

Medicenna Therapeutics Corp.

(MDNA-NASDAQ)

MDNA: On Track to Dose First Patient in MDNA11 Phase 1 Trial in 3Q21...

Based on our probability adjusted DCF model that takes into account potential future revenues of MDNA55 and MDNA11, MDNA is valued at \$12/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 (08/18/21) **\$1.91**
Valuation **\$12.00**

OUTLOOK

On August 13, 2021, Medicenna Therapeutics Corp. announced financial results for the first quarter of fiscal year 2021 that ended June 30, 2021 and provided a business update. The company recently submitted a Clinical Trial Application (CTA) in Australia to initiate a Phase 1/2 clinical trial of MDNA11. We anticipate the Phase 1/2 ABILITY (A Beta-only IL-2 ImmunoTherapy Study) study initiating in the third calendar quarter of 2021. The trial is designed to assess the safety, PK/PD, and effect on various biomarkers of different doses of MDNA11 in patients with advanced solid tumors, with initial data possible by the end of 2021. Once a Phase 2 dose is established, dose expansion cohorts consisting of metastatic melanoma, advanced renal cell carcinoma (RCC) and patients with other solid tumor types will be treated in both monotherapy and combination (with a checkpoint inhibitor) settings, with results expected during 2022. Expansion of the trial to additional sites in the U.S., U.K., and Canada is expected following submissions to those regulatory agencies, which should occur before the end of calendar 2021.

SUMMARY DATA

52-Week High **\$5.97**
52-Week Low **\$1.91**
One-Year Return (%) **-58.04**
Beta **1.24**
Average Daily Volume (sh) **134,075**

Shares Outstanding (mil) **54**
Market Capitalization (C\$mil) **\$103**
Short Interest Ratio (days) **1**
Institutional Ownership (%) **25**
Insider Ownership (%) **33**

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 **Above Avg.**
Type of Stock **Small-Blend**
Industry **Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of \$CAD)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2021	0 A	0 A	0 A	0 A	0 A
2022	0 A	0 E	0 E	0 E	0 E
2023					0 E
2024					0 E

Earnings per Share

(in \$CAD)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2021	-\$0.05 A	-\$0.08 A	-\$0.11 A	-\$0.11 A	-\$0.35 A
2022	-\$0.12 A	-\$0.12 E	-\$0.12 E	-\$0.13 E	-\$0.49 E
2023					-\$0.48 E
2024					-\$0.49 E

WHAT'S NEW

Business Update

CTA Submitted, Phase 1/2 Clinical Trial of MDNA11 to Start in 3Q21

In June 2021, Medicenna Therapeutics Corp. (MDNA) announced it has submitted a Clinical Trial Application (CTA) in Australia in order to initiate the Phase 1/2 ABILITY Study (A Beta-only IL-2 ImmunoTherapY Study) of MDNA11 in patients with advanced solid tumors. We anticipate the trial initiating in the third calendar quarter of 2021. It is designed to assess the safety, PK/PD, and effect on various biomarkers of MDNA11 as both a monotherapy as well as in combination with a checkpoint inhibitor. Initiating the trial in Australia will allow dosing to begin at higher levels in contrast to lower doses which is generally recommended by the FDA, and we anticipate the trial eventually expanding to clinical sites in the U.S., U.K., and Canada, with submissions to their regulatory agencies expected by the end of calendar 2021.

During the quarterly conference call, management indicated that even in light of the Australian government's recent COVID-related lockdowns, the clinical site trial investigators and CRO indicated that cancer treatment is considered an essential service and therefore exempt from COVID restrictions, including travel between different regions. In addition, previous government lockdowns in Australia had minimal impact on Phase 1 cancer trials. Thus, we are confident that the trial will be able to initiate in calendar Q3 as planned.

The first data reported from the trial will include preliminary safety, pharmacokinetics (PK), pharmacodynamics (PD), and biomarker data from the initial dose escalation cohorts, which are expected by end of this calendar year. In regards to PK, the company is hoping to see MDNA11 accumulation in the tumor along with albumin-mediated half-life extension that would support dosing once every two to three weeks. In regards to PD and biomarker data, paired biopsies will be taken from patients before and during treatment and the company will be evaluating various biomarkers and immune cell markers to look for anti-cancer immune cell activation and a lack of regulatory cell activation. Subsequent data including efficacy data readouts will continue throughout 2022 for both monotherapy and combination treatment.

