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David Bautz, PhD
(312) 265-9471
dbautz@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Chicago, IL 60606

Medicenna Therapeutics Corp. (T.MDNA-TSX)

T.MDNA: New Data for MDNA55 and MDNA11 Presented at ASCO 2020…

Based on our probability adjusted DCF model that takes into account potential future revenues of MDNA55 and MDNA19, MDNA.T is valued at CAD$15/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 (06/03/20)	CAD$6.36
Valuation	**CAD$15.00**

OUTLOOK

On May 29, 2020, Medicenna Therapeutics Corp. (MDNA) announced updated efficacy data for the Phase 2b clinical trial of MDNA55 and preclinical data for MDNA11 were presented at ASCO 2020. Updated results for MDNA55 show that the median overall survival (mOS) increased up to 126% compared to a synthetic control arm when examining all patients with high interleukin (IL)-4 receptor (IL4R) expression and ILR4 low patients who received a high dose of MDNA55. The company will be conducting an 'End-of-Phase 2' meeting with the FDA in the third quarter of 2020 at which time the regulatory path forward for the drug will be discussed. MDNA11, one of the lead candidates from the IL-2 Superkine program, showed similar or superior characteristics to MDNA19 (another IL-2 Superkine candidate) in a number of areas and will be advanced into clinical trials in 2021.

SUMMARY DATA

52-Week High	**$7.25**
52-Week Low	**$0.94**
One-Year Return (%)	**389**
Beta	**0.44**
Average Daily Volume (sh)	**144,710**
Shares Outstanding (mil)	**48.5**
Market Capitalization (C$mil)	**$308**
Short Interest Ratio (days)	**N/A**
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	**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)
2020	0 A	0 A	0 A	0 A	0 A
2021	0 E	0 E	0 E	0 E	0 E
2022					0 E
2023					0 E

Earnings per Share

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2020	-$0.05 A	- $0.07 A	-$0.07 A	-$0.07 A	-$0.26 A
2021	-$0.06 E	-$0.06 E	-$0.06 E	-$0.06 E	-$0.23 E
2022					-$0.28 E
2023					-$0.36 E

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Business Update

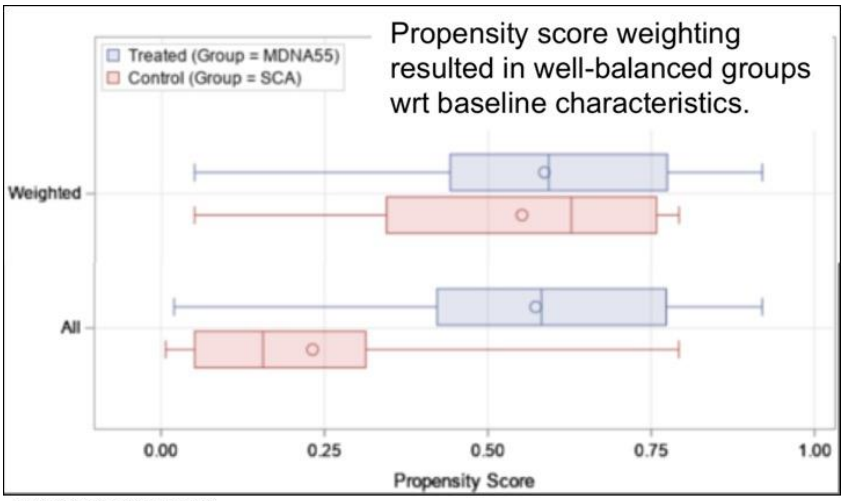
Updated Efficacy Results for MDNA55 Presented at ASCO 2020

On May 29, 2020, Medicenna Therapeutics Corp. (MDNA) announced updated results for the Phase 2b clinical trial of MDNA55 in patients with recurrent glioblastoma (rGBM) were presented at ASCO 2020. A copy of the presentation can be found here. A total of 44 subjects were evaluable for this analysis. The trial is a multi-center, open label, single arm study with the primary endpoint of median overall survival (mOS) and a secondary endpoint of objective response rate (ORR) following a single intra-tumoral infusion of MDNA55 in adult rGBM subjects (NCT02858895). The following table lists the demographic data for the patients. The red box indicates characteristics of rGBM tumors that are associated with worse prognoses, each of which were seen in at least 50% of patients.

