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Oragenics, Inc. (OGEN-AMEX)

OGEN: New Pre-Clinical Data Shows Lantibiotic OG253 Safe and Well Tolerated…

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 (06/07/19)	$0.48
Valuation	**$3.00**

OUTLOOK

On May 13, 2019, Oragenics, Inc. (OGEN) announced the publication of pre-clinical data on lantibiotic OG253 that showed the compound to be safe and well tolerated, even at very high doses. Surprisingly, treatment with OG253 caused a significant decrease in serum cholesterol and triglycerides, although no OG253 was detected in the serum. This observation is currently being investigated to better under the mechanism of action.

Due to its susceptibility to proteolytic cleavage in the stomach, development of OG253 was suspended and the company is now focused on the follow-on compound OG716 for the treatment of *Clostridium difficile* infection. However, the data for OG253 show that lantibiotics are safe and well tolerated and could become a new weapon in the treatment of serious bacterial infections.

SUMMARY DATA

52-Week High	**$3.57**
52-Week Low	**$0.38**
One-Year Return (%)	**-69.14**
Beta	**1.58**
Average Daily Volume (sh)	**1,101,293**
Shares Outstanding (mil)	**46**
Market Capitalization ($mil)	**$22**
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 E	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	-$0.06 E	-$0.06 E	-$0.06 E	-$0.28 E
2020					-$0.23 E
2021					-$0.22 E

WHAT'S NEW

Business Update

80th Patient Enrolled into Phase 2 Trial of AG013

On May 20, 2019, Oragenics, Inc. (OGEN) announced that the 80th patient has been enrolled in the company's ongoing Phase 2 clinical trial of its lead development compound AG013 in the prevention of severe oral mucositis (OM). In addition, the World Health Organization provided the company with the generic name *dapatifagene navolactibac* for AG013. 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 160-180 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.

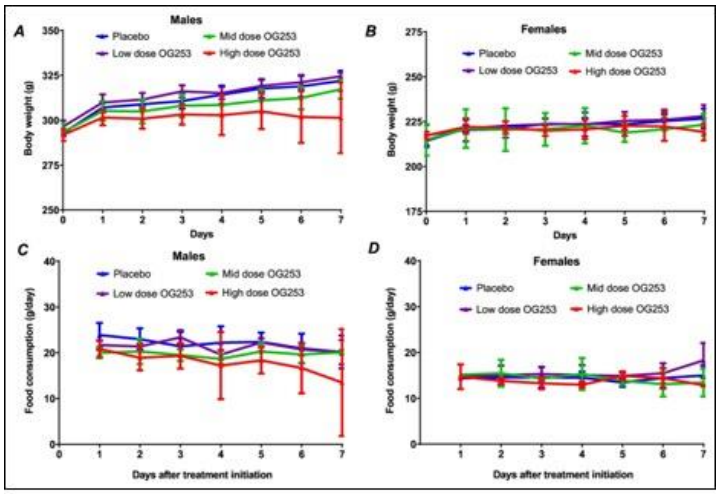
In August 2018, Oragenics announced that the Phase 2 trial was resuming following positive results from an interim safety analysis conducted by a Data and Safety Monitoring Board (DSMB) from 19 patients enrolled in the study. Safety was evaluated based on treatment-emergent adverse events, vital signs, 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.

In October 2018, the company announced that it received clearance from the Belgian Health Authority to enroll Belgium residents in the Phase 2 trial and in November 2018 the company announced that it received clearance to enroll patients in both Germany and the United Kingdom. Patients began enrolling at these sites in early 2019. Given the current rate of enrollment, we anticipate topline results in the first half of 2020.

