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Mateon Therapeutics, Inc.

(OTCQB: MATN)

MATN: Initiating Coverage of Mateon Therapeutics, Inc.; Targeting TGF-β for Treating Cancer and Viral Respiratory Diseases, including COVID-19…

Based on our probability adjusted DCF model that takes into account potential future revenues from OT-101, ArtiShield, OXi-4503, and CA4P, MATN is valued at $0.40 per share. This model is highly dependent upon continued clinical success of the company's assets and will be adjusted accordingly based upon future clinical results and the company's execution.

Current Price (11/23/20)	$0.20
Valuation	**$0.40**

OUTLOOK

We are initiating coverage of Mateon Therapeutics, Inc. (MATN) with a $0.40 valuation. Mateon is a biopharmaceutical company focused on the modulation of transforming growth factor-beta (TGF-β) for the treatment of cancer and infectious diseases, including COVID-19. The company's lead development compound, OT-101 (trabedersen), is a single stranded antisense oligonucleotide targeting the TGF-β2 mRNA. Mateon is conducting a Phase 2/3 clinical trial of OT-101 in patients suffering from COVID-19. In addition, the company has initiated a global Phase 4 clinical trial of ArtiShield™ in India, Africa, and Latin America for the treatment of COVID-19, with results expected in the 4Q20. ArtiShield™ received marketing approval from India Ministry of AYUSH.

SUMMARY DATA

52-Week High	**$0.29**
52-Week Low	**$0.09**
One-Year Return (%)	**-14.13**
Beta	**1.65**
Average Daily Volume (sh)	**66,347**
Shares Outstanding (mil)	**90**
Market Capitalization ($mil)	**$18**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**0**
Insider Ownership (%)	**39**
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 2020 Estimate	**N/A**
P/E using 2021 Estimate	**N/A**

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

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	0.0 A	0.0 A	0.0 A	0.0 A	0.0 A
2020	0.0 A	1.4 A	0.0 A	0.0 E	1.0 E
2021					0.0 E
2022					0.0 E

Earnings Per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	-$0.02 A	-$0.02 A	-$0.01 A	-$0.06 A	-$0.11 A
2020	-$0.04 A	$0.01 A	-$0.02 A	-$0.01 E	-$0.07 E
2021					-$0.03 E
2022					-$0.04 E

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WHAT'S NEW

Initiating Coverage



Source: Mateon Therapeutics, Inc.

We are initiating coverage of Mateon Therapeutics, Inc. (MATN) with a valuation of $0.40. Mateon is a biopharmaceutical company developing drug candidates for difficult to treat cancers and viral respiratory diseases including COVID-19. The lead development compound, OT-101, is an antisense RNA therapeutic that targets transforming growth factor-beta (TGF-β), a cytokine involved in the growth, proliferation, and repair of many different cell types. The compound has exhibited activity against SARS-CoV-2, the virus that causes COVID-19, and the company recently received clearance to initiate a Phase 2/3 clinical trial of OT-101 in Latin America. The company also received marketing approval for ArtiShield™ from the India Ministry of AYUSH for symptoms frequently observed in COVID-19 (e.g., fever and inflammation). The company is conducting clinical trials for the treatment of COVID-19 for ArtiShield™ in India, Africa, and Latin America. The pipeline also includes CA4P and OXi4503, two anti-cancer compounds that have received Rare Pediatric Drug designation and Orphan Drug Designation from the U.S. FDA.

Targeting TGF-β Through Antisense Technology

TGF-β signaling is involved in a wide variety of cellular processes, including, proliferation, development, and immunity. Multiple isoforms of TGF-β exist, thus making it difficult to target a particular isoform through a monoclonal antibody. All of the isoforms are developmentally vital, and TGF-β1 is involved in the immune response, thus complete inhibition through gene knockout has led to adverse side effects. Mateon has developed an antisense RNA molecule that specifically targets TGF-β2, which block TGF-β2 directly and TGF-β1 indirectly (thus avoiding its complete inhibition), which we believe will lead to fewer adverse side effects.

OT-101 Exhibits Antiviral Activity Against SARS-CoV-2

Multiple studies published since the start of the coronavirus pandemic reveal that the level of TGF-β is elevated in COVID-19 patients, thus making it a suitable target for therapeutic intervention. This elevation in TGF-β can result in a number of adverse consequences, including neutrophil recruitment to the lungs, which can lead to the development of neutrophil extracellular traps (NETs), cytokine storm, and thrombosis in adults and multiorgan inflammatory syndrome (Kawasaki syndrome) in children.

Advancing ArtiShield™ as Treatment for COVID-19

ArtiShield consists of an extract of the herb artemisia absinthium. Its use is based on the traditional form of Indian medicine known as Ayurveda. Artemisinin, one of the active components of ArtiShield, is known to inhibit the TGF-β signaling pathway and neutralizes SARS-CoV-2 *in vitro* at a concentration of 0.45 μg/mL while exhibiting a safety index of 140, which is better than remdesivir and chloroquine. The India Ministry of AYUSH has approved ArtiShield™ for treatment of fever and inflammation, which is frequently observed in COVID-19.

Multiple Opportunities for Priority Review Vouchers

Mateon has received Rare Pediatric Drug designation for three of its development compounds: OT-101 for the treatment of diffuse intrinsic pontine glioma (DIPG), a rare and fatal brain tumor; CA4P for the treatment of pediatric melanoma; and OXi4503 for the treatment of pediatric acute myeloid leukemia (AML). Upon approval, products given Rare Pediatric Drug designation are eligible for a priority review voucher (PRV), which are fully transferable and many have recently been sold for approximately $100 million.

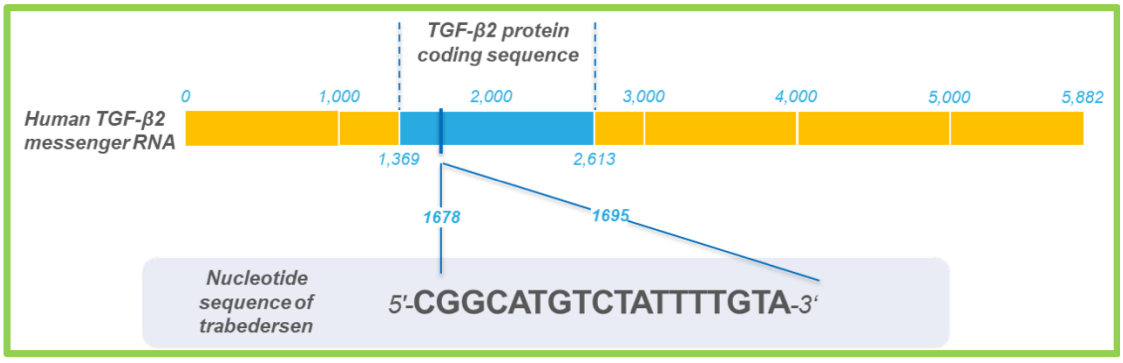
INVESTMENT THESIS

Mateon Therapeutics, Inc. (MATN) is a biopharmaceutical company developing compounds to treat cancer and viral respiratory diseases. The company's lead development asset, OT-101, is an antisense compound that targets transforming growth factor-beta (TGF-β), a cytokine involved in a number of different biological pathways, including growth, proliferation, and immune response. Mateon is also developing ArtiShield™, a readily available and cost-effective agent to combat COVID-19. ArtiShield is currently being studied in ARTI-19, a phase IV study in India. The company is also planning to initiate oncology trials in 2021, as OT-101, CA4P, and OXi4503 each has rare pediatric designation for diffuse intrinsic pontine glioma (DIPG), pediatric melanoma, and pediatric acute myeloid leukemia (AML), respectively. A timeline of the company's upcoming milestones is given below.

- 2H20
    - Initiation of ARTI-19 in India, Africa, and Latin America/Top line data expected end of 4Q20/ Application for global approval if outcome is positive
    - Initiation of C001/C002 for OT-101 against COVID-19 in Latin America/Top line data expected end of 1Q21/ Application for global EUA if outcome is positive
    - Global launch of ArtiShield
- 1H21
    - OT-101: Initiation of Phase 2/3 Trial in Pancreatic Cancer
    - CA4P: Initiation of Phase 2 Trial in Pediatric Melanoma
    - OXi4503: Initiation of Phase 2 Trial in Pediatric AML

OT-101

Mateon's lead development product is OT-101 (trabedersen), a single-stranded phosphorothioate antisense oligodeoxynucleotide (ASO) that targets the TGF-β2 messenger RNA (mRNA). A schematic of the TGF-β2 messenger RNA and where OT-101 binds is shown below.



Source: Mateon Therapeutics, Inc.

ASOs are short oligonucleotides that bind to the complementary mRNA in a sequence-specific manner via Watson-Crick base pairing. Upon binding to the target mRNA, the complex is degraded by various mechanisms depending on the characteristics of the ASO and the location of hybridization (Chen *et al*., 2006). The ultimate outcome of ASO treatment is reduced translation of the target transcript. The following figure depicts various modes of action of ASOs. The ASO is taken up by the cell and hybridizes to its target mRNA. Formation of this complex leads to activation of RNaseH and selective degradation of the bound mRNA. Alternatively, the ASO may prevent binding of the ribosome complex to the mRNA. The ASO can also enter the nucleus and inhibit various parts of mRNA maturation.

