

Avivagen

Avivagen Inc.

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| Ticker (Exchange) | VIV (TSX.V) |
|-----------------------------|-------------------|
| Recent Price (03/07/2017) | C\$0.09 |
| 52-week Range | C\$0.09 – C\$0.22 |
| Shares Outstanding* | ~278 million |
| Market Capitalization | ~C\$28.9 million |
| Average 3-month Volume | 401,886 |
| Insider Ownership +>5% | ~3.1% |
| Institutional Ownership | ~25% |
| EPS (Year ended 10/31/2016) | (C\$0.012) |
| Employees | 17 |

*As of October 31, 2016

VIV (TSX.V) One-year Stock Chart



OxC-beta™ Technology for Livestock



Company Description

Avivagen Inc. (or “the Company”) is a life sciences company developing products to replace the use of antibiotics in livestock feed, among other human and animal health products. In the U.S., 80% of all antibiotics sold are not prescribed to patients, but rather are given to poultry and livestock. These drugs are used to ward off disease among animals raised in close quarters and to promote weight gain in animals intended for slaughter. A consequence of such widespread antibiotic use is “superbugs,” potentially fatal bacteria that have become resistant to antibiotic treatment. Rising **antibiotic resistance†** is one of the foremost human health concerns of the century, and Avivagen believes its proprietary, non-antibiotic, hormone-free OxC-beta™ technology holds the key to balancing the food production industry’s need for the benefits of antibiotics with society’s need to preserve antibiotics for only medically necessary uses. OxC-beta™ is a nature-based ingredient with clinical support for its ability to enhance animal health, immunity, and weight gain. Sales have commenced for its use in livestock feed, with the Company now focused on market access and penetration. Avivagen is also pursuing important opportunities in human health for OxC-beta™ based on discoveries documenting an extensive safety record in nature for its bioactive component. An OxC-beta™-based product for companion animals has also been developed.

Key Points

- Numerous third-party studies of the OxC-beta™ technology as a supplement added to livestock feed have shown that it has a similar impact at promoting animal growth to conventional antibiotics.
- OxC-beta™ Livestock is cleared for sale in the Philippines (where commercial sales started during 2016), Thailand, and Taiwan. Avivagen is pursuing product registration and distribution agreements in other countries as well, including a joint venture recently established in China—the world’s top market for livestock feed. The pet products are available in the U.S.
- OxC-beta™ could eliminate the use of antibiotics as growth promoters in livestock feed—a potential multi-billion-dollar market.
- The Company is led by a skilled executive team that combines scientific expertise (chemists, veterinary scientists, and biomedical researchers) with business acumen from the life sciences, pharmaceutical distribution, and corporate finance worlds.
- Avivagen’s intellectual property encompasses six patent families providing global protection as far out as 2036.
- In a significant industry milestone, on January 3, 2017 the U.S. FDA announced the full implementation of Guidance for Industry (GFI) #213 in a national effort to reduce the use of medically important antibiotics in food-producing animals.
- At January 31, 2017 (Avivagen’s Q1), Avivagen held cash and cash equivalents of over C\$5.4 million, up from C\$5.1 million on October 31, 2016.

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Executive Overview

Avivagen Inc. (“Avivagen” or “the Company”) is developing a suite of products—based on its proprietary scientific platform—that optimizes the immune system of the host, helping it to defend itself from infection. The Company’s first commercial target is the poultry and livestock feed industries. The immediate goal of the Company is to accelerate market access and the commercial uptake of its OxC-beta™ Livestock product, an innovative product that has the potential to eliminate the use of antibiotics as growth promoters in livestock feed, a problem that needs an urgent solution and which represents a multi-billion-dollar market. The Company’s feed additive product, studied and proven in field trials, is a compelling alternative to antibiotics for growth promotion and disease prevention and is currently being adopted by veterinarians, animal nutritionists, and livestock producers looking to reduce their reliance on antibiotics. Importantly, in early 2016, Avivagen published data regarding a notable discovery: the active ingredient forming the basis of the Company’s proprietary OxC-beta™ technology platform for animal health can be found naturally in fruits and vegetables that humans and animals consume every day, suggesting a solid case for safety as Avivagen seeks to pursue regulatory clearance for its natural health products in humans. Ultimately, Avivagen is targeting market opportunities within livestock health and productivity enhancement, including a global animal feed additives market that is projected to cross \$37 billion by early 2022 from \$28.6 billion in 2016, growing at a compound annual growth rate (CAGR) of over 5.3% over the forecast period (Source: Mordor Intelligence), as well as the human health and wellness market.

Avivagen Fills an Industry Gap

Avivagen’s market viability centers on the fact that its products are capable of achieving competitive disease resistance and healthy growth without using any antibiotics or hormones. The use of antibiotics in livestock feed is a massive problem worldwide that many governments, regulators, and even industry are tackling directly. Due to how widespread antibiotic use is in today’s society, many bacteria have developed a resistance to the antibiotic treatments that were designed to cure infections in patients. This is dangerous, and often fatal, to people who are sickened by these new drug-resistant “superbugs,” as they can no longer be treated with conventional medicines. Without any action to curb inappropriate and unnecessary antibiotic use, by 2050, someone could die every three seconds from antimicrobial resistance, which would equate to 10 million people every year. Avivagen’s efforts near term are to directly target one of the causes of antibiotic resistance—animal feed.

In the U.S., 80% of all antibiotics sold are not being prescribed to patients, but rather are given to poultry and livestock (Source: *National Geographic*, February 13, 2015). These drugs are used to ward off disease in animals raised in close quarters and have the added benefit of promoting weight gain among animals intended for slaughter. Despite the serious risks to human health—the Centers for Disease Control and Prevention [CDC] reports two million drug-resistant infections a year—there has been a strong economic benefit for food producers to continue supplementing feed with antibiotics. That is, until recently, when companies such as Avivagen have been able to prove the existence of far safer products capable of achieving similar benefits in animals as antibiotics, but without the risks to society.

The United Nations (UN) has committed to fighting the danger that antibiotic resistance poses to modern medicine, with 193 UN member states signing a declaration to fight the drug-resistant superbugs responsible for over 700,000 human deaths a year. The most vulnerable patients to superbugs are the very young and very old, as well as any patient who may be already immunosuppressed. Beyond the UN, governments around the world have recognized this threat and are taking steps to ban or discourage the use of **antibiotic growth promoters (AGPs)** in livestock. Since the 1980s, Sweden and Denmark have prohibited the routine use of AGPs in livestock. More recently, the EU banned AGPs in 2006, followed by South Korea and Iran in 2011 and 2012, California (U.S.) in 2015, and Vietnam in 2016.

Implementation of Guidance for Industry #213 Completed

In an important step, on January 3, 2017, the U.S. Food and Drug Administration (FDA) announced that it had completed the implementation of Guidance for Industry #213 (a process that began in 2013) to transition antimicrobial drugs with importance in human medicine (medically important antimicrobials) that are used in the feed or drinking water of food-producing animals to veterinary oversight and eliminate the use of these products in animals for production (e.g., growth promotion) purposes. The implementation of GFI #213 represents a significant milestone in national efforts to address the use of medically important antimicrobials in food-producing animals. The reason for this is that illnesses caused by drug-resistant strains of bacteria are more likely to prove fatal when the medicines used to treat them are rendered less effective.

With these FDA Guidelines, some farmers, ranchers, veterinarians, animal nutritionists, and others may face challenges as they adjust to these changes, which is precisely what Avivagen's product has been developed to address. Over the next few years, Canada and China are expected to follow suit. Avivagen believes that its technology is poised to capture the market gap left as food producers are prevented from using AGPs but still need viable, well-tested, and economically competitive ways to increase yield (i.e., promote weight gain among animals), maintain feed efficiency, and strengthen animal immune systems to ward off disease outbreaks.

Technology Platform: OxC-Beta™ (Fully Oxidized β -carotene)

Scientists have recognized for several decades that beta-carotene (β -carotene), a nutrient found in fruits and vegetables such as carrots, sweet potatoes, cantaloupe, among others, is an important component of the human diet. It is a source of vitamin A and supports vision and eye health, strong immune systems, and healthy skin. However, not all of β -carotene's health benefits can be attributed to vitamin A. Recognizing the opportunity that β -carotene and other **carotenoids** held for health but believing that there was another factor enabling carotenoids' immunological activity, Avivagen's founding scientists—while at Canada's National Research Council (NRC)—began studying β -carotene to determine how exactly it reacts with oxygen and how that builds immunity against disease.

Avivagen found that β -carotene was highly susceptible to reacting spontaneously with oxygen to form a new compound called an *oxygen copolymer*, which had previously gone unnoticed in medical research. By discovering these copolymer compounds—the main product of spontaneous carotenoid oxidation—Avivagen was able to isolate the precise molecular agent of immunological activity in animals. The Company has developed and extensively studied a synthetic β -carotene-oxygen copolymer compound, which is the active ingredient in OxC-beta™ today. The Company's data, describing the chemical nature and biological effects of OxC-beta™, has been published in four peer-reviewed journals: the *Canadian Journal of Chemistry*, *PLOS ONE*, the *American Journal of Veterinary Research*, and the *Journal of Agricultural and Food Chemistry*.

Clinical Results Confirm Competitive Advantages

Avivagen, the National Research Council of Canada, and other funding and research partners have invested over two decades and roughly \$30 million into studies of OxC-beta™, ultimately finding that the improvement in animal health using OxC-beta™ is comparable to what occurs using antibiotics.

The biological effects of OxC-beta™ at stimulating the immune system are host-mediated, meaning there are no direct antibacterial effects and thus zero likelihood of creating antibiotic-resistant pathogens. Pages 23-27 of the Core Story detail the product testing that has been performed on the OxC-beta™ platform, *in vitro*, in the field on poultry, swine, cattle, and trout, as well as with companion animals. Through these studies, the active ingredient—the oxidized β -carotene—has been found to consistently achieve each of the following:

- Support and prime innate immune function
- Optimize host defenses against pathogens and reduce incidence of enteric disease, including diarrhea
- Limit or reduce disease-induced inflammation without disrupting immune response to infection

- Retain its activity in all feed formulations tested to date
- *For food animals*, achieve consistent results across species and climates (which is rare for this field)
- *For food animals*, healthier growth, improved weight gain, better utilization of feed, and decreased morbidity
- *For humans*, potential for therapeutic and prophylactic benefits
- *For companion animals*, increased vitality and energy, mobility and joint function, healthier skin, coat, and gut, improved digestive health

Overall, OxC-beta™ technology supports immune function and, under challenging situations, may offer specific benefits to production animals, as listed in Figure 1.

Product: OxC-Beta™ for Livestock and Humans

Avivagen’s OxC-beta™ platform addresses the livestock and human health markets through the products and product candidates listed below.

- *OxC-beta™ Livestock*. As a replacement for antibiotics in livestock feed, OxC-beta™ Livestock is initially being targeted in Asia, the world’s top region for livestock feed consumption and a region where customers are receptive to new technologies in the food production industry and where there are favorable regulatory regimes. Avivagen has commenced sales to the Philippines, has received additional clearances for sale in Thailand and Taiwan, has established a joint venture to enter the Chinese market (the world’s largest for animal feed), and is pursuing additional research and/or distribution relationships around the world (as listed in Figure 23 [page 29]).

Figure 1

Ox-C-BETA™ LIVESTOCK PRODUCT AND ITS BENEFITS



| |
|--|
| <i>Non-antibiotic and non-hormonal method of enhancing animal productivity and profitability</i> |
| Optimizes innate immune function leading to: |
| <ul style="list-style-type: none"> ■ Earlier and enhanced detection of disease-causing microbes |
| <ul style="list-style-type: none"> ■ Potentially arrests infections at an early stage before they take hold, therefore improving productivity |
| <ul style="list-style-type: none"> ■ In-feed and selected novel delivery forms |
| <ul style="list-style-type: none"> ■ Reduces subclinical inflammation in the gut and improved nutrient absorption |
| <ul style="list-style-type: none"> ■ Improves growth, general health, and feed conversion efficiency |

Source: Avivagen Inc.

- *Investigational carotenoid oxidation products for human wellness*. Stemming from one of Avivagen’s most recent discoveries that naturally occurring oxidized copolymer compounds are present in common human food products, including carrots, tomatoes, sweet potatoes, paprika, rosehips, seaweeds, alfalfa, and milk, the Company is investigating carotenoid oxidation products for human wellness. These naturally found compounds are analogous to the active ingredient in OxC-beta™, and their safe, daily consumption may help support the safety of OxC-beta™ technology as well as the Company’s premise that these compounds have far-reaching health implications. Notably, consuming intact carotenoids (such as β-carotene, **lycopene**, and lutein in conventional dietary supplements) does not achieve the same level of enhanced immune function and resistance to chronic diseases as consuming carotenoid-containing fruits and vegetables, which importantly also contain the copolymer compounds.

Other Operating Units

Companion Animals

Figure 2
HEALTH SUPPLEMENTS FOR COMPANION ANIMALS



Source: Avivagen Inc.

- *Vivamune™ Health Chews*. As an all-in-one dietary supplement for dogs containing OxC-beta™, Vivamune™ helps improve dogs' skin and coat health, digestive (gut) health, and mobility and vitality due to healthier joint function. Vivamune™ can also help soothe itchy skin from seasonal allergies. Vivamune™ Health Chews (pictured in Figure 2) are available for sale in the U.S. through Avivagen and hold a quality seal from the National Animal Supplement Council.
- *Oximunol™ Chewable Tablets* (pictured in Figure 2) are hard, chewable, beef-flavored tablets that serve as a daily dietary supplement for mature dogs. They promote canine immune function to optimize health and quality of life for aging pets, including supporting healthier joint function and mobility, a healthy skin and coat, and normal intestinal function.

Chemaphor Chemical Services (A Division of Avivagen)

Avivagen also operates Chemaphor Chemical Services, a synthetic chemistry business that sells **deuterated** vitamins (D and E), deuterated cholesterol, and other deuterated chemicals and chemistry products to universities and research centers. Chemaphor synthesizes deuterated compounds in-house with high purity and high deuterium enrichment, and also manufactures custom-made chemicals ready for shipping, including specialty, non-labelled small-molecule compounds that may be required for screening as drug candidates.

Headquarters and Employees

Avivagen is headquartered in Ottawa, Canada, and maintains two research and development (R&D) facilities in Canada: (1) chemistry operations in the National Research Council (NRC) of Canada's Industrial Partnership Facilities (Ottawa); and (2) biology operations in Charlottetown, Prince Edward Island, Canada. The Company was established in August 2005. It is publicly trading on the TSX Venture Exchange (TSX.V) under the ticker "VIV" and on the OTC Pink Market under the ticker "CHEXF." The Company currently employs 17 individuals, and has two independent directors and two consultants.

Core Story

Bacteria are single-celled organisms found inside and outside the body. While many bacteria are not harmful (with some actually helpful, including the majority of bacteria that live in our intestine [gut]), disease-causing bacteria can cause serious illnesses. Alternatively, viruses are microbes that are even smaller than bacteria that cannot survive outside the body's cells and cause illness by invading healthy cells. Also called antimicrobial drugs, antibiotics are medicines that fight infections caused by bacteria in both humans and animals. These drugs fight infections by either killing the bacteria or making it difficult for them to grow and multiply. Importantly, antibiotics have no effect on viruses whatsoever.

