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Medicenna Therapeutics Corp. (T.MDNA-TSX)

T.MDNA: Meeting Soon with the FDA to Discuss Regulatory Path Forward for MDNA55…

Based on our probability adjusted DCF model that takes into account potential future revenues of MDNA55 and MDNA109, MDNA.T is valued at CAD$5.00/share. This model is highly dependent upon continued clinical success of those compounds and will be adjusted accordingly based upon future clinical results.

Current Price (08/20/19)	CAD$1.20
Valuation	**CAD$5.00**

OUTLOOK

On August 9, 2019, Medicenna Therapeutics Corp. (MDNA.T) announced financial results for the first quarter of fiscal year 2020 and provided a business update. Following the release of positive interim data from the Phase 2b clinical trial of MDNA55 in patients with recurrent glioblastoma in June 2019, we anticipate the company meeting with the FDA in the second half of 2019 to discuss a regulatory path forward for the compound, which may include the potential for accelerated approval in patients that express high levels of IL-4R, which is associated with more aggressive disease and poorer prognosis. The company also recently announced the selection of MDNA19, a long-acting IL-2 that preferentially activates cancer killing immune cells, as its second immuno-oncology clinical candidate. We anticipate MDNA19 entering the clinic in 2020.

SUMMARY DATA

52-Week High	**$2.38**
52-Week Low	**$0.64**
One-Year Return (%)	**2.59**
Beta	**2.79**
Average Daily Volume (sh)	**57,870**
Shares Outstanding (mil)	**29**
Market Capitalization ($mil)	**$35**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**0**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2018 Estimate	**N/A**
P/E using 2019 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Value**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $CAD)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2019	0 A	0 A	0 A	0 A	0 A
2020	0 A	0 E	0 E	0 E	0 E
2021					0 E
2022					0 E

Earnings per Share

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2019	-$0.04 A	- $0.04 A	-$0.07 A	-$0.04 A	-$0.18 A
2020	-$0.05 A	-$0.04 E	-$0.04 E	-$0.04 E	-$0.17 E
2021					-$0.15 E
2022					-$0.14 E

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WHAT'S NEW

Business Update

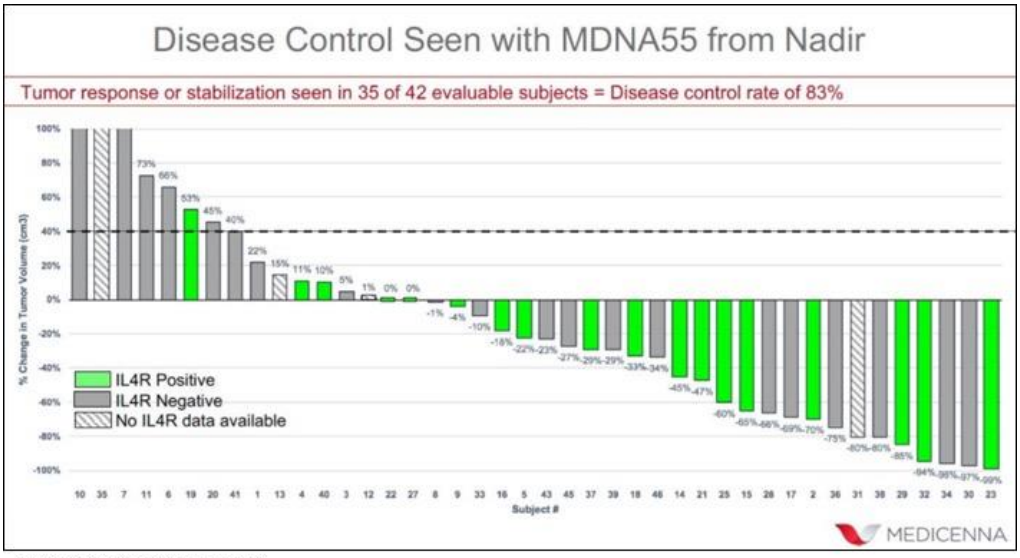
Medicenna Therapeutics Corp. (MDNA) is a clinical stage immuno-oncology company developing novel versions of the cytokines Interleukin (IL)-2, IL-4, and IL-13, which they term 'Superkines'. The Superkines can be utilized as monotherapies, used in combination with other immune modulating agents (e.g., checkpoint inhibitor antibodies), or fused with toxic agents to generate 'Empowered Cytokines' (EC) that precisely deliver cell-killing moieties to tumors. The company has two lead immuno-oncology development products:

MDNA55: This is the company's lead EC asset and consists of an engineered IL-4 with increased affinity to its receptor fused to a fragment of the tumor killing *Pseudomonas* exotoxin as a payload. The company presented positive preliminary Phase 2b data in patients with recurrent glioblastoma (rGBM) in June 2019 and we anticipate overall survival data from this trial in late 2019 or early 2020. Medicenna will be meeting with the FDA in the second half of 2019 to discuss the regulatory path forward for MDNA55, which may include the potential for accelerated approval in patients with high levels of IL-4R.

MDNA19: This is the company's lead 'Superkine' and is an engineered version of IL-2 designed to increase its ability to activate and proliferate effector T cells (which target cancer cells) without promoting the activation of regulatory T cells (which dampen the immune response). Pre-clinical work shows MDNA19 can enhance the activity of anti-PD-1 and anti-CTLA-4 therapy. Pre-IND work is continuing and we anticipate it entering the clinic in 2020.

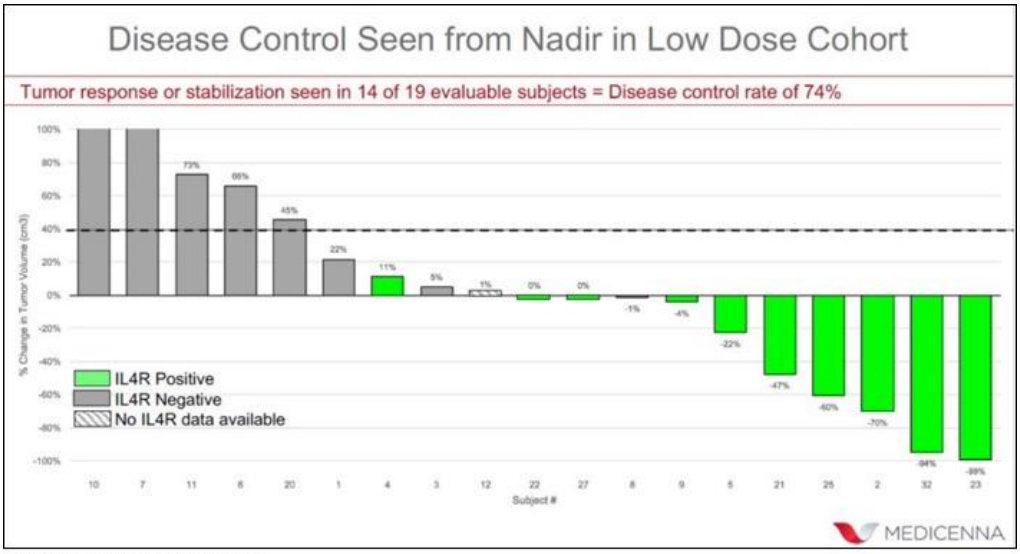
Encouraging Preliminary Data for MDNA55 Phase2b Trial

In June 2019, Medicenna announced the presentation of preliminary topline results from the company's ongoing Phase 2b trial of MDNA55 in patients with rGBM. The trial is not far enough along to report data on the primary outcome, which is overall survival, however Medicenna did present data on the percent change in tumor volume for each patient in the study. To account for the phenomenon of pseudoprogression, in which a treated tumor appears to be growing on subsequent scans following treatment (Van Mieghem *et al*., 2013), assessment as a response from nadir (the largest tumor volume measured) was presented using the criteria for immunotherapy Response Assessment in Neuro-Oncology (iRANO) (Okada *et al*., 2015). The following plot shows that 35/42 evaluable patients experienced either stabilization or a decrease in tumor size from nadir for a disease control rate (DCR) of 83%.