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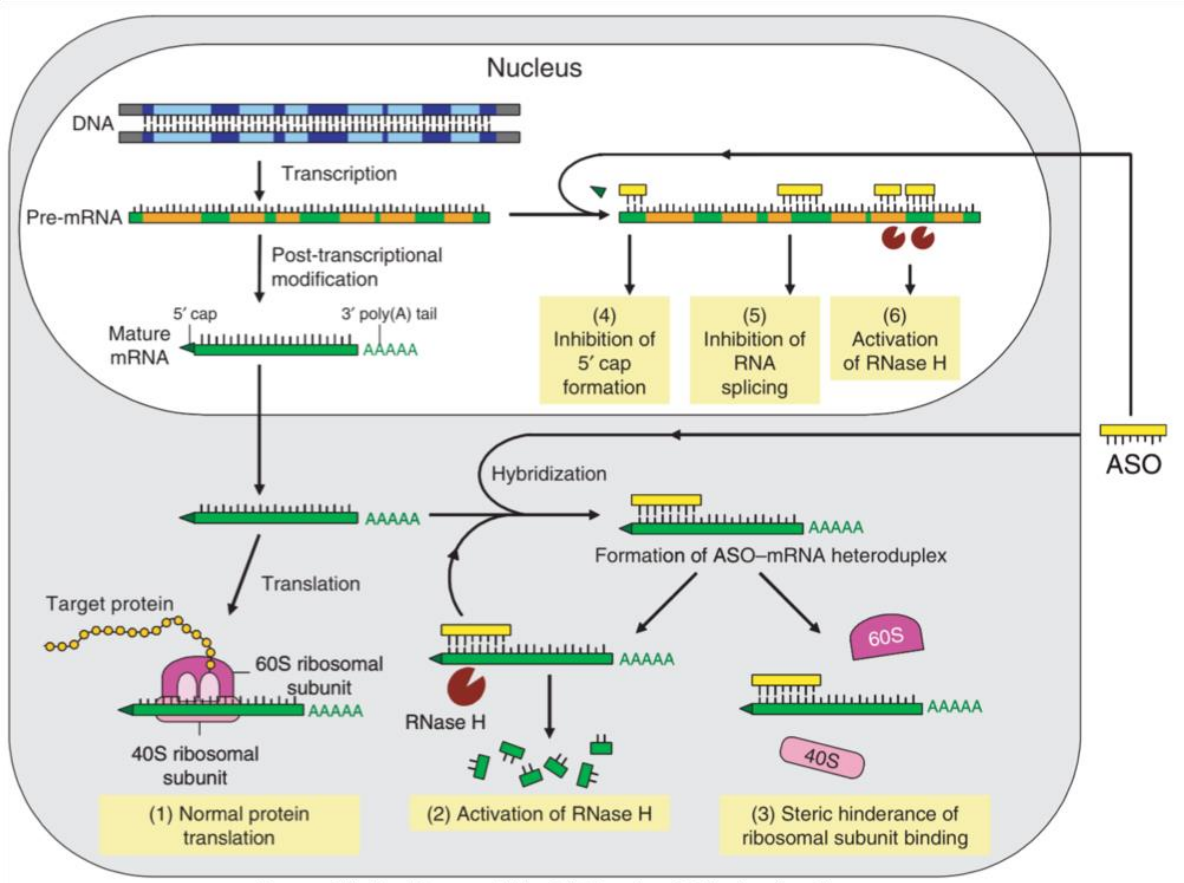


Source: Clin Exp Pharmacol Physiol, May-June 2006, Jasmine Chan.

The first recorded use of antisense technology to inhibit protein production was in the 1970's, when researchers successfully utilized a synthetic oligodeoxynucleotide to inhibit replication of the Rous Sarcoma Virus in chick embryo fibroblasts (Zamecnik *et al*., 1978). Since that time, the production of synthetic oligonucleotides has become routine, and multiple antisense drugs have been approved by the U.S. FDA, as indicated in the table below.

Drug	Target	Disease	Year Approved
Fomivirsen	CMV gene UL123	CMV retinitis	1998
Pegaptanib	VEGF	Wet AMD	2004
Mipomersen	ApoB-100	Familial Hypercholesteremia	2013
Nusinersen	SMN1	SMA	2016
Eteplirsen	Dystrophin	DMD	2016
Voretigene neparvovec	RPE65	Leber Congenital Amaurosis	2017
Inotersen	TTR	Hereditary TTR-mediated Amyloidosis	2018
Patisiran	TTR	Hereditary TTR-mediated Amyloidosis	2018

Sources: Company documents; FDA; Zacks SCR

TGF-β Pathway

Transforming growth factor-beta (TGF-β) signaling is involved in a wide variety of cellular processes, including, proliferation, development, and immunity (Tzavlaki *et al*., 2020). There are three isoforms of TGF-β that share a high degree of homology (>75% at the amino acid level), are often co-expressed and co-localized, and have similar effects on cells *in vitro*. These three isoforms exert their biological effects through binding to three different cell surface receptors (TGFBRI, TGFBRII, TGFBRIII). While each isoform of TGF-β can bind to each of the receptors, they do so with varying degrees of affinity. TGFBRII has high affinity for

TGF-β1 and TGF-β3, but not for TGF-β2 (Lawler *et al*., 1994). TGF-β2 binds with high affinity to a heterooligomer comprised of TGFBRI and TGFBRII. TGFBRIII binds with high affinity to all three isoforms of TGF-β, and functions as a co-receptor to increase ligand binding to TGFBRII (Dong *et al*., 2007). Once bound by TGF-β, TGFBRII autophosphorylates and causes phosphorylation of TGFBRI to initiate its protein kinase activity. Activated TGFBRI phosphorylates the transcription factors Smad2 or Smad3, which bind to Smad4, and the Smad complex then translocates into the nucleus to regulate transcription of a large number of TGF-β regulated genes.

Many companies have attempted to target the TGF-β pathway for therapeutic intervention through either interruption of TGF-β signaling via receptor inhibition by small molecules or to reduce the amount of TGF-β with neutralizing antibodies. Unfortunately, there has been limited success due in part to toxicities observed in clinical testing. Eli Lilly developed a TGF-β monoclonal antibody (mAb) but did not advance it into clinical trials after noting severe toxicity in animals (Herbertz *et al*., 2015). In addition, previous research efforts into inhibition of TGFBRI resulted in severe toxicity in preclinical models (Anderton *et al*., 2011). These results indicate that a systemic 'pan-TGF-β' inhibitor may not be feasible.

Targeted Inhibition of TGF-β Pathway

In contrast to interruption of all TGF-β signaling, targeted inhibition of specific TGF-β isoforms or receptors could alleviate the deleterious effects of non-specific TGF-β inhibitors. With many different components of the TGF-β signaling pathway, there are many options available for therapeutic intervention, but also many different potential consequences.

One way in which researchers learn about the consequences of targeting a specific gene or pathway is through the use of 'knockout' mice. These mice have a disruption in a specific gene that inactivates, or 'knocks out', the function of that particular gene resulting in alterations in phenotype that give clues as to the function of the inactivated gene, as well as potential issues that may arise through its targeted inhibition.

Knockout mice have been generated for each of the TGF-β isoforms:

- For TGF-β1 knockouts, approximately 50% die *in utero* and post-partum mice have severe dysfunctions in the immune and inflammatory systems that results in death by day 20 (Shull *et al*., 1992). T cells appear to play a critical role in this phenotype, as targeted depletion of TGF-β1 in the T cells of adult mice results in a lack of peripheral T cell activation, significant weight loss, decreased cellularity of the thymus and spleen, and a multi-organ hyper-active inflammatory response (Azhar *et al*., 2009).

- For TGF-β2 knockouts, there is also a high degree of perinatal mortality and a wide range of developmental defects, including cardiac, lung, craniofacial, limb, spinal column, eye, inner ear, and urogenital defects (Sanford *et al*., 1997). The development processes most affected by TGF-β2 knockout include epithelial-mesenchymal interactions, cell growth, extracellular matrix production, and tissue remodeling. In adult mice, knocking out TGF-β2 does not interfere with proper immune system function and only affects the extracellular matrix.

- For TGF-β3 knockouts, the mice have delayed lung development, cleft palate, and die shortly after birth (Proetzel *et al*., 1995). However, there are no other obvious gross malformations.

Results of those studies shows that there is no phenotypic overlap between knockouts of TGF-β1, TGF-β2, and TGF-β3, indicating that there are numerous non-compensated functions between the different isoforms (Sanford *et al*., 1997).

