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Avivagen, Inc. (CHEXF-OTC)

CHEXF: Initiating Coverage of Avivagen, Inc.; Combating Antibiotic Resistance at the Source…

Using an EV/EBITDA multiple of 16 applied to 2024 revenues and a discount rate of 20% (derived from CAPM), CHEXF is valued at $2.50/share. This model is highly dependent upon commercial success of OxC-beta™ Livestock and will be adjusted accordingly based on future commercial results.

Current Price (11/19/19)	$0.42
Valuation	**$2.50**

OUTLOOK

We are initiating coverage of Avivagen, Inc. (CHEXF) with a $2.50 valuation. Avivagen is developing products to support animal health, which includes replacing antibiotics in livestock feeds with proprietary compounds that promote the growth and overall health of the animal through support of the host's innate immune system. Avivagen discovered that oxidized β-carotene (OxBC) contains a unique class of polymeric compounds that promote immunological health. Regulatory agencies worldwide are scaling back or outlawing the use of antibiotics in livestock feed due to the ever-increasing prevalence of antibiotic-resistant organisms. OxBC may enable the removal of antibiotics from feeds while offering the same or better growth and health benefits without any risk of the development of antibiotic resistance. OxBC is currently approved in six countries, including the U.S., and registration activity is ongoing in several Asian countries, including China.

SUMMARY DATA

52-Week High	**$0.70**
52-Week Low	**$0.26**
One-Year Return (%)	**4.79**
beta	**3.10**
Average Daily Volume (sh)	**443**
Shares Outstanding (mil)	**35**
Market Capitalization ($mil)	**$15**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**N/A**
Insider Ownership (%)	**4**
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 2019 Estimate	**N/A**
P/E using 2020 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Growth**
Industry	**Med Products**

ZACKS ESTIMATES

Revenue
(in millions of CAD$)

	Q1 (Jan)	Q2 (Apr)	Q3 (Jul)	Q4 (Oct)	Year (Oct)
2018	0 A	0 A	0 A	0 A	0 A
2019	0 A	0 A	0 A	0 E	0 E
2020					0 E
2021					0 E

Earnings per Share
(in CAD$)

	Q1 (Jan)	Q2 (Apr)	Q3 (Jul)	Q4 (Oct)	Year (Oct)
2018	-$0.04 A	-$0.03 A	-$0.03 A	-$0.04 A	-$0.15 A
2019	-$0.03 A	-$0.04 A	-$0.04 A	-$0.04 E	-$0.15 E
2020					-$0.10 E
2021					-$0.07 E

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WHAT'S NEW

Initiating Coverage



Source: Avivagen, Inc.

We are initiating coverage of Avivagen, Inc. (CHEXF) with a valuation of $2.50. Avivagen is developing products to support animal health, which includes replacing antibiotics in livestock feeds with proprietary compounds that promote the growth and overall health of the animal through support of the host's innate immune system. Avivagen discovered that β-carotene polymerizes with oxygen into a unique class of compounds (oxidized β-carotene, OxBC) that promote immunological health and are the basis of Avivagen's OxC-beta™ technology. Antibiotic resistance is a growing worldwide public health problem, and since 80% of antibiotics are used in livestock feeds in the U.S., replacement of antibiotics in animal feed may help alleviate the rise in antibiotic resistant organisms. In addition, regulatory agencies worldwide are calling for the decreased use of or outlawing the use of antibiotics in livestock feed. Numerous studies conducted by Avivagen and its partners has shown that supplementation of feed with parts-per-million levels of OxC-beta Livestock can be used as a replacement for growth-promoting antibiotics while offering the same or better growth and health benefits without contributing to the development of antibiotic resistant organisms. OxC-beta Livestock is currently approved in six countries, including the U.S., and registration activity is ongoing in several Asian countries, including China.

Combating Antibiotic Resistance at the Source
Each year, at least 2 million individuals in the U.S. contract a serious infection involving a bacterium that is resistant to one or more antibiotics, with at least 23,000 people dying each year as a result of antibiotic-resistant infections. The rise in antibiotic resistant bacteria is the result of the overuse of antibiotics, with approximately 80% of antibiotics sold in the U.S. utilized for livestock growth promotion. Avivagen's proprietary OxC-beta technology is a non-antibiotic solution for growth promotion in livestock by enhancing the innate immune system and has no risk of promoting antibiotic resistant organisms.

$1 Billion Market Opportunity
Approximately 32,000 feed mills produce approximately 1.1 billion metric tons of feed every year and the global animal feed market is projected to reach approximately $37 billion in 2022. Even with only very small amounts of OxC-beta Livestock premix required (providing 2 g of the OxBC active/ton of animal feed), this represents an enormous potential market opportunity

Gaining Market Share in Asia
Of the approximately 1.1 billion metric tons of animal feed produced annually worldwide, Asia accounts for approximately 35% of that total. Avivagen is focusing on Asia for initial commercialization efforts for OxC-beta Livestock as a number of successful trials have already been conducted in that region. The company has multiple distribution partnerships in place in the region and is actively working toward attaining regulatory approval in China.

Growth Strategy in Place
Avivagen has a three-pronged growth strategy to capitalize on the enormous potential for OxC-beta Livestock: 1) maximize the company's current partnerships by driving adoption and increasing new applications; 2) support expansion of new markets through regulatory approvals in additional countries; 3) add distribution deals in approved markets to reach the maximum number of customers as possible.

INVESTMENT THESIS

Avivagen, Inc. (V.VIV) is a life sciences company developing products to improve animal health through support of the innate immune system, which may ultimately allow for the removal of antibiotics in livestock feed. Antibiotics in livestock feed make up 80% of all antibiotics sold in the U.S. and it this overuse of antibiotics that is contributing to the growing incidence of antibiotic resistance worldwide.

Avivagen's technology involves a proprietary class of compounds that are derived from the oxidation of β-carotene (OxBC) which creates polymeric oxidation products that are the basis of the OxC-beta technology. These compounds confer immunological health benefits and may be responsible for β-carotene's previously reported non-vitamin A activity.

