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# Medicenna Therapeutics Corp. (T.MDNA-TSX)

## *T.MDNA: Financing Extends Cash Runway Through 2020; Multiple Catalysts on the Horizon…*

Based on our probability adjusted DCF model that takes into account potential future revenues of MDNA55 and MDNA19, MDNA.T is valued at CAD$4.50/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 (10/28/19) | CAD$0.95 |
| **Valuation** | **CAD$4.50** |

## OUTLOOK

On October 17, 2019, Medicenna Therapeutics Corp. (T.MDNA) announced the closing of a public offering of approximately 5.31 million units, which included approximately 0.7 million units issued upon the full exercise of the over-allotment option, with each unit comprising one common share of stock and one-half of one common share purchase warrant for gross proceeds of approximately CAD$6.9 million. The warrants have an exercise price of CAD$1.75 and expire in three years. The financing extends the company's cash runway through 2020 and multiple important upcoming inflection points, including additional OS data from the Phase 2b trial of MDNA55 in the fourth quarter of 2019 and an 'end-of-Phase 2' meeting with the FDA in the first quarter of 2020.

## SUMMARY DATA

| | |
|---|---|
| **52-Week High** | **$1.74** |
| **52-Week Low** | **$0.50** |
| **One-Year Return (%)** | **-21.71** |
| **Beta** | **2.43** |
| **Average Daily Volume (sh)** | **14,180** |
| **Shares Outstanding (mil)** | **40** |
| **Market Capitalization ($mil)** | **$44** |
| **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

**Financial Update**

On October 17, 2019, Medicenna Therapeutics Corp. (MDNA) announced the closing of a previously announced public offering in which the company issued a total of 5,307,695 units, with each unit comprising one common share of stock and one-half of one common share purchase warrant, which resulted in gross proceeds of approximately CAD$6.9 million. The warrants have an exercise price of CAD$1.75 and expire in Oct. 2022. Based on decreased spending over the next year due to the end of the Phase 2b trial, we estimate that the company is now funded through the end of 2020 and importantly through important upcoming inflection points, including additional overall survival data from the Phase 2b trial of MDNA55 before the end of 2019 and an 'end-of-Phase 2' meeting with the FDA in the first quarter of 2020.

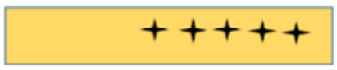
**Business Update**

*Encouraging Preclinical Results for MDNA19*

On September 30, 2019, Medicenna announced a poster presentation at the International Cancer Immunotherapy Conference entitled "Long-acting MDNA109: Emerging IL-2 Superkines displaying potent anti-tumoral responses". The presentation included additional preclinical data on the company's long-acting IL-2 programs, including the lead clinical candidate MDNA19.