MDNA11 Background

MDNA11 is a long-acting variant of interleukin (IL)-2 that is engineered to have enhanced binding to CD122 and no affinity for CD25. IL-2 is a 16 kDa protein that activates a wide range of leukocytes, including T cells and natural killer (NK) cells through binding IL-2 receptors (IL-2R α [CD25], IL-2R β [CD122], and IL-2R γ [CD132]), with the arrangement of these receptors dictating the response seen. Binding of IL-2 to a heterodimer consisting of CD122 and CD132 is of "intermediate 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 CD122/CD132 complex could enhance T cell activation while diminishing the effect of regulatory T cells.

The following table shows that MDNA11 (and MDNA19, the company's other long-acting IL-2 variant) binds to CD122 with enhanced affinity compared to native IL-2 (as shown by the lower K_D value), and that neither compound binds to CD25, thus preferentially activating immune effector cells but not T regulatory cells.

	K_D [CD25 (IL-2R α)]	K_D [CD122 (IL-2R β)]
IL-2 ^a	24 nM	210 nM
MDNA109 (1 st Gen.) ^a	26 nM	1.8 nM
MDNA109-Fc (2 nd Gen.) ^b	14 nM	2.7 nM
MDNA109-Alb (2 nd Gen.) ^b	56 nM	3.5 nM
MDNA19 (3rd Gen.)^b	No binding	2.1 nM
MDNA11 (3rd Gen.)^b	No binding	6.6 nM

Source: Medicenna Therapeutics Corp.

"Improved IL-2" Landscape

The "improved IL-2" landscape is quickly becoming quite crowded, with a number of different strategies being developed to enhance IL-2 activity and minimize potential side effects. While there are a large number of

companies that could be considered potential competitors to Medicenna, we believe investors would be wise to pay close attention to the following companies, which we believe are the best current comparators:

Neoleukin Therapeutics (NLTX): Neoleukin is developing NL-201, which was produced using the company's platform technology of *in silico* protein design. NL-201 is a "non-alpha" IL-2 mimetic that shares only 14% homology with native IL-2. Pre-clinical studies show that the drug stimulates CD8 effector T cells more effectively than native IL-2 and promotes durable anti-tumor activity in pre-clinical mouse tumor models. Half-life extension is achieved through PEGylation. The company recently initiated a Phase 1 clinical trial of NL-201 in patients with solid tumors, with dose expansion cohorts planned in RCC and melanoma. A potential issue for NL-201 is immunogenicity, which is of concern since the protein shares only 14% homology with native IL-2 and non-human primates (NHP) developed anti-drug antibodies to NL-201 in pre-clinical studies.

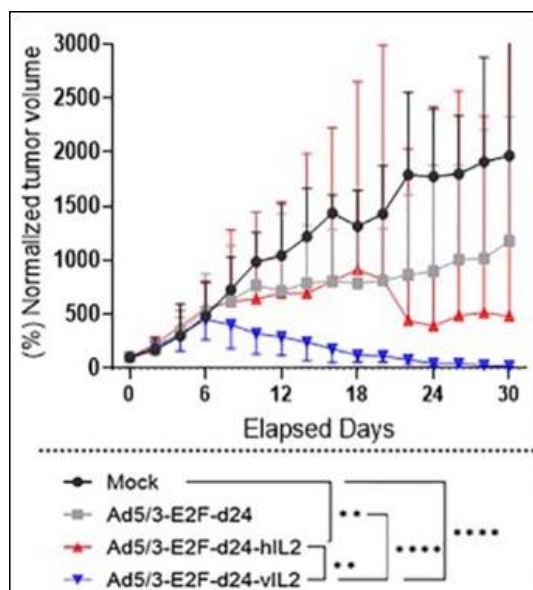
Werewolf Therapeutics (HOWL): Werewolf is developing WTX-124, an IL-2 prodrug that is conditionally activated in tumors by tumor-specific proteases. The compound consists of IL-2, an "inactivation domain" that is cleaved by a tumor specific protease, and a "half-life extension domain". Preclinical data shows the compound is efficacious in mouse tumor models and there is minimal release of free IL-2 in the periphery. A potential issue for WTX-124 is that since no modifications were made to the IL-2 portion of the compound, it can still activate T regulatory cells through binding of CD25, which may ultimately decrease efficacy.

Synthekine (private): Synthekine is developing STK-012, a CD25/CD122 selective IL-2 mutein that is designed to selectively bind to activated T cells without binding to naïve T cells or natural killer (NK) cells. Half-life extension is achieved through PEGylation. The compound is derived from work in Dr. Chris Garcia's lab at Stanford (same lab that produced the precursor molecule to MDNA11). Potential issues for STK-012 include: activated T cells express CD25 transiently; no activation of NK cells will miss anti-tumor activities of those cells; and no activation of naïve T cells will ultimately decrease available pool of T cells to become effector cells.