The immunological health benefits shown for the OxC-beta product could allow for it to be used as a replacement for antibiotics in animal feed. Antibiotics have been added to livestock feed since the 1940's when it was discovered that their inclusion resulted in animals growing faster and larger. The amount of antibiotics in feed has increased over time, however with the rise in antibiotic resistant organisms their use has come under scrutiny. The EU banned the use of antibiotics as growth promoters in animal feed over 10 years ago, and there is pressure being exerted on the industry from governments, health agencies, and consumers to remove them entirely. Avivagen has evaluated OxC-beta Livestock in a number of trials as a non-antibiotic feed additive and shown that it performs on par or better than antibiotics in a number of growth and health outcomes.

Antibiotic Resistance

Sir Alexander Fleming, the discoverer of penicillin, first warned against the potential of antibiotic resistance during his acceptance speech for the Nobel Prize in 1945 (Fleming, 1945). It was a rather prescient warning; the rate of antibiotic resistant strains of bacteria has been growing rapidly since the 1980's, with more than 70% of hospital acquired infections resistant to at least one of the drugs commonly used to treat them.

Antibiotic resistance is fueled by the misuse (Dr. Fleming warned about the "…danger that the ignorant man may easily underdose himself…") and overuse of antibiotics in both the clinical and veterinary settings. The widespread use of antibiotics results in the survival and selection of organisms that harbor mechanisms for self-preservation, and with the ability of microorganisms to share genetic material these self-preserving principles are spreading rapidly and leading to an abundance of antibiotic resistant microbes.

Regarding the overuse of antibiotics, the FDA estimates that approximately 10.9 million kg of antibiotics were sold in the U.S. in 2017 for both food-producing and nonfood-producing animals (FDA, 2017). While this is a 22% decrease from 2016, it still represents a substantial amount of antibiotics utilized in animal care and accounts for approximately 80% of all antibiotics sold in the U.S.

The Centers for Disease Control (CDC) published a report in 2013 on antibiotic resistance in the U.S. and the potential for catastrophic consequences if nothing is done to correct the problem. Each year, at least 2 million individuals in the U.S. contract a serious infection involving a bacterium that is resistant to one or more antibiotics, with at least 23,000 people dying each year as a result of antibiotic-resistant infections. In fact, methicillin-resistant *Staphylococcus aureus* (MRSA) infections in U.S. hospitals are responsible for more deaths than HIV/AIDS and tuberculosis combined (Klevens *et al*., 2006; Boucher *et al*., 2009). The rise of antibiotic resistance not only affects the ability to fight routine infections, but it also undermines the treatment of infectious diseases in patients with other diseases. A number of medical advancements were possible due to the ability to fight infections with antibiotics. These include joint replacements, organ transplants, cancer therapy, and the treatment of various chronic diseases. The continued increase in antibiotic resistant bacteria could raise the risks for those treatments and procedures to the point where they are unable to be performed.

Antibiotics in Animal Feed

Improved growth rates in animals due to the addition of antibiotic growth promoters (AGPs) was first described in the mid 1940's (Moore *et al*., 1946), and by the 1950's the addition of AGP's to animal feed became standard practice. The average amount of antibiotics in animal feed has increased over time, from approximately 10-20 g/ton of feed in the 1950's to approximately 30-100 g/ton of feed today. The highest average amounts of antibiotics are used in the U.S. (30% higher than the global average) while China is second on the list (12% higher than the global average). Food producers point to increased body weights, growth rates, and feed conversion ratios (FCR; how efficient animals are at converting feed administered to a given output, such as weight or milk output) in animals administered AGPs as justification for their continued use. However, epidemiological studies have linked the use of AGPs to the emergence of antibiotic resistant bacteria (Wegener, 2003).

With the increased incidence of antibiotic resistant organisms, the use of AGP's has come under increased scrutiny in the past several years. In 2016, a coalition of 54 institutional investors representing over $1 trillion under management launched a campaign against the 10 largest restaurant chains in the U.S. and U.K. to call for an end to the non-therapeutic use of antibiotics important to human health in their meat supply chains. In addition, the National Resources Defense Council publishes an annual report on the 25 largest fast food and fast casual restaurant chains on their antibiotics policies in an effort to end the routine use of antibiotics. Companies are responding to this pressure, with 14 of the 25 taking at least some steps to limit the use of antibiotics in their supply chains. However, as of now this is mostly confined to chicken production.

Governments have also responded to the rise in antibiotic resistant organisms through plans to reduce or eliminate the use of AGP's:

- In 1986, Sweden became the first country to ban the use of AGP's followed in 1989 by Denmark.
- In 2006, the EU placed a ban on the use of antibiotics as growth promoters while still allowing their use to control infections and disease.
- China banned the use of colistin in 2016 and the government has announced a plan to eliminate the use of all AGP's by 2020.
- As of Dec. 1, 2018, Canada requires all medically important antimicrobials (MIAs) to be sold by prescription only and to remove any growth promotion claims from their labels. MIAs consist of antibiotics deemed important for human health.
- In 2017 the FDA issued Guidance for Industry (GFI) #213 that bans all MIAs for animal weight gain and limits their use to veterinary oversight.

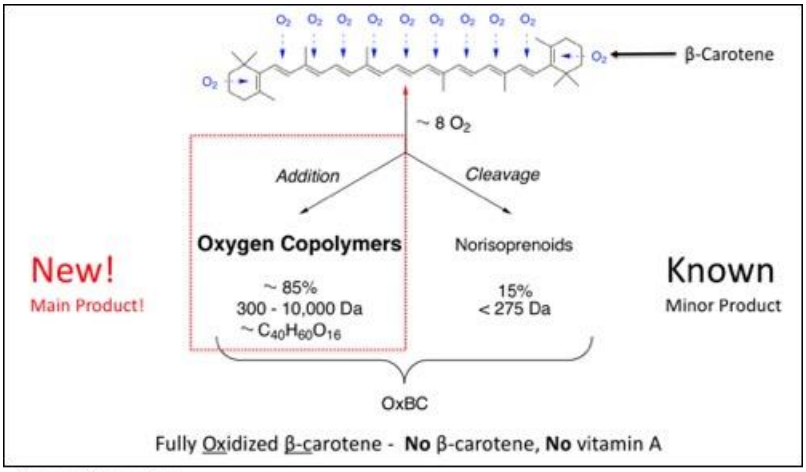
The implementation of GFI #213 is an important milestone in the U.S. to address antibiotic resistance, and with countries worldwide implementing similar measures it could create a potential issue for farmers, ranchers, and animal producers who have relied on AGPs to meet the needs of an ever-increasing population that consumes billions of pounds of animal protein every year. Thus, what is needed is a viable, proven alternative to AGPs that offers the same benefits in terms of weight gain, growth rate, and overall animal health without the risk of increasing antibiotic resistance.

