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Oragenics, Inc. (OGEN-AMEX)

OGEN: Enrollment in Phase 2 Trial of AG013 to Complete in 4Q19…

Based on our probability adjusted DCF model that takes into account potential future revenues from AG013 and OG716, OGEN is valued at $3.00/share. This model is highly dependent upon the continued clinical success of those programs and will be adjusted accordingly based upon future clinical outcomes.

Current Price (08/20/19)	$0.38
Valuation	**$3.00**

OUTLOOK

Oragenics, Inc. (OGEN) is currently conducting a Phase 2 clinical trial of its lead development candidate, AG013, for the prevention of oral mucositis in patients undergoing traditional chemotherapy and radiation treatment for head and neck cancer. The company has enrolled a total of 126 patients with an anticipated total enrollment of 200. We anticipate enrollment completing in the fourth quarter of 2019 and top line results being released in the first half of 2020.

In June 2019, Oragenics announced the publication of results showing that the company's lantibiotic compounds exhibit a novel mechanism of action involving the formation of water permeating pores across bacterial cell membranes, which is believed to contribute to the compounds' anti-microbial properties.

SUMMARY DATA

52-Week High	**$3.74**
52-Week Low	**$0.35**
One-Year Return (%)	**-12.65**
Beta	**1.89**
Average Daily Volume (sh)	**758,330**
Shares Outstanding (mil)	**46**
Market Capitalization ($mil)	**$17**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**24**
Insider Ownership (%)	**8**
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	**-1.7**
P/E using 2019 Estimate	**-1.8**

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)
2018	0 A	0 A	0 A	0 A	0 A
2019	0 A	0 A	0 E	0 E	0 E
2020					0 E
2021					0 E

Earnings Per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	-$0.42 A	-$0.38 A	-$0.35 A	-$0.09 A	-$0.87 A
2019	-$0.11 A	-$0.10 A	-$0.06 E	-$0.06 E	-$0.33 E
2020					-$0.23 E
2021					-$0.22 E

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WHAT'S NEW

Business Update

Enrollment of Phase 2 Trial of AG013 to Complete in 4Q19

Oragenics, Inc. (OGEN) is currently conducting a Phase 2 clinical trial of its lead development compound AG013 in the prevention of severe oral mucositis (OM). AG013 is an oral mouth rinse composed of a recombinant *Lactococcus lactis* strain that contains the coding sequence for human trefoil family factor 1 (hTFF1), which is continually secreted by the bacteria. The trefoil factor family (TFF) is a family of three different peptides secreted by epithelial cells of the gastrointestinal tract in response to injury (Hoffman, 2004). Their presence has been implicated in reducing chemotherapy- and radiation-induced injury, both in preclinical studies (Beck *et al*., 2004) and in clinical trials (Peterson *et al*., 2009).

The Phase 2 trial (NCT03234465) is expected to enroll approximately 200 subjects with head and neck cancer receiving chemotherapy and radiation who will receive either AG013 (2.0×10^{11} CFU) or placebo administered three times a day over 7-9 weeks (depending on the subject's treatment plan). This will be followed by a four-week follow-up phase with a long-term follow up until 12 months past the end of chemotherapy treatment. OM will be assessed at the start of chemotherapy treatment and will continue until the subject has completed the short-term follow up phase or until OM resolves (WHO score ≤ 1). The purpose of the long-term follow up is to assess whether AG013 has any effect on the tumor response to chemotherapy treatment. Thus far, the company has enrolled 126 patients and we anticipate enrollment completing in the fourth quarter of 2019.

In August 2018, Oragenics announced that the Phase 2 trial was resuming following positive results from an interim safety analysis conducted by a Data and Safety Monitoring Board (DSMB) from 19 patients enrolled in the study. Safety was evaluated based on treatment-emergent adverse events, vital signs, weight, physical examinations, clinical assessments, and the presence/absence of AG013 in the blood. The Data Safety Monitoring Board (DSMB) concluded that the trial could continue with no changes to the study protocol. The incidence of adverse events between AG013 and placebo-treated patients was the same. Reports of serious adverse events were typical for a population of head and neck cancer patients undergoing chemotherapy and there were no reports of sepsis or bacteremia. Of particular note is the fact that only a few patients discontinued due to the development of severe OM, which could be an early indication of efficacy. We anticipate top line results from the trial in the first half of 2020.