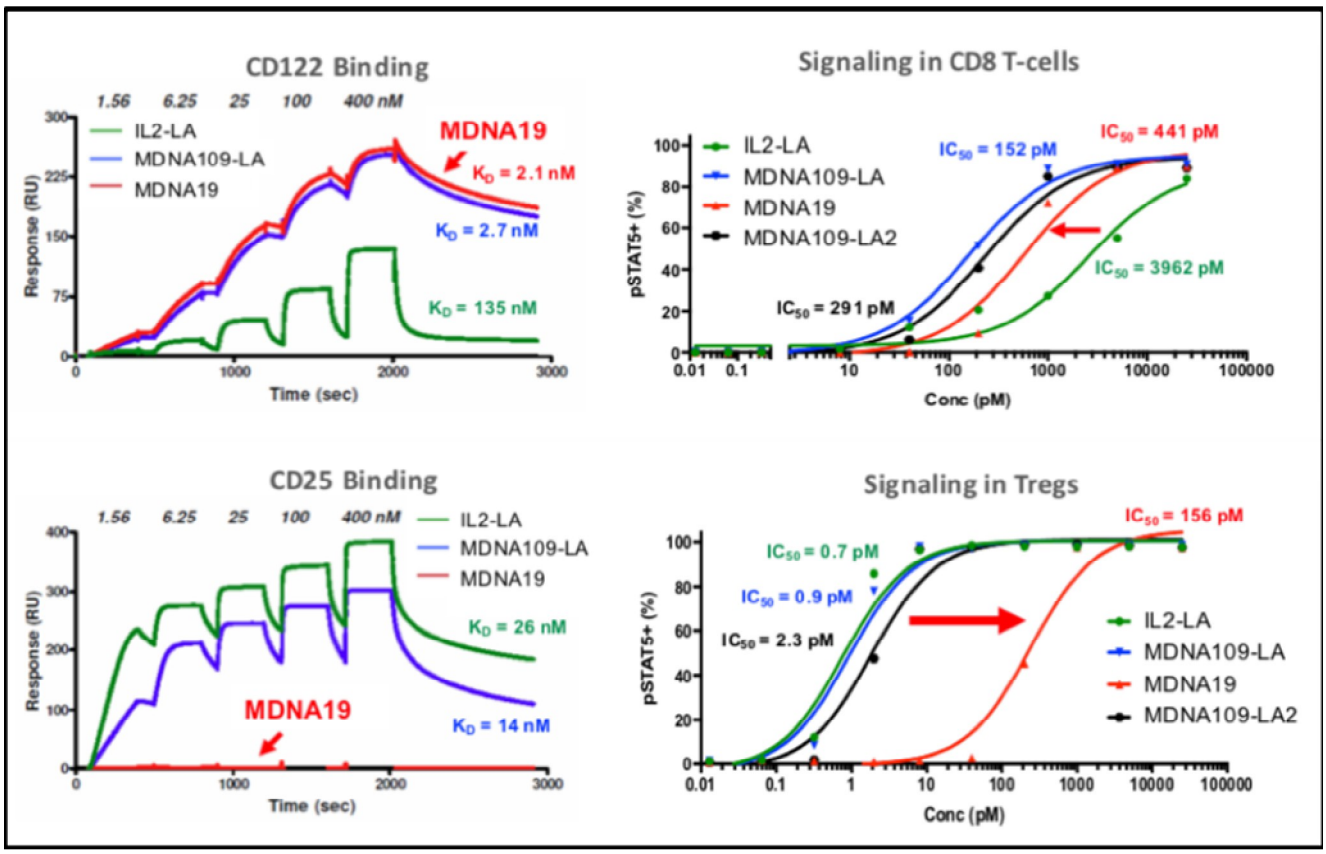
IL-2 is a 16 kDa protein that activates a wide range of leukocytes, including T cells and natural killer (NK) cells through binding IL-2 receptors (IL-2Rα [CD25], IL-2Rβ [CD122], and IL-2Rγ [CD132]), with the arrangement of these receptors dictating the response seen. Binding of IL-2 to a heterodimer 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) while naïve T 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. 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. The long-acting IL-2 Superkines are listed in the table below.

**MDNA109 Family of Long-Acting 'IL-2 Superkines'**

| Compound | Features | Advantages |
|---|---|---|
| MDNA109 |  | IL-2 with 5 core mutations to enhance activity towards CD8 T cells |
| MDNA109-LA |  | MDNA109 fused to a protein scaffold to improve PK profile |
| MDNA19 (MDNA109-LA1) |  | MDNA109-LA with 2 additional mutations to limit expansion of Tregs |
| MDNA109-LA2 |  | MDNA109 fused to an alternative protein scaffold to improve PK profile |
| IL2-LA |  | IL2 fused to a protein scaffold for use as control |