Similar studies have been performed for the TGF-β receptors:

- For Tgfbr2 knockouts, embryos develop normally, however there is a defect in the yolk sac hematopoiesis and vasculogenesis that results in embryo lethality at approximately 10.5 days of gestation (Oshima *et al*., 1996). Targeted depletion of Tgfbr2 in $CD4^+$ T cells results in a fatal

autoimmune condition that is just as severe as seen in TGF-β1 knockout mice, with activated CD4+ and CD8+ T cells expressing increased levels of FasL and INF-γ (Marie *et al*., 2006). Dendritic cells with Tgfbr2 depletion are proinflammatory and less immunosuppressive and mice harboring those cells die by 14 weeks of age with multi-organ autoimmune inflammation (Ramalingam *et al*., 2012).

- For Tgfbr1 knockouts, embryos die at midgestation from severe defects in vascular development of the yolk sac and placenta, along with an absence of circulating red blood cells (Larsson *et al*., 2001). Targeted depletion of Tgfbr1 in adult mice smooth muscle cells resulted in rapid and severe aneurysmal degeneration with 100% penetration of ascending thoracic aortas (Yang *et al*., 2016).

In summary, all of the TGF-β isoforms and receptors are critical for development, as knocking them out results in embryonic lethality or death shortly after birth. In addition, TGF-β1 is critical for proper functioning of the immune system, as its elimination in adult mice results in an inflammatory autoimmune response. In contrast, TGF-β2 elimination has no effect on the immune system. Thus, we believe that inhibition of TGF-β1 has the potential to lead to undesirable side effects while inhibition of TGF-β2 would not have those same consequences.

Indication #1: COVID-19

The ongoing coronavirus epidemic caused by the novel coronavirus SARS-CoV-2 has resulted in more than seven million cases and over one million deaths globally (Johns Hopkins coronavirus resource center). While most cases are not serious, approximately 15% of infected adults develop severe pneumonia and approximately 5% of adult patients progress to acute respiratory distress syndrome (ARDS) and multiorgan failure that requires mechanical ventilation (Wu *et al*., 2020).

Thus far, there are no approved vaccines to prevent the spread of SARS-CoV-2 and while remdesivir has been approved through the FDA's Emergency Use Authorization (EUA) based on the results of a clinical trial in 1063 patients (Beigel *et al*., 2020), it exhibited limited efficacy and has a limited supply. In addition, the WHO Solidarity Therapeutics Trial showed that remdesivir, hydroxychloroquine, lopinavir, and interferon had little to no effect on hospitalized COVID-19 patients as judged by overall mortality, initiation of ventilation, and duration of hospital stay (WHO Solidarity trial consortium *et al*., 2020). Thus, additional treatments for SARS-CoV-2 infection are warranted and needed.

The Role of TGF-β in COVID-19

As mentioned previously, TGF-β is involved in immune responses, and that is true for those suffering from COVID-19 as well. There are many examples in the literature of elevated levels of TGF-β in patients suffering from COVID-19:

- Xiong *et al*., 2020: This study reported on transcriptomic analysis of bronchoalveolar lavage fluid from COVID-19 patients. The researchers found that TGF-β levels were increased upon infection with SARS-CoV-2, similar to what occurred in patients infected with SARS-CoV-1 (Huang *et al*., 2005). In addition, the authors speculated that since TGF-β signaling can lead to the development of pulmonary fibrosis (Yu *et al*., 2017), the fibrosis and inflammation seen in the lungs of COVID-19 patients may be a result of TGF-β signaling.

- Agrati *et al*., 2020: This study examined immune and inflammation markers in eight patients with severe (n=4) and mild (n=4) COVID-19. Severe patients were shown to have higher serum concentrations of IL-6 and TGF-β compared to patients with mild disease.

- Mann *et al*., 2020: This study examined longitudinal immune profiling of whole blood and peripheral blood mononuclear cells (PBMCs) of patients hospitalized with COVID-19 in the UK. The results showed that compared to healthy controls (n=7), patients with mild (n=12), moderate (n=7), or severe (n=7) COVID-19 had elevated levels of TGF-β in their serum.

- Ferreira-Gomes *et al*., 2020: This study examined the adaptive immune response in patients with severe COVID-19 through an in-depth analysis of B cell responses. The data showed that the immune response is primarily driven by TGF-β in patients with severe COVID-19, and the authors speculate that given the role of TGF-β in fibrosis, targeting TGF-β therapeutically may be a way to ameliorate severe COVID-19.

Consequences of TGF-β Elevation in COVID-19

Given that TGF-β is involved in a great number of signaling pathways, including inflammatory responses, it is no surprise that there are a number of adverse consequences to increased TGF-β signaling in COVID-19 patients, particularly those suffering from severe disease and/or ARDS.

A) TGB-β induces the expression of IL-6 (Elias *et al*., 1991). While IL-6 is necessary for a proper host defense against infections and injuries, excessive levels of IL-6 can lead to an acute severe inflammatory response known as a 'cytokine storm' (Tanaka *et al*., 2016). The cytokine storm can lead to activation of the coagulation pathway, hypotension, and myocardial dysfunction and eventually lead to multiple organ failure.
B) TGF-β promotes internalization of the αβγ epithelial sodium channel (ENaC), which facilitates Na+ reabsorption across epithelial membranes (Peters *et al*., 2014). Since Na+ concentration is directly related to extracellular fluid osmolarity, any changes in Na+ concentration can affect the accumulation of fluids and potentially lead to pulmonary edema. In a model of acute lung injury, inhibition of TGF-β protected mice from pulmonary edema induced by bleomycin or *Escherichia coli* endotoxin (Pittet *et al*., 2001).
C) Transforming growth factor beta induced protein (TGFBIp) is an extracellular matrix protein that is induced by TGB-β (Skonier *et al*., 1992). While investigating potential biomarkers for severity of COVID-19, researchers found that TGFBIp and its derivative, TGFBIp acetylated K676Ac (TGFBIp K676Ac), were consistently elevated in patients with SARS-CoV-2 pneumonia, in particular in patients in the intensive care unit (Park *et al*., 2020). This indicates that TGF-β signaling is active in patients with COVID-19.
D) TGF-β is a potent regulatory cytokine involved in the initiation and resolution of the inflammatory process, including the chemotaxis of neutrophils to promote their migration to sites of injury (Li *et al*., 2006). One of the ways neutrophils contain infections is through the production of neutrophil extracellular traps (NETs), which are extracellular webs of DNA and antimicrobial enzymes. When not properly regulated, NETs can ultimately lead to increased inflammation and thrombosis. Multiple reports have shown that patients with severe COVID-19 have increased markers for NETs, which may be a novel therapeutic target for those patients (Zuo *et al*., 2020; Barnes *et al*., 2020).
E) In a study of 53 ARDS patients and 53 controls, researchers identified a specific microRNA (miR-425) that was reduced in ARDS patients (Wang *et al*., 2019). miR-425 downregulates TGF-β/SMAD signaling, and its reduction in ARDS patients resulted in an increase in lung fibrosis, showing that upregulated TGF-β signaling can promote fibrosis formation leading to acute lung injury.

OT-101 Activity Against SARS-CoV-2

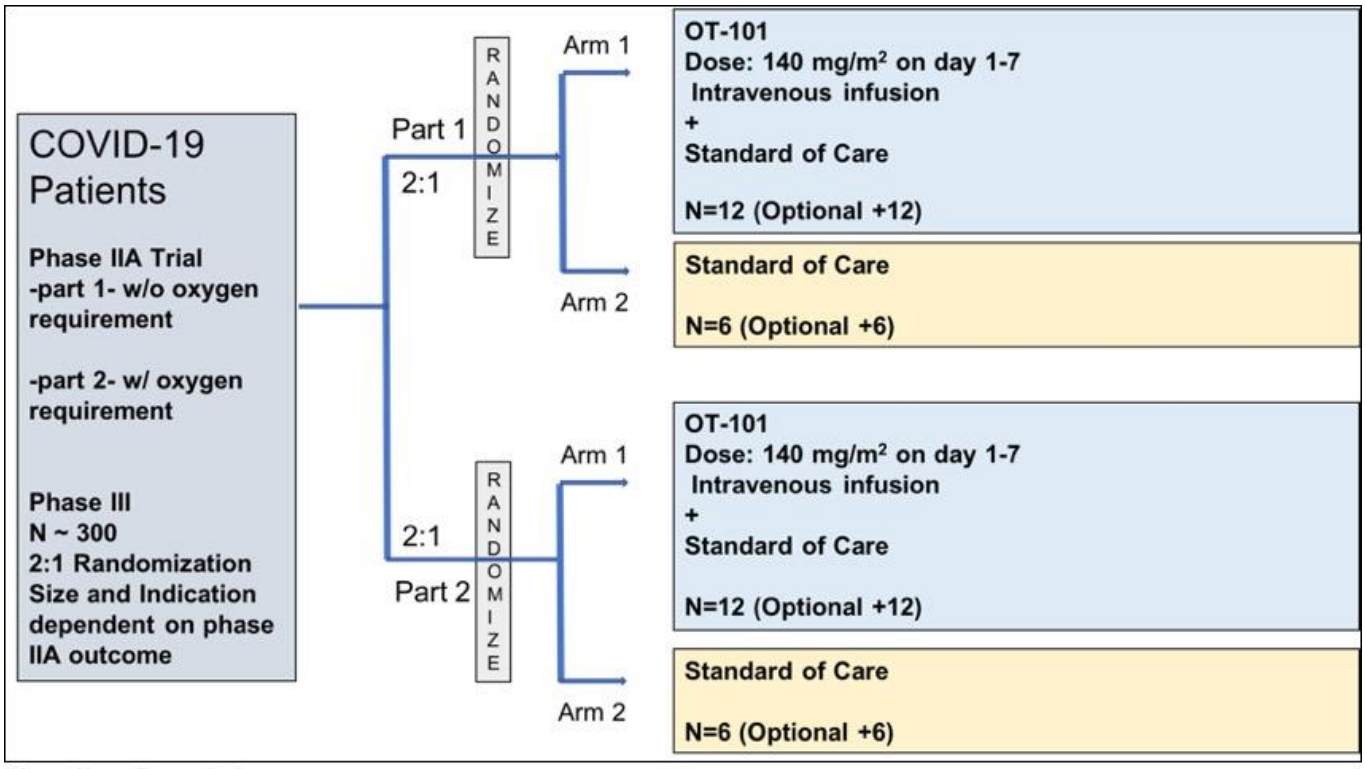
OT-101 was tested against both SARS-CoV-1 and SARS-CoV-2 in collaboration with Dr. Brett Hurst at Utah State University. The antiviral activity of OT-101 was tested against both viruses using Vero 76 cells. The following chart shows that OT-101 inhibits SARS-CoV-2 with a lower EC_{50} value (0.33 μM) compared to remdesivir, which has been approved by the FDA for the treatment of COVID-19 through an Emergency Use Authorization. In addition, OT-101 does not show any signs of cytotoxicity, with a CC_{50} value of >1000 μM (CC_{50} represents the concentration at which there is 50% cytotoxicity in the absence of virus).