Antibiotics are widely used in food-producing animals, with more kilograms of antibiotics sold in the U.S. for food-producing animals than for people (Source: U.S. FDA). Such widespread use has been the key contributing factor to the development of antibiotic-resistant bacteria in food-producing animals, which is a great concern as these animals serve as carriers. Resistant bacteria can contaminate the foods that come from those animals; as well, people who consume these foods can develop antibiotic-resistant infections. As such, antibiotics must be used judiciously in humans and animals because both uses contribute not only to the emergence, but also the persistence and spread of antibiotic-resistant bacteria. There has been widespread evidence reported by scientists around the world that use of antibiotics in food-producing animals can harm public health in the following ways:

- it creates an environment favoring the development of antibiotic-resistant bacteria;
- it allows resistant bacteria to thrive because susceptible bacteria are suppressed or die and therefore they do not compete for resources;
- resistant bacteria can be transmitted from food-producing animals to humans through the food supply or by environmental exposure; and
- infections caused by resistant bacteria are challenging to treat and can result in adverse health consequences for humans.

THE PROBLEM: ANTIBIOTIC/ANTIMICROBIAL RESISTANCE (AMR) This Century's Single Greatest Health Threat

Antibiotic or **antimicrobial resistance (AMR)** in humans—the ability of bacteria to withstand exposure to an antibiotic—is considered to be this century's single greatest global health threat. So much so that the United Nations (UN) has committed to fighting this danger to modern medicine with 193 UN member states signing a declaration to fight drug-resistant 'superbugs'.

The most commonly reported superbug found in hospitals, **Methicillin-Resistant Staphylococcus Aureus (MRSA)**, leads to thousands of deaths every year and is among those superbugs that fail to respond to or be killed by the standard antibiotics. On a larger scale, it is these superbugs that may actually be responsible for killing more than 700,000 people annually, with the most vulnerable patients being the very young or very old who are most at risk. Importantly, while some people are at greater risk than others, there is no individual that can altogether avoid the risk of antibiotic resistant infections. An *Oxford Journals' Clinical Infectious Diseases* article states "*The ongoing explosion of antibiotic-resistant infections...could mean a literal return to the pre-antibiotic era for many types of infections.*" Warnings with regard to antimicrobial resistance are not new, with Alexander Fleming reportedly warning about the development of drug-resistance in his 1945 Nobel Prize acceptance speech.

Therefore, because of the direct link between antibiotic use in food-producing animals and the emergence of antibiotic-resistant infections in humans, it is recommended that antibiotics should be used in food-producing animals only under the oversight of a veterinarian and only to manage and treat infectious diseases (as further described on pages 4 and 16, describing the completion of the implementation of Guidance for Industry #213). The CDC further encourages and supports efforts to minimize inappropriate use of antibiotics in humans and animals, including promoting the judicious use of antibiotics that are important in treating humans.

Improper or Overuse of Antibiotics and its Effects on Human Health

Development of antibiotic-resistant bacteria has resulted from overuse and misuse of antibiotics. For example, each time an individual takes antibiotics, sensitive bacteria (bacteria that antibiotics can still attack) are killed, leaving resistant bacteria to grow and multiply. This process, repeated over and over, is the reason that antibiotics have increased the number of drug-resistant bacteria. Additionally, even while antibiotics are not effective against viral infections such as the common cold, flu, most sore throats, bronchitis, and some sinus and ear infections, they are still prescribed for these illnesses—further promoting the spread of antibiotic resistance, as further described on pages 10-12. Intelligent use of antibiotics is crucial to controlling the spread of resistance.

In livestock, low doses of antibiotics are fed to food animals to promote growth with the intent of reliably preventing disease. During 2014 in the U.S. alone, there were 15,358,210 kg of antibiotics given to livestock, according to the U.S. Food and Drug Administration (FDA). The problem has become that use of these antibiotics in the food chain has led to drug-resistant bacteria, which has become a global human health concern with massive worldwide economic impacts. Among the main causes of antibiotic resistance include the common and widespread use of antibiotics in animal feeds to produce meat consumed by humans, as well as over-prescribing of antibiotics by physicians. For the purposes of this discussion, we will focus on antibiotics used in animal feed. In the U.S., the FDA reports that more than 62% of the antibiotics defined as “medically important” for humans are sold for agricultural use.

Traditionally, on farms with limited alternatives, antibiotics have been used to treat not only existing illness in animals but also to prevent potential disease and certain infections in livestock, as well as to increase the feed conversion ratio of animals, thus improving the efficiency of the farm. Leading scientific and healthcare organizations worldwide agree that the use of antibiotic growth promoters (AGPs) for enhancing growth and preventing disease in commercial livestock production has, and, for as long as it continues to be used, will contribute significantly to the rise of drug-resistant strains of bacteria that threaten human health, hence the call for a global ban on AGP use.

Seeing the issues that were stemming from overuse of antibiotics in the food chain, the European Union (beginning with Sweden and Denmark) prohibited the routine use of AGPs beginning in the 1980s. Today, advocating for the same restrictions, the U.S., Canada, and much of Asia are following suit. Recognizing the problem and the most immediate need to address it, governments have taken steps to restrict antibiotic use in livestock. The evolution (including country and year that prohibition of AGPs began) of such efforts is outlined below.

- Sweden and Denmark (1986 & 1989)
- The European Union (2006)
- South Korea and Iran (2011 & 2012)
- California (2015) Vietnam (2016)
- United States and Canada (2017), China (2020) expected to take place

While various categories of AGP substitutes are available (as described under *Competition*, pages 41-42), no single product has proven effective as a standalone alternative to antibiotics and producers must often use a combination of different products to replace antibiotics. In addition, many of the alternative products have poorly defined chemical composition and modes of action that are not well understood. As a result, their effectiveness in the field is inconsistent and many producers remain reluctant to adopt the use of these products.

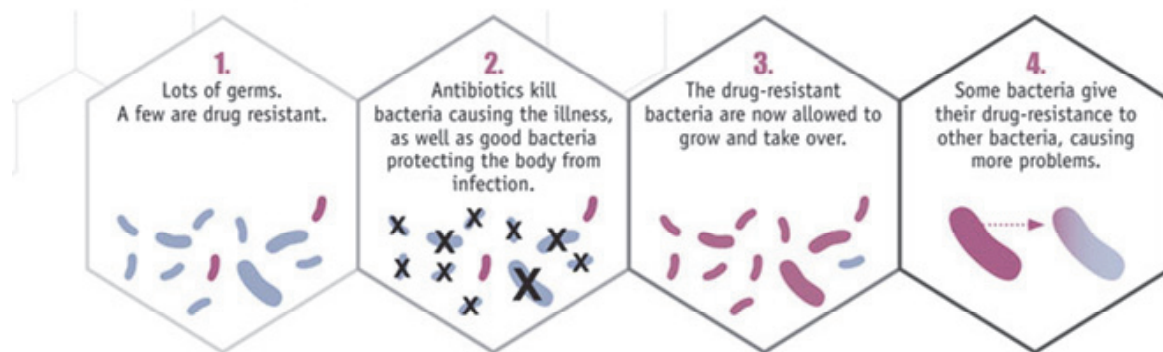
Reasons Bacteria Have Become Resistant to Antibiotics

There are several ways that bacteria can become resistant to antibiotics. One way is that some bacteria are able to 'neutralize' an antibiotic through enzymatically modifying the antibiotic in a way that renders it harmless. Alternatively, bacteria have learned how to pump an antibiotic back outside itself prior to it taking effect and doing any harm. Moreover, certain bacteria are able to alter their outer structure in such a way as to make it impossible for the antibiotic to attach to the bacteria. There are times, however, that after being exposed to antibiotics, a bacterium can survive, having found a way to resist the antibiotic. If even one bacterium becomes resistant to antibiotics, it can then multiply and replace all the bacteria that were killed off. This means that exposure to antibiotics provides selective pressure that creates an environment where the surviving bacteria is more likely to be resistant. Another way in which bacteria can become resistant is through mutation of their genetic material.

What Happens During Antibiotic Resistance

As described above, antibiotic resistance occurs when bacteria change in a way that reduces the effectiveness of drugs, chemicals, or other agents designed to prevent infections. Moreover, antibiotic-resistant bacteria are able to survive and continue to multiply, causing more harm. Figure 3 provides a summary of the effects of antibiotic resistance.

Figure 3
HOW ANTIBIOTIC RESISTANCE HAPPENS



Source: CDC.gov.

Currently being called one of the world's most urgent public health problems, antibiotic resistance can cause illnesses that were once easily treatable with antibiotics to become dangerous infections. As well, antibiotic-resistant bacteria can easily spread to family members, classmates, and co-workers, and may threaten communities. Antibiotic-resistant bacteria are frequently more difficult to kill, costly to treat, and may lead to serious disability or even death in some situations. Importantly, it is the bacteria that becomes resistant to specific drugs—not the person. The accompanying section below describes an example of a fatal superbug infection that resisted all FDA approved antibiotics, where ultimately the patient ended up dying from septic shock.

Example of Fatal Superbug Infection That Resisted All FDA-Approved Antibiotics

In early January 2017, it was reported by the U.S. Centers for Disease Control and Prevention (CDC) that a worst-case scenario had taken place—a 70-year-old Nevada woman with a bacterial infection was resistant to all antibiotics available in the U.S. after being infected with a drug-resistant bacterium, *Klebsiella pneumoniae*. The woman arrived at a hospital in August 2016 with signs of sepsis. According to the CDC, this woman had been in India years before and had been treated for a broken leg and bone infection. After undergoing testing, her doctors found the bacteria, which belonged to a class of drug-resistant bugs called carbapenem-resistant Enterobacteriaceae (CRE), were resistant to all forms of FDA-approved antibiotics. The patient died in September after going into septic shock.

Carbapenem-resistant Enterobacteriaceae (CRE) infections are an immediate public health threat that requires urgent and aggressive action, as the CDC estimates that these bacteria cause 9,000 drug-resistant infections per year and 600 related deaths. While most CRE bacteria are still susceptible to one or more antibiotics, in the infection of the woman in her 70s reported by the CDC, the bacteria were resistant to all FDA-approved antibiotics (noting that common *E. coli* and *Klebsiella* bacteria are among CRE strains). It is important to point out that while this recently reported case is alarming, it is still also unusual as this patient had been in and out of hospitals in India for two years after fracturing a femur and developing a bone infection. However, extensive stays in hospitals, especially in India, combined with exposure to different antibiotics, can increase one's likelihood of eventually developing a drug-resistant bacterial infection.

This woman's death caused by a rare infection has once again brought attention to the increasing problems surrounding these drug-resistant infections and the deficiency of antibiotics available to treat them. It also highlights the fact that no matter how effective an antibiotic is at killing bacteria, new drugs are needed as the bacteria mutate and grow more resistant to existing drugs. That said, the number of drug applications for novel antibiotics being developed by pharmaceutical companies have been dropping steadily over the last three decades, where from 1980 to 1984, there were nearly 20 FDA drug applications approved for new antibiotics but from 2005 to 2009, there were fewer than five applications approved.

Ways in Which Antibiotic Resistance Spreads

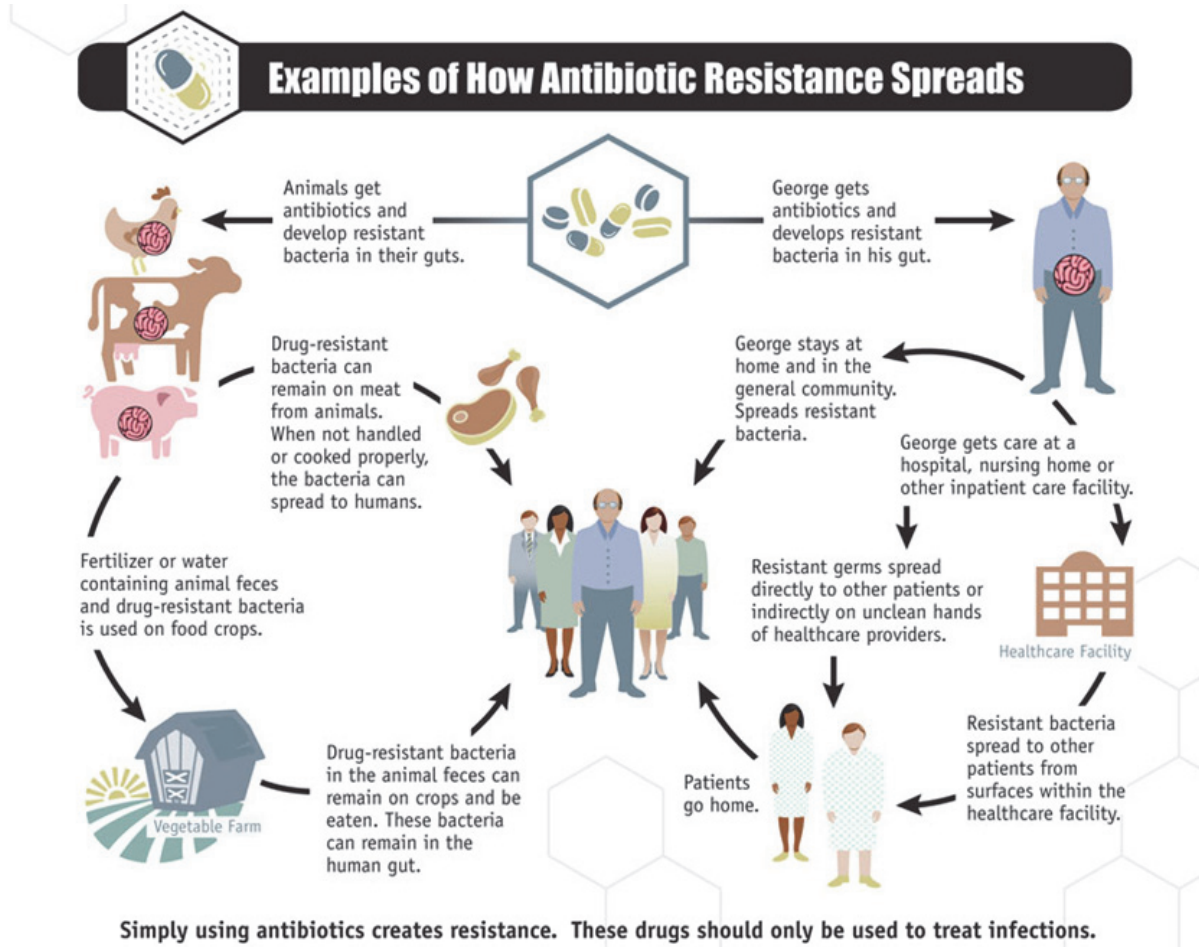
Figure 4 (page 11) provides a sampling of some of the ways in which antibiotic resistance can spread. Antibiotic resistance can be prevented from spreading in a number of ways, including by prescribing an antibiotic only when it is likely to benefit the patient; prescribing an antibiotic that targets the bacteria that is most likely causing their patient's illness; encouraging patients to use the antibiotic as instructed; and reviewing and following the latest clinical practice guidelines for common infections.

As well, for the animal feed process in particular, antibiotics should only be administered when medically necessary (as described on the accompanying section). Avivagen has developed a non-antibiotic replacement for growth promotion and prophylaxis in livestock, with results similar to those provided by the use of AGPs.

Superbugs Can Be Passed to Humans in a Variety of Ways

In 2013, the FDA announced it would *request* pharmaceutical companies to voluntarily stop labeling antibiotics necessary for use in humans as acceptable for growth promotion purposes in animals. This move effectively made it illegal for producers to use certain antibiotics for any reason other than the medically necessary treatment of disease. This is based on the concern that the widespread use of antibiotics in livestock is a significant contributor to the development of bacterial resistance to antibiotics. Outbreaks of Methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitals worldwide are another example of the need to protect human health from the development of antibiotic resistant "superbugs."