Patient Demographics	N=44
Age	56 years (34 – 77)
Sex (Male)	27 / 44 (61%)
KPS: 70, 80	22 / 44 (50%)
90, 100	22 / 44 (50%)
De novo GBM	44 / 44 (100%)
No resection at recurrence	44 / 44 (100%)
IDH WT	37 / 37 (100%)
Unmethylated MGMT	23 / 40 (58%)
IL4R over-expression	21 / 40 (53%)
Steroid use > 4mg/day	23 / 44 (52%)
Max Tumor Diameter	30 mm (12 – 65)
# Prior Relapse: 1 , 2	35 (80%) , 9 (20%)

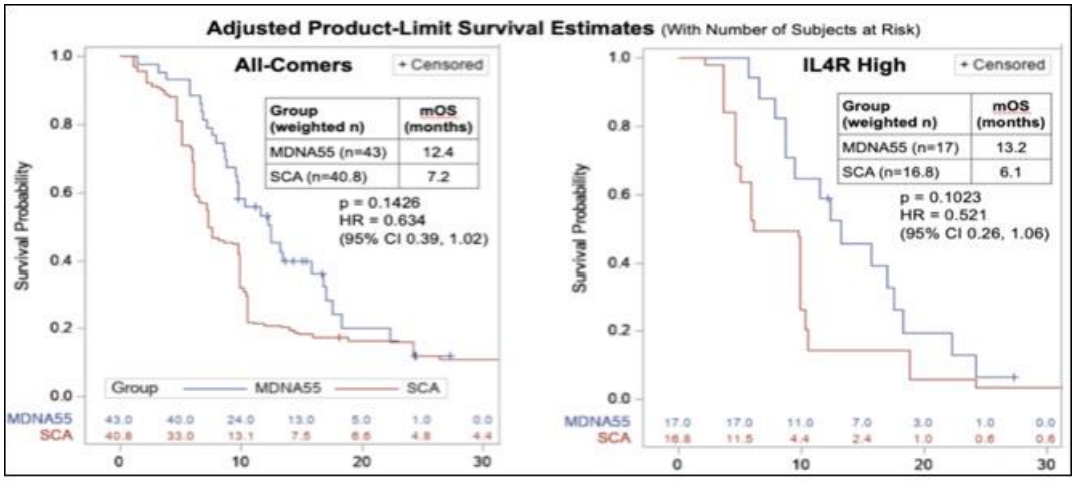
Source: Medicenna Therapeutics Corp.

To compare the survival of patients receiving MDNA55, a synthetic control arm (SCA) was established to identify rGBM patients matched on eligibility and prognostic characteristics including those with *de novo* GBM, wild-type IDH, and not eligible for resection. A propensity score weighting was then used to balance the baseline characteristics between the MDNA55 cohort and the SCA. Propensity scoring is a statistical method utilized to better align a treated group and an observational cohort. As the following graph shows, when using propensity score weighting the SCA is much better aligned (according to the propensity score) with the MDNA55-treated cohort than if it were not adjusted. Aligning the baseline characteristics between the two groups allows a more rigorous comparison to be made.



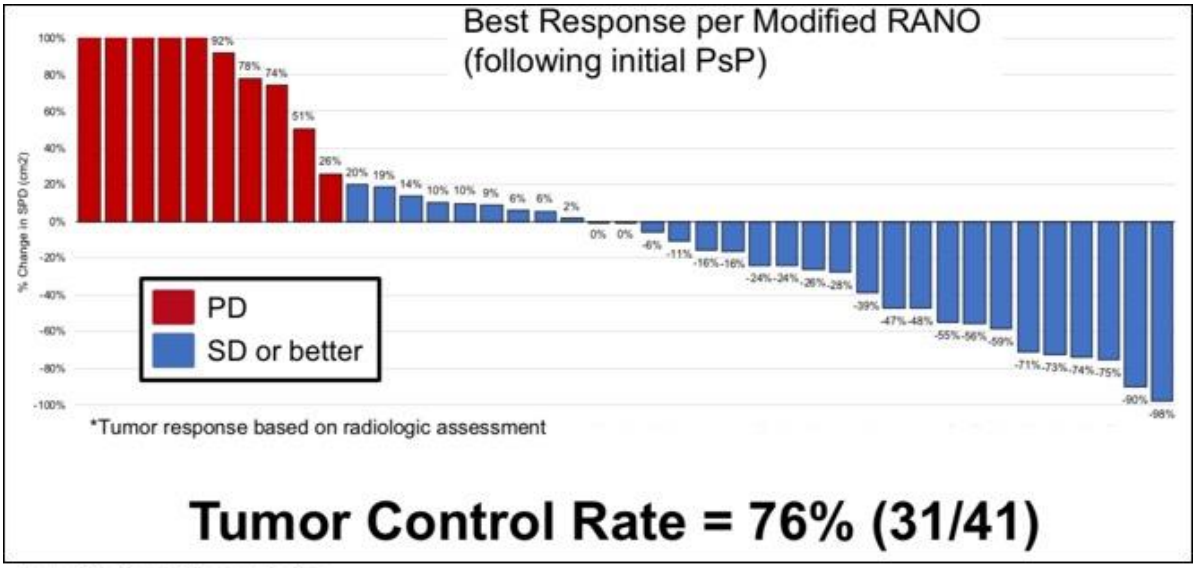
Source: Medicenna Therapeutics Corp.