Compound	Virus	EC_{50}	CC_{50}	SI
OT-101	SARS-CoV-1 (Urbani strain)[1]	7.6 (1.24 uM)	>1000	>130
OT-101	SARS-CoV-1 (Urbani strain)[1]	26 (4.23 uM)	>1000	>38
OT-101	SARS-COV-2 USA_WA1/2020[2]	2.0 (0.33 uM)	>1000	>500
RSV	SARS-COV-2 USA_WA1/2020[2]	620.0	>1000	>1.6
M128533	SARS-COV-2 USA_WA1/2020[2]	0.012	>10	>830
Remdesivir	SARS-COV-2 (Wang M. et al., 2020, Cell Res. 30:269-271)	(0.77 uM)	(>100 uM)	>129.87

Source: Mateon Therapeutics, Inc.

OT-101 Clinical Trial for COVID-19

Mateon has designed a Phase 2a/3 clinical trial for testing OT-101 in patients with COVID-19. An overview of the Phase 2a portion is shown below. It will consist of two parts, the first will involve patients who have mild or moderate disease with part 2 involving patients requiring mechanical ventilation or intubation. Part 1 of the trial will involve up to 36 patients randomized 2:1 to receive OT-101 administered intravenously at a dose of 140 mg/m^2 for seven days along with standard of care compared to standard of care only. Assuming positive results, a Phase 3 trial involving approximately 300 patients randomized 2:1 to receive either OT-101 plus standard of care or standard of care only will be conducted, however the size of the trial and which patient population will be included is dependent on the outcome of the Phase 2a trial.



Source: Mateon Therapeutics, Inc.

The company recently announced clearance for the trial to initiate in Argentina, which now has the fifth highest number of confirmed coronavirus cases in the world. Approximately 24 patients are expected to be enrolled in Argentina with a total planned enrollment of up to 72 patients worldwide. The primary efficacy endpoint is the proportion of subjects with clinical improvement score (measured using an 8-point WHO COVID-19 Clinical Improvement Ordinal Scale) as assessed by the Odds Ratio at Day 14.

Indication #2: Pancreatic Cancer

Pancreatic cancer is responsible for 7% of all cancer deaths in both men and women, making it the fourth leading cause of cancer death in the U.S. (American Cancer Society). The disease is notoriously difficult to diagnose in early stages due to initial symptoms (anorexia, malaise, nausea, fatigue, and back pain) quite often being nonspecific and subtle in nature.

Surgical resection is the only potential curative therapy for pancreatic cancer. Due to differences in locations of the tumors and their proximity to nearby blood vessels, only 20% of cases are eligible for surgery. Of the tumors that are surgically resected, 80% of those patients will still develop metastatic disease within two to three years following surgery (Daniel *et al*., 2008). For those with pancreatic cancer that cannot be surgically removed, the median overall survival is 10 to 14 months. For those with Stage IV disease (meaning the cancer has metastasized), the 5-year survival rate is 9% (American Cancer Society).

Gemcitabine is the standard of care chemotherapy agent for metastatic pancreatic cancer. The FDA has approved its use in combination with two other chemotherapeutic agents: erlotinib (Tarceva®) and nab-paclitaxel (Abraxane®). FOLFIRINOX (leucovorin + 5-fluorouracil + oxaliplatin + irinotecan) is a combination regimen that significantly improved overall survival compared to treatment with gemcitabine, however it is accompanied by serious adverse events and for that reason is only recommended for the healthiest patients. Onivyde® (irinotecan liposome injection) was approved by the FDA in 2015 in combination with fluorouracil and leucovorin to treat patients with metastatic pancreatic cancer who failed treatment with gemcitabine-based chemotherapy.

Pancreatic Cancer Market Analysis

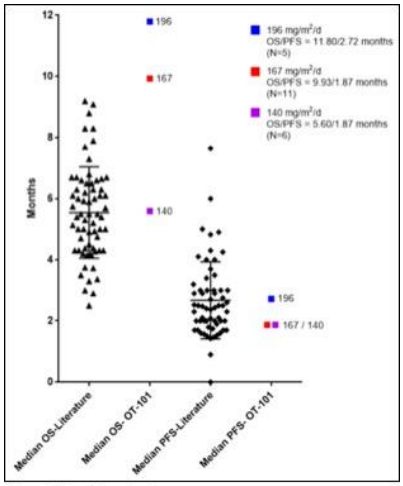
It is estimated that in 2020 approximately 57,600 people will be diagnosed with pancreatic cancer in the U.S. (American Cancer Society). More than half of these patients will be diagnosed with metastatic disease. The 5-year survival rates for patients with pancreatic cancer are dismal 9%) and are particularly bad for those with metastatic disease (~3%).

The current standard of care for patients with metastatic pancreatic cancer includes gemcitabine combined with either erlotinib or nab-paclitaxel. Gemzar® (gemcitabine) is now available as a generic, however prior to losing patent protection the drug generated peak revenues of approximately $700 million in the U.S. for Eli Lilly. Tarceva® (erlotinib) is also available as a generic, however prior to losing patent protection it generated sales of $1.4 billion in 2014 (Evaluate Pharma). Abraxane® (nab-paclitaxel), which was approved for the treatment of breast cancer in 2005 and non-small cell lung cancer in 2012, was approved by the FDA in 2013 for the treatment of metastatic pancreatic cancer. Sales of Abraxane® totaled $1.6 billion in 2019 for all indications (Evaluate Pharma).

OT-101 in Pancreatic Cancer

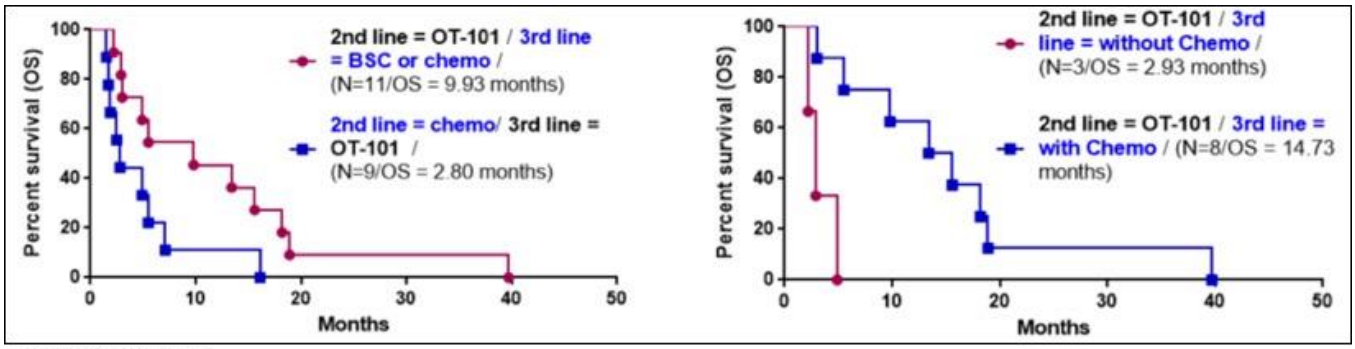
OT-101 was evaluated in a Phase 1/2 clinical trial in patients with pancreatic cancer, melanoma, or colorectal cancer (NCT00844064). OT-101 was administered in escalating doses in two treatment schedules; the first schedule was seven days on and seven days off while the second schedule was four days on and 10 days off. The results showed that OT-101 was safe and well-tolerated with the only expected adverse reaction being a non-serious and transient thrombocytopenia. The maximum tolerated dose (MTD) for the 7/7 regimen (n=11) was 160 mg/m^2/day while the MTD for the 4/10 regimen (n=27) was not reached even at the highest dose of 330 mg/m^2/day. There were two serious adverse events possibly related to study medication (gastrointestinal hemorrhage and pyrexia).