While the above-mentioned companies are all early-stage, the more advanced development products in this class include Nektar's NKTR-214 and Alkermes ALKS 4230 (in Phase 3 and Phase 2, respectively), which have both underwhelmed as monotherapy treatments but have shown more encouraging results in combination with checkpoint inhibitors.

External Validation of IL-2 Superkine Platform

In July 2021, Medicenna announced a peer-reviewed publication in *Frontiers in Immunology* featuring preclinical data on MDNA109, the company's IL-2 Superkine platform that forms the basis of MDNA11 ([Quixabeira et al., 2021](#)). The preclinical study featured oncolytic adenoviruses that were either unarmed, armed with MDNA109, or armed with wild type IL-2 and evaluated in a hamster pancreatic cancer model. The following figure shows that the oncolytic virus armed with MDNA109 (labeled "vIL2") severely restricted tumor growth with a clear trend toward complete tumor regression.



Source: Quixabeira et al., 2021

Additional data from the study showed that MDNA109 was able to reprogram the tumor microenvironment, induced efficient T cell receptor signaling, activated cytotoxic anti-cancer immune cells, and inhibited myeloid cells in the tumor microenvironment. These results highlight the therapeutic potential of the MDNA109 platform for difficult to treat tumor types such as pancreatic cancer.

Financial Update

On August 13, 2021, Medicenna announced financial results for the first quarter of fiscal year 2022 that ended June 30, 2021. The company reported a net loss for the first quarter of fiscal year 2022 of CAD\$6.4 million, or CAD\$0.12 per share, compared to a net loss of CAD\$2.4 million, or CAD\$0.05 per share, for the three months ending June 30, 2020. R&D expenses for the first quarter of fiscal year 2022 were CAD\$4.3 million compared to CAD\$1.8 million for the first quarter of fiscal year 2021. The increase in expenses was primarily due to increased manufacturing and development expenditures for the MDNA11 program, increased clinical costs due to preparation of the ABILITY study, and higher salary and benefits costs. G&A expenses for the first quarter of fiscal year 2022 were CAD\$1.9 million compared to CAD\$0.7 million for the three months ending June 30, 2020. The increase was primarily due to public company expenses associated with the Nasdaq listing and related directors and officer's liability insurance premiums.

As of June 30, 2021, Medicenna had approximately CAD\$35.9 million in cash, cash equivalents, and marketable securities. We estimate Medicenna has sufficient capital to fund operations through the end of calendar 2022. As of August 13, 2021, Medicenna had approximately 53.7 million shares outstanding and, when factoring in options and warrants, a fully diluted share count of approximately 62.0 million.

Conclusion

We look forward to the initiation of the ABILITY trial in the third calendar quarter of 2021 along with the initial PK/PD and biomarker data by the end of calendar 2021. MDNA11 has a number of attributes that could lead it to be a 'best-in-class' molecule and we will be very interested to see if it can match Proleukin's efficacy (approximately 15-20% ORR in RCC and melanoma) but without the serious side effects, which includes cytokine storm and capillary leak syndrome. Our valuation remains at \$12 per share, and with the stock not performing well recently despite multiple upcoming catalysts investors have a nice opportunity to initiate or add to a position prior to the first data readouts from the ABILITY trial.