OxC-beta Technology

Avivagen's technology centers on the discovery that fully oxidized β-carotene (OxBC), the active ingredient in OxC-beta Livestock, has positive effects on the innate immune system and can provide natural protection against infectious organisms, similar to feeding low level amounts of antibiotics, without the risk of breeding antibiotic resistant bacteria.

Modulation of the immune system by carotenoids has been known for some time, however it has always appeared to be independent of their role as precursors to vitamin A (Bendich *et al*., 1989). One possible explanation for this activity is related to the antioxidant action of intact carotenoids (Burton *et al*., 1984). An alternative explanation, which had not been fully investigated until more recently, has to do with the oxidation products of carotenoids (Burton *et al*., 2014). Autoxidation of β-carotene occurs through oxygen copolymerization that results in a reproducible product following incorporation of 8 molar equivalents of

oxygen. This product (OxBC) contains >30% oxygen by weight and 85% β-carotene oxygen copolymers with no vitamin A present.



Source: Avivagen, Inc.

To determine the biological activity of fully oxidized β-carotene, studies were conducted with OxBC in normal human fibroblasts. Cells were treated with 5 μM OxBC followed by treatment with lipopolysaccharide (LPS), which was utilized to mimic infection conditions. Results of the experiment are shown in the following table and show that OxBC increases the expression of genes associated with pathogen recognition and innate immunity, for example toll-like receptors (TLRs), and decreases the expression of inflammatory genes such as cytokines and cytokine receptors. These findings suggest that OxBC could potentially impact a number of diverse pathways involved in the immune response and highlight that the product appears to have both immune priming activity as well as anti-inflammatory or pro-resolution effects.

Gene ID	Name	Fold regulation
Pathogen defense		
IFNGR1	Interferon-γ receptor	191
TLR4	Toll-like receptor 4	68
TLR2	Toll-like receptor 2	63
CD14	Cluster of differentiation 14	12
LY96/MD2	Lymphocyte antigen 96	7.4
Inflammation		
CD55/DAF	Complement decay accelerating factor	22
TNFRSF1 A	TNF receptor	−4.4
CCL2/MCP-1	Monocyte chemotactic protein	−4.7
IL1B	Interleukin-1β	−6.6
TNF	Tumour necrosis factor	−7.1
IL1RAP	IL-1 receptor accessory protein	−8.1
NOS2	Nitric oxide synthase (inducible)	−8.7
IL-6	Interleukin-6	−11
CASP1	Caspase-1	−16
Signal transduction		
CHUK/IKKa	Inhibitor of NFκB kinase	27
NFκBIA/IκBα	Inhibitor of NFκB	15
IRF1	Interferon regulatory factor 1	−4.7
TRAF6	TNF receptor associated factor 6	−5.4
IRAK1	IL-1 receptor associated kinase 1	−5.7
NFKB2	Nuclear factor κ-light-chain enhancer of activated B-cells	−7.6
MYD88	Myeloid differentiation gene 88	−9.3

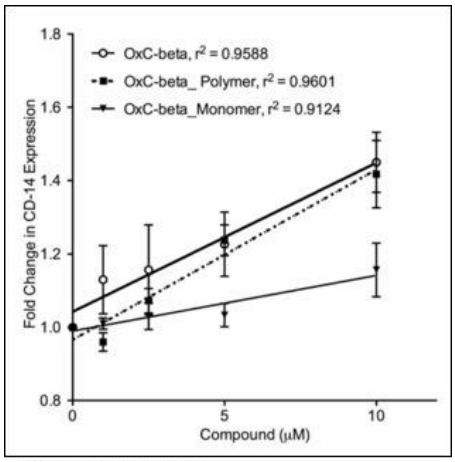
Source: Burton *et al.*, 2014

Immune Priming Actions

To follow up on the results showing increased expression of several genes associated with pathogen recognition and host defense, studies were performed to evaluate the ability of OxBC to directly affect innate immune function and determine the source of activity for OxBC (Johnston *et al.*, 2014). In a confirmation of the gene expression data shown above, flow cytometry data showed that OxBC treatment increased plasma membrane levels of TLRs and CD14 in monocytes, fibroblasts, and endothelial cells. Interestingly, OxBC treatment of naïve monocytes does not impact the production of various cytokines, including TNFα, IL-1β, IL-6, IFNγ, and IL-8. However, LPS challenge following treatment with OxBC leads to enhanced production of several cytokines over what is seen following LPS challenge only, including increases in TNFα (25%), IL-6 (48%), and IL-1β (40%). A further series of experiments were conducted in mice to confirm that the effect of OxBC on receptor levels observed in cell culture also occurred in an animal model. The results of the feeding

trials in mice showed that dietary supplementation with OxBC led to increased receptor levels in the intestinal tissues of mice and thus confirmed the findings of the cell culture work.