Publication Highlights Tolerability of Lantibiotic OG253

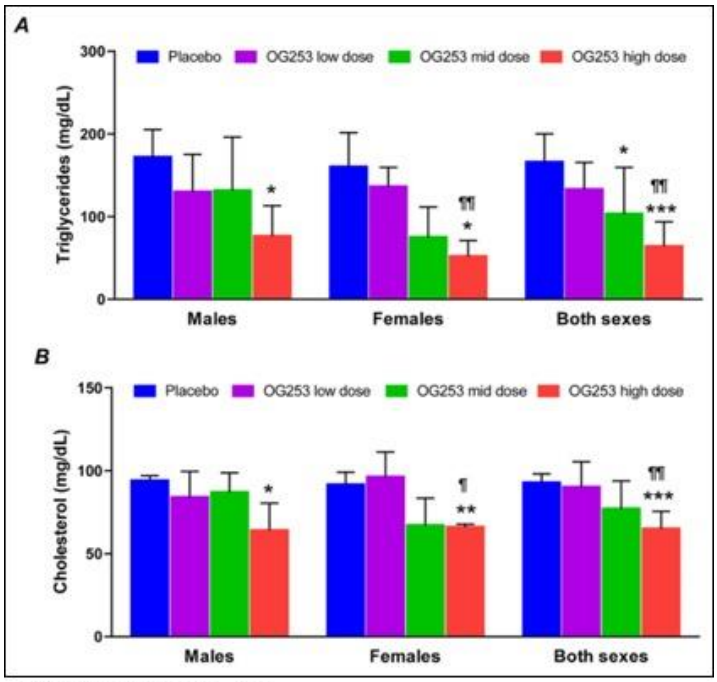
On May 13, 2019, Oragenics announced the publication of new preclinical data on the lantibiotic compound OG253, a predecessor of the company's lead lantibiotic compound OG716, in the peer reviewed journal *Toxicology and Applied Pharmacology*.

The study examined the tolerability of three doses of OG253 in healthy rats both as a single dose and a seven-day repeated dose. The drug was administered three times a day, and all three doses (6.75, 27, and 108 mg/day) were well tolerated with no treatment-related clinical signs of toxicity, including changes in body weights or feeding behavior, as shown in the following figure. In addition, there were no changes in organ weights, hematologic parameters, or histopathologic evidence of toxicity in the gastrointestinal (GI) tract. Importantly, OG253 was not detected in the plasma, meaning that it stays sequestered in the GI tract. The conclusion from the study was a recommendation for a maximum tolerated dose of 425.7 mg/kg/day.



Source: Rajeshkumar *et al.*, 2019

Surprisingly, one effect that was seen was a dramatic decrease in cholesterol and triglycerides. The mean decrease in triglycerides and cholesterol was 61.38% and 29.98%, respectively, after seven days of OG253 treatment. The differences between OG253- and placebo-treated animals for both triglycerides (*P*=0.0002) and cholesterol (*P*=0.0002) were statistically significant. At this point it is unclear exactly why treatment with OG253 would cause such a dramatic decrease in cholesterol and triglycerides, although antibiotics have previously been shown to cause a similar effect (Jenkins *et al.*, 2005). Research into the mechanism of this effect are currently underway.



Source: Rajeshkumar *et al.*, 2019

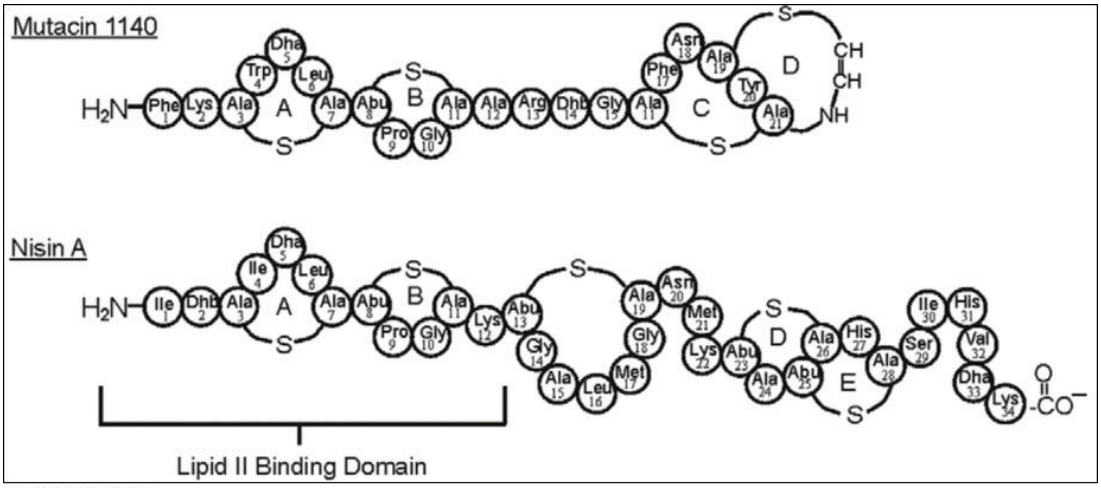
OG253 was originally developed as a derivative of mutacin 1140 based on its ability to eradicate *Clostridium difficile* infection. Unfortunately, OG253 is not orally active as the drug is degraded by digestive proteases. Thus, Oragenics selected a second compound, OG716, which is orally active and also active against *C. difficile* and for which the company is currently continuing pre-IND activities.