Figure 4
EXAMPLE OF HOW ANTIBIOTIC RESISTANCE SPREADS



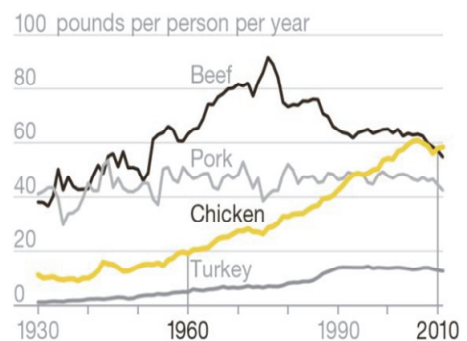
Source: CDC.gov.

Antibiotics in the Meat and Poultry Food Chain: A Leading Culprit in Antibiotic Resistance

America’s biggest restaurant chains feed millions of people billions of pounds of beef, chicken, turkey, and pork every year. In fact, Americans today eat three times as much poultry as they did in the 1960s (with Figure 5 illustrating this increase in consumption over the past 80-plus years). Poultry, egg, and meat production account for more than 40% of global compound feed consumption. Because feed costs account for a significant part (up to 70%) of total production costs, feeding strategy is a crucial point.

The vast majority of this meat is produced at industrial-scale facilities where thousands and even tens of thousands of animals at a time are routinely fed antibiotics to help them survive and make them grow faster—many times in unsanitary, crowded, and stressful conditions. According to a recent scientific study, the poultry industry’s global consumption of AGPs is three times higher than that of cattle. Researchers estimate that the global average annual consumption of antimicrobials per kilogram of animal produced was 45 mg/kg, 148 mg/kg, and 172 mg/kg for cattle, chicken, and pigs, respectively. Such misuse of antibiotics has been the leading contributor to antibiotic resistance.

Figure 5
U.S. CHICKEN AND TURKEY CONSUMPTION



Source: National Geographic Partners, LLC.

Antibiotic resistance makes treatment of bacterial infections harder, increases how long people are sick, and makes it more likely that patients will die. Because of this, consumer demand for antibiotic-free meat has seen a strong upsurge. Certain industry groups have urged producers to thoughtfully weigh the use of AGPs in the context of overall profitability in light of domestic consumer demand and export requirements, where curbing the misuse of antibiotics in the meat industry has become a public health imperative.

Food Companies Are Responding: Commitments to Reduce Use of Antibiotics

Understanding the critical nature of the problem, food companies are responding. Figures 6-8 (pages 13-15) provide a breakdown not only by restaurant but food distributor, producer, or supermarket and each respective effort to be a part of the solution of antibiotic resistance, according to The Pew Charitable Trusts (an independent nonprofit organization whose stated goal is to apply an analytical approach to improve public policy, inform the public, and invigorate civic life). These companies' antibiotic use policies, for major food animal species and associated labels, are defined by the U.S. Department of Agriculture (USDA) or FDA as follows:

- **Organic.** A standard that includes no use of antibiotics during production stages.
- **No antibiotics ever/no antibiotics/raised without antibiotics.** A label used when sufficient documentation demonstrates that no antibiotics were used during the food animal's life.
- **No medically important antibiotics.** A label indicating that antibiotic drugs important for therapeutic use in humans cannot be used; some antibiotics with no relevance in human medicine can be used.
- **Judicious use.** A standard that follows the judicious use principles outlined by FDA and the American Veterinary Medical Association; unnecessary or inappropriate use of antibiotics should be avoided.

Other antibiotic policies and company labels may have variations of the descriptions above—antibiotic free; routine use prohibited; or no growth-promoting antibiotics. **Importantly with regard to these Figures, they are not intended to represent all companies encouraging the responsible use of antibiotics in meat and poultry production.** Restaurants and food service companies listed are limited to those with at least 20 locations, with the list providing examples of companies with an antibiotic policy found on their website or in a news release (or in certain cases via email to The Pew Charitable Trust prior to Feb. 29, 2016, according to their website).

Figure 6
RESTAURANT AND FOOD SERVICE COMPANIES OFFERING RESPONSIBLY RAISED MEAT AND POULTRY

📄 Antibiotic use policy announced. (See comments for implementation status.)
 🚫 No policy announced.
 🚫 The company does not serve the protein.

| Restaurant or food service company | Number of U.S. locations* | Chicken | Pork | Turkey | Beef | Policy/implementation status (as stated by the company's website or news release) |
|------------------------------------|----------------------------------|------------------------|--------------|-----------------|------------------------|---|
| Au Bon Pain | 300 | 📄 | 📄 | 📄 | 🚫 | No antibiotics ever—chicken and turkey (sandwiches and salad only, excludes hot bowl/wrap); pork (Niman Ranch sausage only, excludes ham and bacon) |
| Boloco | 20 | 📄 | 🚫 | 🚫 | 📄 | No antibiotics ever |
| Bon Appétit Management Co. | 650 | 📄 | 📄 | 📄 | 📄 | No antibiotics ever—pork and ground beef (excludes primal cut beef †) Routine nontherapeutic use of antibiotics prohibited chicken and turkey |
| BurgerFi | 77 | 📄 | 🚫 | 🚫 | 📄 | No antibiotics ever |
| Burgerville | 46 | 📄 | 📄 | 📄 | 📄 | No antibiotics ever |
| Carl's Jr. | 1,495 | 🚫 | 🚫 | 🚫 | 📄 | No antibiotics ("All-Natural Burger" only) |
| Chick-fil-A | 1,962 | Target: 2019 | 🚫 | 🚫 | 🚫 | No antibiotics ever (Status: 23% of supply as of Q2 2015) |
| Chipotle Mexican Grill | 1,931 | 📄 | 📄 | 🚫 | 📄 | Raised without antibiotics |
| Chopt | 35 | 📄 | 📄 | 🚫 | 🚫 | No antibiotics ever |
| Culver's | 544 | 📄 | 🚫 | 🚫 | 🚫 | Raised without antibiotics |
| Dunkin' Donuts | 8,299 | 📄 | 📄 | 📄 | 📄 | Judicious use |
| Elevation Burger | 33 | 📄 | 📄 | 🚫 | 📄 | No antibiotics ever (chicken, beef, and bacon only) |
| Farmer Boys | 79 | 🚫 | 🚫 | 🚫 | 📄 | Antibiotic free (beef in "The Natural" burger only) |
| Good Times | 36 | 📄 | 📄 | 🚫 | 📄 | No antibiotics ever (chicken, beef, and bacon only) |
| Houlihan's | 104 | 📄 | 🚫 | 🚫 | 🚫 | Antibiotic free (in some locations) |
| McDonald's USA | 14,304 | Target: March 2017 | 🚫 | 🚫 | 🚫 | No medically important antibiotics |
| Noodles & Co. | 330 | Target: Q1 2017 | 📄 | 🚫 | Target: mid-/late 2016 | Antibiotic free |
| Panera Bread | 1,972 (U.S. and Ontario, Canada) | 📄 | 📄 | 📄 | 🚫 | No antibiotics ever |
| Papa John's | 3,075 | Target: summer 2016 | 🚫 | 🚫 | 🚫 | Antibiotic free |
| Pret A Manger | 66 | 📄 | 📄 | 📄 | 🚫 | Antibiotic free (excludes prosciutto and Korean pulled pork products) |
| Restaurant Associates | 100 | 📄 | 📄 | 📄 | 🚫 | Routine use of medically important antibiotics prohibited |
| Roti | 21 | 📄 | 🚫 | 🚫 | 🚫 | No antibiotics ever |
| Shake Shack | 49 | 📄 | 📄 | 🚫 | 📄 | No antibiotics ever |
| Subway | 27,463 | Target: end of 2016 | Target: 2025 | Target: 2018-19 | Target: 2025 | Raised without antibiotics |
| Sweetgreen | 36 | 📄 | 📄 | 🚫 | 🚫 | Organic (chicken and bacon products only) |
| Taco Bell | 6,824 | Target: end of Q1 2017 | 🚫 | 🚫 | 🚫 | No medically important antibiotics |
| Wendy's | 6,058 | 📄 | 📄 | 🚫 | 📄 | Judicious use |

* As of Feb. 29, 2016.

† The U.S. Department of Agriculture defines primal cut beef as chuck, loin, rib, and round.

Source: The Pew Charitable Trust.

Figure 7
FOOD PRODUCERS OFFERING RESPONSIBLY RAISED MEAT AND POULTRY

📄 Antibiotic use policy announced. (See comments for implementation status.)
🚫 No policy announced.
🚫 The company does not serve the protein.

| Food producer | Chicken | Pork | Turkey | Beef | Policy/implementation status (as stated by the company's website or news release) |
|---------------------------|---------|------|--------|------|---|
| Applegate | 📄 | 📄 | 📄 | 📄 | Antibiotic free |
| Bell & Evans | 📄 | 🚫 | 🚫 | 🚫 | No antibiotics ever |
| DaBecca Natural Foods | 🚫 | 📄 | 📄 | 📄 | No antibiotics ever (with the exception of bacon for food service and some retail outlets) |
| Estancia Beef | 🚫 | 🚫 | 🚫 | 📄 | No growth-promoting antibiotics |
| Evol Foods | 📄 | 📄 | 🚫 | 📄 | No antibiotics |
| Foster Farms | 📄 | 🚫 | 🚫 | 🚫 | Judicious use (for disease treatment and control, and no use of antibiotics critical to human medicine) No antibiotics ever (Foster Farms Certified Organic and Simply Raised brands) |
| FreeBird | 📄 | 🚫 | 🚫 | 🚫 | No antibiotics ever |
| Hormel | 🚫 | 📄 | 📄 | 🚫 | Judicious use |
| Luvo | 📄 | 🚫 | 📄 | 📄 | Raised without antibiotics |
| MamaMancini's | 🚫 | 🚫 | 📄 | 📄 | Raised without antibiotics (meats with "antibiotic free" label only) |
| Meyer Natural Angus | 🚫 | 🚫 | 🚫 | 📄 | No antibiotics ever |
| Miller Poultry | 📄 | 🚫 | 🚫 | 🚫 | Raised without antibiotics/antibiotic free |
| Mom Made Foods | 📄 | 🚫 | 📄 | 📄 | Raised without antibiotics |
| Murray's | 📄 | 🚫 | 📄 | 🚫 | Antibiotic free |
| Niman Ranch | 🚫 | 📄 | 🚫 | 📄 | No antibiotics ever |
| Perdue Farms Inc. | 📄 | 📄 | 🚫 | 🚫 | No antibiotics ever (Simply Smart chicken, Harvestland poultry and pork) Judicious use |
| Ranch Foods Direct | 📄 | 📄 | 📄 | 📄 | No subtherapeutic antibiotics/routine use prohibited |
| Red Bird Farms | 📄 | 🚫 | 🚫 | 🚫 | Antibiotic free/raised without antibiotics (98% of retail chicken, except 50% dark/50% white ground chicken) |
| Saffron Road | 📄 | 🚫 | 🚫 | 📄 | Raised without antibiotics |
| Smart Chicken | 📄 | 🚫 | 🚫 | 🚫 | Raised without antibiotics (applies to entire production—egg and life of chicken) |
| Smithfield | 🚫 | 📄 | 🚫 | 🚫 | Judicious use |
| Springer Mountain Farms | 📄 | 🚫 | 🚫 | 🚫 | No antibiotics ever |
| Thousand Hills Cattle Co. | 🚫 | 🚫 | 🚫 | 📄 | No antibiotics ever |
| Tyson Foods | 📄 | 🚫 | 🚫 | 📄 | No antibiotics ever (hatcheries; Nature Raised Farms, Open Prairie Natural Angus brands) Judicious use (reduced use of human antibiotics in broiler flocks more than 80%; target: end of September 2017—no medically important antibiotics in U.S. broilers) |
| White Oak Pastures | 📄 | 📄 | 📄 | 📄 | No antibiotics |

Source: The Pew Charitable Trust.

Figure 8
SUPERMARKETS OFFERING RESPONSIBLY RAISED MEAT AND POULTRY

Antibiotic use policy announced. (See comments for implementation status.)
 No policy announced.
 The company does not serve the protein.

| Supermarket | Number of U.S. locations* | Chicken | Pork | Turkey | Beef | Policy/implementation status (as stated by the company's website or news release) |
|---|---|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|---|
| Ahold USA (Giant Food, Giant Food Stores, Martin's Food, Peapod, Stop & Shop) | Giant Food: 213 Giant Food Stores: 196 Martin's Food: 51 Stop & Shop: 395 | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | No antibiotics ever (Nature's Promise brand and USDA Organic labels only) |
| ALDI | 1,500 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> | No antibiotics (Kirkwood Never Any! chicken, SimplyNature Organic beef brands only) |
| Delhaize America (Food Lion, Hannaford) | Food Lion: 1,103 Hannaford: 227 | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | Antibiotic free (Nature's Place label only) |
| H-E-B | 294 | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | Antibiotic free/no antibiotics ever (H-E-B Fresh Local Chicken, H-E-B Organics labels only) |
| Kroger | 3,934 (Includes subsidiaries) | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | Antibiotic free/no antibiotics ever (Simple Truth and Simple Truth Organic labels only) |
| Publix | 1,115 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> | Antibiotic free (Publix GreenWise brand only) |
| Safeway | 1,270 | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | No antibiotics ever (Open Nature and O Organics brands only) |
| Supervalu (Cub Foods, Farm Fresh, Hornbacher's, Shop 'n Save, and Shoppers Food & Pharmacy) | 1,363 | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | Raised without antibiotics (Wild Harvest brand only) |
| Trader Joe's | 456 | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | Raised without antibiotics (Trader Joe's Organic brands, "antibiotic free" labels only) |
| Walmart (Sam's Club) | 5,310 retail stores 3,466 supercenters 449 discount stores 699 neighborhood markets 41 small formats 655 Sam's Clubs | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | Judicious use (including compliance agreement to suppliers) |
| Wegmans | 88 | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | No antibiotics ever (Food You Feel Good About brand and USDA Organic labels only) |
| Whole Foods Markets | 433 | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | No antibiotics ever |

* As of Feb. 29, 2016.

Source: The Pew Charitable Trust.

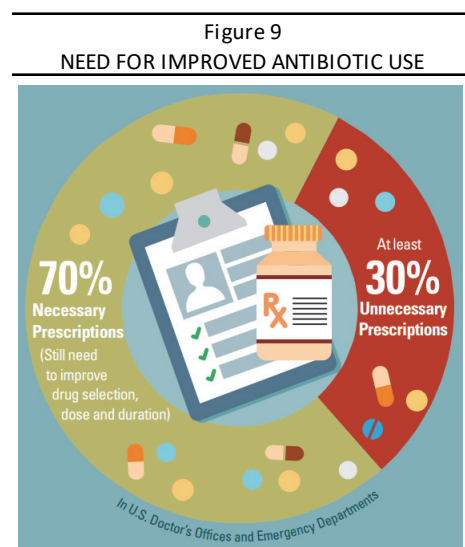
Need for Non-Antibiotic Replacements in Food-Producing Animals

On January 3, 2017, the FDA announced that it had completed the implementation of Guidance for Industry #213, (a process that began in 2013) to transition antimicrobial drugs with importance in human medicine (medically important antimicrobials) that are used in the feed or drinking water of food-producing animals to veterinary oversight and eliminate the use of these products in animals for production (e.g., growth promotion) purposes. These are antibiotics that are added to the animal feed or drinking water of cattle, hogs, poultry, and other food-producing animals to help them gain weight faster or use less food to gain weight. Since all uses of antimicrobial drugs in both humans and animals contribute to the development of antimicrobial resistance, use of these drugs should be for medical need only. The reason for this is that illnesses caused by drug-resistant strains of bacteria are more likely to prove fatal when the medicines used to treat them are rendered less effective.