PROJECTED FINANCIALS

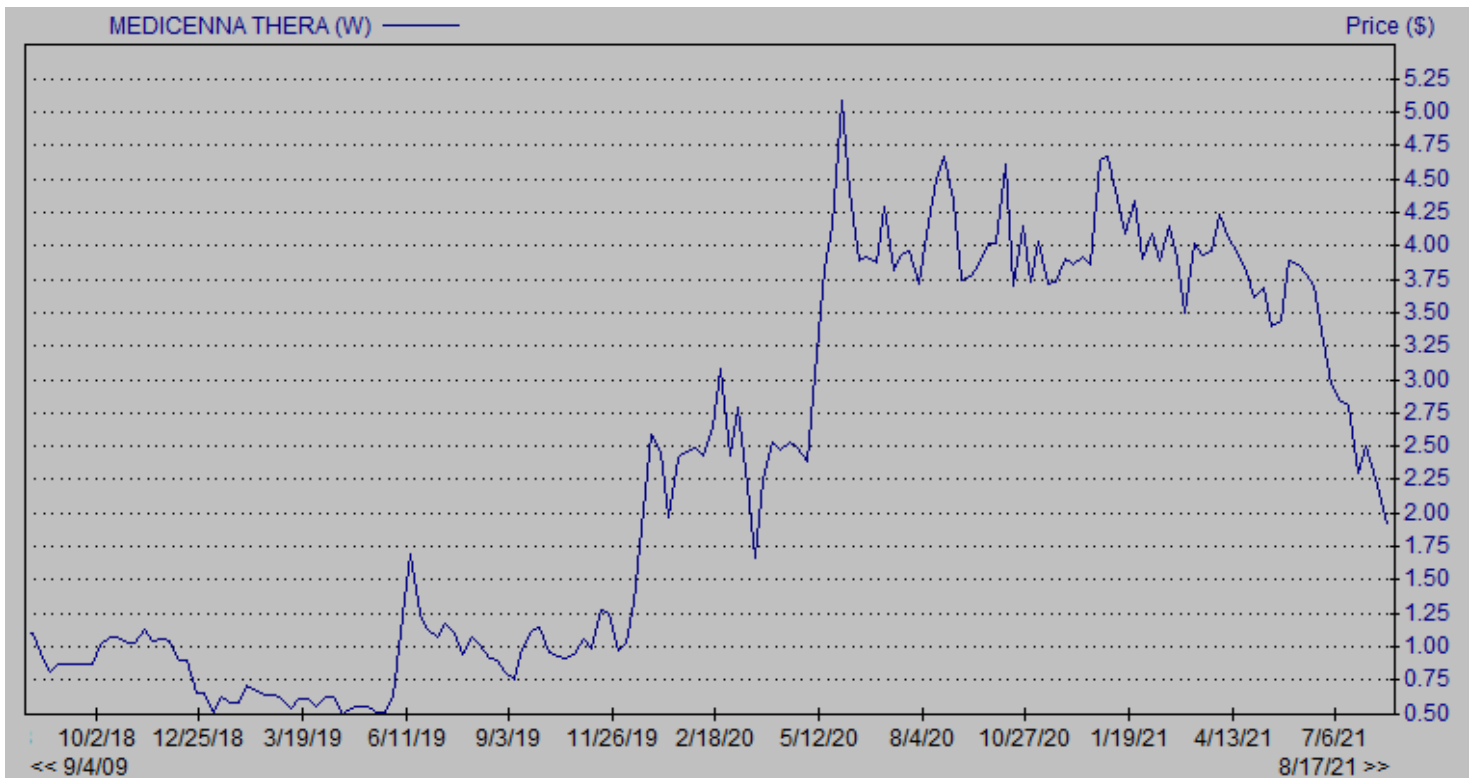
Medicenna Therapeutics Corp. Income Statement

Medicenna Therapeutics Corp. In Canadian Dollars	FY 2021 A	Q1 FY22 A	Q2 FY22 E	Q3 FY22 E	Q4 FY22 E	FY 2022 E	FY 2023 E	FY 2024 E
MDNA55	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
MDNA11	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
Other Income	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
Total Revenues	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
Cost of Sales	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>Product Gross Margin</i>	-	-	-	-	-	-	-	-
Research & Development	\$10.9	\$4.3	\$4.5	\$4.5	\$4.7	\$18.0	\$20.0	\$22.0
General & Administrative	\$6.5	\$1.9	\$2.0	\$2.2	\$2.5	\$8.6	\$9.0	\$10.0
Other (Income) Expense	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0
Operating Income	(\$17.4)	(\$6.2)	(\$6.5)	(\$6.7)	(\$7.2)	(\$26.6)	(\$29.0)	(\$32.0)
<i>Operating Margin</i>	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	(\$0.1)	\$0.2	(\$0.1)	(\$0.1)	(\$0.1)	(\$0.1)	(\$0.4)	(\$0.4)
Pre-Tax Income	(\$17.3)	(\$6.4)	(\$6.4)	(\$6.6)	(\$7.1)	(\$26.5)	(\$28.6)	(\$31.6)
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	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0
Net Income	(\$17.3)	(\$6.4)	(\$6.4)	(\$6.6)	(\$7.1)	(\$26.5)	(\$28.6)	(\$31.6)
<i>Net Margin</i>	-	-	-	-	-	-	-	-
Reported EPS	(\$0.35)	(\$0.12)	(\$0.12)	(\$0.12)	(\$0.13)	(\$0.49)	(\$0.48)	(\$0.49)
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
Basic Shares Outstanding	49.7	53.6	54.0	54.2	54.5	54.1	60.0	65.0

Source: Zacks Investment Research, Inc.

David Bautz, PhD

HISTORICAL STOCK PRICE



Source: Zacks Small Cap Research

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