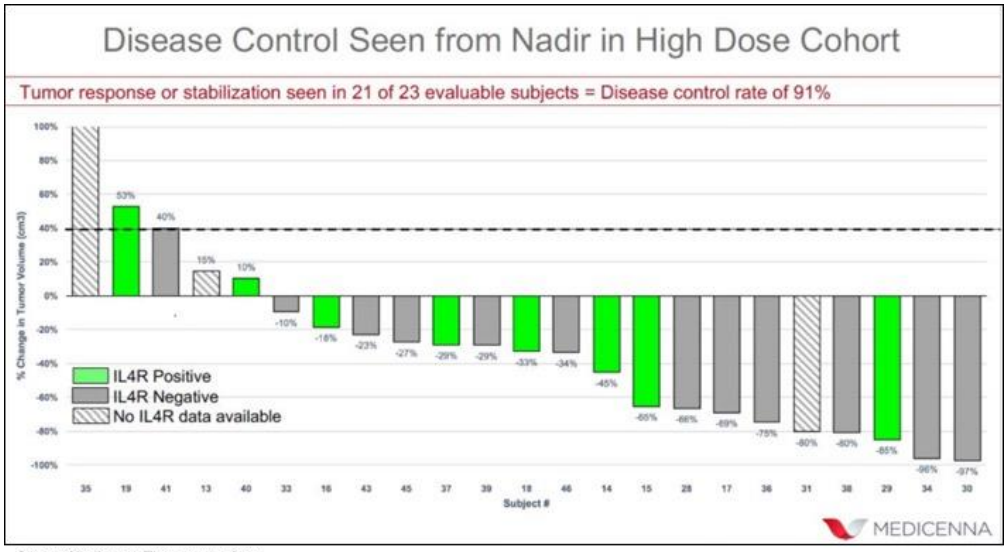
Source: Medicenna Therapeutics Corp.

When the patient population is subdivided into the low-dose and high-dose cohorts an interesting dose response is evident. The following chart shows disease control for patients in the low-dose cohort (median dose of 63 μg), in which a decrease in tumor size is essentially limited to only those with high IL-4R expression.



Source: Medicenna Therapeutics Corp.

This is in contrast to the high-dose group, where a decrease in tumor volume is seen equally in those with both high and low IL-4R expression.

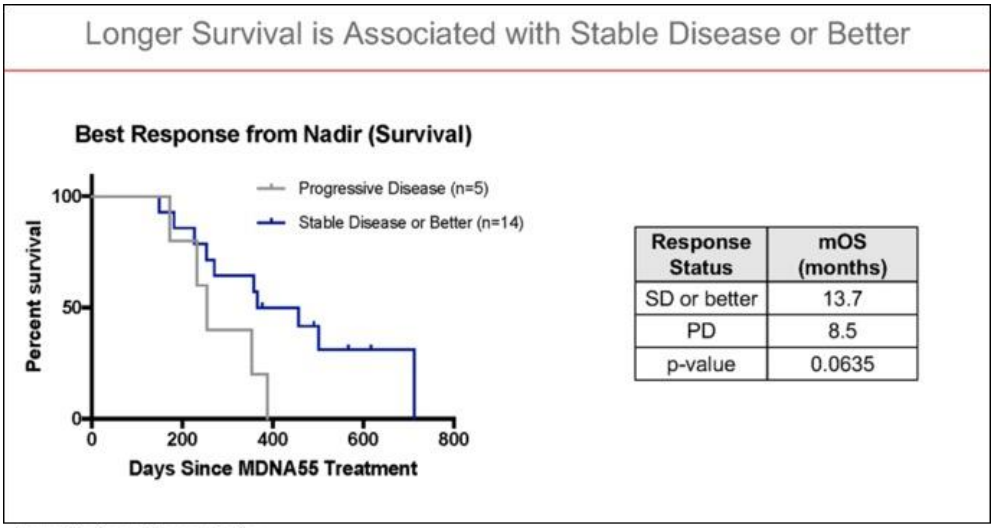


Source: Medicenna Therapeutics Corp.

While we are uncertain about what exactly is driving the phenomenon of tumor response in patients with low IL-4R expression, we believe there are at least two possibilities (which may not be mutually exclusive):

1) The amount of MDNA55 in the low-dose cohort may only be enough to trigger a response in patients who express a high level of IL-4R, while the high-dose cohort may be receiving enough drug that even tumors with low level expression of IL-4R respond.
2) IL-4R is expressed on myeloid derived suppressor cells (MDSCs), which dampen the immune system's response to tumors. Thus, MDNA55 may be depleting the MDSC population and allowing an immunological response to the tumor.