The FDA is working to address the use of “medically important” antibiotics in food-producing animals for production uses, such as to enhance growth or improve feed efficiency. These drugs are deemed important because they are also used to treat human disease and might not work if the bacteria they target become resistant to the drugs’ effects. Importantly, the antibiotic resistance crisis cannot be solved without addressing how animals are raised for food. The reason is that 80% of all antibiotics sold in the U.S. each year, which also includes a significant number of medically important antibiotics, are used by food animal producers and a substantial fraction of the antibiotics consumed by food animals are excreted in their waste. This means that antibiotic residues and resistant bacteria in the waste can enter waterways from lagoon leaks and soil runoff, drift off farm in dust and air, or be carried off farm by workers and wildlife.

Protecting antibiotics requires treating food animals better. This includes providing clean, comfortable housing, more nutritious and naturally-suited diets, and sufficient space to keep animals healthy and reduce reliance on routine antibiotics. Strong animal welfare benefits not just animals, but also public health and the environment. Animals should only be given antibiotics to control or treat infectious diseases and the use of anything otherwise, including for routine disease prevention, should be eliminated.

Need for Improved Antibiotic Prescribing Practices



Source: CDC.gov.

Overuse and misuse of antibiotics threatens the usefulness of these drugs, thus decreasing inappropriate antibiotic use is a key strategy to control antibiotic resistance. Of particular concern is antibiotic resistance in children and older adults, as these age groups have the highest rates of antibiotic use. For people who have common infections that once were easily treatable with antibiotics, antibiotic resistance can cause significant suffering. This is because when antibiotics do not work, infections often last longer, causing more severe illness, requiring more doctor visits or longer hospital stays, and involving more costly and toxic medications. Unfortunately, for some individuals, these resistant infections can lead to death.

It is estimated that a minimum of 30% of antibiotic courses prescribed in the outpatient setting are unnecessary (Figure 9). The majority of these antibiotics are being prescribed unnecessarily for acute respiratory conditions such as colds, bronchitis, sore throats caused by viruses, and even some sinus and ear infections. Inappropriate antibiotic use (unnecessary antibiotic use plus inappropriate antibiotic selection, dosing, and duration) may approach half of all outpatient antibiotics prescribed.

Many advances in medical treatment—joint replacements, organ transplants, cancer therapy, and treatment of chronic diseases such as diabetes, asthma, rheumatoid arthritis—are dependent on the ability to fight infections with antibiotics. If that ability is lost, the ability to safely provide life-saving and life-improving modern medical advantages will be lost. An example of some of the highest risk patients who are at danger from the effects of antibiotic resistance are listed in Figure 10.

Figure 10
HIGH RISK PATIENTS

CANCER CHEMOTHERAPY

People receiving chemotherapy are often at risk for developing an infection when their white blood cell count is low. For these patients, any infection can quickly become serious and effective antibiotics are critical for protecting the patient from severe complications or death.

COMPLEX SURGERY

Patients who receive cardiac bypass, joint replacements, and other complex surgeries are at risk of a surgical site infection (SSI). These infections can make recovery from surgery more difficult because they can cause additional illness, stress, cost, and even death. For some, but not all surgeries, antibiotics are given before surgery to help prevent infections.

RHEUMATOID ARTHRITIS

Inflammatory arthritis affects the immune system, which controls how well the body fights off infections. People with certain types of arthritis have a higher risk of getting infections. Also, many medications given to treat inflammatory arthritis can weaken the immune system. Effective antibiotics help ensure that arthritis patients can continue to receive treatment.

DIALYSIS FOR END-STAGE RENAL DISEASE

Patients who undergo dialysis treatment have an increased risk for getting a bloodstream infection. In fact, bloodstream infections are the second leading cause of death in dialysis patients. Infections also complicate heart disease, the leading cause of death in dialysis patients. Infection risk is higher in these patients because they have weakened immune systems and often require catheters or needles to enter their bloodstream. Effective antibiotics help ensure that dialysis patients can continue to receive life-saving treatment.

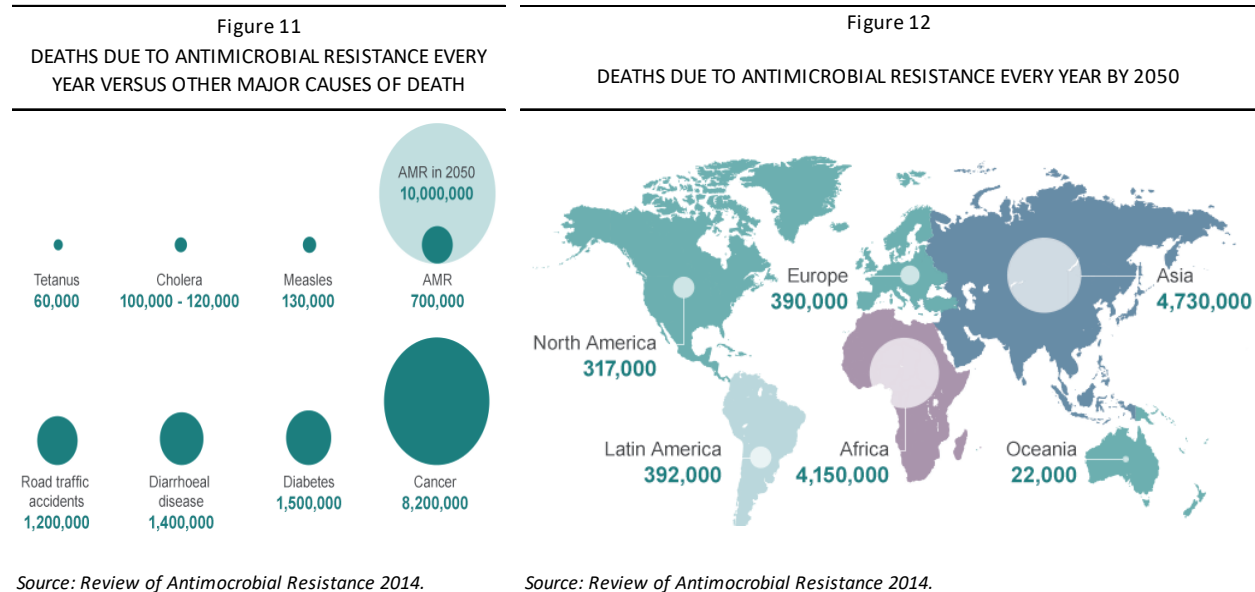
ORGAN AND BONE MARROW TRANSPLANTS

Transplant recipients are more vulnerable to infections. Because a patient undergoes complex surgery and receives medicine to weaken the immune system for a year or more, the risk of infection is high. It is estimated that 1% of organs transplanted in the United States each year carry a disease that comes from the donor—either an infection or cancer. Effective antibiotics help ensure that organ transplants remain possible.

Source: CDC.gov.

The Global Picture

Without any action to curb inappropriate and unnecessary antibiotic use, by 2050, someone could die every three seconds from antimicrobial resistance, which would equate to 10 million people every year (Figure 11). The majority of deaths would occur in Africa and Asia, with over four million in each region. For the rest of the world, the estimated death toll would be lower but could still reach nearly 400,000 in both Latin America and Europe (Figure 12).



Market Opportunities: Trends in Antibiotic Growth Promoter (AGP) Use

The global animal feed additives market is projected to cross \$37 billion by early 2022 from \$28.6 billion in 2016, growing at a CAGR of over 5.3% over the forecast period (Source: Mordor Intelligence). Worldwide, approximately 32,000 feed mills produce approximately 1,000,000,000 tons of feed with the great majority of that volume manufactured by a small number of organizations that integrate milling of feed production with the raising of the animals. Based on the global compound feed production and antibiotic consumption data, each ton of compound feed in the world contains an average of 66 grams of antibiotics.

Without indicating any relationship between resistance level and antibiotic usage, the recommended dosage of subtherapeutic antibiotics has increased during the past 60 years from 10 to 20 grams/ton in the early 1950s to 40 to 50 grams/ton in the 1970s. Today, the dosage runs from 30 to 110 grams/ton. The average antibiotic use per ton of feed is highest in the U.S., followed by China. Overall, antibiotic usage per ton of feed is 30% higher in the U.S. and 12% higher in China than the global average. Importantly, China and the U.S. are taking measures to reduce their use of antibiotics in livestock production. In the EU, antibiotic usage is 21% less than the global average, in part, due to efforts such as the European Union’s 2006 ban on the use of antibiotics as growth promoters in animal feed.

Avivagen: Addressing Unmet Needs

With world population continuing to steadily climb, the demand for animal protein will continue to grow. The need to improve efficiencies in animal production will remain a top priority for producers and governments. Natural, safe, and effective alternatives to antibiotics are being sought by an industry that needs to maintain a high level of efficiency in order to simultaneously maintain profits and protect human health. **Avivagen has developed a natural product-based, non-antibiotic, non-hormonal platform as an alternative to antibiotics in food animals—representing a significant opportunity for future growth and profitability.**

PROPRIETARY TECHNOLOGY PLATFORM

Avivagen operates under the premise that there will be significant changes coming forth to livestock feeding practices. Specifically, a coalition of 54 institutional investors managing over one trillion U.S. dollars published a letter demanding that the 10 largest food companies in the U.S. and U.K. require their supply chains to halt the use of non-therapeutic antibiotics in livestock production. This is an important step given the fact that more antibiotics are given to livestock than to people, which is leading humans into a post-antibiotic era where routine surgical operations may not be possible and where infections may no longer be treatable. The coalition also cites research suggesting the global cost of such a scenario could exceed a staggering \$100 trillion.

Currently, the Centers for Disease Control and Prevention (CDC) states that resistant bacteria cause two million infections and 23,000 deaths every year, which already has a cost of \$20 billion for eight million hospital days. Moreover, a recent scientific article raises greater concerns with regard to the unregulated use of antibiotics in livestock feeds. Specifically, it cites that antibiotic resistance genes “cluster” together in gut bacteria where treatment with even a single antibiotic can activate multi-drug resistance and that multi-drug resistant bacteria in livestock may be far more common than anyone had ever realized. Such evidence further shows the hazards of current antibiotic feeding practices and why it is so necessary to implement strong antibiotic restrictions.

The Company believes that it is well positioned to help address changes in feeding practices. For example, on March 22, 2016, Avivagen announced positive results from a trial of OxC-beta™ as a feed additive in swine run by COFCO Nutrition and Health Research Institute Co., Ltd. (COFCO NHRI) in Beijing, China, and has now established a joint venture alliance to be funded by the Jintai companies to launch OxC-beta™ in that country. Additional confirmatory trials have been completed in **broiler poultry** in Spain, the Philippines, and Korea, and in swine in Vietnam. To date, Avivagen’s OxC-beta™ has performed well versus multiple types of antibiotics, including those deemed critically important to human medicine.

OxC-Beta™ (Fully Oxidized Beta-Carotene)

Avivagen’s product development centers on its OxC-beta™ (fully oxidized beta-carotene) technology, which has already been commercialized for use in livestock feeds where it promotes animal growth and helps prevent disease without the use of antibiotics or hormones. To avoid the need for traditional antibiotics, Avivagen’s technology capitalizes on its ability to modulate natural immunological mechanisms present in both humans and animals, to develop products that enhance immune defenses and maintain optimal health.

Avivagen’s OxC-beta™ platform addresses target markets for livestock and humans, as well as companion animal health through the OxC-beta™ Livestock product, investigational carotenoid oxidation products, and Vivamune™ Health Chews and Oximuno™ Chewable Tablets, respectively. The Company’s primary focus at this time is its livestock and human health opportunities, as further detailed in the accompanying section.

Core Technology: Fully Oxidized β-carotene

Avivagen’s technology centers on understanding the origin of the beneficial health impacts of β-carotene, which most people know as the component in carrots that gives them their orange color. β-carotene belongs to a family of carotenoids found in a number of yellow, orange, and green fruits and vegetables, from carrots to tomatoes, sweet potatoes, cantaloupe, some squash varieties, and even spinach, lettuce, and broccoli (as illustrated in Figure 13, page 20). It is one of the best-known dietary sources of vitamin A and is important for vision and eye health, strong immune systems, and healthy skin. According to the University of Maryland Medical Center, a rough guideline to measuring β-carotene is by color: the more intense the color of the fruit or vegetable, generally the more β-carotene found in it.

Figure 13

β -CAROTENE (BETA-CAROTENE)

β -carotene Chemical Structure



Carotenoids are naturally found in fruits/vegetables...



Sources: Avivagen Inc., Wikimedia Commons, and Crystal Research Associates, LLC.

In addition to providing the body with vitamin A, β -carotene has been thought to be an antioxidant that provides protection from damaging molecules, called free radicals. Free radicals are a type of highly reactive oxygen molecule known to cause oxidative stress, which triggers harmful inflammatory responses and cell death as the free radicals attack DNA, lipids, proteins, and other cell components. These oxygen molecules are believed to accelerate the progression of cancer, cardiovascular disease, and age-related diseases, including cataracts, arthritis, Alzheimer’s disease, and diabetes. In normal, healthy cells, an antioxidant defense system can both minimize and repair free radical-induced damage. To this end, as far back as the 1980s, medical research has documented the impact of a diet high in β -carotene, and its effect at reducing chronic diseases such as certain cancers, heart disease, and other age-related illnesses.

Not Just a Source of Vitamin A:

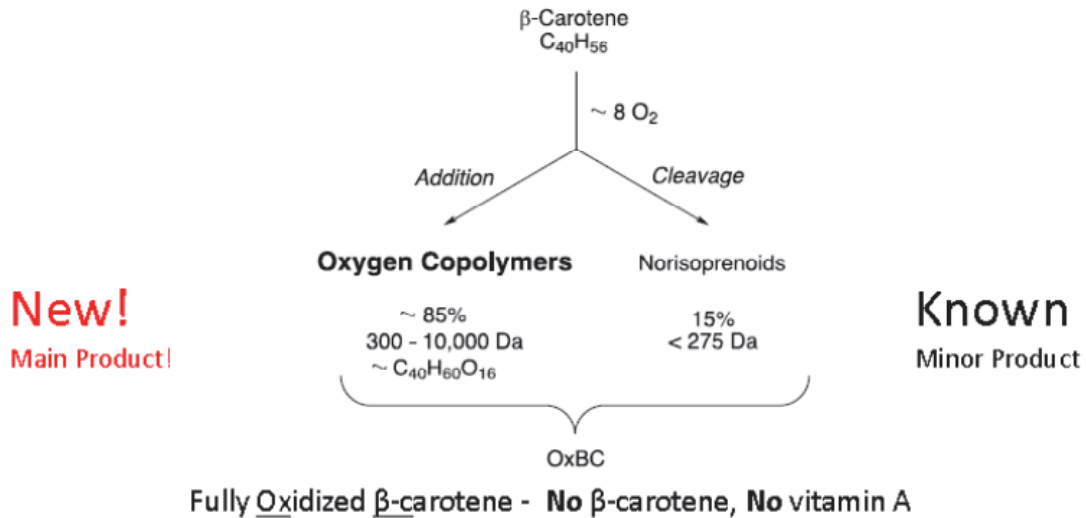
β -carotene is transformed by Spontaneous Oxidation into Much-needed Copolymer Compounds

Recognizing the opportunity that β -carotene and other carotenoids held for health but believing that something other than an antioxidant was at play, Avivagen’s founding scientists—while at Canada’s National Research Council (NRC)—sought to determine exactly how β -carotene reacts with oxygen and how that builds immunity against disease, since not all of the molecule’s health benefits can be attributed to vitamin A or antioxidant properties. In the course of the Company’s research, Avivagen found that β -carotene was highly susceptible to reacting spontaneously with oxygen to form a new compound called *oxygen copolymers*, which had previously gone unnoticed. Further studies elucidated that copolymer compounds are directly immunologically active. Avivagen believes, and its scientific studies confirm that oxygen copolymers resulting from carotenoid oxidation are the actual agents of immunological activity in animals—not the β -carotene itself.