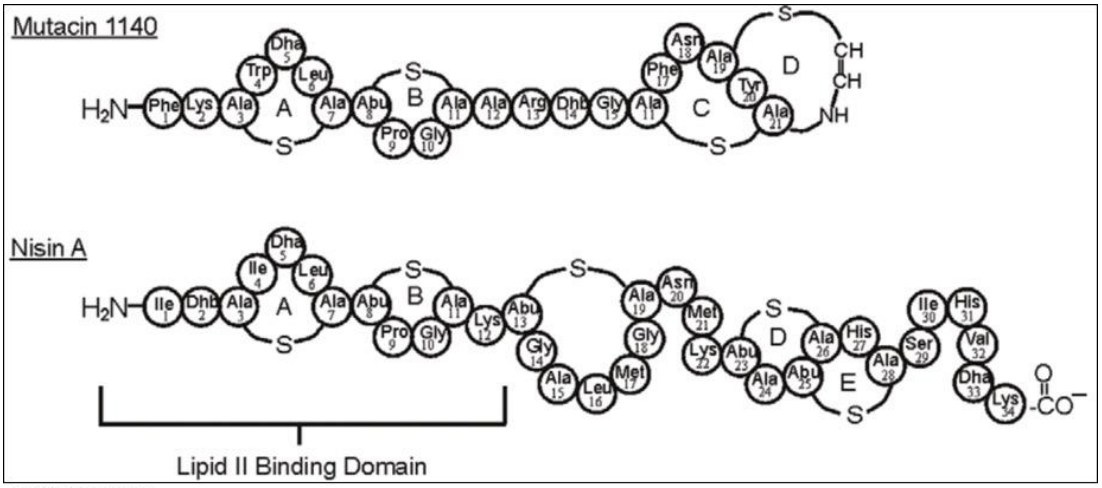
Novel Mechanism of Action for Lantibiotics

In June 2019, Oragenics announced the publication of research describing a novel mechanism of action for the company's lantibiotic compounds in the journal *Physical Chemistry Chemical Physics*. The study examined the interaction of the lantibioitic compound mutacin 1140 (MU1140) with lipid II along with the mechanism of membrane pore formation in Gram positive bacteria using molecular dynamics simulations. The results showed that MU1140-lipid II complexes form functional, water permeating membrane pores that ultimately results in the disruption of the bacterial membrane. This anti-microbial mechanism of action is in addition to the previously described mechanism of action of lipid II sequestration and disruption of cell membrane formation (Hasper *et al*., 2006; Smith *et al*., 2008). The results of these studies give greater insight into a novel mode of action of MU1140 and other lantibiotics and could lead to optimized lantibiotic variants with improved properties.

Background on Lantibiotics

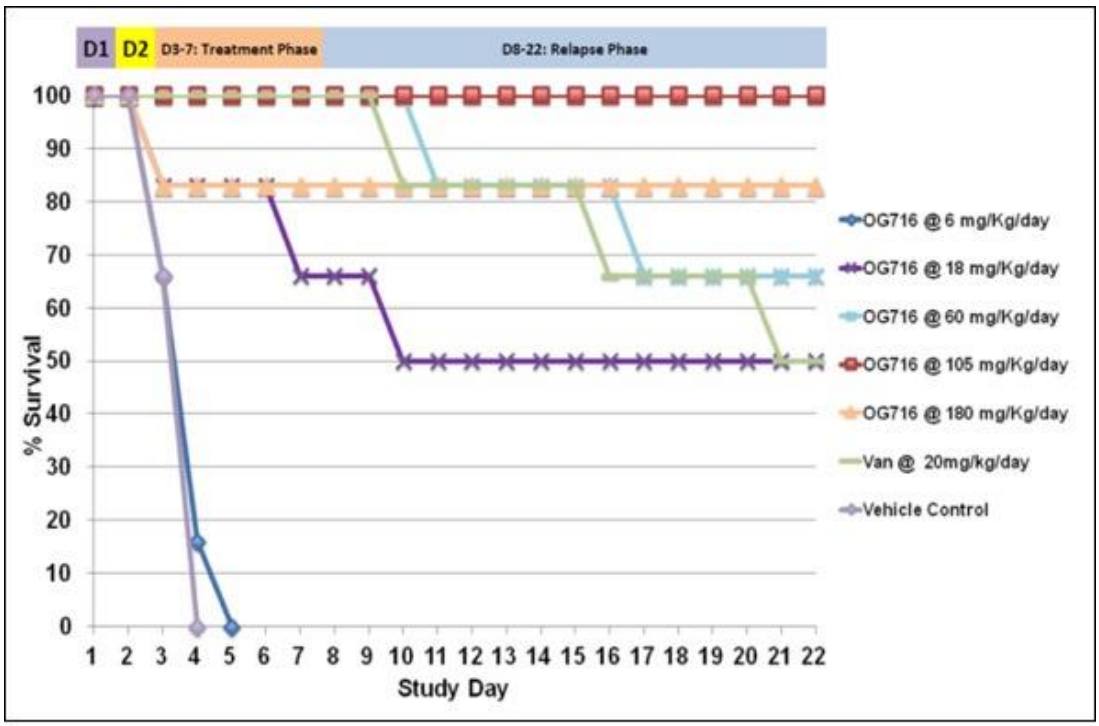
Lantibiotics are a class of peptide antibiotics that are produced by certain Gram-positive bacterial strains. The compounds range in size from 22 to 34 amino acids and typically go through a number of posttranslational modifications that results in novel serine and threonine derivatives, multiple types of sulfhydryl bonds, and the presence of the uncommon amino acids lanthionine (Lan) and B-methyllanthionine (MeLan), from which the lantibiotic name is derived. The compounds are classified based on their length, structure, and heat stability as Type A, Type B, Type IIa, and Type IIb.