The following graphs show the survival curves for all patients and for those with high expression of IL4R compared to the SCA. The mOS was 12.4 months for all MDNA55-treated patients compared to a mOS of 7.2 months in the SCA. When examining only those patients who had high expression of IL4R the mOS was 13.2 months compared to 6.1 months for the SCA. This is particularly impressive given that high IL4R expression is associated with poor outcomes.



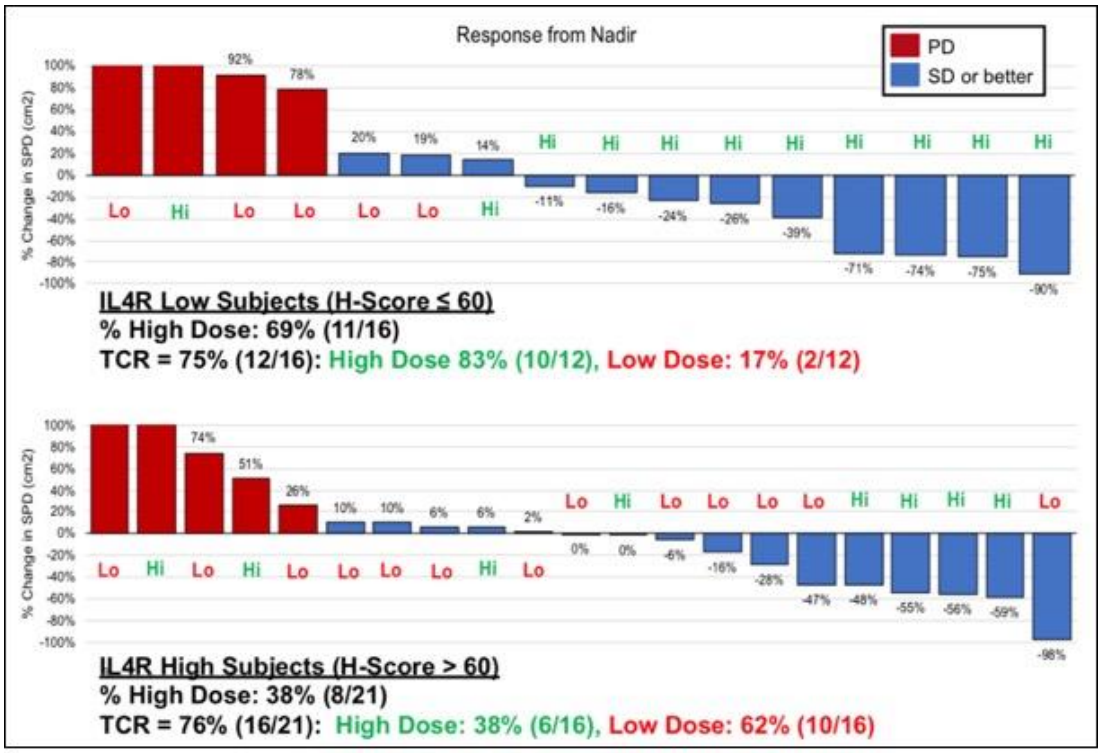
Source: Medicenna Therapeutics Corp.

The following graph shows tumor response rate for the 41 patients for which scans were available. The data is presented as the best response following pseudo-progression, in which a tumor appears to be growing on radiographic imaging (due to an inflammatory response to treatment and not due to an increase in tumor mass) before decreasing in size. To account for this phenomenon, assessment of tumor response was analyzed using the criteria for modified Response Assessment in Neuro-Oncology (mRANO) (Ellingson *et al*., 2017). Approximately three-quarters of patients had a best response of less than 20% tumor growth (or tumor shrinkage).