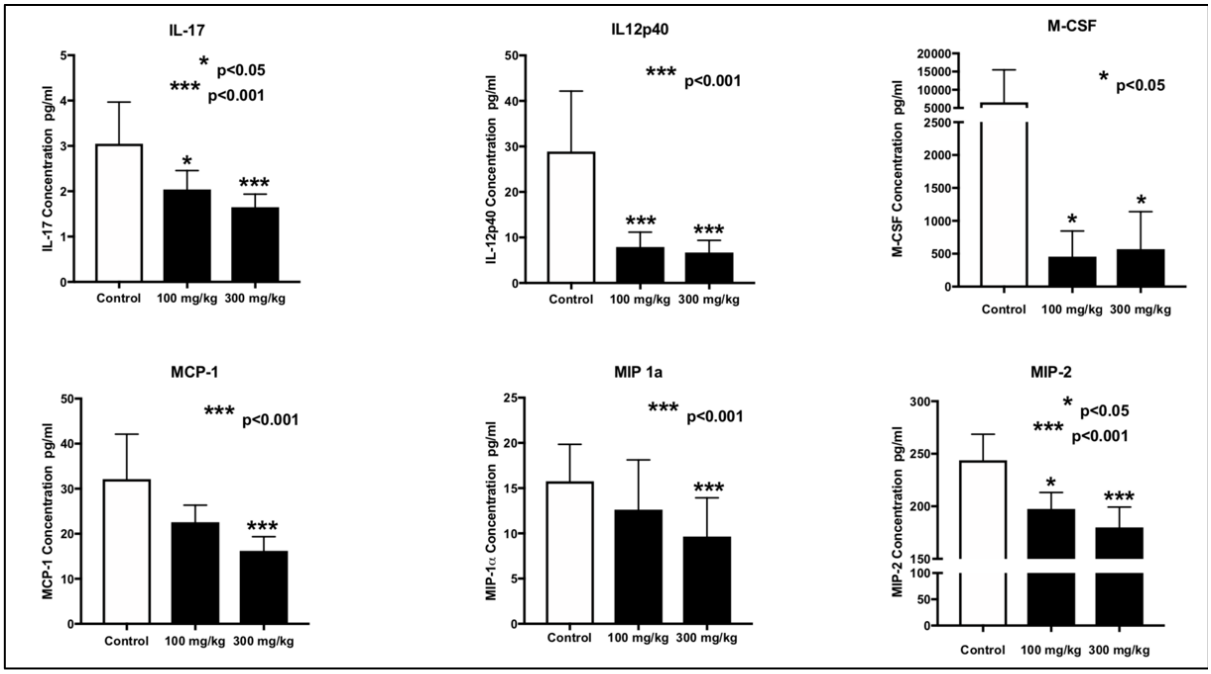
Lastly, to determine the identity of the compound(s) responsible for the immunological activity, a FACS assay was performed to determine the change in CD-14 expression following treatment with OxBC or its isolated polymeric or monomeric fractions. The following graph shows that CD-14 expression increases similarly when cells are treated with OxBC or the polymeric fraction with a much smaller increase seen with the monomeric fraction. These results support the idea that it is the β-carotene/oxygen polymers that are biologically active.



Source: Johnston *et al.*, 2014

Anti-Inflammatory Actions

The ability of OxBC to limit the extent of background or over-zealous inflammation was further investigated in a mouse trial. The results, shown in the figure below, demonstrate significantly reduced levels of six different pro-inflammatory chemokines/cytokines in blood samples from mice receiving two weeks of treatment with OxBC compared to controls.



Source: Avivagen, Inc.

Naturally Occurring OxBC

Following the discovery of the β-carotene/oxygen polymers, scientists at Avivagen then set out to determine if these same polymers are found naturally in foods (Burton *et al*., 2016). Since β-carotene/oxygen polymers are difficult to detect in a food matrix, geronic acid (GA) was utilized as a marker to measure the extent of oxidation and polymer formation. Oxygen polymers comprise approximately 85% of the products of β-carotene oxidation, however GA, the most abundant norisoprenoid breakdown product, accounts for 1-3% of the total reaction by product weight (Burton *et al*., 2014). Thus, using an average 2% of the total product weight for GA, oxidation of β-carotene leads to an approximately 50:1 polymer:GA ratio (although it likely ranges from 25:1 to 100:1 based on the 1-3% range). The following table shows the estimated amounts of GA, OxPVA (oxidized provitamin A), PVA, and the percentage of OxPVA/PVA. The upper value for full conversion of PVA to OxPVA is 130% (OxPVA is ~1.3 times heavier than PVA), and carrot powder had the highest value with approximately 55% conversion of the original carotenes to the oxidized form. Some OxPVA/PVA values are >130% due to the uncertainty of the amount of β-carotene in the raw fruit and low levels of β-carotene in some foods, which makes accurately determining the concentration of GA more difficult. While the absolute numbers aren't important to focus on, what is important is that oxidized β-carotene polymers are found naturally occurring in a wide variety of foods and thus fully supports the safety of β-carotene/oxygen polymers and may help to explain the non-vitamin A immunological activities of β-carotene.

Table 2. Measured Concentrations in Foods of Geronic Acid, GA, Arising from Oxidation of Provitamin A Carotenoids (PVA)[a]

sample	*n*	GA (ng/g)	OxPVA[b] (μg/g)	PVA[c,d] (μg/g)	OxPVA/PVA[e] (%)	isolated polymer[f] (μg/g)	polymer/OxPVA[g]
carrot juice	4	12.6 ± 0.8	0.63	136	0.5		
carrot powder #1[h]	3	10,590 ± 550	530	965 [118]	55	756	1.4
carrot powder #2[i]	3	5007 ± 119	250	965 [118]	21	404	1.6
tomato, raw	5	1.5 ± 0.9	0.08	5.5	1.4		
tomato powder	3	414 ± 46	21	97	21	2600	126
tomato pomace	3	113 ± 3	6	90	6	1006	178
cranberry, raw	1	3.8	0.19	1.6	12		
cranberry powder	3	338 ± 55	17	12	142		
rosehip powder	4	499 ± 12	25	66 [29]	38	1380	55
paprika[j]	3	364 ± 22	18	243 [21]	7	1080	59
spirulina powder	3	2560 ± 10	128	14,303 [1400]	1		
sweet potato powder #1[k]	3	692 ± 22	35	345 [85]	10		
sweet potato powder #2[l]	3	417 ± 55	21	352 [85]	6		
dulse seaweed powder	3	1603 ± 39	80	194 [31]	41	634	8
nori seaweed flakes	3	2002 ± 33	100	198 [31]	51		
dates, dried	7	32 ± 12	1.6	0.54 [0.37]	296		
alfalfa (sun-cured)	2	869 ± 37	43	643 [148]	7	978	23
wheatgrass powder	3	964 ± 7	48	231 [42]	21	924	19
red palm oil	3	60 ± 1	3.0	506	0.6		
milk (3.25% MF)	2	6.7 ± 2.1	0.34	0.07	479		
milk powder (3.25% MF)	3	2.0 ± 0.1	0.10	0.58	17		
whole egg powder	3	34 ± 2	1.7	0.37 [0.09]	463		

[a]GA values provide estimates of total PVA oxidation products, OxPVA, that may be compared to literature or dry weight-adjusted PVA levels and to levels of carotenoid-oxygen copolymer products isolated from ethyl acetate extracts of some powdered foods. [b]Estimated approximate total amount of provitamin A carotenoid oxidation products (OxPVA) = 50 × GA, assuming that GA production parallels that for the model *β*-carotene oxidation in solution. OxPVA implicitly includes any, mostly minor, contributions from two other provitamin A carotenoids, *α*-carotene and cryptoxanthin (Table 2S), which can in principle each contribute one molecule of GA per carotenoid molecule, compared to two from *β*-carotene. [c]Sum of provitamin A carotenoid levels, PVA = *α*- + *β*-carotenes + cryptoxanthin, using literature values for raw food and expressed as nominal original amounts for dehydrated forms after adjusting for water losses (Table 2S). [d]Values in square brackets are for parent raw form. [e]Estimated total provitamin A carotenoid oxidation products, OxPVA, as a percentage of the sum of literature-based initial provitamin A carotenoid levels, PVA. [f]Weight (*μ*g) of carotenoid-oxygen copolymer fraction per gram of dehydrated food isolated by successive precipitations from ethyl acetate extract with hexane. [g]Ratio of isolated polymer fraction to OxPVA. [h]Light brown powder. [i]Orange powder. [j]Comparison with raw, sweet red pepper. [k]Drum-dried. [l]Air-dried.