Regardless of the mechanism, we believe the data shown thus far by Medicenna is clearly indicative of a dose response in patients treated with MDNA55 and the tumor regressions seen are highly encouraging in this patient population. We anticipate survival data for the entire cohort of patients to be available toward the end of 2019 or early 2020, however the following chart does show that for the low-dose cohort, experiencing stable disease or better is a good prognosticator for an improvement in overall survival. Thus, with a disease control rate of 91% for the high-dose cohort, we are looking forward to seeing if that will translate to an improvement in overall survival beyond the six to nine months that is expected for patients with rGBM.



Source: Medicenna Therapeutics Corp.

MDNA19 Selected as Lead 'Superkine' Clinical Candidate

In July 2019, Medicenna announced the selection of MDNA19 (formerly MDNA109-LA1) as its second immuno-oncology clinical candidate. MDNA19 is an engineered IL-2 designed to increase the ability of T cells to fight cancer.

IL-2 (Proleukin®) was one of the first cancer immunotherapies approved by the FDA based on data showing a 16% ORR in patients with metastatic melanoma (Atkins *et al*., 2000). IL-2 activates a wide range of leukocytes, including T cells and natural killer (NK) cells. While effective as an anti-cancer agent, its use has been limited by a range of adverse side effects, including the potentially deadly capillary leak syndrome, as well as its necessity for frequent dosing and ability to stimulate regulatory T cells along with effector T cells (Boyman *et al*., 2012).

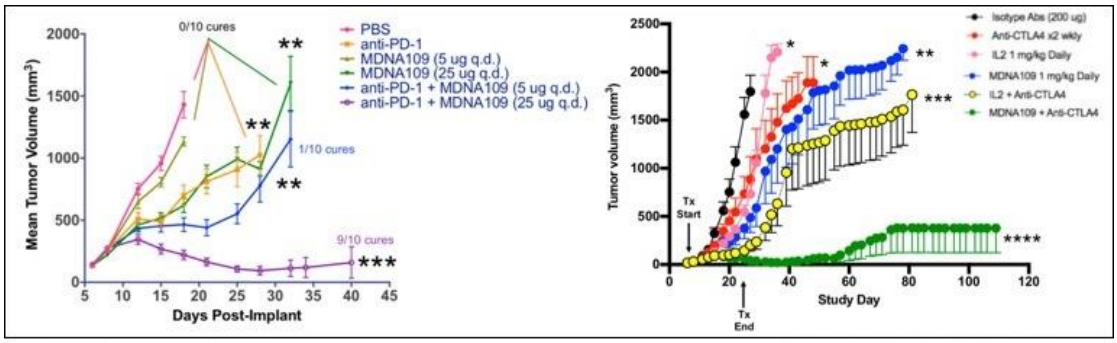
IL-2 is a 16 kDa protein that exerts its effects through binding various IL-2Rs (IL-2Rα, IL-2Rβ, and IL-2Rγ), with the arrangement of these receptors dictating the response seen. Binding of IL-2 to a heterodimer consisting of IL-2Rβ and IL-2Rγ is relatively 'low affinity', whereas a heterotrimer consisting of all three IL-2Rs is a 'high affinity' complex. The heterotrimer is typically found on activated T cells (including regulatory T cells) while naïve T cells and NK cells only express the heterodimer. Thus, modifying IL-2 signaling to enhance binding to the β–γ complex could enhance T cell activation while diminishing the effect of regulatory T cells.

An engineered version of IL-2 that exhibited increased affinity to IL-2Rβ was first described in 2012 (Levin *et al*., 2012). The researchers used *in vitro* evolution in which point mutations were randomly created in the IL-2 coding sequence, with each of the mutated versions of IL-2 tested for IL-2Rβ affinity. Following the first round of *in vitro* evolution, a predominant IL-2 variant was identified containing a L85V mutation in the hydrophobic core of the protein, and not a direct IL-2Rβ contact residue. For the second round of *in vitro* evolution, mutations were restricted to six amino acids in the hydrophobic core. The following table shows the consensus sequence that resulted in the identification of MDNA109 (denoted as H9 in the table), which exhibited high affinity binding to IL-2Rβ.