Oxygen Copolymer Compounds

Essentially, when carotenoids such as β -carotene or lycopene react chemically in the presence of oxygen, copolymer compounds are created that have chemical characteristics distinct from β -carotene on its own. Figure 14 (page 21) depicts the formation of oxygen copolymers, which occurs when β -carotene O_2 adds to the β -carotene molecule. This Figure also highlights another part of Avivagen’s initial discoveries surrounding β -carotene: oxygen copolymers represent roughly 85% of the products created in the spontaneous oxidation of β -carotene. This aspect had eluded the focus of the scientific community until Avivagen’s founding scientists began to theorize that something aside from vitamin A was contributing to β -carotene’s considerable health impacts. Avivagen has found that these copolymer compounds have a direct beneficial impact on immune function, including moderating inflammation.

Figure 14
FORMATION OF OXYGEN COPOLYMERS THROUGH SPONTANEOUS OXIDATION OF BETA-CAROTENE

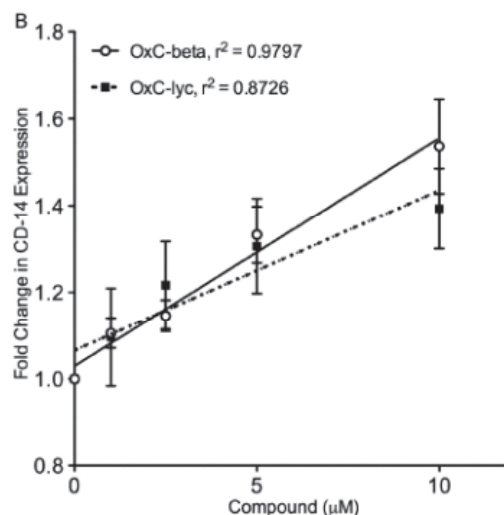


Source: Burton et al., *Can. J. Chem.*, 92: 305-316 (2014) dx.doi.org/10.1139/cjc-2013-0494.

Beyond β -carotene, the carotenoid family encompasses roughly 600 molecules, including popular health supplements lycopene (which gives tomatoes their red color), lutein, and astaxanthin. Each of these generates oxygen copolymers during spontaneous oxidation. Avivagen’s research shows that all such copolymers are immunologically active, as is illustrated for example in Figure 15 using fully oxidized β -carotene and lycopene. This Figure illustrates the increase in the level of an innate immune receptor, **CD14**. The CD14 receptor plays a critical role in the innate immune system’s recognition of pathogenic bacteria. Results show that the copolymer compounds present in oxidized β -carotene and oxidized lycopene are biologically active, with an ability to prime innate immune function, which is associated with enabling animals to more rapidly respond to subsequent microbial challenges (Source: *PLOS ONE*, 2014, Vol. 9, Issue 10). Moreover, the formation of oxygen copolymers may help explain why increased dietary consumption of carotenoid-rich fruits and vegetables is associated with decreased incidence of diseases of aging, e.g., cancer, heart disease.

Figure 15
COPOLYMERS STIMULATE IMMUNE ACTIVITY

Oxidized β -carotene and lycopene are equally active (CD14 Receptor Expression)



Source: Johnston et al., *PLOS ONE*, Oct 2014, Vol 9, Issue 10, e111346.

Creation of Commercially Viable OxBC: Avivagen's Active Ingredient

The outcome of Avivagen's study of copolymer compounds was the development of a fully oxidized, synthetic β -carotene mixture containing mostly copolymers. This mixture, referred to technically as OxBC, is produced via the same oxidation reaction that occurs in nature and is highly similar to the chemical structure of the natural product. To make the OxBC mixture, Avivagen takes pure β -carotene and simply allows it to react with oxygen—a process that occurs naturally all the time. Once β -carotene has fully oxidized, the resulting mixture has a consistency similar to molasses (as illustrated in Figure 16), which is then formulated as an OxC-beta™ powder by mixing with cornstarch.

OxBC—or synthetic β -carotene-oxygen copolymer compound—is the active ingredient and basis of the Company's OxC-beta™ technology, from which its immune-strengthening products for livestock, humans, and pets are derived.

Figure 16

CREATING SYNTHETIC B-CAROTENE COPOLYMER COMPOUNDS



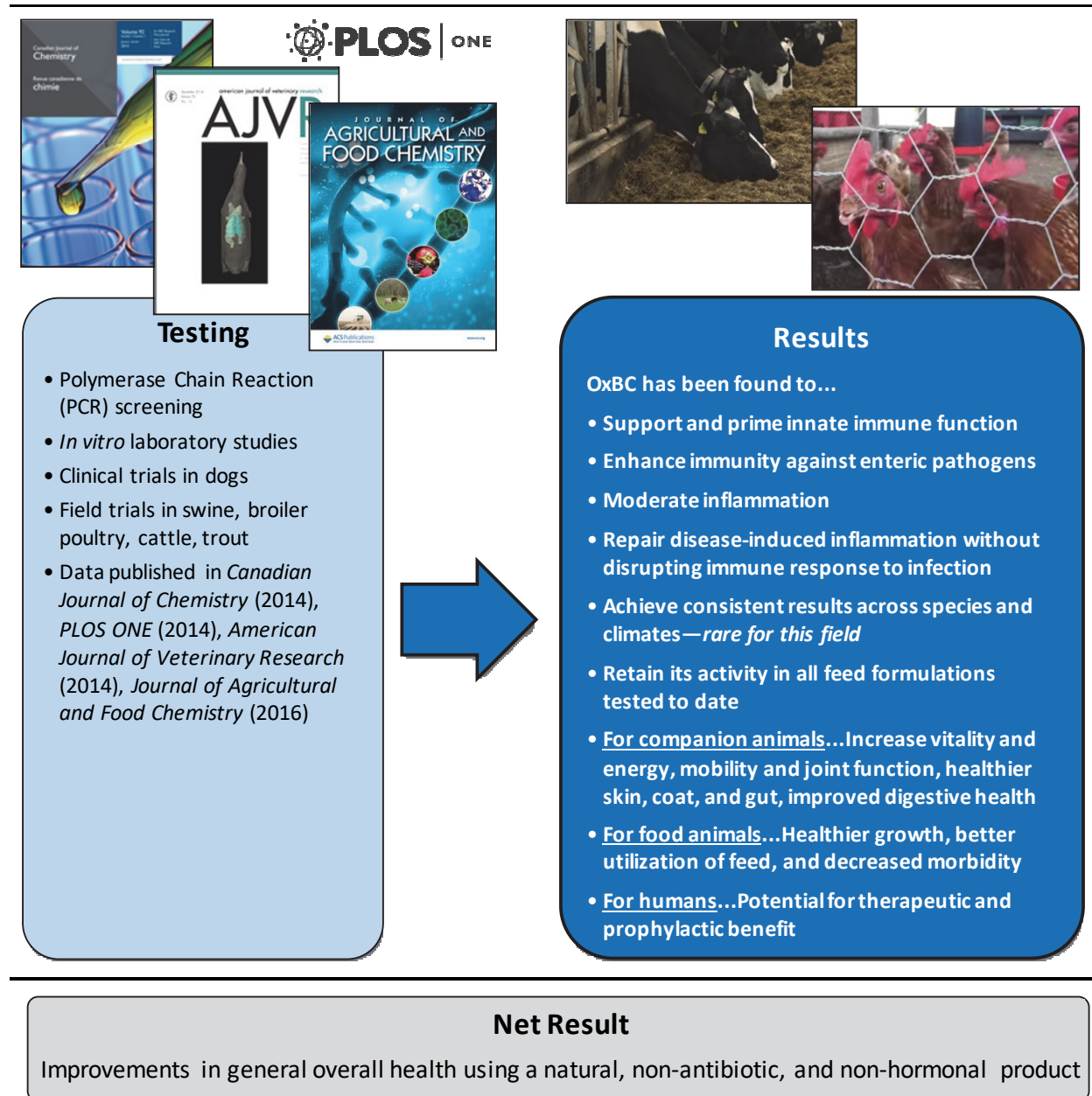
Source: Avivagen Inc.

OxBC (OxC-beta™) Clinical Trials

Avivagen and its funding and research partners have invested over two decades and roughly \$30 million into extensive studies of its proprietary technology, ultimately finding that the improvement in animal health using OxC-beta™ is comparable to what occurs using antibiotics. The Company’s scientific results reporting the chemical composition and immunological mode of action of OxC-beta have been published in four different peer-reviewed journals: the *Canadian Journal of Chemistry*, *PLOS ONE*, the *American Journal of Veterinary Research*, and the *Journal of Agricultural and Food Chemistry*. Highlights of these results are summarized in Figure 17 and detailed on the accompanying pages.

Figure 17

OxBC CLINICALLY-PROVEN VETERINARY HEALTH BENEFIT SUMMARY



Sources: Avivagen Inc. and Crystal Research Associates, LLC.

Safety and Efficacy in Livestock

Broiler Poultry and Swine

To date, Avivagen and its collaborators have conducted 13 trials of OxC-beta™ Livestock in broiler poultry and swine. Figure 18 summarizes these trials, which are composed of seven broiler poultry and six swine trials that have occurred across Canada, Europe, and Asia. The Company’s partners in these studies are typically from both academia and industry, which helps facilitate the logistics and economics of running large-scale, commercially-oriented trials in broiler poultry and swine.

Results of the trials listed in Figure 18 have indicated meaningful intestinal disease protection and growth promotion, as measured by average daily growth (ADG), final body weight (FBW), and feed conversion ratio (FCR). To read Figure 18, look for increases (+) in ADG and FBW and decreases (-) in FCR. In addition, the more recent trials, which have been conducted in Asia, have demonstrated important regional results—namely that OxC-beta™ Livestock can be effective under Asian livestock production conditions. These trials further served to clarify optimal dosages and efficacy levels for OxC-beta™ in livestock.

Figure 18
OxC-BETA™ LIVESTOCK TRIALS

| Broiler Poultry (Seven Trials) | | | | |
|--------------------------------|-------------------------------|--------------|----------|---------------------|
| Location | Trial Type | # of Animals | Duration | Results |
| Canada | Proof of concept | 1,600 | 38 days | +FBW, +ADG, -CFU |
| Canada | Dosing* | 2,500 | 39 days | +ADG, +FBW, -FCR |
| UK | Confirmatory | 4,655 | 35 days | +ADG, +FBW, -FCR |
| Canada | Necrotic enteritis challenge* | 450 | 21 days | +FBW, -FCR |
| Korea | Necrotic enteritis challenge* | 280 | 28 days | +FBW, -lesion, -CFU |
| Spain | Diet and crowding challenge | 714 | 35 days | +FBW |
| Philippines | Recycled litter* | 768 | 36 days | +FBW |

| Swine (Six Trials) | | | | |
|--------------------|---------------------------|--------------|----------|---------------------------|
| Location | Trial Type | # of Animals | Duration | Results |
| Canada | Proof of concept, starter | 96 | 28 days | +ADG, -FCR |
| Canada | Dosing and challenges* | 240 | 35 days | +health |
| Vietnam | Full post-wean grow-out* | 500 | 140 days | +ADG, +FBW, -FCR, +health |
| China | Starter* | 144 | 28 days | +ADG |
| Vietnam | Creep/starter* | 420 | 49 days | +ADG, +FBW, -FCR, +health |
| Philippines | Starter | 480 | 28 days | +health |

*These trials included both negative and antibiotic growth promoter (AGP) control arms.

ADG: Average Daily Growth FBW: Final Body Weight FCR: Feed Conversion Ratio (kg feed/kg of weight gain; smaller is better)
CFU: Colony-forming units

Source: Avivagen Inc.

Broiler poultry is the number one global feed market, consisting of approximately 295 million tons of feed. Swine is the number two feed market globally, consisting of roughly 254 million tons of feed. Avivagen has tested its product in almost 11,000 meat birds and 1,880 swine, demonstrating that OxC-beta™ can maintain feed efficiency and weight gain in multiple species with equal or better efficacy than antibiotics currently in use.

- In poultry, daily weight gain was improved by up to 12%, feed conversion by up to 4%, and protection from enteric (intestinal) disease was equal to that of antibiotics.
- In swine, daily weight gain was improved by up to 23%, feed conversion by up to 11%, and protection from **Enterotoxigenic *E. coli* (ETEC)** diarrhea was better than that with antibiotics.

Cattle

Avivagen, in partnership with the University of Calgary and University of Alberta (Canada), has conducted studies of OxC-beta™ in cattle by way of an experimental model of **bovine respiratory disease complex (BRDC)**. BRDC is one of the most devastating diseases to affect cattle, and represents a major economic burden to the beef industry from animal death, decreased weight gain, and the extensive time, labor, and medicine costs that go into preventative antibiotics and vaccines as well as treatments. It is estimated that BRDC affects up to 20% of beef cattle in North America.

In a BRDC challenge study, 25 young Holstein calves were fed a diet that was supplemented with OxC-beta™ for 28 days and were then inoculated with *M haemolytica* bacterium (causing BRDC). Three Angus **heifers** also provided blood for *in vitro* studies of OxC-beta™. Results of this study found that OxC-beta™ helped to resolve pathogen-driven inflammation in the lung—suggesting the potential of OxC-beta™ Livestock at becoming a novel nutraceutical strategy conferring benefits for cattle with respiratory disease (Source: *American Journal of Veterinary Research*, December 2014, 75:1064-1075).

Fish (Trout)

A proof-of-concept study has also been performed in trout, which demonstrated enhanced bacterial killing ability of innate immune cells from OxC-beta-fed fish.

Safety

Avivagen has conducted safety studies that show OxC-beta™ can be used safely for an extended period of time. Such studies have occurred in companion animals and food animals with no ill effects. Animals, including thousands of dogs, have received daily doses of the active ingredient in the Company's products, sometimes as much as 10 times the quantity normally administered, and have not experienced adverse clinical effects according to Avivagen. Altogether, there have been over 1,000,000 daily doses of OxC-beta™ given to pets without adverse effects. Hundreds of thousands of doses have been given to livestock in field trials as well, including at up to 50 times the effective dose (in swine, up to 15 times in poultry), with no attributable adverse effects. There has also not been any evidence of side effects in food-allergic pets. Of note is that Avivagen completed a feline safety trial and launched a cat-oriented SKU of its Vivamune pet product line. However, with limited marketing, it has since reduced the range of SKUs to focus solely on dogs.

Furthermore, OxC-beta™ does not have any direct antibacterial effects, and thus, is highly unlikely to trigger the creation of antibiotic-resistant pathogens. Its effects are host-mediated (immune system-driven), so the product is widely considered a safer alternative to current antibiotics and hormones both for the animals that receive supplements and for the human population as a whole. In addition, the copolymer compounds used in OxC-beta™ are also found naturally in foods that humans consume on a daily basis. The Company believes that the maximum possible human exposure from meat residue is well below that of normal dietary exposure from eating plant-based foods.

PRODUCT: OxC-BETA™ FOR LIVESTOCK AND HUMANS

OxC-beta™ is commercially available in multiple countries, as listed in Figure 19. Demand for OxC-beta™ Livestock in Asia is driven by first-followers of Europe’s 2006 ban on antibiotics in livestock feed, in anticipation that such regulations will eventually come to other global markets as well. In addition to the Philippines, Thailand, and Taiwan, Avivagen reports that negotiations are ongoing in other jurisdictions as well to promote adoption of OxC-beta™.

Figure 19

GLOBAL AVAILABILITY

OxC-beta™ Livestock

- o Cleared for marketing in the Philippines, Thailand, and Taiwan, and is available in bulk in Thailand and the Philippines
- o Sales and distribution agreement is in place with a Philippine producer of pig and poultry feed, UNAHCO
- o Joint venture established in China, the world’s largest market for animal feed

OxC-beta™ for Companion Animals

- o Vivamune Health Chews™ are available for purchase from Avivagen in the U.S.