Source: Burton *et al*., 2016

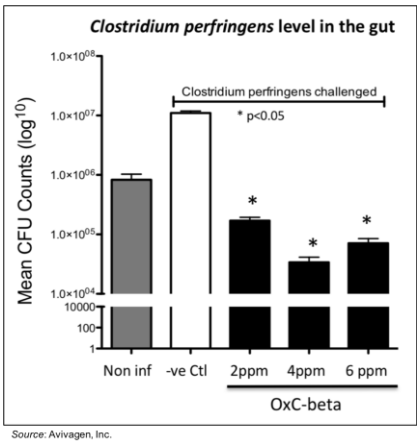
OxC-beta Livestock Trials

OxC-beta Livestock premix containing 10% OxBC has been tested in numerous trials in pigs, chickens, and cows to test how it affects a wide range of outcomes, including growth performance, milk production, and bacterial challenge. Below are summaries from a few published trials:

- Hurnik *et al*. (2011): This study examined the effects of OxC-beta Livestock when administered to pigs. Two sets of 48 weaned piglets were divided such that 24 pigs were immunized with a vaccine for the porcine reproductive and respiratory syndrome (PRRS) virus and 24 pigs were injected with placebo. The pigs were then randomly assigned to one of four treatment diet groups of 0 mg/kg, 10 mg/kg, 30 mg/kg, or 100 mg/kg OxBC (i.e., 100, 300 and 1,000 mg/kg OxC-beta Livestock premix). Results showed that feeding with OxC-beta Livestock improved growth performance (as judged by average daily growth and feed conversion ratio), with the 100 mg/kg OxC-beta group performing the best.

- Duquette *et al*. (2014): Bovine respiratory disease (BRD) is caused by *Mannheimia haemolytica* and results in severe inflammatory tissue damage that can lead to respiratory failure and death in many animals. It is the costliest disease of the North American cattle industry with an incidence of 14-20% and a mortality rate of 4%. In this study, 25 Holstein calves were fed a diet supplemented with OxC-beta Livestock for 28 days prior to inoculation with *M. haemolytica*. Results showed administration of OxC-beta Livestock promoted anti-inflammatory and pro-resolution mechanisms and led to an overall decrease of inflammation in the lungs.

- Kang *et al*. (2018): This study examined the effect of OxC-beta Livestock in chickens with necrotic enteritis caused by *Clostridium perfringens*. Results showed that chickens administered OxC-beta Livestock had higher mean body weights, lower intestinal lesion scores, and decreased number of pathogenic clostridial bacteria in the intestine. The following figure shows the level of *C. perfringens* in the gut of chickens, with OxC-beta Livestock-treated chickens having OxBC levels up to 2-log lower than negative controls and 1-log lower than non-infected chickens.



Source: Avivagen, Inc.

Avivagen has also conducted studies in cooperation with various food producers in pigs, chickens, and cattle. The following slide shows the results of seven studies performed in pigs with outcomes for average daily gain (ADG), FCR, and clinical health. Compared to negative control groups, the animals fed OxC-beta Livestock showed higher ADG and FCR values as well as better health outcomes such as decreases in incidence of diarrhea.

Location	Type	Δ ADG versus control	Δ FCR versus control	Clinical Health
Canada	Performance	**12%**	**8%**	Trend for ↑ vaccine response (PRRS)
Vietnam	Performance	**23%**	**8%**	↓ Incidence of Diarrhea
China	Performance	**5 %**	**-2%**	↓ Incidence of Diarrhea
Vietnam	Performance	**5%**	**6%**	Trend for ↑ vaccine response (PRRS)
USA	Performance	**8%**	**U/C***	Improved fecal scores
Thailand**	Performance	**5%**	**3%**	No effect observed
China	Sow & Piglet Health	**Improved Sow Health, Increased Milk Quality, Improved Piglet Health**		

* U/C= Under confidentiality ** Negative control group received antibiotic growth promoters

Source: Avivagen, Inc.

Similar results were seen in chickens in both performance studies, where outcomes such as ADG and FCR were of primary importance, as well as in necrotic enteritis challenge studies, where the primary outcome measure was clinical health.

Location	Type	*Δ ADG versus control*	*Δ FCR versus control*	Clinical Health
Canada	Performance	**4.3 %**	**1.3 %**	**No Effect Reported**
Canada	Performance	**4.1 %**	**3.3 %**	**No Effect Reported**
UK	Performance	**3.7 %**	**0.7 %**	**No Observed Effect**
Canada	NE Challenge	**3.7 %**	**4.7 %**	**↓lesion scores**
S. Korea	NE Challenge	**12.1 %**	**N/R****	**↓lesion scores, ↓ C. perf CFU**
USA	NE Challenge	**-3.7 %**	**5.5 %**	**↓ Mortality by 16%, ↓lesion scores**
USA	NE Challenge	**2.6 %**	**4.3 %**	**↓lesion scores**

* Performance in the control group was already exceeding the reference standard for the birds
** N/R = Result not reported
NE Challenge = birds challenged with *Clostridium perfringens* to induce subclinical necrotic enteritis

Source: Avivagen, Inc.

The safety of OxBC has been established through administration of the compound for extended periods of time in companion and food animals with no ill effects reported. Daily doses of OxBC have been administered to animals as doses up to 10 times the amount normally given without any evidence of adverse clinical effects. Hundreds of thousands of doses of OxBC have been administered to food animals, including doses up to 50 times the normal dose in pigs and 15 times the normal dose in chickens, with no negative clinical outcomes. Lastly, the fact that oxidized β-carotene is found naturally occurring in foods that are eaten on a regular basis (discussed previously) means that people are continually exposed to the compounds, thus any exposure from consuming animals administered OxBC should not involve any type of safety issue.