									Affinity for IL-2Rβ		
residue #	74	80	81	85	86	89	92	93	K_d(nM)	k_{on}(1/ms)	k_{off}(1/s)
WT hIL-2	Q	L	R	L	I	I	I	V	280	$7.9x10^5$	0.22
6-6			I	V					49	$1.2x10^6$	0.061
D10	H	F	D	V	V		F		1.3	$4.1x10^6$	0.0051
H9		F	D	V	V		F		1.4	$4.1x10^6$	0.0056
CONSENSUS		F	D	V	V		F				

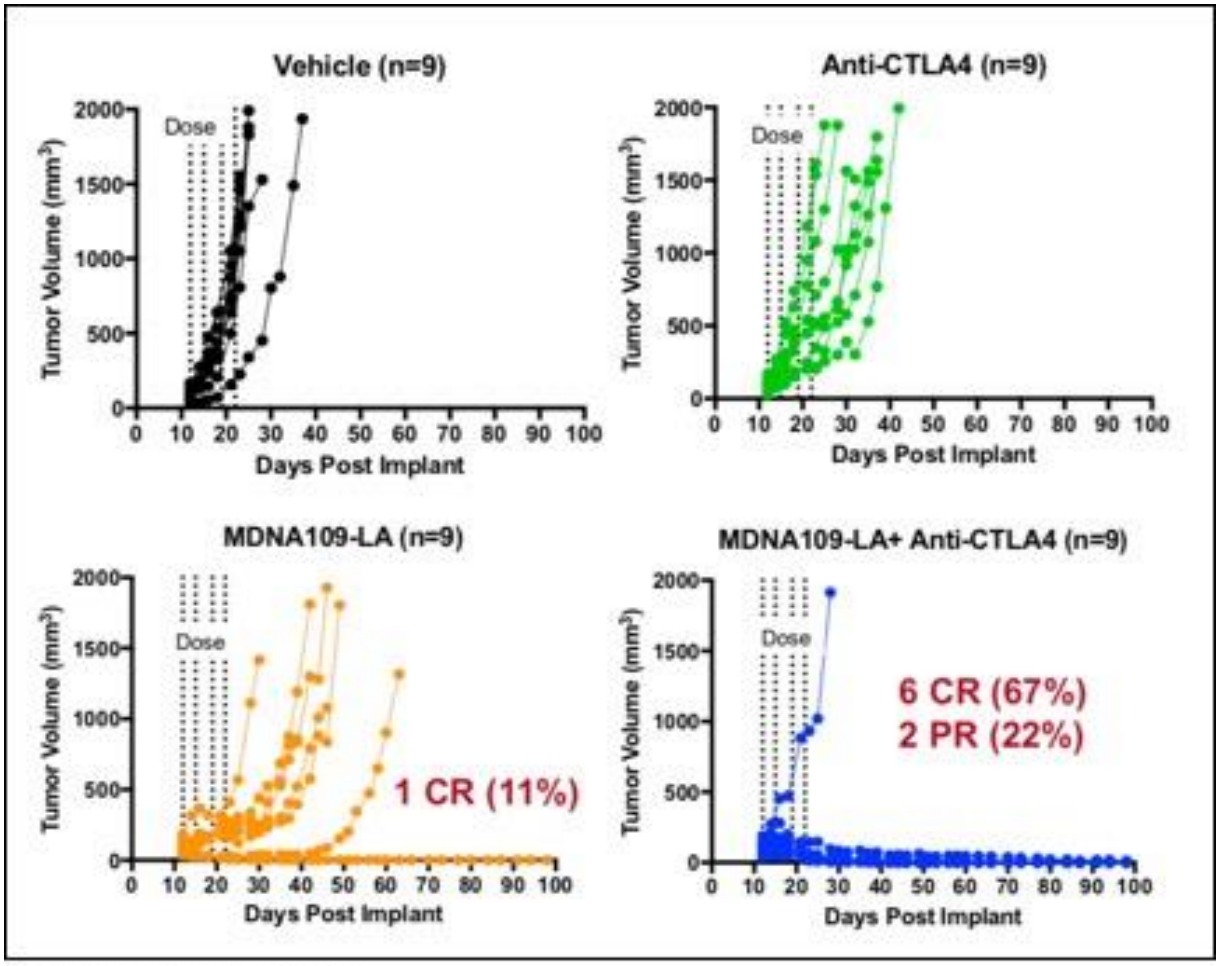
Source: Levin *et al*., 2012

MDNA109 showed excellent *in vivo* synergism with the checkpoint inhibitor (CPI) antibodies targeted against PD-1 and CTLA-4. The following figures show synergistic anti-tumor activity of MDNA109 when combined with anti-PD-1 in a syngeneic M38 murine colon cancer model (left panel) and also when combined with anti-CTLA-4 in a CT26 colon cancer model (right panel).