Sources: Avivagen Inc. and Crystal Research Associates, LLC.

For Food Animals

OxC-beta™ Livestock

In livestock feeds, OxC-beta™ replaces the antibiotics typically used for disease prevention and growth promotion of food animals. Because livestock given OxC-beta™ in their feed grow to be healthier, they utilize that feed more efficiently. The end result is that these animals use less feed but grow faster, which has a significant impact on the bottom line of the food production industry. Faster animal growth also increases the productivity of food producers’ operations. Thus, Avivagen’s value proposition for food producers centers on improving productivity and saving costs since livestock consuming OxC-beta™ require less feed and need less disease intervention.

Figure 20

OxC-BETA™ LIVESTOCK

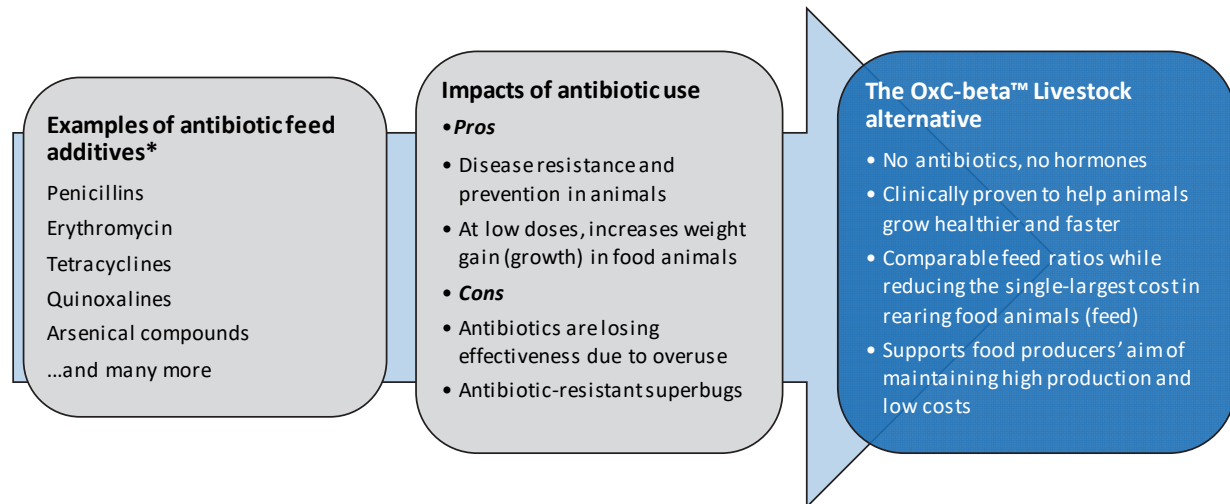


OxC-beta™ Livestock offers dual capabilities of priming the innate immune response to respond more effectively when challenged by a pathogen (e.g., enteric or respiratory diseases) and moderates inflammation arising from chronic inflammatory conditions. These two benefits in particular help control common and costly problems of rearing food animals.

OxC-beta™ Livestock (illustrated as a powder in Figure 20) is effective in very small quantities; for example, 2 grams in 1 ton of animal feed. The Company believes that it is competitively priced to be economically advantageous to livestock producers. Figure 21 (page 27) summarizes the advantages that OxC-beta™ may offer the global food production industry as it is further commercialized around the world.

Source: Avivagen Inc.

Figure 21
THE OxC-BETA™ LIVESTOCK ADVANTAGE



*Some countries, particularly in Europe, have already banned antibiotics in feed. This regulatory trend will likely ultimately force food producers to choose non-antibiotic solutions for preventing disease in food animals raised in dense, close quarters where a disease outbreak could spread quickly.

Sources: Avivagen Inc. and Crystal Research Associates, LLC.

For Humans

Carotenoid Oxidation Products (Human Health and Wellness)

OxC-beta™ has further shown that it may help humans maintain optimal health as well. One of Avivagen’s most recent discoveries arising from its research was the finding that OxC-beta™ has naturally occurring counterparts—oxidized copolymer compounds—that are present in common human food products, including carrots, tomatoes, sweet potatoes, paprika, rosehips, seaweeds, alfalfa, and milk (Source: *Journal of Agricultural and Food Chemistry*, April 2016, 64: 3767-3777). The existence of β-carotene and other carotenoid copolymer compounds in human foods consumed on a daily basis helps support the safety of Avivagen’s OxC-beta™ technology and the Company’s premise that these compounds have far-reaching nutritional implications.

Moreover, the distinction between the health impacts of carotenoids themselves and the copolymer compounds created from the breakdown of carotenoids is critically important, and was fully explained in Avivagen’s latest published research: *Discovery and Characterization of Carotenoid-Oxygen Copolymers in Fruits and Vegetables with Potential Health Benefits* by Graham W. Burton, Janusz Daroszewski, Trevor J. Mogg, Grigory B. Nikiforov, and James G. Nickerson (*Journal of Agricultural and Food Chemistry*, April 2016, 64: 3767-3777). This article details how some foods contain carotenoids (β-carotene) and some contain the naturally occurring copolymers. Both offer a beneficial impact on human health, but consuming intact carotenoids (such as β-carotene, lycopene, and lutein in conventional dietary supplements) does not achieve the same level of enhanced immune function and resistance to chronic diseases as consuming carotenoid-containing fruits and vegetables, which importantly also contain the copolymer compounds.

Avivagen’s OxC-beta™ products may become a preferred alternative in the human health dietary supplement market because of their ability to tap into, and replicate, the effects of copolymer compounds.

Growth Strategy

Avivagen pursues scientifically supported alternatives to conventional therapies that promote feed efficiency, growth, and animal and human health, but lack harmful side effects and do not contribute to the global problem of antibiotic resistance. Avivagen is commercializing novel products and focusing on the following four strategic operational goals:

- Securing additional licensing agreements;
- Building collaborations and alliances with selected industry partners;
- Continuing to launch pet products in the U.S., Canada, and internationally; and
- Further strengthening its intellectual property (IP) position (as detailed on page 35).

Product-specific Goals

OxC-beta™ Livestock

For its OxC-beta™ Livestock product, which is available for sales in the Philippines, Thailand, and Taiwan thus far, Avivagen has opted to focus initial efforts on poultry (broilers) and swine markets. These are animal species where the Company can rapidly generate data through its industry and academic relationships, and at the same time, are animal species that are largely impacted by regulations on the use of antibiotics in feed. Avivagen has conducted confirmatory trials with major Asian livestock integrators and exploratory trials with qualified universities and research institutes (trial information is provided on pages 23-27) and is currently filing for national registrations to expand the global reach of OxC-beta™. In addition to expanding geographically (a joint venture in China was established in November 2016), Avivagen is also generating data in beef cattle. Over the medium to long term, the Company believes potential new markets exist for laying hens, **dairy ruminants**, and **aquaculture**.

Altogether, it is estimated that the quantity of feed for poultry, swine, and cattle that could include OxC-beta™ is roughly 995 million tons worldwide. Asia—the first target market for OxC-beta™ commercialization—represents approximately 35% of this demand. Avivagen has also found Asia to have industry clients that are receptive to non-antibiotic solutions as well as favorable regulatory regimes and market sizes. Figure 22 summarizes market sizes for OxC-beta™, highlighting Avivagen’s work in pursuing worldwide sales and relationships.

Figure 22

AVIVAGEN'S GLOBAL COMMERCIALIZATION OPPORTUNITIES AND PROGRESS

Targeting a global market of approximately 995 million tons of livestock feed (poultry, swine, and cattle) per year

| Countries where OxC-beta™ is available for sale with commercial discussions ongoing |
|--|
| Thailand (17.9 million metric tons of feed), Philippines (12.8), Taiwan (7.3) |
| Countries where registration and distribution discussions have been initiated |
| China (180 million metric tons of feed), U.S.* (173.7), South Korea (19), Thailand (17.9), Vietnam (14.8), Philippines (12.8), Taiwan (7.3) |
| Countries where Avivagen has existing or planned relationships for product trials |
| China (180 million metric tons of feed), U.S. (173.7), Spain (29.4), Canada (20.4), South Korea (19), Thailand (17.9), Vietnam (14.8), Philippines (12.8) |

Bolded countries are among the world's top 10 markets for livestock feed. *OxC-beta™ pet products are available for sale.

Sources: Avivagen Inc. and Alltech Global Feed Survey (2016) for tonnage data.

With prices for a ton of feed typically in the US\$350 to US\$400 range, Avivagen believes there is a compelling argument for supplementing feed with OxC-beta™ to achieve greater animal productivity and disease resistance given that the amount of OxC-beta™ needed per ton of feed only has a cost of roughly US\$5 to US\$10 MSRP.

Carotenoid Oxidation Products (Human Health and Wellness)

Avivagen is also actively exploring applications of the OxC-beta™ technology for human health and wellness. The Company may ultimately pursue the introduction of OxC-beta™ through a class of carotenoid oxidation products to the human supplement, prophylactic, or therapeutic healthcare markets.

Vivamune Health Chews™ and Oximunol™ Chewable Tablets

Avivagen has further commercialized OxC-beta™ technology into products for companion animals to improve and maintain quality of life in pets. These products are non-drug nutritional supplements, regulated by the National Animal Supplement Council (NASC), to improve pets’ digestive functions (a healthy gut), joints, and coat. These products are approved for sale in the U.S. and Avivagen is looking to register its ingredient for pet products in Canada under the Government’s Low-Risk Veterinary Health Products (LRVHP) program. One or more pet approvals may also be pursued in Asia.

Corporate Partnerships

Avivagen collaborates with animal health companies and other academic, institutional, and industrial research partners in the U.S., Canada, Philippines, Korea, Vietnam, and Thailand, and continues to seek further strategic relationships around the world. Such partnerships (Figure 23) aid research and testing as well as distribution and commercialization of the OxC-beta™ technology and products to veterinarians, farmers and food producers, pet owners, and retailers. Ongoing applied research through some of these partnerships is aimed at expanding the applications of OxC-beta™ to additional livestock species.

Figure 23

A SELECTION OF AVIVAGEN'S CORPORATE PARTNERS



Source: Avivagen Inc.

Milestones

Recent Milestones (2016)

During 2016, Avivagen further confirmed the benefits of its products with trial results from additional studies in swine and poultry. The Company also achieved product registrations in several Asian countries, and entered into distribution and joint venture relationships with local partners (the joint venture in particular being an important first step toward product registration in China). Following product registrations, Avivagen was able to commence material product sales into Asia during 2016. Milestone highlights are presented below.

- In March 2016, the COFCO Nutrition and Health Institute of Beijing, China, reported favorable findings of a comparative trial of OxC-beta™ Livestock in swine feed. Researchers studied the impact on piglets that received feed supplemented with OxC-beta™, no supplements, or a regimen of two antibiotics, and found that OxC-beta™ enhanced piglet growth and reduced the incidence of diarrhea.
- In April 2016, Avivagen authored a peer-reviewed article published in the *Journal of Agricultural and Food Chemistry* detailing a discovery that the bioactive component of OxC-beta™ occurs naturally in human foodstuffs. These findings are helping drive the Company's human health platform, and are expected to favorably impact the ability of Avivagen to gain regulatory acceptance for its OxC-beta™ technology in humans given the inherent safety of its primary ingredient. New patent applications have also stemmed from this discovery.
- In June 2016, Avivagen raised approximately \$3.6 million in a private placement, and released results of three new trials of OxC-beta™ Livestock in swine and broiler poultry. The trials occurred in the Philippines and Vietnam.
 - Findings from the National Institute of Animal Sciences (NIAS) for Vietnam confirmed that OxC-beta™ in swine is comparable to antibiotics in terms of weight gain, feed efficiency, and diarrhea and mortality prevention, and was superior on all measures versus no supplement at all.
 - A prospective customer in the Philippines found a reduction in morbidity and mortality in swine given OxC-beta™ versus other forms of non-antibiotic supplements or no supplements. In addition, a UNAHCO (the feed and veterinary subsidiary of the Philippines' largest pharmaceutical company, Unilab Inc.)-cosponsored trial in broiler poultry found that OxC-beta™ matches the performance of antibiotics plus antiparasitics.
- In July 2016, Avivagen received notice of registration of OxC-beta™ Livestock in the Philippines, enabling its use as a livestock feed additive for all animal species in the Philippines.
- In October 2016, Avivagen and UNAHCO entered into a sales and distribution agreement. Under the agreement, UNAHCO serves as Avivagen's exclusive supplier of OxC-beta™ to the Philippines, which began with the purchase of OxC-beta™ for inclusion in certain UNAHCO-branded feeds. UNAHCO is a major producer of pig and poultry feed and has a distribution network that serves more than 3,000 outlets, supported by over 100 field personnel.
 - Initial sales to UNAHCO were in an amount of OxC-beta™ sufficient to supplement the feed of approximately three million broiler chickens (full grow) or 350,000 piglets (first month post-weaning).
- In November 2016, Avivagen formed a joint venture (JV) with a Chinese company, Shaanxi Jintai Mining Co. Ltd., that is held 49% by Avivagen and 51% by Jintai. Under the terms of the JV, there will be a partial capital injection of 25% by the partner shortly after the JV is formally approved by the Government. Thereafter, further capital will be added on an as-needed basis.

Potential Milestones (2017 and Beyond)

Going forward, during 2017, Avivagen aims to further international recognition of the OxC-beta™ science, engage with the U.S. and other new regulators, and advance its human health initiatives.

- Avivagen aims to have registration, distribution, and sales in place for all of the following countries in the near term: China, Korea, Philippines, Taiwan, Thailand, and Vietnam.
- The Company aims to commence multiple new product trials, including for swine in China (through the COFCO Nutrition and Health Institute of Beijing) and for broilers in the Philippines (through UNAHCO).
- Over the longer term, Avivagen could expand OxC-beta™ Livestock into the U.S. (where its pet supplements are already sold), the European Union (where antibiotics are already banned in livestock feeds), and Brazil as well as into new species, such as laying hens, beef cattle, dairy cattle, and aquaculture.
- Having already identified human applications for its OxC-beta™ technology, Avivagen also seeks to show proof-of-concept in human wellness and may enter into collaborations to do so.

Company Leadership

Executive Management

Figure 24 summarizes the Company’s executive leadership team, followed by brief biographies.

Figure 24
EXECUTIVE LEADERSHIP

| | |
|-------------------------------------|--|
| Kym Anthony | Chairman of the Board and Interim CEO |
| Graham Burton, Ph.D. | Co-founder and Director, Commercialization Science |
| Janusz Daroszewski, Ph.D. | Co-founder and Director, Process Validation |
| James Nickerson, Ph.D. | Director, Product Validation |
| Tracy Gillett, BVSC | Marketing Manager |
| Mr. Louis Hui | Director, Business Development |
| Mr. Drew Basek | Director, Investor Relations |
| Chris Boland, CPA, CA, CMA, B.Comm. | Chief Financial Officer |

Source: Avivagen Inc.

Kym Anthony, Chairman of the Board and Interim Chief Executive Officer (CEO)

Mr. Anthony has extensive experience in capital markets, agriculture, and life sciences and invested in the Company concurrent with his appointment. He was currently chair of the Audit Committee and vice chair of the Board of ComDev International until its sale in February 2016. From 2011 to May 2014, he served as chair of Prometic Life Sciences Inc.; from 2007 to present, as the chair of Hybrid Partners and executive chair of Top Meadow Investments, Inc.; from 2005 to 2007, with Dundee Securities; from 1998 to 2005, with First Marathon – National Bank Financial – as president and CEO; from 1993 to 1998, as CEO and vice chair of Toronto Dominion – TD Securities; and from 1980 to 1993, with Wood Gundy (CIBC World Markets).