Commercial Sales of OxC-beta Livestock

OxC-beta Livestock 10% is formulated as a premix containing 10% OxBC active ingredient mixed with cornstarch. It is recommended to be used at a rate of 20-80 g of 10% premix / ton of compound feed (2-8 g of OxBC active compound / ton of compound feed). The price for a ton of animal feed in the U.S. costs $350-$400 and OxC-beta Livestock is competitively priced ($5-$10/ton of feed) such that it will be economically advantageous to livestock producers.

The product is currently approved for sale in the Philippines, Mexico, Thailand, Taiwan, New Zealand and Australia. The company self-affirmed generally regarded as safe (GRAS) status for OxBC to allow its sale in the U.S. Avivagen is targeting Asia for initial commercialization, with registration activities ongoing in South Korea, China, Vietnam, and Malaysia. Asia represents approximately 35% of the world's total animal feed consumption.

In 2017, Avivagen delivered its first industrial-scale orders of OxC-beta Livestock to UNAHCO, Inc., the company's distribution partner in the Philippines. A total of 1,100 kg of OxC-beta Livestock was purchased by UNAHCO.

For the fiscal year ending Oct. 31, 2018, Avivagen delivered a total of 6,000 kg of OxC-beta Livestock 10% premix to UNAHCO along with 100 kg of OxC-beta Livestock 10% premix to Thailand. The amount of OxC-beta Livestock delivered to UNAHCO in 2018 was sufficient to supplement approximately 300 million kg of commercial feed, which is enough to feed approximately 120 million broiler chickens or 14 million piglets. For the first 9-months of fiscal year 2019 that ends Oct. 31, 2019, Avivagen has delivered 4,000 kg of OxC-beta

Livestock 10% premix to UNAHCO and the company recently announced an additional 2.1 metric ton order by UNAHCO, which represents the fourth multi-metric ton order by UNAHCO in the past calendar year.

Distribution Agreements

Avivagen collaborates with a number of different animal health companies as well as academic, institutional, and industrial researchers both in countries where OxC-beta Livestock is approved as well as in countries where the company is working for approval. The company has a number of distribution agreements through which it sells OxC-beta Livestock in the countries for which it is approved or seeking approval:

CSA Animal Nutrition – United States: Avivagen signed a sales and distribution agreement with CSA in February 2019. The agreement grants CSA the exclusive rights to distribute and sell OxC-beta Livestock 10% for swine, poultry, and dairy cattle within the U.S. The U.S. accounts for approximately 20% of the world's animal feed. CSA is an independent firm, thus allowing it to reach a number of different customers across numerous species and companies representing over 60% of broiler production have been contacted thus far. The agreement stipulates minimum performance targets CSA must meet in order to maintain exclusivity.

UNAHCO Inc. – Philippines: UNAHCO is a subsidiary of Unilab Inc., the largest pharmaceutical company in the Philippines. The Philippines produced approximately 19 million metric tons of feed in 2019, which was up from 11.75 million metric tons in 2016. Avivagen has delivered 4 metric tons of OxC-beta Livestock 10% to UNAHCO thus far in fiscal year 2019.

FAITH – Thailand: In June 2018, Avivagen signed a non-exclusive distribution agreement with FAITH (Feed and Ingredients Technology Hub), a member of the BIS Group of Companies. The agreement covers Thailand, Myanmar, Cambodia, Laos, Malaysia, Vietnam, and Indonesia. OxC-beta Livestock is approved for sale in Thailand as well as Myanmar and Cambodia as both those countries follow Thailand's regulatory authority. The first order for 100 kg of OxC-beta Livestock 10% in Thailand occurred in Sep. 2018.

TLC Veterinary Services – Malaysia: In Oct. 2018, Avivagen signed a distribution agreement for OxC-beta Livestock 10% in Malaysia with the principal supplier to farms that supply KFC, the leading fast food chain in Malaysia. TLC Veterinary Services will also undertake the registration process for Avivagen in Malaysia. The Malaysian government has stated a goal of producing antibiotic-free chicken by 2020, thus the company is ideally positioned to take advantage of this country-wide mandate.

Competition

We were not able to uncover any other company that is developing technology similar to OxC-beta Livestock, however there are a number of antibiotic alternative products that are available and could be considered competition to Avivagen and OxC-beta Livestock. The modes of action of these products are all unique and work to prevent the spread and proliferation of bacterial and viral infections, to enhance the overall health of the animal, and/or to optimize animal growth, however each of them has disadvantages when compared to OxC-beta Livestock. These products include:

Vaccines: There are a number of vaccines that are regularly employed in veterinary medicine to protect against both viral and bacterial infections. However, each vaccine is unique to each particular pathogen and there is no overall immune system enhancement to guard against bacteria/viruses not vaccinated against.

Immunomodulators: These are compounds that non-specifically enhance the innate immune system to improve the host's defense mechanism. Examples of immunostimulants include plant extracts, minerals, vitamins, and bacterial extracts. However, immunostimulants show different effects in different species and there is usually no linear relationship between dose and effect.

Bacteriophages: These are viruses that infect and replicate in bacterial cells. They were first discovered in 1915, however research into them waned following the discovery of antibiotics. In 2006, the FDA approved a bacteriophage cocktail as a food additive for the prevention of meat contamination with *Listeria*. Another bacteriophage product was approved for the disinfection of *E. coli* in cattle. While they can be effective, they have strict host strain specificity, thus the pathogenic microorganism needs to be positively identified before treatment.

Probiotics: These are live microorganisms that can improve the overall microbiological environment of the gastrointestinal tract. Typical probiotics include *Bacillus*, *Lactobacillus*, *Lactococcus*, and *Pediococcus*. Many different types of probiotics are used as feed additives in the E.U. However, contradictory results have been reported using probiotics in controlled trials and some probiotics can have detrimental effects on the normal gut flora.

Phytobiotics: These are plant extracts or biologically active constituents of plants (e.g., terpenoids, phenolics, glycosides, and alkaloids). Due to the fact that many phytobiotics are complex blends of bioactive compounds there is a lot of variation in their composition, manufacturing, and storage. Consequently, consistency in performance is lacking and more uniformity in the aforementioned parameters is necessary before they can be applied more extensively in animal feeds.

