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Medicenna Therapeutics Corp. (MDNA-NASDAQ)

MDNA: CTA Submitted in Australia; Phase 1 Trial of MDNA11 to Initiate 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 (06/28/21)	$3.27
Valuation	**$12.00**

OUTLOOK

On June 23, 2021, Medicenna Therapeutics Corp. announced the submission of a Clinical Trial Application (CTA) in Australia to initiate a Phase 1/2 clinical trial of MDNA11. Upon acceptance of the CTA by Australia's Therapeutics Goods Administration (TGA), we anticipate the Phase 1/2 ABILITY (A Beta-only IL-2 ImmunoTherapY Study) study initiating in the third 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, a dose expansion cohort consisting of metastatic melanoma and advanced renal cell carcinoma (RCC) patients will be treated, with results expected in 2022.

SUMMARY DATA

52-Week High	**$5.97**
52-Week Low	**$3.24**
One-Year Return (%)	**-12.57**
Beta	**1.28**
Average Daily Volume (sh)	**96,508**
Shares Outstanding (mil)	**54**
Market Capitalization (C$mil)	**$175**
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-Growth**
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 E	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	-$0.06 E	-$0.08 E	-$0.10 E	-$0.12 E	-$0.37 E
2023					-$0.44 E
2024					-$0.46 E

WHAT'S NEW

Business Update

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

On June 23, 2021, Medicenna Therapeutics Corp. (MDNA) announced it has submitted a Clinical Trial Application (CTA) in Australia such that upon approval by the Human Research Ethics Committee (HREC) and acceptance by the Therapeutics Goods Administration (TGA) the company can 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 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 than what the FDA would recommend, and we anticipate the trial eventually expanding to clinical sites in the U.S., U.K., and Canada. Initial safety, PK/PD, and biomarker data (including flow cytometry analysis on cell populations along with pre- and on-treatment biopsies) is expected by the end of 2021.

Following the dose escalation phase of the trial examining MDNA11 as a monotherapy, the company will be performing the dose expansion portion of the trial in patients with melanoma and renal cell carcinoma (RCC), two indications for which Proleukin® (native IL-2) is FDA approved. Efficacy data for the expansion cohorts is likely in 2022.

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-2Rα [CD25], IL-2Rβ [CD122], and IL-2Rγ [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-2Rα)]	K_D [CD122 (IL-2Rβ)]
IL-2[a]	24 nM	210 nM
MDNA109 (*1st Gen.*)[a]	26 nM	1.8 nM
MDNA109-Fc (*2nd Gen.*)[b]	14 nM	2.7 nM
MDNA109-Alb (*2nd Gen.*)[a]	56 nM	3.5 nM
MDNA19 (*3rd Gen.*)[b]	**No binding**	**2.1 nM**
MDNA11 (*3rd Gen.*)[a]	**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.

Conclusion

We are glad to see Medicenna has filed the CTA such that the Phase 1/2 trial can initiate in the third quarter of 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. Initial safety, PK/PD, and biomarker data is likely before the end of 2021 and initial efficacy data will be available in 2022. Coupled with an expected update on MDNA55 partnering discussions in the second half of 2021, there exist multiple catalysts over the next 6-12 months. With no changes to our model the valuation remains at $12 per share.