Graham Burton, Ph.D., Co-founder and Director, Commercialization Science

Dr. Burton co-founded Avivagen after 19 years of biomedical research at the National Research Council of Canada (NRC). 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.

Janusz Daroszewski, Ph.D., Co-founder and Director, Process Validation

Dr. Daroszewski co-founded Avivagen after 21 years of work in chemical industry, research institutions, and academia. He has a broad background in organic synthetic chemistry and extensive experience in research of biologically active substances.

James Nickerson, Ph.D., Director, Product Validation

Dr. Nickerson joined Avivagen as a senior research biologist and has held various research and management positions during his career with the company. Dr. Nickerson established Avivagen’s biological research facility and has directed the Company’s biology research program for the past 10 years. He holds graduate degrees and postdoctoral research experience in the fields of molecular biology and physiology.

Tracy Gillett, BVSC, 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. Ms. Gillett gained valuable experience within one of the world’s largest multinational pharmaceutical companies.

Mr. Louis Hui, Director, Business Development

Mr. Hui is a life science executive with over ten years of direct business development, technology transfer, and venture capital experience. His entrepreneurial spirit enabled him to garner broad leadership experience in early-stage life science and animal health companies. Mr. Hui’s past experiences include co-founding Healthy Cow, a biotech for the dairy industry commercializing non-antibiotic and non-hormonal therapies to address mastitis, reproductive, and metabolic ailments. In a prior role as the founding employee of OtoSim Inc., a developer of interactive medical simulation devices, he helped build the company from concept-stage to global sales with installations into leading U.S. military and medical institutions in North America, Europe, Middle East, and Asia.

Mr. Drew Basek, Director, Investor Relations

Mr. Basek’s twenty-five plus years of experience within the investment industry include working on Fixed Income and Foreign Exchange desks (Merrill Lynch Canada, Bankers Trust Canada), and spending the last fifteen years as an Institutional Equity Salesperson (Deutsche Bank, Levesque Beaubien), including the position of Head of Institutional Sales at Dundee Securities. Born in Manhattan and growing up in the Tri-State Area, he spent his final four years of high school attending Ridley College in St. Catharines, Ontario. Realizing that Canada was where he wanted to make his permanent home, he then attended Queen’s University, graduating with a B.A. Honours, (Economics), followed six years later with an MBA (Finance and Marketing) from The Rotman School of Management (U of T).

Chris Boland, CPA, CA, CMA, B.Comm., Chief Financial Officer

Mr. Boland has completed the CICA Advanced Taxation and Advanced IFRS studies. He also has 25 years of experience in corporate finance, IFRS, SOX, ERM, public reporting, anti-fraud measures, and corporate governance. He serves on the Board of Directors of CMAO and was previously on the Board of ICAO, CPA of Ontario.

Board of Directors

The Board of Directors oversees the conduct of and supervises the Company’s management. Figure 25 provides a summary of Board members, followed by detailed biographies.

Figure 25
BOARD OF DIRECTORS

| | |
|----------------------|--|
| Kym Anthony | Chairman |
| Graham Burton, Ph.D. | Co-founder and Director, Commercialization Science |
| Vanessa Grant | Director, Chair of Governance and HR Committee |
| Paul Mesburis | Lead Director and Chair of Audit Committee |
| David Hankinson | Director, Member of Audit Committee |

Source: Avivagen Inc.

Kym Anthony, Chairman

Biography provided on page 32

Graham Burton, Ph.D., Co-founder and Director, Commercialization Science

Biography provided on page 32.

Vanessa Grant, Director, Chair of Governance and HR Committee

Ms. Grant is co-director of York University's Osgoode Hall Law School part-time LLM in business law (Master of Laws degree). She is a business law partner in the Toronto office of the firm of Norton Rose Fulbright Canada LLP, and has substantial expertise in corporate governance, capital markets, life sciences, and agriculture.

Paul Mesburis, Lead Director and Chair of Audit Committee

Mr. Mesburis is a CPA and CFA, with more than 20 years of international experience in financial and capital markets. On the buy-side, he has managed portfolios for investment strategies in both debt and equities. On the sell-side, his investment experience includes senior roles in mergers and acquisitions, investment banking, and institutional equity research at both global and domestic bank-owned investment dealers. In 2012, he was honored with a Canadian Lipper Fund Award, which recognizes funds that have excelled in delivering consistently strong risk-adjusted performance, relative to their peers. Mr. Mesburis is a director and chair of the Audit and Risk Committee of ProMetic Life Sciences Inc. and a director, Co-Chair of the Board, and chair of the Audit Committee of EESor Corp.

David Hankinson, Director, Member of Audit Committee

Mr. Hankinson brings more than 30 years of pharmaceutical industry experience to the organization. From 1991-99, he was President and CEO of Canadian operations for Solvay Pharma Inc. Prior to that Mr. Hankinson served as 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. From 1964-1980, Mr. Hankinson 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. Mr. Hankinson graduated as a Pharmaceutical Chemist (Ph.C.) from the College of Pharmacy at Dalhousie University, Halifax, Nova Scotia.

Intellectual Property

Avivagen holds a number of issued and pending patents that can be categorized into six different patent families. The Company's intellectual property (IP) provides it with protections as far out as 2036.

The patent families are listed below in order of oldest to most recently discovered/filed:

- (1) Enhancing weight gain and feed conversion;
- (2) Enhancing immunity to prevent or treat disease in animals;
- (3) Improving health of animals, including pets;
- (4) Compositions, uses, and methods for aquaculture;
- (5) Uses and methods to prevent livestock disease; and
- (6) Compositions, uses, and methods for further sources of Avivagen's compounds.

Within the above patent families, Avivagen holds an issued U.S. patent (# 8,211,461) for its compositions and methods for promoting weight gain and feed conversion, which has a corresponding internationally published patent application (# WO 2006/034570) filed under the Patent Cooperation Treaty (PCT). The PCT entails a unified procedure for simultaneously filing the same patent application in up to 151 countries. Under the PCT structure, a single international patent application is examined for its patentability, which includes a search of other published documents that might affect the patentability of the application, and is then published by the World Intellectual Property Organization (WIPO). The PCT process greatly facilitates filing patent applications in multiple jurisdictions worldwide; however, it does not grant an "international patent," which does not exist. Each country under the PCT must still review and choose to grant the patent on its own. Avivagen's U.S. patent # 8,211,461 has been granted to date by Argentina, Australia, Canada, Indonesia, Mexico, New Zealand, Russia, Singapore, South Africa, and South Korea, and is pending in Brazil, Chile, and Europe. Most all of the Company's IP has been filed globally in this manner.

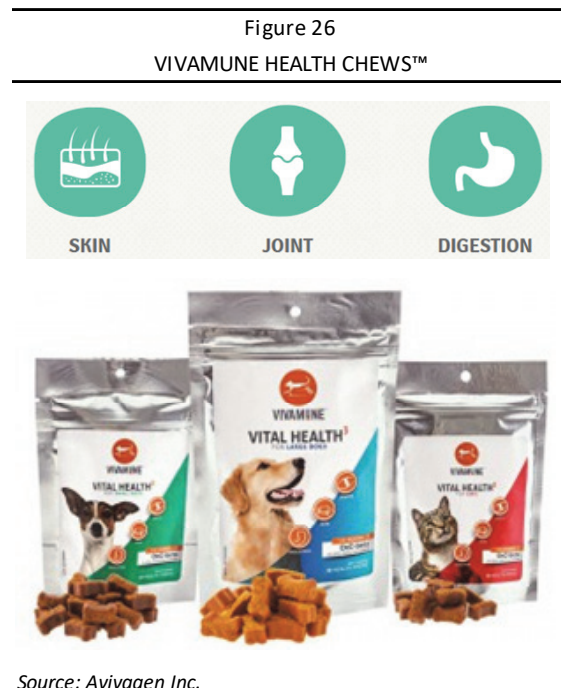
The Company also holds trademarks in multiple national jurisdictions on OxC-beta, Avivagen, and Oximunol.

Other Operating Units

Companion Animals

OxC-beta™ is also available for use in companion animals to help enhance their quality of life.

Vivamune Health Chews™
www.vivamunehealth.com



Source: Avivagen Inc.

OxC-beta™ is the active ingredient in Vivamune Health Chews™, which are intended to be a tasty daily treat (dietary supplement) for dogs. Vivamune is an all-in-one supplement to help improve pet health inside and out. Avivagen states pet owners should expect to see an improvement in the health of their pet's skin and coat as well as better digestive (gut) health and an increase in mobility and vitality due to healthier joint function. Vivamune can also help soothe itchy skin from seasonal allergies. Vivamune Health Chews™ are suitable for dogs older than six weeks of age, but are generally most useful for aging pets needing joint, gut, and overall health support.

As shown in Figure 26, Vivamune is sold as a soft chew in resealable foil packs of 30 or 60 chews. It may take up to four weeks of continued use before pet owners observe a change in their pets. Avivagen holds a quality seal from the National Animal Supplement Council (NASC) for Vivamune Health Chews™, indicating that these chews meet NASC guidelines for quality, integrity, and truth in labeling. Vivamune Health Chews™ are available for purchase directly from Avivagen at www.vivamunehealth.com. Vivamune was softly re-launched

as a single 10mg SKU for dogs in 2016. The product is safe for cats, however, is not currently being marketed for that application.

Oximunol™ Chewable Tablets
www.oximunol.com

As with Avivagen's other products, the Oximunol™ Chewable Tablets are built on the OxC-beta™ technology platform. Oximunol™ is a hard, chewable, beef-flavored tablet that serves as a daily dietary supplement for mature dogs. Oximunol™ promotes canine immune function to optimize health and quality of life for aging pets, including supporting healthier joint function and mobility, a healthy skin and coat, and normal intestinal function.

Oximunol™ can be purchased in the U.S. The product was formerly also available in Canada, though its sale has been temporarily suspended in Canada due to changes in Canadian animal health regulations in 2013. Canada's regulatory path for low-risk veterinary health products (LRVHP) is presently difficult and cumbersome for animal health product manufacturers due to safety and efficacy requirements that are often more stringent than similar natural health products for humans would have to endure. While regulators and producers work to sort-out how each product must conform to new laws, Oximunol™ Chewable Tablets are unavailable while Avivagen prepares an application for the product's return to the Canadian marketplace. The primary difference between the two product lines is in their format (tablet versus chew). The intention was to have one product line available only via veterinarians, while the other could be bought directly by consumers. Avivagen currently offers Vivamune in the U.S.

Formulation Options

Pending the outcome of further development and as resources allow, carotenoid oxidation products may ultimately be suitable for a number of different commercial applications, including the following: (1) an aid for maintaining general health using oxygen copolymer compounds derived from their natural plant sources; (2) a dietary supplement using 85% polymer concentration, such as OxC-beta™ currently does; or (3) a pharmaceutical drug using 95% to 99% polymer content and enhanced purity. The last of these routes would require considerable testing and development.

Chemaphor Chemical Services (A Division of Avivagen)

<http://chemaphor.com/>

Avivagen's management and team of chemists also operates Chemaphor Chemical Services, a synthetic chemistry business that sells deuterated vitamins (D and E), deuterated cholesterol, and other deuterated chemicals and chemistry products to universities and research centers. Chemaphor synthesizes deuterated compounds in-house with high purity and high deuterium enrichment, and also manufactures custom-made chemicals ready for shipping, including specialty, non-labelled small-molecule compounds as may be required for screening as drug candidates.

Chemaphor was founded as a spin-off from the National Research Council (NRC) of Canada, and now operates as a division of Avivagen. Avivagen's OxBC (Fully Oxidized β -carotene) is available for sale at quantities suitable for laboratory research through Chemaphor.

Historical Financial Results

Figures 27, 28, and 29 (pages 38-40) provide a summary of Avivagen's key historical financial statements: Audited Consolidated Interim Statement of Comprehensive Income, Financial Position, and Cash Flows, as presented in the Company's December 20, 2016, "audited annual financial statements" filing on the Canadian System for Electronic Document Analysis and Retrieval (SEDAR). As a note, Avivagen's fiscal year ends October 31st. As well, notes to the Audited Consolidated Financial Statements, as referenced in the accompanying Figures, can be founded at <http://www.avivagen.com/wp-content/uploads/Avivagen-FS-YE-2016-Oct-31-SEDAR.pdf>.

Avivagen reports that its monthly burn rate, excluding cash flow from sales, is approximately C\$250,000.

All financial tables are in Canadian dollars (C\$).

As of October 31, 2016, C\$1.00 ≈ US\$0.75.

As of October 31, 2015, C\$1.00 ≈ US\$0.76.

| Figure 27 Avivagen Inc. CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME For the years ending | | | |
|---|----------------|--------------------|--------------------|
| | Note | 31 October 2016 | 31 October 2015 |
| Revenue | | | |
| Chemistry Products | 3(c), 6 | \$ 150,634 | \$ 155,743 |
| OxC-beta Products | 3(c), 6 | 10,556 | 8,223 |
| Total Revenue | | \$ 161,190 | \$ 163,966 |
| | | | |
| Cost of OxC-beta products sold | 13 | 2,444 | 1,112 |
| Gross Margin | | 158,746 | 162,854 |
| | | | |
| Selling, general and administration | 20 | 1,938,868 | 1,594,813 |
| Research and development | 20 | 795,213 | 551,173 |
| Depreciation of equipment | 9 | 11,726 | 20,823 |
| Interest on long-term debt | 11 | 143,664 | - |
| Amortization of transaction costs on long-term debt | 11 | 21,773 | - |
| Total expenses | | 2,911,244 | 2,166,809 |
| Income (loss) before income taxes | | (2,752,498) | (2,003,955) |
| | | | |
| Income Taxes | | | |
| Current and deferred income tax expense | 3(d), 7 | - | - |
| Total comprehensive income (loss) for the period | | (2,752,498) | (2,003,955) |
| | | | |
| Profit (loss) per Share, Basic and Diluted | 8 | \$ (0.012) | \$ (0.010) |
| | | | |
| Weighted Average Common Shares Issued and Outstanding Basic and Diluted | 8 | 223,574,408 | 193,419,351 |

Source: Avivagen Inc.

Figure 28
Avivagen Inc.
CONSOLIDATED STATEMENTS OF FINANCIAL POSITION
As at

| | Note | October 31, 2016 | October 31, 2015 |
|--|------|---------------------|---------------------|
| Assets | | | |
| Current Assets | | | |
| Cash and cash equivalents | | 5,142,401 | 632,247 |
| Trade and other accounts receivable | 14 | 40,732 | 37,482 |
| Prepaid expenses | 15 | 10,562 | 10,255 |
| Inventories | 13 | 2,500 | 1,000 |
| Total Current Assets | | 5,196,195 | 680,984 |
| Non-current Assets | | | |
| Laboratory equipment | 9 | - | 11,726 |
| Total Non-current Assets | | - | 11,726 |
| Total Assets | | 5,196,195 | 692,710 |
| Liabilities and Shareholders' Equity (Deficiency) | | | |
| Current Liabilities | | | |
| Accounts payables and accrued liabilities | 19 | 480,271 | 279,209 |
| Research and development repayable funding | 10 | 1,055 | 822 |
| Long-term debt | 11 | 147,129 | - |
| Total Current Liabilities | | 628,455 | 280,031 |
| Non-current Liabilities | | | |
| Research and development repayable funding | 10 | 3,369,518 | 3,323,582 |
| Long-term debt | 11 | 797,694 | (85,839) |
| Total Non-current Liabilities | | 4,167,212 | 3,237,743 |
| Total Liabilities | | 4,795,667 | 3,517,774 |
| Shareholders' Equity (Deficiency) | | | |
| Share Capital | 16.1 | 18,119,041 | 12,675,922 |
| Contributed surplus | 17 | 2,995,099 | 2,842,013 |
| Accumulated deficit | | (20,713,612) | (18,342,999) |
| Total Shareholders' Equity (Deficiency) | | 400,528 | (2,825,064) |
| Total Liabilities and Shareholders' Equity (Deficiency) | | 5,196,195 | 692,710 |

Source: Avivagen Inc.