The OxC-beta product has a number of advantages when compared to AGP's and AGP alternatives, particularly in regard to the large number of positive efficacy trials, the ability to be used in multiple species, and the necessity for very low quantities in feed. The following chart summarizes the advantages of OxC-beta Livestock compared to AGP's and AGP alternatives.

	Disease Protection	Growth Promotion	Well-Proven MOA	Handling/ Stability	Consistent Quality	Environmental Health/Safety	Social Acceptability	Uniqueness & IP
Antibiotic Growth Promoters	+++	+++	+++	+++	+++	+	+	+
Existing AGP Alternatives	++	++	++	+	+	+	+++	+
OxC-beta™	**+++**	**+++**	**+++**	**+++**	**+++**	**+++**	**+++**	**+++**

Source: Avivagen Inc. / Zacks SCR

Companion Animal Product

While Avivagen's main focus is on the sale of the OxC-beta product to livestock producers, the company has a companion animal product based on the OxC-beta technology. Vivamune™ Chews are an OxC-beta technology-based health supplement for use in companion animals to improve or maintain quality of life and are designed to improve the pet's skin, coat, and joints. The product holds a quality seal from the National Animal Supplemental Council (NASC) indicating that the chews meet NASC guidelines for quality, integrity, and truth in labeling.

In June 2019, Avivagen announced a joint venture with Mimi's Rock Corp., an online dietary supplement and wellness company with significant sales on the Amazon.com platform. Under the terms of the agreement, Avivagen will supply its products for Mimi's Rock to market and sell through its e-commerce platform. All sales will be conducted by a newly formed corporation jointly owned by Avivagen and Mimi's Rock and profits will be split evenly between the two companies.



Source: www.avivagen.com/products

Financials and Capital Structure

On September 6, 2019, Avivagen announced financial results for the third quarter of fiscal year 2019 that ended July 31, 2019. The company reported revenues of CAD$12,484, which was a decrease of CAD$351,729 compared to the three months ending July 31, 2018. The difference was due to the timing of sales, with sales expected to take place during the third quarter of fiscal year 2019 instead taking place in August 2019. Expenses from continuing operations totaled CAD$1.29 million for the three months ending July 31, 2019 compared to CAD$1.26 million for the three months ending July 31, 2018. The slight decrease was mainly due to decreased salaries and stock-based expenses partially offset by an increase in finance costs. Net loss for the third quarter of 2019 was CAD$1.28 million compared to CAD$1.03 million for the three months ending July 31, 2018. The difference was mainly due to increased expenses related to finance cost and decreased product revenues.

As of July 31, 2019, Avivagen had approximately CAD$1.88 million in cash and cash equivalents. We estimate that this will be sufficient to fund operations through the end of 2019. As of July 31, 2019, the company had approximately 34.9 million shares of stock outstanding and when factoring in the 2.3 million stock options and 7.0 million warrants a fully diluted share count of approximately 44.2 million.

Risks to Consider

Regulatory Risks: Avivagen is dependent upon the regulatory approval of its products. Animal healthcare laws differ from country to country and compliance with laws and regulations can require substantial expenses. Failure to abide by those laws and regulations could result in the suspension or revocation of the right to sell in a country, which would be highly detrimental to the company.

Development Risk: While previous trials involving OxC-beta Livestock have been successful and the compound has exhibited few adverse side effects, there is no guarantee that those results will be replicated in future trials. There can be no assurance that future trials will yield positive results and allow the continued development of OxC-beta Livestock.

Financing Risk: We estimate that Avivagen currently only has sufficient capital to fund operations through the end of 2019. If the company is not able to obtain funding it may have to curtail or cease operations, or any financing obtained may result in significant dilution to existing shareholders. The company is not currently profitable and there is no guarantee that profitability will ever be obtained, thus successive financings may be required to keep the business solvent.

Stock Risk: The company's share price has been volatile in the past and will likely continue to be so in the near future. Avivagen's stock is currently traded on the TSX Venture Exchange, however there is no assurance that the company will be able to maintain that listing. The sale of a large number of shares and the issuance of shares in connection with partnerships or financings could result in the market price of Avivagen's shares to decline significantly.

MANAGEMENT PROFILES

Kym Anthony – Chief Executive Officer
Mr. Anthony has extensive experience in capital markets, agriculture, and life sciences. He is currently the chair of Hybrid Partners and the executive chair of Top Meadow Investments, Inc. Previously, Mr. Anthony was vice chair of the Board of ComDev International until its sale in February 2016. He was chair of Prometic Life Sciences Inc. from 2011 to 2014 and held previous positions with Dundee Securities, First Marathon – National Bank Financial, Toronto Dominion – TD Securities, and Wood Gundy.

Graham Burton, PhD – Chief Scientific Officer
Dr. Burton co-founded Avivagen after 19 years of biomedical research at the National Research Council of Canada (NRC). While at NRC, he developed the foundation for Avivagen's oxidized β-carotene technology. Dr. Burton is internationally known as a leading scientist in vitamin E research.

Chris Boland – Chief Financial Officer
Mr. Boland has 25 years of experience in corporate finance, IFRS, SOX, ERM, public reporting, anti-fraud measures and corporate governance. He currently serves on the board of CMAO and was previously on the board of ICAO, CPA of Ontario. Mr. Boland has completed the CICA Advanced Taxation and Advanced IFRS studies.

James Nickerson, PhD – Executive Vice President of Business Development and Innovation
Dr. Nickerson joined Avivagen as a senior research biologist and has held various research and management position during his career with the company. He established Avivagen's biological research facility and directed the company's biology research program for 10 years. Dr. Nickerson hold graduate degrees and postdoctoral research experience in the fields of molecular biology and physiology.

David Hankinson – Vice Chairman of the Board
Mr. Hankinson has more than 30 years of pharmaceutical industry experience. From 1991-1999 he was President and CEO of Canadian operations for Solvay Pharma Inc. Prior to that, he was the Vice President of Kingswood Canada Inc., a pharmaceutical distribution operation and contract sales force group that he co-founded in 1983 and then sold to Solvay in 1990. Prior to that he held various management positions at Eli Lilly and company in both Canada and the U.S., including Manager of Pharmaceutical (New Product Planning) and Manager International Marketing.