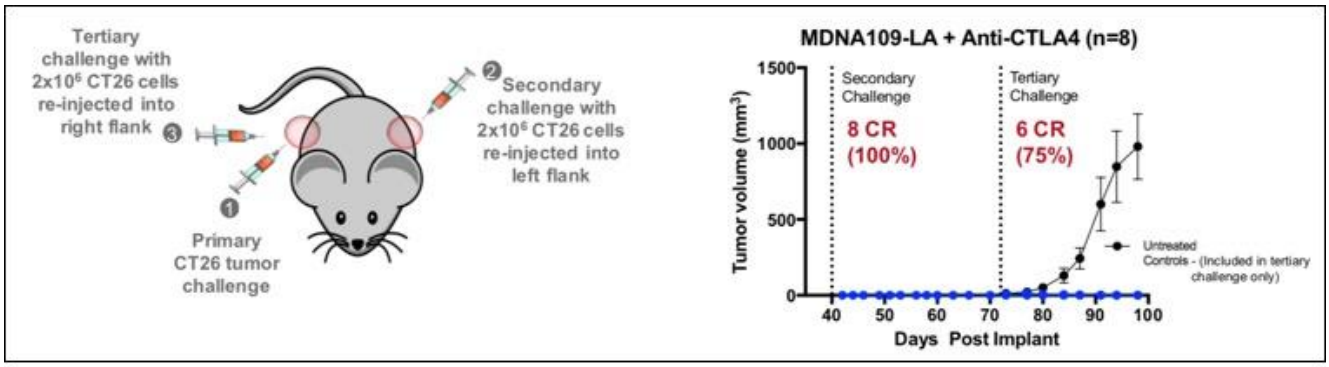
Source: Medicenna Therapeutics Corp.

Medicenna recently presented data on long-acting versions of MDNA109, MDNA109-LA and MDNA-LA1 (which also has low IL-2Rα affinity). MDNA109-LA was shown to synergize with anti-CTLA-4 therapy in a CT26 colon cancer mouse model, as shown in the following figures. MDNA109-LA treatment showed minimal activity as a monotherapy (1 complete response [CR] out of 9 mice treated), however the combo therapy of MDNA109-LA and anti-CTLA-4 resulted in 6 CR and 2 partial responses (PR) out of 9 mice treated.



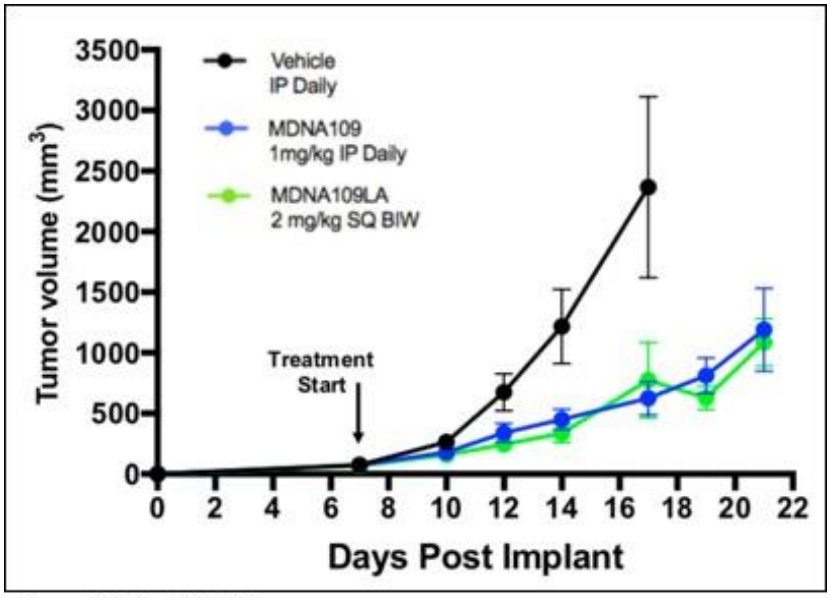
Source: Rafei *et al.*, 2019

MDNA109-LA treatment results in immunological memory as shown by tumor rejection upon re-challenge. The following figure shows the experimental design for tumor re-challenge in mice that achieved a CR upon treatment with MDNA109-LA and anti-CTLA-4 following injection with CT26 tumor cells. All mice maintained a CR upon the secondary challenge and 75% maintained a CR on the tertiary challenge. Note that there was no additional treatment with MDNA109-LA following the secondary or tertiary tumor challenges.