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

Lantibiotics exert their bactericidal activity through a number of different mechanisms, including transmembrane pore formation, lipid II-mediated pore formation, and lipid II abduction from physiological domains. Type A lantibiotics have a net positive charge, and it is believed that an electrostatic interaction between the positively charged lantibiotic and the negatively charged bacterial cell membrane is required for initial binding. In addition, Type A lantibiotics bind to lipid II (a precursor molecule in the synthesis of the bacterial cell wall) and cluster it away from the bacterial membrane where cell wall synthesis is occurring, thus ensuring that not enough lipid II is available and consequently inhibiting bacterial cell growth (Hasper *et al*., 2006). Mutacin 1140 does not appear to form pores like nisin A, thus suggesting that only sequestration of lipid II is responsible for its bactericidal activity. Vancomycin also targets lipid II, however it is at a unique site away from where lantibiotics bind. In addition, vancomycin does not sequester lipid II from its normal physiological locations (Daniel *et al*., 2003).

Scientists have been aware of lantibiotics for decades, however they have not been studied as extensively as other classes of antibiotics due to the difficultly in producing sufficient quantities of the compounds. As naturally occurring molecules, lantibiotics are usually produced and secreted into a cell's immediate environment, thus preventing other bacterial cells from infiltrating the area around them. When produced in culture there is a powerful feedback mechanism that works to prevent a bacterium from producing excess lantibiotic that would ultimately kill the host. This results in very low yields of lantibiotics when grown in culture, thus presenting a significant obstacle to their widespread commercial use. Oragenics overcame this obstacle by developing a methodology to produce sufficient quantities of lantibiotics, and through a collaboration with Intrexon Corp. it is developing a means to produce commercial-scale quantities of the drugs.

Financial Update

On May 13, 2019, Oragenics filed form 10-Q with financial results for the first quarter of 2019. As expected, the company did not report any revenue during the first quarter of 2019. R&D expenses were $2.4 million for the first quarter of 2019 compared to $1.3 million for the first quarter of 2018. The increase was due to increased clinical trial costs. G&A expenses for the first quarter of 2019 were $1.0 million compared to $0.8 million in the first quarter of 2018. The increase was due to increased consulting, stock-based compensation, insurance, and salary costs. Net loss for the first quarter of 2019 was $3.3 million, or $0.11 per share, compared to a net loss of $2.1 million, or $0.42 per share, in the first quarter of 2018.

Oragenics exited the first quarter of 2019 with approximately $29.3 million in cash and cash equivalents. This was partially due to an underwritten public offering in March 2019 that resulted in gross proceeds of $12.5 million. We estimate that the company has sufficient capital to fund operations into the fourth quarter of 2020.

As of May 10, 2019, Oragenics 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 E	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	$1.6	$1.7	$1.7	$7.4	$7.0	$7.3
General & Administrative	$4.0	$1.0	$1.1	$1.2	$1.2	$4.5	$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)	($2.7)	($2.9)	($2.9)	($11.9)	($11.7)	($12.3)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.1	$0.1	$0.0	$0.0	$0.0	$0.1	$0.0	$0.0
Pre-Tax Income	($9.9)	($3.3)	($2.7)	($2.9)	($2.9)	($11.8)	($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)	($2.7)	($2.9)	($2.9)	($11.8)	($11.7)	($12.3)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.87)**	**($0.11)**	**($0.06)**	**($0.06)**	**($0.06)**	**($0.28)**	**($0.23)**	**($0.22)**
YOY Growth	*-36%*	-	-	-	-	*-68%*	*-16%*	*-4%*
Basic Shares Outstanding	13.0	30.6	46.2	46.3	46.4	42.4	50.0	55.0

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

HISTORICAL STOCK PRICE

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