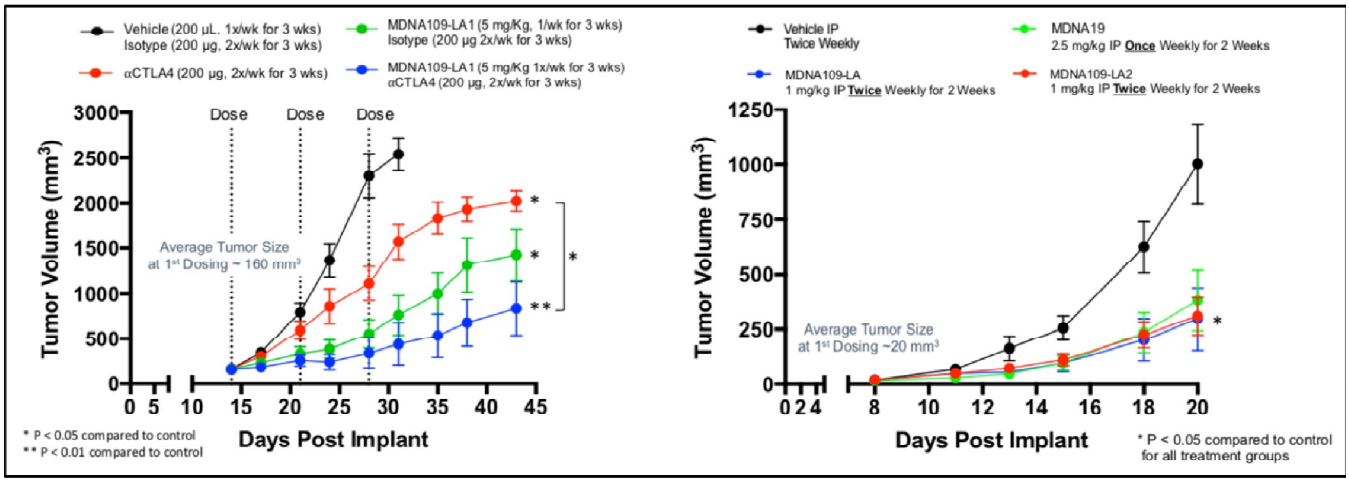
*Source*: Rafei *et al*., 2019

MDNA19 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 T regulatory cells (Tregs), as shown in the following figures. For the binding assays, a lower number signifies decreased affinity while for the signaling assays, a lower number corresponds to higher signaling.




***Source:* Rafei *et al.*, 2019**

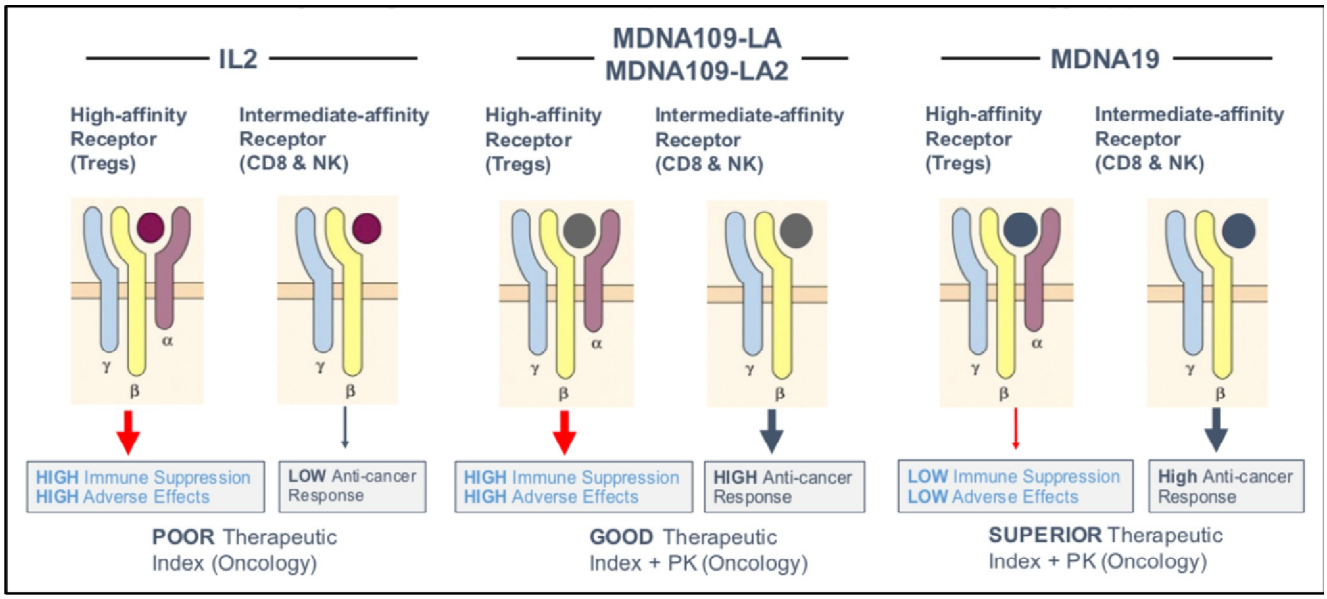
MDNA19 shows activity as both a monotherapy and in combination with α-CTLA4 therapy in a CT26 colon cancer mouse model. The following figure on the left shows decreased tumor growth in mice treated with MDNA19 (green line) and enhanced anti-tumor activity when MDNA19 is administered along with an α-CTLA4 antibody (blue line). The figure on the right shows that MDNA19 achieves similar efficacy to other MDNA109 family members with less frequent dosing in an aggressive B16F10 melanoma mouse model.