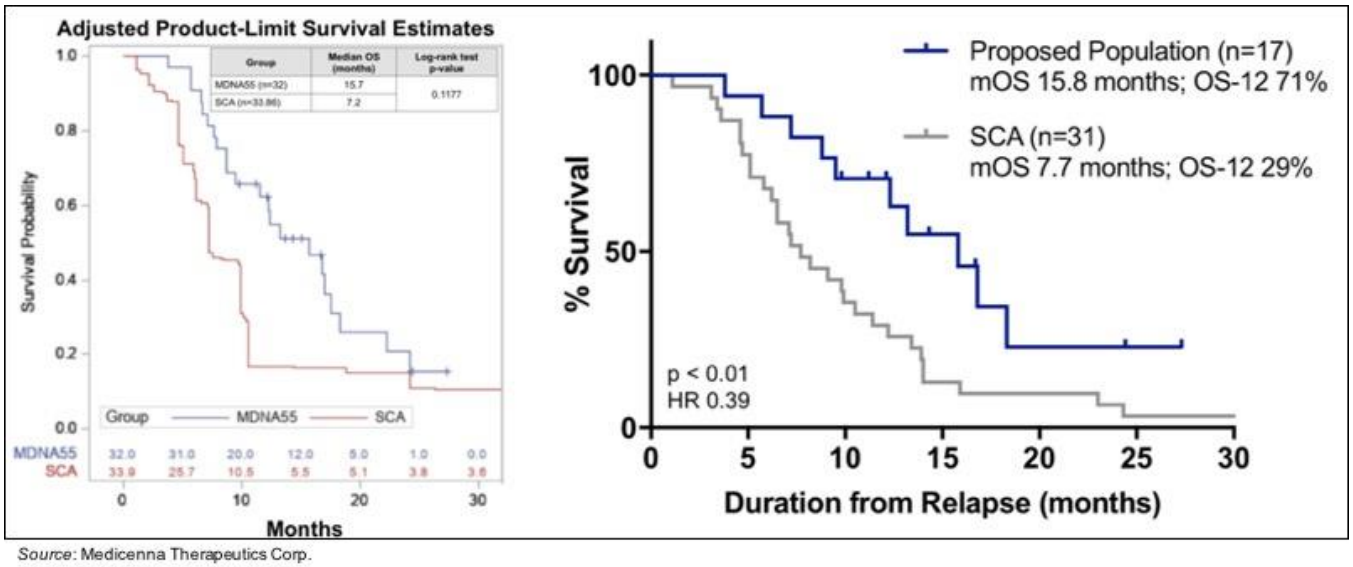
Source: Medicenna Therapeutics Corp.

The most interesting new data presented at ASCO 2020 had to do with the response to treatment in IL4R high and low patients. The following two graphs show tumor response from nadir in patients who had low IL4R expression (n=16) and high IL4R expression (n=21). Almost all of those who exhibited tumor control in the IL4R low group received a high dose of MDNA55. Conversely, there was no association with the amount of MDNA55 received and response in those with high IL4R expression. What this signifies is that in the IL4R low group a sufficient amount of MDNA55 is required in order to see a response since as there is a limited amount of receptor available for the drug to bind. In contrast, in the IL4R high group, the amount of MDNA55 given is of less importance because there is more receptor available for the drug to interact with.



Source: Medicenna Therapeutics Corp.

These data indicate that MDNA55 could be utilized to treat all rGBM patients regardless of IL4R status as the safety of the high dose (180 μg) was similar to that of the low dose. The proposed patient population (n=32 from the Phase 2b trial that were either IL4R high or IL4R low with a high dose of MDNA55) had a mOS of 15.7 months compared to a mOS of 7.2 months for the SCA (graph on lower left). In addition, MGMT unmethylated patients in the proposed patient population (n=17) had a mOS of 15.8 months compared to a mOS of 7.7 months in the SCA (graph on lower right). As a reminder, unmethylated MGMT is associated with a worse prognosis in GBM patients, thus it is very encouraging to see MDNA55 having a positive effect in that patient cohort.



Source: Medicenna Therapeutics Corp.

Medicenna will be conducting an 'End-of-Phase 2' meeting with the FDA during the third quarter of 2020. At that time the company will present data from the IL4R high subjects along with the IL4R low subjects that received a high dose of MDNA55, with the goal now being to target 'all comer' rGBM patients regardless of IL4R status. This will alleviate the company from having to develop and validate an IL4R expression assay and increases the potential patient population. Additional topics that could be discussed at the meeting include:

- Does the FDA want a Phase 3 trial conducted or to just expand the number of patients in the Phase 2b trial?
- If a Phase 3 trial is required, what will the control arm look like? Will Medicenna be able to use a synthetic control arm?