Tracy Gillett – Marketing Manager
Ms. Gillett holds a bachelor's of veterinary science from the University of Queensland, Australia. She has 10 years of experience in companion and mixed animal practice in Australia and the UK and worked for Bayer Animal Health, New Zealand prior to her position with Avivagen.

VALUATION

We are initiating coverage of Avivagen, Inc. (CHEXF) with a valuation of $2.50. Avivagen is developing products to support animal health, which includes replacing antibiotics in livestock feeds with proprietary compounds that promote the growth and overall health of the animal through support of the host's innate immune system. Avivagen discovered that β-carotene polymerizes with oxygen into a unique class of compounds (oxidized β-carotene, OxBC) that promote immunological health and are the basis of Avivagen's OxC-beta technology. Antibiotic resistance is a growing worldwide public health problem, and since 80% of antibiotics are used in livestock feeds in the U.S., replacement of antibiotics in animal feed may help alleviate the rise in antibiotic resistant organisms. In addition, regulatory agencies worldwide are calling for the decreased use of or outlawing the use of antibiotics in livestock feed. Numerous studies conducted by Avivagen and its partners has shown that supplementation of feed with parts-per-million levels of OxC-beta Livestock can be used as a replacement for growth-promoting antibiotics while offering the same or better growth and health benefits without contributing to the development of antibiotic resistant organisms. OxC-beta Livestock is currently approved in six countries, including the U.S., and registration activity is ongoing in several Asian countries, including China.

OxC-beta Livestock

Avivagen's technology centers on the discovery that fully oxidized β-carotene (OxBC), the active ingredient in OxC-beta Livestock, has positive effects on the innate immune system and can provide natural protection against infectious organisms, similar to feeding low level amounts of antibiotics, without the risk of breeding antibiotic resistant bacteria.

OxC-beta Livestock 10% is formulated as a premix containing 10% OxBC active ingredient mixed with cornstarch. It is recommended to be used at a rate of 20-80 g of 10% premix / ton of compound feed (2-8 g of OxBC active compound / ton of compound feed). The price for a ton of animal feed in the U.S. costs $350-$400 and OxC-beta Livestock is competitively priced ($5-$10/ton of feed) such that it will be economically advantageous to livestock producers.

For the fiscal year ending Oct. 31, 2018, Avivagen delivered a total of 6,000 kg of OxC-beta Livestock 10% premix to UNAHCO along with 100 kg of OxC-beta Livestock 10% premix to Thailand. The amount of OxC-beta Livestock delivered to UNAHCO in 2018 was sufficient to supplement approximately 300 million kg of commercial feed, which is enough to feed approximately 120 million broiler chickens or 14 million piglets. For the first 9-months of fiscal year 2019 that ends Oct. 31, 2019, Avivagen has delivered 4,000 kg of OxC-beta Livestock 10% premix to UNAHCO and the company recently announced an additional 2.1 metric ton order by UNAHCO, which represents the fourth multi-metric ton order by UNAHCO in the past calendar year.

Valuation

We value Avivagen using an EV/EBITDA multiple based on projected revenues of OxC-beta Livestock. We believe Avivagen is laying the groundwork for a very steep growth rate in revenues in the coming years through a combination of new market opportunities and market expansion. For example, the company is making steady progress on sales in the Philippines and we believe it is only a matter of time before sales begin to ramp up considerably in Asia and other parts of the world, particularly as additional data showing the benefits of the OxBC technology is published.

Due to the fact that Avivagen has a limited commercial history, the financial forecasts we have prepared are educated guesses and are heavily reliant on the company continuing to execute on its business plan to get OxC-beta Livestock approved in as many jurisdictions as possible, signing distribution agreements in each of those jurisdictions, and continuing market expansion through adoption of OxC-beta Livestock by major animal producers.

Our model estimates sales of OxC-beta Livestock of CAD$50 million in 2024, as we believe the company will hit an inflection point following the adoption of OxC-beta Livestock by multiple major animal producers over the next couple of years. Using an EV/EBITDA ratio of 16 (which is derived from the average for pharmaceutical companies found here) and an EBITDA of CAD$21 million leads to an EV of CAD$336 million. Using a discount rate of 20% (derived from CAPM) we arrive at a present day EV of approximately CAD$135 million. The company has approximately CAD$3.5 million in debt, CAD$1.9 million in cash, and CAD$7 million in potential financing from warrant exercises. Accounting for that leads to a NPV of CAD$140 million. Dividing this by the fully diluted share count of 44.2 million leads to a valuation of approximately CAD$3.20 per share. Using the current exchange ratio of $1 CAD = $0.76 USD leads to a valuation for CHEXF of approximately $2.50.

PROJECTED FINANCIALS

Avivagen, Inc. (in Canadian Dollars)	FY2018 A	1QFY19 A	2QFY19 A	3QFY19 A	4QFY19 E	FY2019 E	FY2020 E	FY2021 E
OxC-beta Livestock	$1.1	$0.3	$0.3	$0.0	$0.3	$0.9	$2.0	$5.0
Other Income	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Total Revenues	**$1.1**	**$0.3**	**$0.3**	**$0.0**	**$0.3**	**$0.9**	**$2.0**	**$5.0**
Cost of Sales	$0.4	$0.1	$0.1	$0.0	$0.2	$0.5	$0.9	$2.2
Product Gross Margin	*61%*	*57%*	*51%*	*91%*	*27%*	*46%*	*55%*	*56%*
Selling, General and Administration	$4.3	$1.1	$0.9	$0.9	$1.1	$3.9	$4.5	$5.0
Research	$0.5	$0.2	$0.3	$0.1	$0.2	$0.8	$1.0	$1.4
Depreciation of Equipment	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Finance Cost	$0.4	$0.1	$0.2	$0.3	$0.3	$0.9	$1.0	$1.0
Joint Venture Termination	$0.3	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($4.8)	($1.1)	($1.3)	($1.3)	($1.5)	($5.2)	($4.4)	($3.6)
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	($4.8)	($1.1)	($1.3)	($1.3)	($1.5)	($5.2)	($4.4)	($3.6)
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	**($4.8)**	**($1.1)**	**($1.3)**	**($1.3)**	**($1.5)**	**($5.2)**	**($4.4)**	**($3.6)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.15)**	**($0.03)**	**($0.04)**	**($0.04)**	**($0.04)**	**($0.15)**	**($0.10)**	**($0.07)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	33.1	33.6	33.8	34.9	35.2	34.4	45.0	55.0

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

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