There were 11 2nd line pancreatic cancer patients and 16 3rd line pancreatic cancer patients that received the 4/10 regimen. The progression free survival/overall survival (PFS/OS) at mean doses of 140, 167, and 196 mg/m^2/day were 1.87/5.60 (n=6), 1.87/9.93 (n=11) and 2.72/11.8 months (n=5), respectively. The OS of 9.93 and 11.8 months were higher than the highest reported OS in 65 clinical trials reported in the literature from 1997-2015 (range = 2.50-9.20 / median = 5.50 months) while the PFS values were in line with the reported literature (range = 0.00-7.65 / median = 2.43). The following graph shows that OS and PFS from those 65 reference trials along with the OS and PFS seen in the Phase 2 trial of OT-101 at the various dosing levels. There was a dose dependent increase seen in OS, however no such correlation was seen for PFS.



Source: Mateon Therapeutics, Inc.

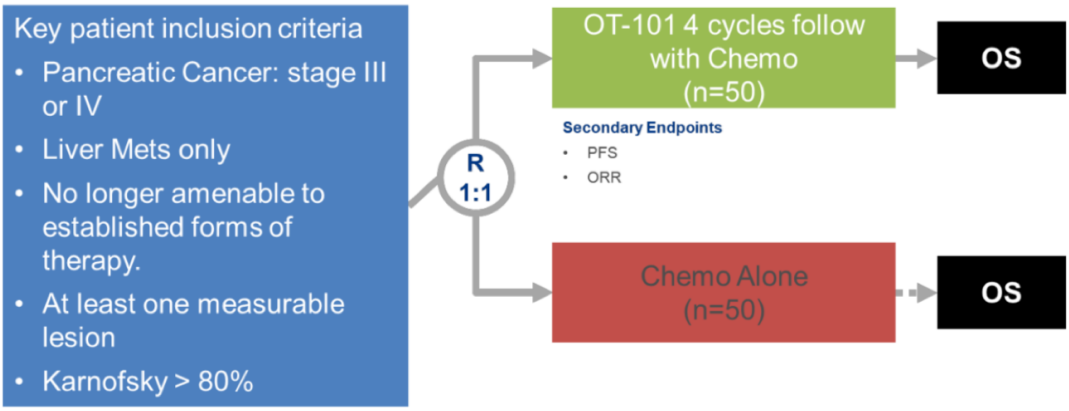
There were also interesting correlations between overall survival and the order of treatment. The following graph on the left shows that patients lived longer when 2nd line therapy was OT-101 followed by chemotherapy compared to 2nd line therapy of chemotherapy followed by OT-101. The following figure on the right shows that patients who follow 2nd line therapy of OT-101 with 3rd line therapy of chemotherapy do much better than patients who do not follow up 2nd line therapy of OT-101 with chemotherapy.



Source: Mateon Therapeutics, Inc.

Proposed Phase 2/3 Trial in Pancreatic Cancer

The following figure gives an overview of the proposed Phase 2/3 clinical trial for OT-101 in patients with pancreatic cancer. The primary endpoint will be improved OS when comparing four cycles of OT-101 treatment followed by chemotherapy to chemotherapy alone. The target patient population is those with end-stage pancreatic cancer with liver metastases only. We anticipate the company waiting for the COVID-19 pandemic to end before initiating the trial.



Source: Mateon Therapeutics, Inc.

Indication #3: High-Grade Glioma

Gliomas are a type of brain tumor that originate in the glial cells that surround and support neurons in the brain. There are four grades of glioma (denoted I, II, III, and IV), with grades I and II referred to as “low grade” and grades III and IV referred to as “high-grade”. Of high-grade gliomas, glioblastoma multiforme (GBM) accounts for 60-70%, anaplastic astrocytomas (AA) for 10-15%, anaplastic oligodendrogliomas and anaplastic oligoastrocytomas for ~10%, and anaplastic ependymoma and anaplastic ganglioglioma make up the rest.

Standard of care for HGG always begins with surgical resection of the tumor, unless the tumor is deemed inoperable due to its location near vital centers of the brain. This is performed both to alleviate the symptoms associated with the disease as well as to facilitate treatment of any residual tumor cells. Even with advances in surgical technique, complete removal of the tumor with clean margins is almost never possible, as the tumors are highly infiltrative and typically extend into the normal brain parenchyma. Due to this, almost all HGG patients have recurrence of the tumor (rGBM), with 90% occurring at the primary site (Wen *et al*., 2008).

Due to the invasive nature of the tumors, surgical resection is followed by radiotherapy coupled with the use of chemotherapeutic agents. Radiotherapy involves the administration of irradiation to the whole brain (Grossman *et al*., 2004). While nitrosoureas were the most common chemotherapeutic agents used for a number of decades, in 1999 temozolomide (TMZ) became available and is now a part of the standard of care. This is due to a clinical trial that showed the addition of TMZ to surgery and radiation increased median survival in newly diagnosed GBM patients to 14.6 months compared to 12.1 months for the surgery and radiation only group (Stupp *et al*., 2005).

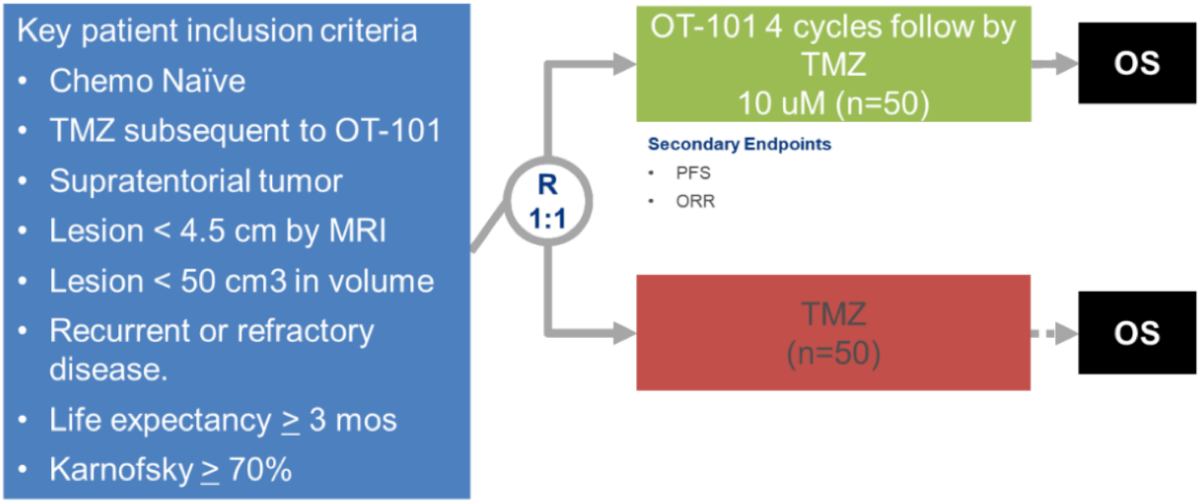
OT-101 in HGG

OT-101 was evaluated in a Phase 2 clinical trial in patients with recurrent and/or refractory HGG (NCT00431561). A total of 145 patients were randomized to receive either 10 μM OT-101, 80 μM OT-101, or standard chemotherapy (TMZ or procarbazine, PCV). OT-101 was administered through intratumoral catheter using a convection enhanced delivery (CED) system. The results showed that the tumor control rate at six months was non-significantly higher in the 10 μM OT-101 group (33%) compared to the 80 μM OT-101 group (20%; *P*=0.1298) and the standard chemotherapy group (27%; *P*=0.6219) (Bogdahn *et al*., 2011).

A post-hoc analysis was performed regarding the safety and efficacy of OT-101 that included a multivariate analysis of parameters that predicted a favorable overall response and survival outcome (Uckun *et al*., 2019). A total of 89 patients received OT-101 (n=27, AA; n=62, GBM) and 77 patients (n=26, AA; n=51, GBM) received at least four OT-101 treatment cycles. Nineteen patients had a complete response (CR) or partial response (PR) with a slow time to maximal size reduction. For the 26 AA/GBM patients with a favorable response, the median progression-free survival (PFS) was 1109 days and overall survival (OS) was 1280 days.

Proposed Phase 2/3 Trial in HGG

The following figure gives an overview of the proposed Phase 2/3 clinical trial for OT-101 in patients with HGG. The primary endpoint will be improved OS when comparing four cycles of OT-101 treatment followed by TMZ to TMZ alone. The target patient population is chemotherapy naïve recurrent glioma patients. We anticipate the company waiting for the COVID-19 pandemic to end before initiating the trial.