We anticipate the company receiving the minutes from that meeting early in the fourth quarter of 2020.

Preclinical Data on MDNA11 Presented at ASCO 2020

On May 29, 2020, Medicenna announced that preclinical data on MDNA11, one of the lead candidates from the interleukin (IL)-2 Superkine program, was presented at ASCO 2020. A copy of the presentation can be found here. 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 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, Tregs) while naïve T cells only express the heterodimer. Thus, modifying IL-2 signaling to enhance binding to the CD122/CD132 heterodimer complex could enhance T cell activation while diminishing the effect of regulatory T cells. An enhanced version of IL-2 that exhibited increased affinity to CD122 was first described in 2012 (Levin *et al*., 2012) and additional work has yielded a family of long-acting 'IL-2 Superkines' with enhanced features compared to IL-2.

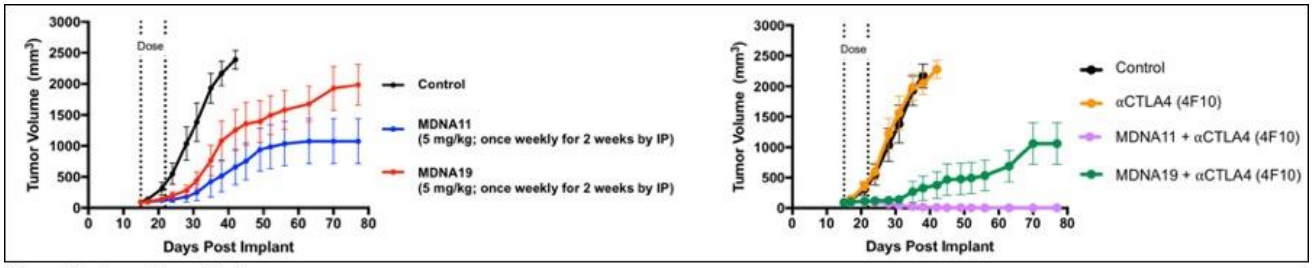
We previously discussed another lead candidate from the company's IL-2 Superkine program, MDNA19, which is differentiated from IL-2 in that it has enhanced affinity for CD122, which results in increased signaling in CD8 T cells, and does not bind to CD25, leading to substantially decreased signaling in Tregs. MDNA19 consists of the modified IL-2 covalently attached to the Fc domain of IgG, which is intended to increase its pharmacokinetic (PK) profile and extend its half-life. MDNA11 consists of the same modified IL-2 domain covalently attached to human albumin, which is another means to increase the compounds half-life and limit the frequency of infusions.

Similar to MDNA19, MDNA11 shows high affinity binding to CD122 (K_D = 6.6 nM) and no binding to CD25. In addition, MDNA11 shows enhanced potency on CD8+ T cells and natural killer (NK) cells along with reduced activity on Tregs. The following table shows the EC_{50} values (a measure of potency with greater potency (corresponding to smaller numbers) for recombinant, human IL-2 and MDNA11 on naïve CD8+ T cells and Tregs.

	Naïve CD8⁺ T cells (EC_{50}, pM)	Treg (EC_{50}, pM)
rhIL-2	3390	5.6
MDNA11	460	160

Source: Medicenna Therapeutics Corp.

Interestingly, as a monotherapy MDNA11 shows enhanced activity in a CT26 tumor model compared to MDNA19, as shown in the following figure on the left. MDNA11 also shows enhanced activity when used in combination with αCTLA4 therapy, as shown in the following figure on the right. All nine mice treated with MDNA11 + αCTLA4 exhibited complete regression of tumor while only 3/9 mice treated with MDNA19 + αCTLA4 showed complete regression of tumor.



Source: Medicenna Therapeutics Corp.

There are multiple factors that may contribute to the enhanced *in vivo* activity of MDNA11 compared to MDNA19. MDNA11 shows a longer half-life than MDNA19 in non-human primates (NHP), with a $T_{1/2}$ of 12.8 – 24.7 hours for MDNA11 compared to 7.3 – 9.1 hours for MDNA19. In addition, MDNA11 has a stronger effect on lymphocyte expansion and on non-Treg CD4 T cell expansion in NHPs at multiple doses. Lastly, the use of albumin to extend the half-life of MDNA11 could allow accumulation of the compound at tumor sites, as tumor cells are known to use albumin as a major energy source and a source of nitrogen (Stehle *et al*., 1997). The following chart shows various phenotypes and how MDNA11 and MDNA19 compare in regards to those phenotypes, with MDNA11 superior in a number of attributes.