***Source:* Rafei *et al.*, 2019**

The following chart summarizes the differences between IL-2, MDNA109LA/MDNA109LA-2, and MDNA19. Due to the increased affinity for CD122 along with no binding to CD25, MDNA19 shows low immune suppression and

adverse effects (which are the result of binding to the heterotrimer complex that includes CD25) and a high anti-cancer response (which is the result of increased binding to the heterodimer complex of CD122/CD132 that activates T cells and NK cells).




***Source*: Rafei *et al.*, 2019**

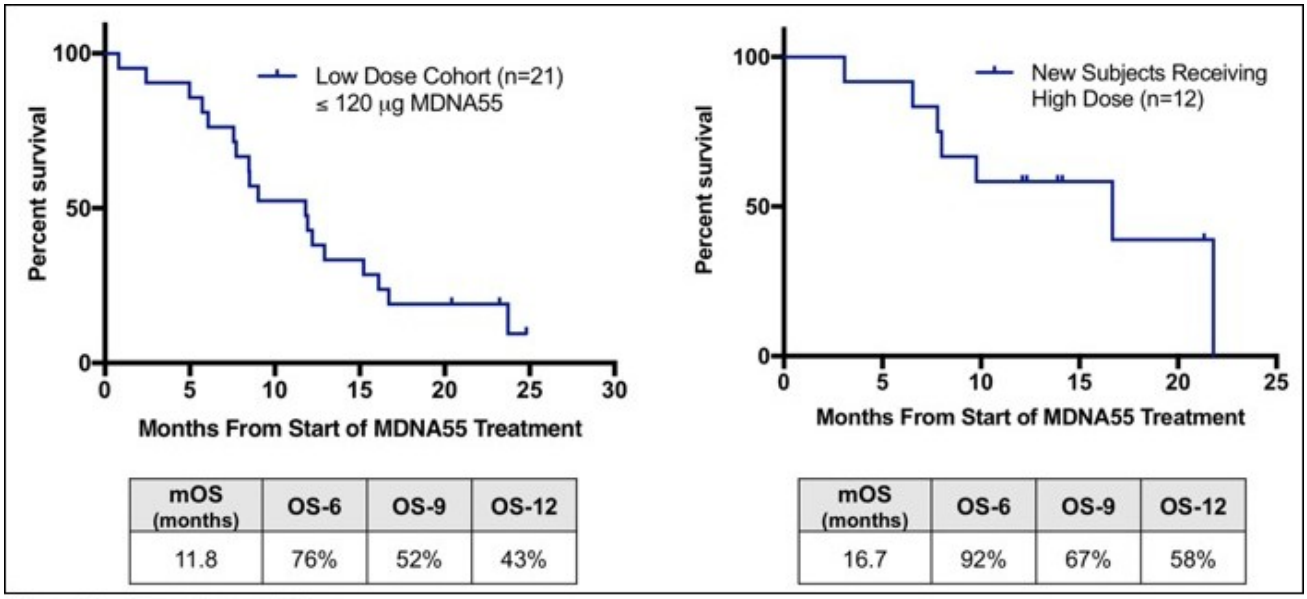
In summary, Medicenna will be advancing MDNA19 into clinical development as the lead IL-2 'Superkine' based on the lack of affinity for CD25 and enhanced affinity for CD122. We believe this is the only enhanced long-acting IL-2 in development that combines both of those characteristics, and it likely has potential in a number of therapeutic applications, including in combination with checkpoint inhibitor therapy, as part of an 'armed' oncolytic virus, or as a fusion protein with antibodies or other cytokines. Pre-IND work is continuing on MDNA19 such that it can be advanced into the clinic and we anticipate an update on the program in 2020.