Source: Mateon Therapeutics, Inc.

ArtiShield™ for Treating COVID-19

In addition to targeting TGF-β with OT-101, Mateon is also developing ArtiShield™ as a treatment for patients suffering from COVID-19. ArtiShield is a capsule that contains the herb extract artemisia absinthium. Its use is based on the traditional form of Indian medicine known as Ayurveda and it is being developed as a potential treatment of COVID-19 in India, Africa, and Latin America. The approved use for artemisia absinthium according to Ayurvedic text is for fever and inflammation.

Artemisinin is one of the active components of ArtiShield and is known to inhibit the TGF-β signaling pathway and neutralize SARS-CoV-2 *in vitro* at a concentration of 0.45 μg/mL while exhibiting a safety index of 140, which is better than remdesivir and chloroquine. Thus, ArtiShield may target multiple pathogenic pathways in patients suffering from COVID-19 through suppression of viral replication and alleviating clinical symptoms that arise from infection.

Mateon recently launched the ARTI-19 clinical trial in India to test ArtiShield 500 mg capsule with standard of care versus standard of care alone. ArtiShield will be administered for five days per cycle with the option to repeat up to three cycles. Outcomes for the trial include safety and efficacy, which is defined as 1) relief from the signs and symptoms of COVID-19 per the WHO Clinical Progression Scale and 2) relief in the sign of symptoms of COVID-19 per the Duration of Symptoms. The trial is being conducted in collaboration with Windlas Biotech Private Ltd., a contract development and manufacturing organization with large scale manufacturing facilities located in India. Results from the trial are anticipated in the fourth quarter of 2020.

COVID-19 is taking a particularly hard toll on India thus necessitating the need for effective therapies that are also affordable. India has a population of approximately 1.4 billion people, and as of Oct. 11, 2020, a total of 7.1 million people have contracted SARS-CoV-2 with 109,184 people dying from the disease. India also currently has the highest rate in the world of daily new cases.

Rare Pediatric Disease Indications

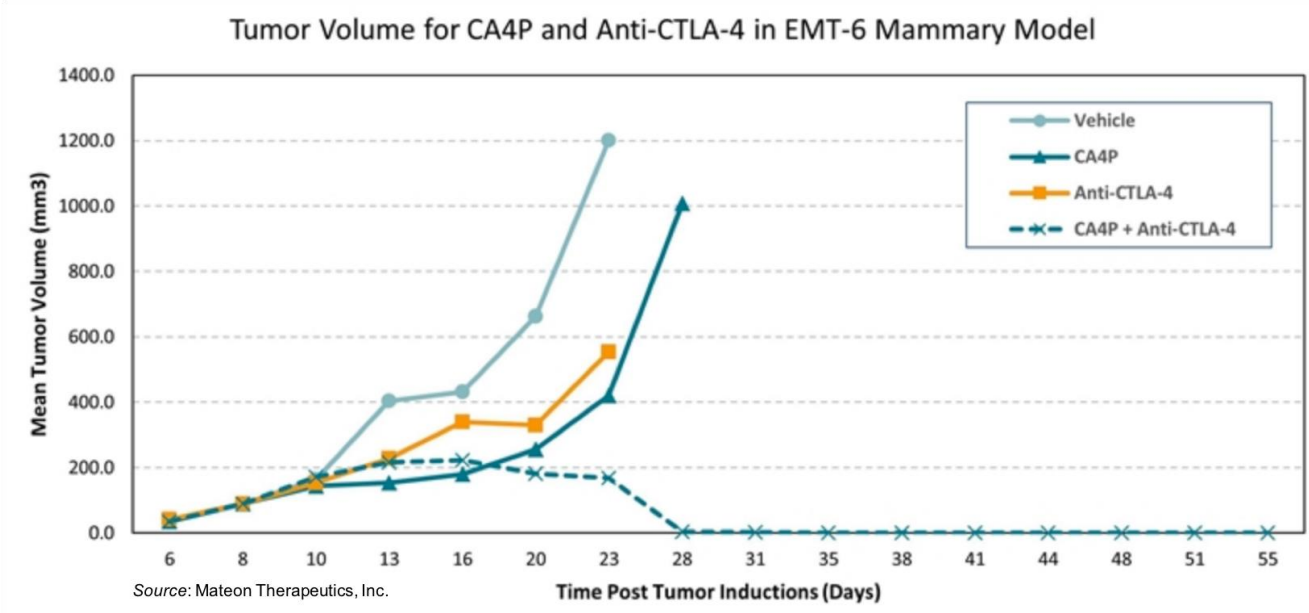
Over the past year, Mateon has announced the receipt of Rare Pediatric Disease designation for three of its development products:

- OT-101 for the treatment of diffuse intrinsic pontine glioma (DIPG)
- CA4P (combretastatin A4) for the treatment of stage IIB-IV melanoma due to genetic mutations that disproportionately affect pediatric patients
- OXi4503 (combretastatin A1-diphosphate) for the treatment of acute myeloid leukemia (AML) due to genetic mutations that disproportionately affect pediatric patients.

DIPG: DIPG is a highly infiltrative brainstem high grade glioma that occurs mostly in children. The tumors are aggressively infiltrative such that cancer tissue typically cannot be differentiated from normal brain tissue. The overall median survival of children with DIPG is approximately 9 months, and remains unchanged despite decades of clinical trial research. The only standard of care is palliative focal radiotherapy, but this has minimal effect on survival and essentially all children die of this disease. Surgical resection is unavailable due to the location of the tumor in the brainstem. New therapeutic strategies are urgently needed. Approximately 1,000 individuals worldwide are diagnosed with DIPG each year.

Pediatric Melanoma: Melanoma is the most common skin cancer seen in children, with approximately 300-500 cases diagnosed each year in the U.S. (Tracy *et al*., 2016). The incidence of melanoma has increased markedly over the past three decades in both adult and pediatric populations. In addition, different genetic predispositions can increase the risk of developing melanoma in the pediatric population. Approximately 5-13% of children with xeroderma pigmentosum, an autosomal recessive disorder affecting DNA repair after ultraviolet exposure, will develop melanoma by the age of 21. Mutations in *CDKN2A* (cyclin-dependent kinase 2A) are also associated with multiple primary melanomas (Kumar *et al*., 2016).

CA4P (combretastatin A4) is a microtubule depolymerizing agent that binds to tubulin leading to morphological changes in endothelial cells (West *et al*., 2004). This ultimately increases vascular permeability and disrupts blood flow to tumor cells. The following figure shows that combination therapy of CA4P and anti-CTLA-4 results in complete tumor regression in the EMT-6 mouse mammary model, while treatment with either agent alone does not affect tumor growth.



Pediatric AML: AML is characterized by an abnormal proliferation and differentiation of a clonal population of myeloid stem cells. Large chromosomal rearrangements that result in the production of chimeric proteins can cause the disease through alteration of the normal myeloid maturation process. It is a heterogeneous disease that can be divided into different subsets based on specific chromosomal abnormalities or mutations. A 2018 study involving 1,000 patients with pediatric AML identified genetic mutations that were more common in pediatric than adult AML and also identified previously unrecognized mutations that were frequent in pediatric AML (Bolouri *et al*., 2018).

OXi4503 (combretastatin A1) has both vascular disrupting and cytotoxic properties and has exhibited single agent activity in mouse xenograft models and a Phase 1 clinical trial in adult AML. A Phase 1b trial of OXi4503 in combination with cytarabine in 26 evaluable adult AML patients showed 4 complete remissions (CR/CRi) and one PR (Uckun *et al*., 2019). The CRs were associated with >1-yr survival overall survival times. The combination therapy also exhibited a manageable toxicity profile.

Potential for Priority Review Vouchers

Rare Pediatric Disease designation makes products eligible for a Priority Review Voucher (PRV) upon approval. A PRV allows the holder of the voucher to receive an expedited six-month review from the FDA for an NDA or biologics license application (BLA) instead of the usual ten-month review. The Food and Drug Administration Safety and Innovation Act (FDASIA) created the rare pediatric voucher in 2012 to specifically target the need for additional therapies for rare pediatric subsets of diseases (affect fewer than 200,000 individuals in the U.S.). PRVs are also awarded for the development of treatments for certain tropical diseases and medical countermeasures.

PRVs are fully transferrable, and a number of companies that have been issued the vouchers in the past have sold them, including one that was sold to AbbVie (ABBV) in Aug. 2015 for $350 million. The four most recent purchases are by Biohaven Pharmaceutical Holding Company for $105 million in Mar. 2019, AstraZeneca (AZN) for $95 million in Aug. 2019, an undisclosed buy for $95 million in Dec. 2019, and Vifor for $111 million in Feb. 2020. While prices for PRVs have come down since AbbVie purchased one for $350 million in 2015, the price for them appears to have settled to approximately $100 million. The following table shows how many PRVs have been issued along with the current status of the voucher, if known.

