBM"). The majority of cancer biopsy samples from adult and pediatric CNS tumors, including recurrent GBM, over-express the IL4R while there is little or no IL4R expression in normal adult and pediatric brain tissue.⁴ Expression of IL4R correlates with increased tumorigenicity in mouse models and poor long term survival in clinical studies of patients with GBM^{5,6}. In addition, the IL4R is known to be expressed by Myeloid Derived Suppressor Cells and Tumor Associated Macrophages, which are known to be key components of the immunosuppressive tumor micro-environment (TME), which hides the tumor from cancer killing immune cells^{7,8}.

About the MDNA55-05 Clinical Trial

MDNA55-05 is a Phase 2b study of the safety and efficacy of MDNA55, an IL4R-directed toxin, in patients with *de novo* GBM at first or second relapse where the tumor is not amenable to surgical resection. In the study, investigators administer MDNA55 once directly into the brain tumor using a technique known as Convection Enhanced Delivery (CED). CED allows precision delivery of MDNA55 into the tumor and the surrounding healthy brain containing infiltrative tumor cells, while avoiding systemic exposure.

The primary endpoint of the study is median Overall Survival (mOS) comparing a null survival rate of 8.0 months (based on historical control) with an alternative pursue rate of 11.5 months (1-sided alpha = 0.10 and 80% power for 46 ITT subjects). The secondary endpoint is objective response rate (ORR) assessed by the modified Response Assessment in Neuro-Oncology (mRANO)-based criteria incorporating advanced imaging modalities with a null response rate of 6% and an alternative pursue rate of 18% (1-sided alpha = 0.10 and 80% power for at least 35 subjects evaluable for response).

About Medicenna Therapeutics Corp.

Medicenna is a clinical stage immunotherapy company focused on oncology and the development and commercialization of novel, highly selective versions of IL-2, IL-4 and IL-13 Superkines and first in class Empowered Cytokines™ (ECs) for the treatment of a broad range of cancers. Supported by a US\$14.1M non-dilutive grant from CPRIT (Cancer Prevention and Research Institute of Texas), Medicenna's lead IL4-EC, MDNA55, has completed enrolling patients in a Phase 2b clinical trial for rGBM, the most common and uniformly fatal form of brain cancer, at top-ranked brain cancer centres in the US. MDNA55 has been studied in five clinical trials involving 132 patients, including 112 adults with rGBM. MDNA55 has demonstrated compelling efficacy and has obtained Fast-Track and Orphan Drug status from the FDA and FDA/EMA respectively. For more information, please visit www.medicenna.com.

References

1. Friedman et al., Bevacizumab Alone and in Combination With Irinotecan in Recurrent Glioblastoma. J Clin Oncol. 2009 Oct 1;27(28):4733-40.
2. Taal et al, Single-agent bevacizumab or lomustine versus a combination of bevacizumab plus lomustine in patients with recurrent glioblastoma (BELOB trial): a randomised controlled phase 2 trial. Lancet Oncol 2014 Aug;15(9):943-53
3. Kim et al., Outcome of salvage treatment for recurrent glioblastoma. J Clin Neuroscience 22 (2015) 468–473, 2015.
4. Joshi BH, Leland P, Asher A, Prayson RA, Varricchio F, Puri RK. In situ expression of interleukin- 4 (IL-4) receptors in human brain tumors and cytotoxicity of a recombinant IL-4 cytotoxin in primary glioblastoma cell cultures. Cancer Res 2001;61:8058-8061.
5. Kohanbash G, McKaveney K, Sakaki M, Ueda R, Mintz AH, Amankulor N, Fujita M, Ohlfest JR, Okada H. GM-CSF promotes the immunosuppressive activity of glioma-infiltrating myeloid cells through interleukin-4 receptor- α . Cancer Res. 2013 Nov 1;73(21):6413-23.
6. Han J and Puri RK. Analysis of the cancer genome atlas (TCGA) database identifies an inverse relationship between interleukin-13 receptor $\alpha 1$ and $\alpha 2$ gene expression and poor prognosis and drug resistance in subjects with glioblastoma multiforme. J Neurooncol. 2018 Feb;136(3):463-474.
7. Roth F, De La Fuente AC, Vella JL, et al. Aptamer-mediated blockade of IL4R α triggers apoptosis of MDSCs and limits tumor progression. Cancer Res. 2012;72(6):1373-83.
8. Bankaitis KV and Fingleton B. Targeting IL4/IL4R for the treatment of epithelial cancer metastasis. Clin Exp Metastasis. 2015 Dec;32(8):847-56.

This news release contains forward-looking statements relating to the future operations of the Company and other statements that are not historical facts. Forward-looking statements are often identified by terms such as "will", "may", "should", "anticipate", "expects" and similar expressions. All statements other than statements of historical fact, included in this release, including, without limitation, statements related to the recently completed Phase 2b clinical trial of MDNA55 for the treatment of rGBM including, without limitation, the use of the IL4R as a biomarker to treat rGBM, ability to develop a viable IL4R companion diagnostic, use of novel imaging modalities for measuring tumor response, the acceptance of primary and secondary endpoints by regulatory agencies, the expectation that patients receiving higher doses of MDNA55 will have similar or better outcomes and that MDNA55 offers promise for patients with aggressive forms of GBM and the future plans and objectives of the Company, are forward-looking statements that involve 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 annual information form of the Company dated June 26, 2018 and in other filings made by the Company with the applicable securities regulators from time to time.

The reader is cautioned that assumptions used in the preparation of any forward-looking information (including, without limitation, the ability of the Company to fully replicate these interim data results) 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 at the time of preparation, 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 of this news release and the Company will update or revise publicly any of the included forward-looking statements only as expressly required by Canadian securities law.

SOURCE Medicenna Therapeutics Corp.



For further information: Fahar Merchant, President and Chief Executive Officer, 604-671-6673, fmerchant@medicenna.com; Elizabeth Williams, Chief Financial Officer, 416-648-5555, ewilliams@medicenna.com