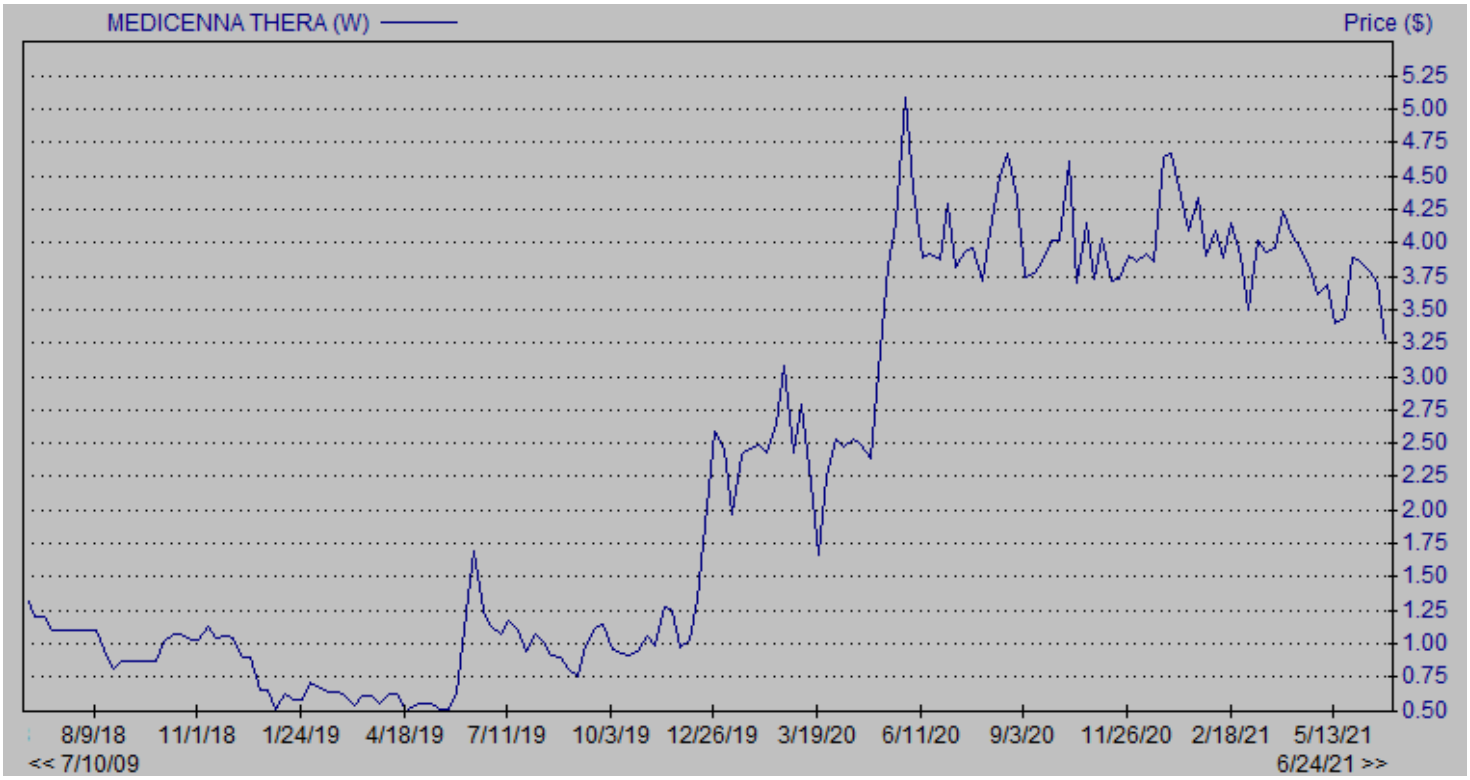
PROJECTED FINANCIALS

Medicenna Therapeutics Corp.
Income Statement

Medicenna Therapeutics Corp. In Canadian Dollars	**FY 2021 A**	**Q1 FY22 E**	**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
YOY Growth	-	-	-	-	-	-	-	-
MDNA11	$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	$10.9	$2.0	$2.8	$3.5	$4.0	$12.3	$18.0	$20.0
General & Administrative	$6.5	$1.5	$1.8	$2.2	$2.5	$8.0	$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)	($3.5)	($4.6)	($5.7)	($6.5)	($20.3)	($27.0)	($30.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	($0.1)	($0.1)	($0.1)	($0.1)	($0.1)	($0.4)	($0.4)	($0.4)
Pre-Tax Income	($17.3)	($3.4)	($4.5)	($5.6)	($6.4)	($19.9)	($26.6)	($29.6)
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)**	**($3.4)**	**($4.5)**	**($5.6)**	**($6.4)**	**($19.9)**	**($26.6)**	**($29.6)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.35)**	**($0.06)**	**($0.08)**	**($0.10)**	**($0.12)**	**($0.37)**	**($0.44)**	**($0.46)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	49.7	53.5	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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