Priority Review Vouchers

Voucher Award Date	Voucher Type	Voucher Awardee	Voucher Status
2009	Tropical Disease	Novartis	Used for BLA for canakinumab
2012	Tropical Disease	Janssen	Used to accelerate approval of Tremfya (guselkumab) for plaque psoriasis
2014	Rare Pediatric Disease	BioMarin	Sold to Sanofi for $67.5M in Jul 2014; used for approval of Praluent
2014	Tropical Disease	Knight Therapeutics	Sold to Gilead for $125M in Nov 2014; used for approval of Odefsey
2015	Rare Pediatric Disease	United Therapeutics	Sold to AbbVie for $350M in Aug 2015
2015	Rare Pediatric Disease	Asklepion Pharmaceuticals	Transferred to Retrophin and sold to Sanofi for $245M in May 2015
2015	Rare Pediatric Disease	Wellstat Therapeutics	Transferred to AstraZeneca
2015	Rare Pediatric Disease	Alexion Pharmaceuticals	Used for approval of ALXN1210
2015	Rare Pediatric Disease	Alexion Pharmaceuticals	Not used
2016	Tropical Disease	PaxVax Bermuda	Not used (possibly sold to Gilead for ~$200M in 2Q16)
2016	Rare Pediatric Disease	Sarepta Therapeutics	Sold to Gilead for $125M in Feb 2017; used for approval of HIV treatment
2016	Rare Pediatric Disease	Ionis Pharmaceuticals	Not used
2017	Rare Pediatric Disease	Marathon Pharmaceuticals	Not used
2017	Rare Pediatric Disease	BioMarin	Sold for $125 million in Nov 2017
2017	Tropical Disease	Chemo Research, S.L.	Not used
2017	Rare Pediatric Disease	Novartis	Used for brolucizumab for wetAMD
2017	Rare Pediatric Disease	Ultragenyx Pharmaceutical	Sold to Novartis for $130 million in Dec. 2017; used for approval of siponimod
2017	Rare Pediatric Disease	Spark Therapeutics	Sold to Jazz Pharmaceuticals for $110 million in Apr 2018
2018	Rare Pediatric Disease	Ultragenyx Pharmaceutical	Sold to Gilead for $80.6 million in Aug. 2018
2018	Rare Pediatric Disease	Medicines Development	Sold to Novo Nordisk for undisclosed amt
2018	Rare Pediatric Disease	GW Pharma	Sold to Biohaven for $105 million on Mar. 18, 2019
2018	Material Threat Medical Countermeasure	SIGA Technologies	Sold to Eli Lilly for $80 million on Nov. 1, 2018
2018	Tropical Disease	GlaxoSmithKline	Used by ViiV Healthcare for NDA for HIV-1 infection
2018	Rare Pediatric Disease	Leadiant Bioscience Inc	Not used
2018	Rare Pediatric Disease	Sobi and Novimmune	Sold to AZN for $95 million in Aug 2019
2019	Tropical Disease	Novartis	Used for BLA fr ofatumumab
2019	Rare Pediatric Disease	Vertex	Not used
2019	Rare Pediatric Disease	Alexion Pharmaceuticals	Not used
2019	Tropical Disease	Sanofi	Not used
2019	Rare Pediatric Disease	Novartis	Used for BLA for secukinumab
2019	Tropical Disease	TB Alliance	Not used
2019	Material Threat Medical Countermeasure	Bavarian Nordic	Sold to undisclosed buyer for $95 million in Dec. 2019
2019	Rare Pediatric Disease	Vertex	Not used
2019	Rare Pediatric Disease	Sarepta Therapeutics	Sold to Vifor in Feb. 2020 for $111 million
2019	Tropical Disease	Merck	Not used

Source: raps.org / Zacks SCR

Financial Update

On November 16, 2020, Mateon announced financial results for the third quarter of 2020.
R&D expenses in the third quarter of 2020 were $0.9 million compared to $0.3 million for the third quarter of 2019. The increase was primarily due to higher amortization of intangibles and personnel costs. G&A expenses were $0.7 million for the third quarter of 2020 compared to $0.6 million for the third quarter of 2019. The increase was primarily due to increased personnel costs.

As of September 30, 2020, Mateon had approximately $1.4 million in cash and cash equivalents due in part to the company raising net proceeds of approximately $2.3 million through the sale of 50 units at a price per unit of $50,000. Each unit allows for the purchase of 25,000 shares of EdgePoint (Mateon's artificial intelligence division) and one note issue by Mateon, with each note convertible into up to 25,000 shares of EdgePoint's

common stock (conversion price $1.00 per share) or up to 138,889 shares of Mateon's common stock (conversion price of $0.18 per share). Each unit also includes 100,000 warrants, 50,000 warrants each to purchase one share of EdgePoint's common stock at $1.00 per share, and 50,000 warrants each to purchase one share of Mateon's common stock at $0.20 per share.

As of November 11, 2020, Mateon had approximately 89.6 million shares of common stock outstanding. However, the company also had 278,188 shares of Series A preferred stock outstanding, with each share of Series A preferred stock convertible into 1,000 shares of common stock. The Series A preferred stock was automatically converted following stockholder approval of the increase in the number of authorized shares from 150 million to 750 million. Thus, when considering stock options, warrants, and conversion of the preferred shares, we estimate the company has a fully diluted share count of 412.3 million shares.

Risks to Consider

Clinical Risks: Mateon is currently developing both OT-101 and ArtiShield for the treatment of COVID-19. While OT-101 has shown good *in vitro* anti-viral activity, those results may not translate into clinical success. As an anti-cancer agent, OT-101 has shown some success in past trials, but there is no guarantee those results could be replicated in future clinical studies.

Development Risks: The company has two development programs for COVID-19. There are an enormous number of therapies that are currently being tested as treatments for COVID-19, thus even if OT-101 or ArtiShield is successful in the clinic, it may not translate into commercial success.

Stock Risk: The company currently has 278,188 Series A Convertible Preferred Shares outstanding. Each of those Convertible Preferred shares converts into 1,000 shares of common stock, with the conversion having already occurred following shareholder approval. Thus, while the conversion has not been officially recorded, we estimate that the company currently has approximately 367.8 million shares outstanding, which is significantly more than the 89.6 million that was last reported.

Financing Risk: The company only reported approximately $1.4 million in cash and cash equivalents as of Sep. 30, 2020, thus significant additional financing will be required to advance the company's development assets into and through clinical testing. Obtaining additional financing could result in significant dilution to current shareholders, or financing may not be able to be obtained, which may result in the company having to scale back or eliminate some or all of its programs.

MANAGEMENT PROFILES

Vuong Trieu – Chief Executive Officer, Chairman

Dr. Trieu currently serves as CEO/Chairman of Oncotelic Inc.. Previously he was President and CEO of Igdrasol, the developer of 2nd generation Abraxane, where he pioneered the regulatory pathway for approval of paclitaxel nanomedicine through a single bioequivalence trial against Abraxane. When Igdrasol merged with Sorrento Therapeutics, he became CSO and Board Director. He was also a Board Director of Cenomed, a company focusing on CNS drug development. Before that he was Director of Pharmacology, Pharmacokinetics, and Biology at Abraxis where he led the development of albumin encapsulated therapeutics along with building a high throughput platform for small molecules, mirRNA, and kinases. Prior to that he was Group Leader at Applied Molecular Evolution, where he was developing a biosimilar for Humira and Enbrel. Before that he was Director of Cardiovascular Biology at Parker Hughes Institute. Dr. Trieu holds a PhD in Microbiology and a BS in Microbiology and Botany. He is member of ENDO, ASCO, AACR, and many other professional organizations. Dr. Trieu has published widely in the fields of oncology, cardiovascular disease, and drug development and has over 100 patent applications and 39 issued US patents.

Seymour Fein – Chief Medical Officer

Dr. Fein's professional activities have been focused on drug development research for over 35 years. He has been extensively involved in the successful development of numerous drugs, biologics, and medical devices over his career leading to FDA approvals for over 20 drugs (NDAs, sNDAs, BLAs) and devices (PMAs). Dr. Fein began his career at Hoffmann-La Roche Ltd. as a senior research physician and was responsible for a clinical development program that led to U.S. FDA approval of recombinant interferon-alpha for cancer treatment. Dr. Fein was also the medical director of Bayer Healthcare Pharmaceuticals (U.S.) where he was responsible for therapeutic areas including gastroenterology, oncology, and cardiology. He later served as medical director for Rorer Group (now part of Sanofi) and Ohmeda (now part of Baxter). Dr. Fein founded and has been managing partner of a clinical and regulatory consulting organization and has worked closely with the Division of Gastroenterology and Inborn Errors Products at the FDA. Dr. Fein received his B.A. degree from the University of Pennsylvania and his M.D. degree with honors from New York Medical College. He completed a three-year residency in internal medicine at Dartmouth and a three-year fellowship in medical oncology and hematology at Harvard Medical School, where he served as an instructor of medicine during his final fellowship year. Dr. Fein is board-certified in both oncology and internal medicine.