Type A lantibiotics fall into two subcategories: compounds that are similar to nisin A (Gross *et al*., 1971) and those that are similar to mutacin 1140 (Smith *et al*., 2000). Nisin A is produced by *Lactobacillus lactis* while mutacin 1140 is produced by *Streptococcus mutans*. The structures of each of those compounds is shown below.



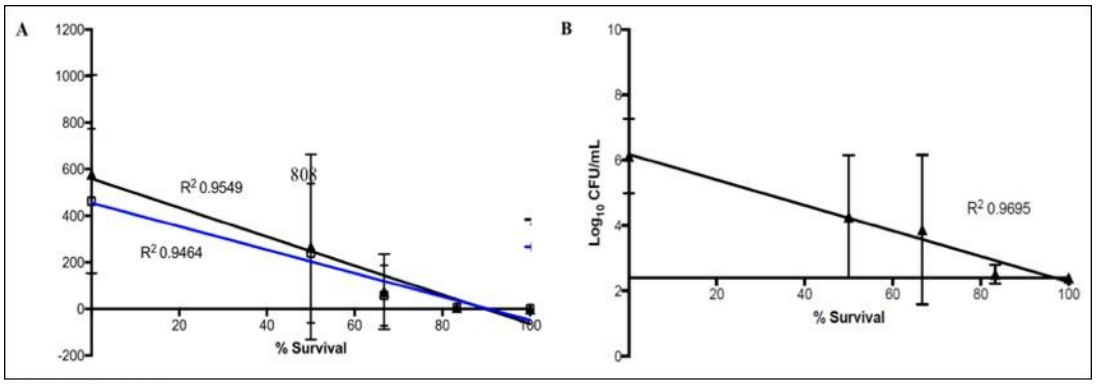
Source: Smith *et al.*, 2008

Oragenics lead lantibiotic development compound is OG716, a derivative of mutacin 1140. Earlier in 2019, new preclinical data was published for OG716 showing its activity in the Golden Syrian hamster model of *Clostridium difficile* associated disease (CDAD) (Pulse *et al.*, 2019). As the following figure shows, all treatments using >18 mg/kg/day OG716 resulted in a statistically significant improvement in survival. The ED_{50} (which measures the concentration of a compound required for 50% maximal activity) was 23.85 mg/kg/day. On a molar basis, this compares quite favorably to vancomycin, which was dosed at 20 mg/kg/day. The ED_{50} of vancomycin was calculated as 13.8 μmole/kg/day compared to OG716 at 10.97 μmole/kg/day.



Source: Pulse *et al.*, 2019

The researchers found a correlation between survival and both cecal CFU counts and levels of toxins A and B, the major virulence factors of C. difficile (Carter *et al.*, 2010). The following figures show the correlation between A) titer levels of toxins A and B and survival and B) cecal CFU and survival. The data suggest that survival as a result of OG716 treatment is affected by the amounts of toxin and how much *C. difficile* is present in the ceca of infected animals.



Source: Pulse *et al.*, 2019

Lastly, the researchers determined the maximum tolerated dose (MTD) of OG716, which included a pharmacokinetic (PK) analysis. Doses tested included 639 mg/kg/day, 1000 mg/kg/day, and 1,917 mg/kg/day (639 mg/kg dose 3 times). Following administration of those doses there were no deaths or significant clinical signs noted in any of the animals, except for a hunched posture noted in one animal following a single dose of OG716 at 639 mg/kg that lasted for only one day. PK analysis showed no prolonged systemic exposure of OG716 following doses at 1,000 and 1,917 mg/kg/day. Two animals from the 1,917 mg/kg/day group showed transient plasma elevations of OG716 of 10.3 ng/mL and 13.6 ng/mL. Of note, the lower limit of detection for that assay is 10 ng/mL Given that the molecular weight of OG716 (approximately 2.2 kDa) is larger than the maximum molecular weight for compounds to be able to pass freely through the gastrointestinal wall (approximately 500 Da), it is not surprising that there was very little systemic exposure of the drug even when dosed at very high levels.