Source: Rafei *et al.*, 2019

In addition, MDNA109-LA exhibits superior pharmacokinetics (PK) compared to MDNA109. The following figure shows that MDNA109-LA gives similar tumor control in an aggressive B16F10 melanoma tumor model when dosed biweekly compared to MDNA109 dosed daily. Finally, MDNA109-LA1, with reduced binding to CD25, achieved similar tumor control with a weekly dosing schedule, which is similar to what is seen with other long-acting IL-2 variants in development, such as Nektar Therapeutics' NKTR-214.



Source: Rafei *et al.*, 2019

Financial Update

On August 9, 2019, Medicenna announced financial results for the first quarter of fiscal year 2020 ending June 30, 2019. The company reported a net loss for the first quarter of fiscal year 2020 of CAD$1.3 million, or CAD$0.05 per share, compared to a net loss of CAD$1.0 million, or CAD$0.04 per share, for the three months ending June 30, 2018. R&D expenses for the first quarter of fiscal year 2020 were CAD$0.8 million compared to CAD$0.6 million for the three months ending June 30, 2018. The increase in expenses was mainly due to increased regulatory costs and increased expenses associated with the development of MDNA19. G&A expenses in the first quarter of fiscal year 2020 were CAD$0.5 million compared to $0.4 million for the first quarter of fiscal year 2019. The increase was primarily due to a lower amount of expenses reimbursed from the Cancer Prevention and Research Institute of Texas (CPRIT).

As of June 30, 2019, Medicenna had approximately CAD$1.1 million in cash and cash equivalents. In May 2019 and July 2019, the company received payments of US$0.76 million (approximately CAD$1.02 million) and US$1.9 million (approximately CAD$2.5 million), respectively, from CPRIT, which are part of a US$14.1 million grant related to the development of MDNA55. Medicenna has approximately US$1.4 million remaining on the grant.

Medicenna has approximately 28.8 million shares outstanding and when factoring in the approximately 3.3 million stock options and 4.9 million warrants a fully diluted share count of approximately 37.1 million.

Conclusion

We look forward to the results of the upcoming meeting with the FDA regarding the regulatory path forward for MDNA55 as well as whether the opportunity exists for accelerated approval. We are also eagerly awaiting the final OS data for the MDNA55 Phase 2b data, which should be available in late 2019 or early 2020. The selection of MDNA19 as the lead 'Superkine' clinical candidate is an important step forward for the company and we anticipate that compound entering the clinic in 2020. We are maintaining our valuation of CAD$5.00 per share.

PROJECTED FINANCIALS

Medicenna Therapeutics Corp.
Income Statement

Medicenna Therapeutics Corp. In Canadian Dollars	FY 2019 A	Q1 FY20 A	Q2 FY20 E	Q3 FY20 E	Q4 FY20 E	FY 2020 E	FY 2021 E	FY 2022 E
MDNA55	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
MDNA109	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Other Income	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$3.0	$0.8	$0.9	$1.0	$1.1	$3.8	$4.0	$4.1
General & Administrative	$1.7	$0.5	$0.4	$0.4	$0.4	$1.7	$2.0	$2.2
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($4.7)	($1.3)	($1.3)	($1.4)	($1.5)	($5.6)	($6.0)	($6.3)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	($0.0)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	($4.7)	($1.3)	($1.3)	($1.4)	($1.5)	($5.6)	($6.0)	($6.3)
Income Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Cumulative translation adjustment	$0.0	$0.0	$0.0	$0.1	$0.0	$0.0	$0.0	$0.0
Net Income	**($4.7)**	**($1.3)**	**($1.4)**	**($1.4)**	**($1.5)**	**($5.6)**	**($6.0)**	**($6.3)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.18)**	**($0.05)**	**($0.04)**	**($0.04)**	**($0.04)**	**($0.17)**	**($0.15)**	**($0.14)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	25.7	28.6	33.0	33.3	35.0	32.5	40.0	45.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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