Amit Shah – Chief Financial Officer

Mr. Shah has served as a senior financial officer for a number of life science companies, including Chief Financial Officer at Marina Biotech, Inc., a publicly traded biotechnology company (2017 to 2018); Vice President of Finance & Accounting and Acting Chief Financial Officer at Insightra Medical Inc. (2014 to 2015); VP Finance and Acting Chief Financial Officer at IgDraSol Inc. (2013); Corporate Controller & Director of Finance at ISTA Pharmaceuticals (2010 to 2012); Corporate Controller at Spectrum Pharmaceuticals (2007 to 2010): and as Controller / Senior Manager Internal Audits at Caraco Pharmaceuticals Laboratories (2000 to 2007). In addition to his work with life sciences companies, Mr. Shah served as the Chief Financial Officer at Eagle Business Performance Services, a management consulting and business advisory firm (2018 through March 2019) and as a consultant and ultimately Senior Director of Finance – ERP, at Young's Market Company (2015 to 2017). Mr. Shah received a Bachelor's of Commerce degree from the University of Mumbai, and is an Associate Chartered Accountant from The Institute of Chartered Accountants of India. Mr. Shah is also an inactive CPA from Colorado.

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VALUATION

We are initiating coverage of Mateon Therapeutics, Inc. (MATN) with a valuation of $0.40. Mateon is a biopharmaceutical company developing drug candidates for difficult to treat cancers and viral respiratory diseases including COVID-19. The lead development compound, OT-101, is an antisense RNA therapeutic that targets transforming growth factor-beta (TGF-β), a cytokine involved in the growth, proliferation, and repair of many different cell types. The compound has exhibited activity against SARS-CoV-2, the virus that causes COVID-19, and the company recently received clearance to initiate a Phase 2/3 clinical trial of OT-101 in Latin America. The company also received marketing approval for ArtiShield™ from the India Ministry of AYUSH for symptoms frequently observed in COVID-19 (e.g., fever and inflammation). The company is conducting clinical trials for the treatment of COVID-19 for ArtiShield™ in India, Africa, and Latin America. The pipeline also includes CA4P and OXi4503, two anti-cancer compounds that have received Rare Pediatric Drug designation and Orphan Drug Designation from the U.S. FDA.

Valuation

We value Mateon using a probability adjusted discounted cash flow model that takes into account potential future revenues from OT-101 and the rare pediatric designations. We do not anticipate sales of ArtiShield having a significant impact on the company's finances.

For OT-101 as an antiviral, we model for the company to file for emergency use authorization in 2021 and begin selling the drug shortly thereafter. We model for peak sales of approximately $100 million, with sales decreasing over the subsequent years as the pandemic comes under control. Using a 15% discount rate and a 50% probability of approval leads to a net present value for OT-101 as an antiviral of $52 million.

For OT-101 in pancreatic cancer, we anticipate a Phase 2/3 clinical trial initiating in the first half of 2021 with an NDA filing in 2024 and approval in 2025. We model for peak sales of approximately $1.5 billion worldwide and for the company to receive a 15% royalty on net sales. Using a 15% discount rate and a 20% probability of approval leads to a net present value for OT-101 in pancreatic cancer of approximately $55 million. In addition, we value potential future indications for OT-101 at $50 million.

For the rare pediatric disease indications, we estimate for PRV's to be issued in 2026, 2027, and 2028 following approvals of OT-101 in DIPG, CA4P for pediatric melanoma, and OXi4503 for pediatric AML, respectively. We estimate that PRV selling prices will remain at approximately $100 million each and using a 15% discount rate and a 40% probability of approval leads to a net present value for the rare pediatric disease indications of $68 million.

Combining the net present value for the company's development pipeline along with the company's current cash position and the potential cash from warrant exercises leads to a combined value of approximately $168 million. Diving by the fully diluted share count of approximately 412.3 million shares leads to a valuation of approximately $0.40.

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PROJECTED FINANCIALS

Mateon Therapeutics, Inc.	2019 A	Q1 A	Q2 A	Q3 A	Q4 E	2020 E	2021 E	2022 E
OT-101 (Cancer)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
CA4P	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Oxi4503	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
ArtiShield	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Other Income	$0.1	$0.3	$1.4	$0.0	$0.0	$1.7	$0.0	$0.0
Total Revenues	**$0.1**	**$0.3**	**$1.4**	**$0.0**	**$0.0**	**$1.7**	**$0.0**	**$0.0**
Cost of Sales	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Product Gross Margin	*100%*					*100%*	*#DIV/0!*	*#DIV/0!*
Research & Development	$1.4	$0.3	$0.5	$0.9	$0.6	$2.3	$5.0	$8.0
General & Administrative	$2.9	$2.7	$0.9	$0.7	$1.0	$5.3	$6.0	$7.0
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($4.2)	($2.6)	$0.0	($1.6)	($1.6)	($5.9)	($11.0)	($15.0)
Non-Operating Expenses (Net)	($2.2)	($2.0)	$0.6	($0.4)	($1.0)	($2.8)	($1.0)	($1.0)
Pre-Tax Income	($6.4)	($4.6)	$0.6	($2.0)	($2.6)	($8.7)	($12.0)	($16.0)
Income Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($6.4)**	**($4.6)**	**$0.6**	**($2.0)**	**($2.6)**	**($8.7)**	**($12.0)**	**($16.0)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.11)**	**($0.05)**	**$0.01**	**($0.02)**	**($0.01)**	**($0.07)**	**($0.03)**	**($0.04)**
Basic Shares Outstanding	60.0	84.9	88.2	89.0	200.0	115.5	400.0	425.0

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

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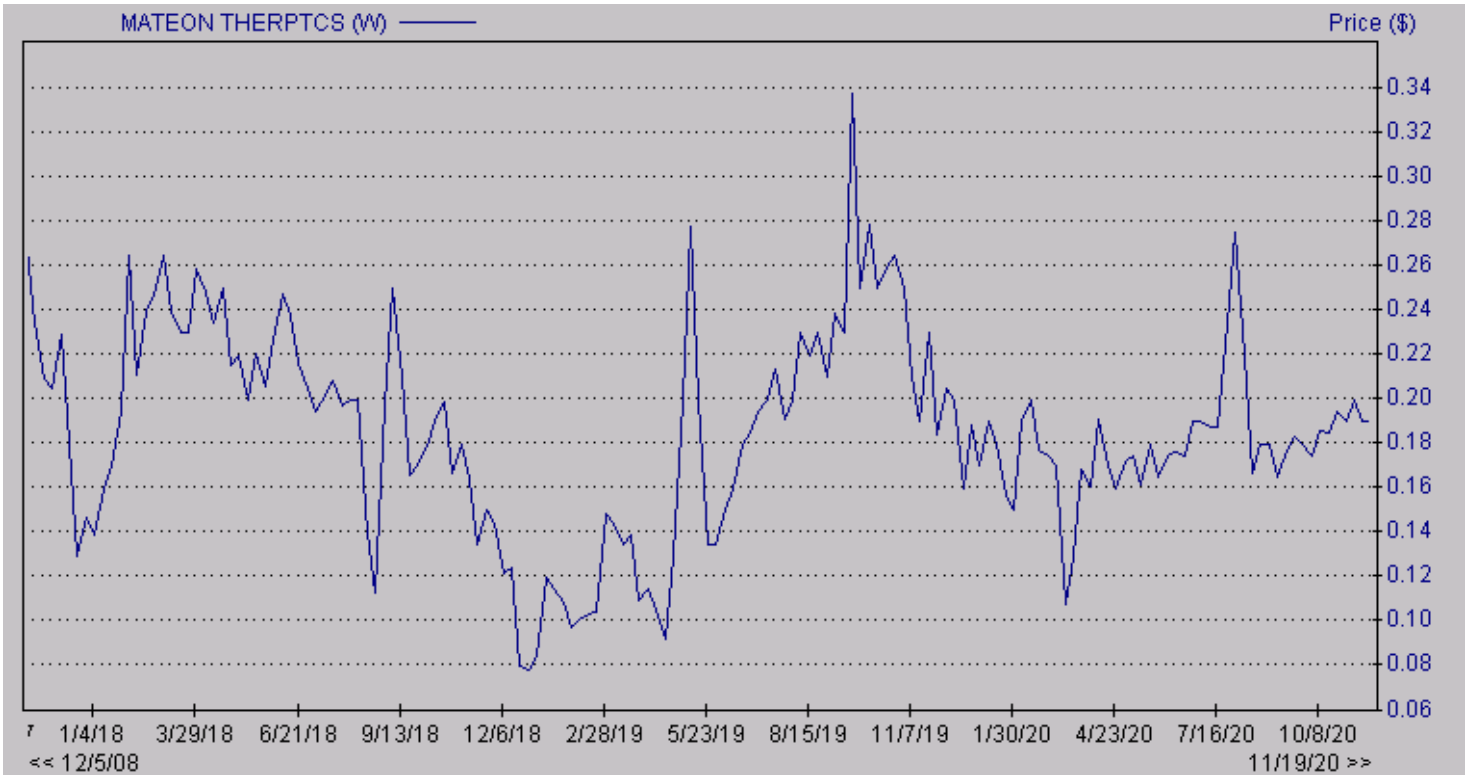
HISTORICAL STOCK PRICE



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