Phenotype/Parameter	Comparison
Activity in Human PBMC P-STAT5 Assay	MDNA11 ~ MDNA19
Receptor Selectivity Based on Affinity Studies	MDNA11 ~ MDNA19
Efficacy: Monotherapy in CT26 Tumor Model	MDNA11 > MDNA19
Efficacy: Combination with Anti-CTLA4 in CT26 Tumor Model	MDNA11 >> MDNA19
Half-Life in Mice	MDNA11 ≥ MDNA19
Half-Life in NHP	MDNA11 >> MDNA19
Effect on Lymphocyte Expansion in NHP	MDNA11 ≥ MDNA19
Effect on CD8 T-cell vs. Treg Proliferation in NHP	MDNA11 ~ MDNA19
Effect on CD4 T-cell Expansion in NHP	MDNA11 ≥ MDNA19
Low Immunogenicity (ADA response) in NHP	MDNA11 ~ MDNA19
Overall Safety Profile in NHP	MDNA11 ~ MDNA19

Source: Medicenna Therapeutics Corp.

Conclusion

We are very interested to hear the outcome of the 'End-of-Phase 2' meeting with the FDA regarding the regulatory pathway for MDNA55, particularly on the possibility for accelerated approval. While still a low probability event, there is precedent for submitting a BLA following a successful single arm, open-label Phase 2 clinical trial. Morphosys AG recently submitted a BLA for tafasitamab, the company's anti-CD19 antibody, based on positive results from the company's Phase 2 L-MIND clinical trial and the retrospective observational matched control cohort RE-MIND trial. This is a very similar situation to what Medicenna has with the results of the Phase 2b clinical trial and the SCA, however the L-MIND trial had results from 80 patients while Medicenna is going to the FDA with results from 32 patients. Regardless of whether Medicenna is allowed to apply for accelerated approval or not, we believe MDNA55 is a very promising clinical candidate for rGBM.

The news for the IL-2 Superkine program continues to get better as MDNA11 appears to be superior to MDNA19 and thus will be advanced into clinical testing in 2021. The IL-2 Superkine platform has enormous potential for the company as shown by the acquisition of SynthoRx, and the enhanced IL-2 THOR-707, by Sanofi for $2.5 billion. With multiple suitors bidding on SynthoRx we believe there are other companies who are eager to have an enhanced IL-2 asset, particularly one like MDNA11, which we view as having potential 'best-in-class' attributes.

Based on the data for MDNA55 presented at ASCO 2020 showing that the compound is active in rGBM patients regardless of IL4R status we have increased our potential worldwide peak sales for the drug to $1.2 billion in rGBM. This has increased our valuation to CAD$15 and Medicenna continues to be one of our top picks in the small-cap biotech sector.

PROJECTED FINANCIALS

Medicenna Therapeutics Corp.
Income Statement

Medicenna Therapeutics Corp. In Canadian Dollars	FY 2020 E	Q1 FY21 E	Q2 FY21 E	Q3 FY21 E	Q4 FY21 E	FY 2021 E	FY 2022 E	FY 2023 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	$5.9	$2.0	$2.0	$2.0	$2.0	$8.0	$10.0	$13.0
General & Administrative	$2.4	$0.7	$0.7	$0.8	$0.8	$3.0	$3.3	$3.8
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($8.2)	($2.7)	($2.7)	($2.8)	($2.8)	($11.0)	($13.3)	($16.8)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	($0.0)	$0.0	$0.0	$0.0	$0.0	$0.1	$0.1	$0.1
Pre-Tax Income	($8.3)	($2.7)	($2.7)	($2.8)	($2.8)	($10.9)	($13.2)	($16.7)
Income Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Cumulative translation adjustment	$0.1	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Net Income	**($8.2)**	**($2.7)**	**($2.7)**	**($2.8)**	**($2.8)**	**($10.9)**	**($13.2)**	**($16.7)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.26)**	**($0.06)**	**($0.06)**	**($0.06)**	**($0.06)**	**($0.23)**	**($0.28)**	**($0.36)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	31.9	46.8	46.8	46.8	46.8	46.8	47.0	47.0

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

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