*Updated Data from Phase 2b Trial Presented at Targeting Innate Immunity Congress*

On September 25, 2019, Medicenna Therapeutics Corp. (MDNA) announced the presentation of updated clinical data from the ongoing Phase 2b trial of MDNA55, an IL-4 targeted toxin, in patients with recurrent glioblastoma (rGBM). The Phase 2b clinical trial enrolled a total of 46 rGBM patients experiencing their first or second GBM relapse (NCT02858895). It 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.

The company had previously announced preliminary topline results for the 21 patients enrolled in the 'low-dose' cohort, in which patients received a median of 63 μg of MDNA55, with a mOS of 11.8 months. In addition, patients in the low-dose cohort experienced a disease control rate of 74%, with 14/19 patients having their tumors stabilize or decrease in size when compared to nadir (the largest tumor volume measured). Assessment of tumor response from nadir was utilized using the criteria for immunotherapy Response Assessment in Neuro-Oncology (iRANO) (Okada *et al.*, 2015) 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).

The updated results show that the 12 evaluable patients in the 'high-dose' group had a mOS of 16.7 months. In addition, the percentage of patients alive at six, nine, and 12 months was increased compared to the low-dose cohort, as shown in the following figure.

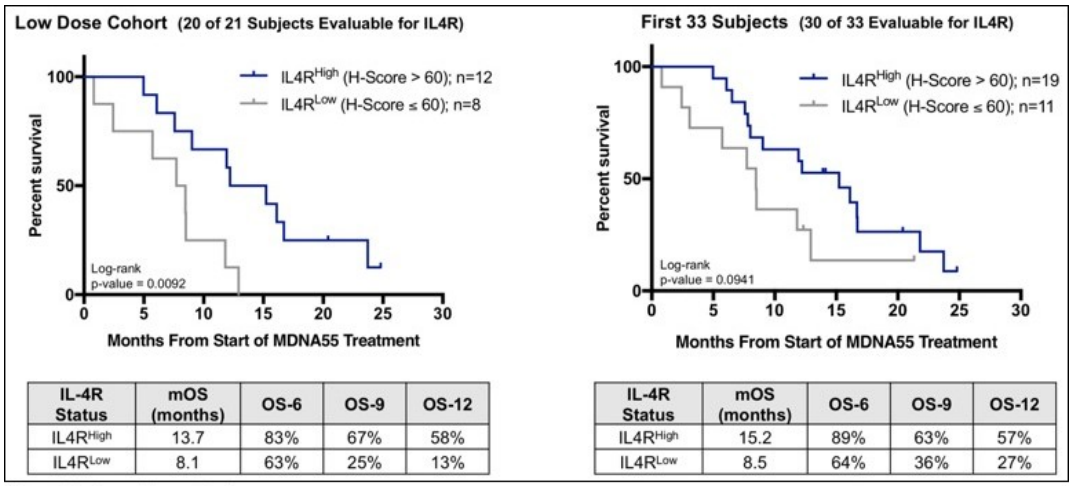



| mOS (months) | OS-6 | OS-9 | OS-12 |
|---|---|---|---|
| 11.8 | 76% | 52% | 43% |

| mOS (months) | OS-6 | OS-9 | OS-12 |
|---|---|---|---|
| 16.7 | 92% | 67% | 58% |

*Source*: Medicenna Therapeutics Corp.