Overall, these experiments confirm that OG716 has the potential to be an effective treatment for CDAD while also exhibiting an excellent safety profile. The company is continuing additional pre-IND activities, including animal toxicity studies and manufacturing additional material for stability studies. We believe the company will be in a position to file an IND in mid-2020.

Financial Update

On August 14, 2019, Oragenics filed form 10-Q with financial results for the second quarter of 2019. As expected, the company did not report any revenue during the second quarter of 2019. R&D expenses were $3.9 million for the second quarter of 2019 compared to $1.3 million for the second quarter of 2018. The increase was primarily due to increased costs associated with the company's Phase 2 trial for AG013. G&A expenses were $1.0 million for both the second quarter of 2019 and 2018. Net loss for the second quarter of 2019 was $4.8 million, or $0.10, compared to a net loss of $2.3 million, or $0.38 per share, in the second quarter of 2019.

Oragenics exited the second quarter of 2019 with approximately $25.7 in cash and cash equivalents. We estimate that the company has sufficient capital to fund operations into the fourth quarter of 2020. As of August 12, 2019, the company had approximately 46.1 million shares of common stock outstanding and when factoring in stock options and warrants a fully diluted share count of 78.8 million.

Valuation

We value Oragenics using a probability adjusted discounted cash flow model that takes into account future revenues from AG013 and OG716. For modeling purposes, we anticipate AG013 entering a Phase 3 trial in 2020, an NDA filing in 2022, and approval in 2023 in the U.S. and Europe, with approval one year later in Japan. For OG716, we forecast for clinical trials to start in 2020, an NDA filing in 2024, and approval in 2025.

There are approximately 700,000 newly diagnosed cancer patients in the U.S. that could potentially develop OM, with another 1.3 million in the E.U. and 20,000 in Japan. Patients who develop OM currently have few treatment options available to them outside of palliative care. We believe that a successful treatment that both prevented the incidence of OM and also decreased the incidence of severe OM in those that develop it would be very appealing to oncologists. An effective OM therapy could also decrease rates of hospitalizations for patients suffering severe OM and limit the need to decrease or stop therapy. We use a very conservative 5% peak market share, an average length of use of 60 days, and a cost of $100/day in the U.S. ($70/day and $75/day for the E.U. and Japan, respectively) to arrive at peak worldwide sales of approximately $350 million. Using a 13% discount rate and a 40% chance of approval leads to a net present value of $210 million.

For OG716, we estimate peak market share of 10% of the approximately 500,000, 200,000, and 100,000 *C. difficile* infections each year in the U.S., E.U., and Japan, respectively. We estimate the cost of treatment of $3,000, $2,000, and $2,250 for the U.S., E.U., and Japan, respectively. This leads to peak worldwide revenues of approximately $275 million. Using a 13% discount rate and a 25% chance of approval leads to a net present value of $14 million.

Combining the net present values for AG013 and OG716 along with the company's current cash position and potential cash from warrant exercises leads to a net present value for the company of $276 million. Dividing by the fully diluted share count of 78.8 million plus an additional 15 million shares for future dilution leads to a current value of $3.00 per share.

PROJECTED FINANCIALS

Oragenics, Inc.	2018 A	Q1 A	Q2 A	Q3 E	Q4 E	2019 E	2020 E	2021 E
AGO13 (Oral Mucositis)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
OG716	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
Licensing & Royalties	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
Total Revenues	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$6.0	$2.4	$3.9	$1.7	$1.7	$9.7	$7.0	$7.3
General & Administrative	$4.0	$1.0	$1.0	$1.2	$1.2	$4.4	$4.7	$5.0
Other Operating Expenses	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($10.0)	($3.4)	($4.9)	($2.9)	($2.9)	($14.1)	($11.7)	($12.3)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.1	$0.1	$0.1	$0.0	$0.0	$0.2	$0.0	$0.0
Pre-Tax Income	($9.9)	($3.3)	($4.8)	($2.9)	($2.9)	($13.9)	($11.7)	($12.3)
Income Taxes	$0	$0	$0	$0	$0	$0	$0	$0
Deemed Dividend of Series D Preferred	$1	$0	$0	$0	$0	$0	$0	$0
Net Income	($11.3)	($3.3)	($4.8)	($2.9)	($2.9)	($13.9)	($11.7)	($12.3)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.87)**	**($0.11)**	**($0.10)**	**($0.06)**	**($0.06)**	**($0.33)**	**($0.23)**	**($0.22)**
YOY Growth	*-36%*	-	-	-	-	*-62%*	*-29%*	*-4%*
Basic Shares Outstanding	13.0	30.6	46.1	46.3	46.4	42.3	50.0	55.0

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

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