A difference in mOS is also seen when examining survival as a function of IL-4R status. For both the low-dose cohort and the combined low-dose and high-dose evaluable patients, IL-4R$^{High}$ patients (defined as an 'H-Score' > 60 based on immunohistochemistry analysis of IL-4R expression) showed both increased mOS as well as increased survival at six, nine, and 12 months. One other note about the data is that approximately 60% of the rGBM patients seen in this study were classified as 'IL-4R$^{High}$', which while lower than what the literature would suggest is still a significant potential market opportunity.

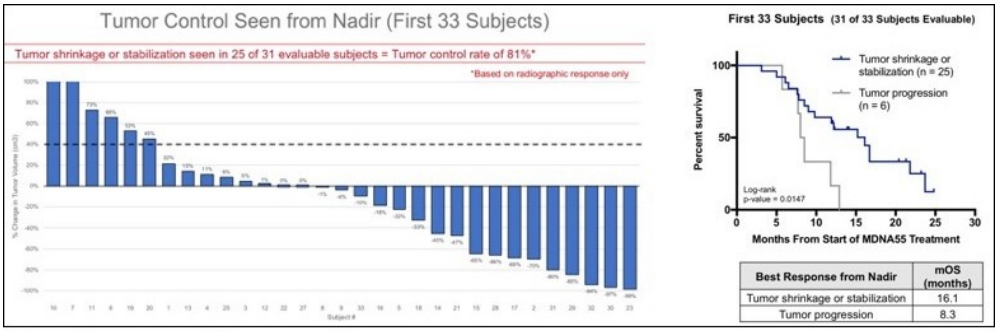



| IL-4R Status | mOS (months) | OS-6 | OS-9 | OS-12 |
|---|---|---|---|---|
| IL4R$^{High}$ | 13.7 | 83% | 67% | 58% |
| IL4R$^{Low}$ | 8.1 | 63% | 25% | 13% |

| IL-4R Status | mOS (months) | OS-6 | OS-9 | OS-12 |
|---|---|---|---|---|
| IL4R$^{High}$ | 15.2 | 89% | 63% | 57% |
| IL4R$^{Low}$ | 8.5 | 64% | 36% | 27% |

*Source*: Medicenna Therapeutics Corp.

Medicenna also reported on tumor control data for the 31 evaluable patients for which there was also OS data. The following figure shows that 25 of 31 (81%) patients saw either stabilization of the tumor or a decrease in tumor size when compared to nadir. There was also an association seen between tumor control and mOS, with those experiencing either tumor shrinkage or stabilization having a mOS of 16.1 months compared to those who saw tumor progression having a mOS of 8.3 months.




*Source*: Medicenna Therapeutics Corp.

The mOS data seen thus far is highly encouraging, particularly in comparison to mOS data seen in trials of other rGBM treatments including Avastin®, lomustine, and temozolomide. The following charts show the mOS results seen from previous clinical trials with those agents, which averaged approximately 8-9 months. This compares to the mOS of 11.9 months seen for the first 33 subjects evaluated in the Phase 2b trial of MDNA55, including a mOS of 16.7 months for the first 12 patients evaluated in the high-dose cohort.

| Approved Therapies | rGBM Population (n) | mOS (months) |
|---|---|---|
| Avastin[1] | n=85 | 9.2 |
| Avastin[2] | n=50 | 8.0 |
| Lomustine[2] | n=46 | 8.0 |
| Lomustine[3] | n=149 | 8.6 |
| Temozolomide[4] | n=31 | 5.6 |
| Temozolomide[5] | n=138 | 5.4 |

1 Friedman et al., J Clin Oncol. 2009 Oct 1;27(28):4733-40.
2 Taal et al., Lancet Oncol 2014 Aug;15(9):943-53.
3 Wick et al., N Engl J Med. 2017 Nov 16;377(20):1954-1963.
4 Kim et al., J Clin Neuroscience 22 (2015) 468–473, 2015.
5 Brada et al., Ann Oncol. 2001;12(2):259–266.

| MDNA55 Patient Groups | rGBM Population (n) | mOS (months) |
|---|---|---|
| Low Dose Cohort | n=21 | 11.8 |
| High Dose Cohort | n=12 (of 25 at high dose) | 16.7 |
| First 33 subjects | n=33 | 11.9 |
| IL4R$^{High}$ - Low Dose Cohort | n=12 (of 20 evaluable) | 13.7 |
| IL4R$^{High}$ - First 33 subjects | n=19 (of 30 evaluable) | 15.2 |
| Tumor control* - Low Dose Cohort | n=14 (of 19 evaluable) | 13.7 |
| Tumor control* - First 33 subjects | n=25 (of 31 evaluable) | 16.1 |

*Source*: Medicenna Therapeutics Corp.

Lastly, we believe the results seen thus far with MDNA55 are all the more impressive when considering the patient population included in the trial, particularly when compared to results seen recently from other clinical trials involving rGBM patients conducted by Ziopharm Oncology (ZIOP) and Tocagen Inc. (TOCA). Ziopharm reported mOS of 12.7 months in a study of a transcriptionally regulated human interleukin-12 gene (Chiocca *et al*., 2019) while Tocagen reported mOS of 11.1 months for a virally delivered cytosine deaminase gene with 5-fluorocytosine (those results were not statistically significant from standard of care). While the mOS numbers look similar to those reported by Medicenna, important differences in inclusion criteria for the Ziopharm and Tocagen studies show that those trials used a more heterogeneous patient population with characteristics known to associate with increased survival.

Medicenna employed strict inclusion criteria for the Phase 2b trial of MDNA55 that included:

1) patients could not be eligible for resection at the time of recurrence
2) patients had to have GBM at recurrence
3) patients needed to have GBM at the initial diagnosis (those with lower grade gliomas were not eligible)
4) patients could not have IDH1 or IDH2 mutations.

Those inclusion criteria are in contrast to the inclusion criteria for the studies conducted by Ziopharm and Tocagen, which included:

1) patients eligible for resection
2) patients with high-grade glioma at recurrence (including GBM and Grade 3 anaplastic astrocytoma)
3) patients originally diagnosed with lower grade glioma but had recurrence with higher grade glioma
4) patients could have IDH1 and/or IDH2 mutations

Surgical resection (Bloch *et al*., 2012), Grade 3 gliomas (Dong *et al*., 2015) and IDH1/IDH2 mutations (Zou *et al*., 2013) are all known to be associated with increased survival in GBM patients compared to those with no surgical resection, Grade 4 gliomas, and no IDH1/IDH2 mutations. Thus, the patient population in the Phase 2b trial of MDNA55 was comprised of patients with worse prognoses than the overall patient populations in the Ziopharm and Tocagen trials. We believe these factors are important to understand and help to differentiate MDNA55 from other GBM therapies currently under development while highlighting what we believe to be impressive results in a very difficult to treat patient population.

We anticipate additional mOS data from the majority of the remaining patients from the high-dose cohort before the end of 2019. The company then anticipates conducting an 'end-of-Phase 2' meeting with the FDA in the first quarter of 2020 to determine the regulatory path forward for MDNA55 and whether the opportunity exists for accelerated approval.

**Conclusion**

Medicenna now has funding in place through 2020 and most importantly, through the near-term inflection points that include the announcement of additional mOS data from the MDNA55 Phase 2b trial and the 'end-of-Phase 2' meeting with the FDA in the first quarter of 2020. Due to the financing we have decreased our valuation slightly to $4.50, however we continue to view the shares as significantly undervalued heading into a very important next couple of months for the company.

## 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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## HISTORICAL STOCK PRICE




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