Figure 29
Avivagen Inc.
CONSOLIDATED STATEMENTS OF CASH FLOWS
For the years ending

| | Note | 31 October 2016 | 31 October 2015 |
|---|--------|---------------------|---------------------|
| Cash Flows from Operating Activities | | | |
| Profit (loss) for period | | \$ (2,752,498) | \$ (2,003,955) |
| Items not affecting cash | | | |
| Share-based compensation | 18 | \$ 194,781 | \$ 166,553 |
| Depreciation of equipment | 9 | \$ 11,726 | \$ 20,823 |
| Changes in non-cash operating working capital items | | | |
| Trade and other accounts receivable | | \$ (3,250) | \$ 11,559 |
| Prepaid expenses | | \$ (307) | \$ (10,255) |
| Inventories | | \$ (1,500) | \$ 17,263 |
| Accounts payable and accrued liabilities | | \$ 201,062 | \$ 135,177 |
| Non-cash debt for equity transaction | | \$ - | \$ 21,000 |
| Total Cash Flows used in Operations - before interest accrued | | (2,349,986) | (1,641,835) |
| Interest accrued and amortization of transaction fees on long-term debt | 11 | 165,437 | - |
| Cash Flows used in Operating Activities | | (2,184,549) | (1,641,835) |
| Cash Flows from Investing Activities | | | |
| | | - | - |
| Cash Flows from Financing Activities | | | |
| Proceeds from research and development repayable funding | 10 | \$ 47,051 | \$ 221,640 |
| Repayment of research and development repayable funding | 10 | \$ (882) | \$ (13,884) |
| Proceeds from issuance of private placement units | 16 | \$ 3,600,000 | \$ 1,500,000 |
| Share issuance cost | 16 | \$ (409,283) | \$ (116,629) |
| Proceeds from long-term debt | 11 | \$ 866,477 | \$ (85,839) |
| Proceeds from the exercise of share purchase warrants | 16, 17 | \$ 2,449,701 | \$ - |
| Proceeds from the exercise of stock options | 16 | \$ 21,300 | \$ - |
| Proceeds from warrants issued with long-term debt | 11 | \$ 133,523 | \$ - |
| Transaction fees on long-term debt | 11 | \$ (1,252) | \$ - |
| Transaction fees on warrants issued with long-term debt | 11 | \$ (11,932) | \$ - |
| Cash Flows from Financing Activities | | 6,694,703 | 1,505,288 |
| Increase (decrease) in cash during the period | | \$ 4,510,154 | \$ (136,547) |
| Cash and cash equivalents, beginning of period | | \$ 632,247 | \$ 768,794 |
| Cash and cash equivalents, end of period | | 5,142,401 | 632,247 |

Source: Avivagen Inc.

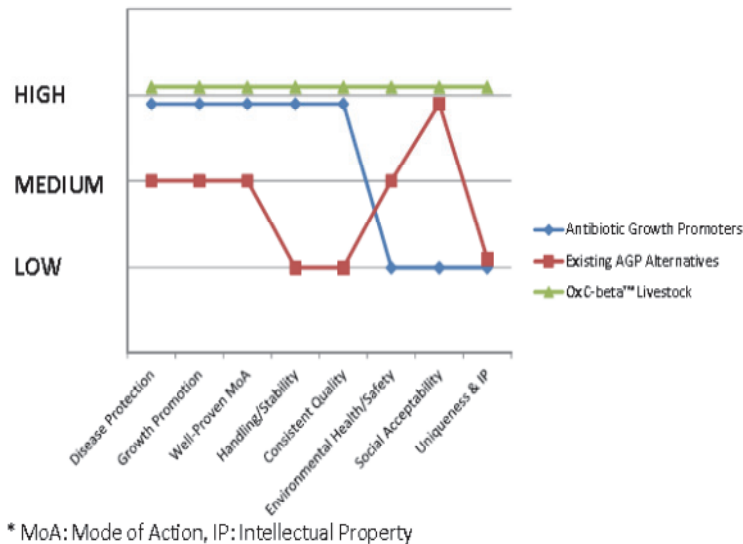
Competition

To Avivagen’s knowledge, the copolymer compounds in the OxC-beta™ technology are not currently being used in any other type of animal health supplement or feed additives. The presence and activity of these compounds are a proprietary discovery by the Company. Although analogous copolymer compounds exist naturally in carotenoid-rich foods, their levels vary widely and they are generally found at concentrations well-below what would be required to see health benefits. The technologies listed on the accompanying pages are not intended to be an exhaustive collection of potential competitors to Avivagen; however, they are believed to be representative of the type of competition the Company may encounter as it seeks to further commercialize its products in agricultural, human health, and veterinary markets, particularly from existing and future alternatives to antibiotic growth promoters (AGPs) used in livestock feed. As represented below, there do exist alternatives to antibiotics in animal feed, but industry experience with such products to date has been hit-or-miss. Some limitations are inconsistent dosages, varied production processes, and non-standardized potency, leading to the perception of such products as just a cocktail of probiotics, pre-biotics, and vitamins with little data to show which products are worth the investment.

Avivagen believes it holds significant competitive advantages in this space, from its data-driven approach to product development to its favorable product characteristics (cross-species efficacy, good handling characteristics and suitability for numerous types of feed, and effectiveness at very low parts-per-million [ppm] levels in feed). Figure 30 summarizes the Company’s potential advantages versus AGPs and existing alternatives to AGPs.

Figure 30

OXC-BETA™ COMPETITIVE ADVANTAGES VERSUS ANTIBIOTIC GROWTH PROMOTERS (AGPs) AND OTHER NON-ANTIBIOTIC DIETARY SUPPLEMENTS



Source: Avivagen Inc.

Alternatives to Antibiotics in Livestock

Below are five examples of alternative products that emphasize disease prevention that may be considered competitive to the technology being developed by Avivagen. Each of these technologies work in different ways (various modes of action) in order to prevent the proliferation of harmful bacteria, to promote health and immune status, and to enhance animal performance. This list is not intended to be comprehensive; however, it offers an overview of some other approaches that are being commercially used.

- **Immune modulators** stimulate the immune system to enhance its overall functioning, making them effective against a broad range of pathogens. For example, the FDA recently granted approval for an immune modulator to reduce infection in dairy cows.
- **Phages** are viruses that infect and kill bacteria, and can be used in a highly targeted way against specific bacterial strains. The FDA has approved use of these products as antimicrobial agents against foodborne pathogens on meat, with other uses currently being developed, for instance, to prevent udder infections in dairy cows.
- **Phytochemicals** are plant-derived compounds, including essential oils, that may have antibacterial and growth-promoting effects. Major chicken production companies use herbs such as oregano and thyme to keep their animals healthy.
- **Probiotics** are live bacterial cultures from microorganisms, such as yeast, fungi, and bacteria, which are added to an animal's diet to improve the balance of microorganisms. This may help to control "bad" bacteria and, at the same time, make a favorable environment within the gut. These cultures can effectively prevent disease in multiple food animal species. As well, probiotics can promote growth in all major food animal species as well.
- **Vaccines** are widely used in veterinary medicine to prevent diseases caused by viruses or certain bacteria, and can also have additional benefit such as enhancing animal productivity. Vaccines are among the most promising alternative approaches to control a host of respiratory and digestive diseases, as well as a number of other health problems.

Sustainable reductions in antibiotic use will depend on research that develops alternatives that are efficient, safe, and cost-effective and that can be incorporated into comprehensive herd or flock health management programs. Avivagen's laboratory, clinical and field trial research programs demonstrate that the Company's scientific platform and resulting products possess these key attributes that producers are seeking in antibiotic alternatives. Its technology has the potential to be adopted worldwide by veterinarians, ranchers, farmers, and animal nutritionists who are seeking viable alternatives to antibiotics for enhancing productivity and reducing disease.

A number of companies offer alternatives to antibiotics, principally in the categories that have been cited. Such companies include the disease-specific vaccines of the major animal healthcare companies such as Elanco, Merck, Merial, Zoetis, etc. For in-feed products, there are companies offering supplements, such as Alltech, Archer Daniels, Biomin, Chr. Hansen, Diamond V, DSM, Lohmann, Kemin, Novus, Nutreco, Olmix, Provimi/Cargill and others. Each have different offerings, but to the Company's knowledge, none are based on any knowledge of carotenoid oxygen copolymers.

Risks and Disclosures

This Executive Informational Overview® (EIO) has been prepared by Avivagen Inc. (“Avivagen” or “the Company”) with the assistance of Crystal Research Associates, LLC (“CRA”) based upon information provided by the Company. CRA has not independently verified such information. Some of the information in this EIO relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in Avivagen’s statements on its financial and other reports filed to the Canadian System for Electronic Document Analysis and Retrieval (SEDAR), as well as other forms filed from time to time.

The content of this report with respect to Avivagen has been compiled primarily from information available to the public released by the Company through news releases, Annual Reports, and SEDAR filings. Avivagen is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by Avivagen or CRA. Certain summaries of activities and outcomes have been condensed to aid the reader in gaining a general understanding. CRA assumes no responsibility to update the information contained in this report. In addition, CRA has been compensated by the Company in cash of forty thousand dollars for its services in creating this report and for updates.

Investors should carefully consider the risks and information about Avivagen’s business, as presented in the Company’s Annual Information Form (AIF) filed to SEDAR. Investors should not interpret the order in which considerations are presented in this or other filings as an indication of their relative importance. In addition, the risks and uncertainties overviewed herein are not the only risks that the Company faces. Additional risks and uncertainties not presently known to Avivagen or that it currently believes to be immaterial may also adversely affect the Company’s business. If any of such risks and uncertainties develops into an actual event, Avivagen’s business, financial condition, and results of operations could be materially and adversely affected, and the trading price of the Company’s shares could decline.

This report is published solely for information purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state. Past performance does not guarantee future performance. Additional information about Avivagen and its public filings, as well as copies of this report, can be obtained in either a paper or electronic format by calling (613) 949-8164.

Going Concern

Avivagen’s ability to continue as a going concern and to realize the carrying value of its assets and discharge its liabilities when due is dependent upon its ability to obtain the ongoing support of its lenders, investors, obtain profitable operations, and/or raise additional capital. The unaudited consolidated interim financial statements presented on pages 38-40 do not include any adjustments to the carrying value and classification of assets and liabilities that would be necessary should Avivagen be unable to continue as a going concern, and such adjustments could be material. The Company has not attained profitable operation to date. The accumulated deficit to date is C\$20,713,612 as of October 31, 2016 (October 31, 2015: \$18,342,999). If Avivagen was not a going concern, possible adjustments could include the reclassification of the research and development repayable funding and long-term debt from non-current to current, a possible impairment of inventory, and a restriction on use of all assets in favor of the outstanding priority creditor, Bloom Burton Healthcare Lending Trust.

Avivagen’s continuance as a going concern is dependent upon its ability to obtain additional equity and/or debt financing in the near term and/or to reach profitable levels of operation. It is not possible to predict whether financing efforts will be successful or if Avivagen will attain profitable levels of operation. In the absence of raising additional funds, there is substantial doubt regarding Avivagen’s ability to continue as a going concern.

The Company may need to raise additional capital.

The need for capital may require the Company to do the following:

- engage in equity financings that could result in significant dilution to existing investors;
- delay or reduce the scope of or eliminate one or more development programs;
- obtain funds through arrangements with collaborators or others that may require the Company to relinquish rights to technologies, product candidates, or products that the Company would otherwise seek to develop or commercialize; or license rights to technologies, product candidates, or products on terms that are less favorable than might otherwise be available;
- considerably reduce operations; or
- cease operations.

The Company may be unable to maintain or obtain partnerships for one or more of its product candidates, which could curtail future development and negatively affect its share price.

The Company's strategy for the research, development, and commercialization of its products may require it to enter into arrangements with corporate collaborators, licensors, licensees, and others. Commercial success is dependent upon these outside parties performing their contractual responsibilities. The amount and timing of resources that these outside parties will devote to these activities may not be within the Company's control. The Company cannot assure shareholders that such parties will perform any of their obligations as expected. The Company also cannot assure shareholders that its current or future collaborators will devote adequate resources to the Company's programs. There is a risk that the Company could become involved in disputes with its collaborators, which could result in a delay or termination of the related development programs. Such disputes could also result in litigation. The Company intends to seek additional collaborative arrangements to develop and commercialize some of its products. The Company may not be able to negotiate collaborative arrangements on favorable terms, or at all, in the future, and it cannot assure shareholders that its current or future collaborative arrangements will be successful. If the Company cannot negotiate collaboration, license, or partnering agreements, it may not achieve profitability and may not be able to continue to develop its product candidates.

The success of the business depends on regulatory approvals.

The animal healthcare field is subject to laws and regulations in every country and that may differ from country to country. Compliance with such laws and regulations can require significant expenditures that may constrain the Company's ability to operate in the applicable jurisdiction. Likewise, a breach of legal or regulatory obligations could lead to suspension or revocation of the right to sell in a country or other penalties, any of which will significantly and negatively impact the Company's position and competitiveness. The Company's research, development, production, and sales depend on regulatory approval of governing bodies for each geographic area in which its products are to be marketed, distributed, or sold. Revocation or denial of regulatory approval will prevent the sale, distribution, and marketing of products in an area.

Only two of its products, Oximunol™ Chewables and Vivamune™ Health Chews, are available for commercial use and sale in North America. The Company's ability to generate revenue is dependent on the successful approval and marketing of OxC-beta™ in livestock. Regulatory approval for additives to feed animals intended for human consumption is a lengthy and uncertain process (see "Regulatory Process"). Further, approval in one country does not assure approval in another country. In general, research and development and clinical studies are required to demonstrate the safety and effectiveness of products before the Company can submit any regulatory applications for approval.

The success of Company-sponsored and customer-sponsored product trials.

In addition, trials of any product candidates could be unsuccessful, which would prevent the Company from advancing, commercializing, or selling its products. Even if the results of trials are initially positive, it is possible that the Company will obtain different results in the later stages of product development or that results seen in trials will not continue. The Company cannot assure shareholders that its trials will generate positive results and it similarly cannot assure shareholders that the results will allow it to move towards the commercial use and sale of its products in livestock. Furthermore, negative trial results may cause its business, financial condition, or results of operations to be materially adversely affected. Preparing, submitting and advancing applications for regulatory approval is complex and expensive. It entails significant uncertainty. A commitment of substantial resources to conduct research and trials will be required if the Company is to complete development of its products for use in livestock. The Company's failure to develop safe, commercially viable products would substantially impair or even altogether negate its ability to generate revenues and sustain its operations. Such a failure would materially harm its business and adversely affect its share price.

The Company may not achieve its projected development goals in the time frames the Company announces and expects.

The Company has set goals for and makes public statements regarding the expected timing of the accomplishment of objectives material to its success, such as the commencement and completion of trials, the partnership of its products, and its ability to secure the financing necessary to continue the development of its products. The actual timing of these events can vary dramatically due to factors such as delays or failures in its trials, the uncertainties inherent in the regulatory approval process, market conditions, and interest by partners in its products, among other things. The Company cannot assure shareholders that its trials will be completed, that it will make regulatory submissions or receive regulatory approvals as planned, or that it will secure partnerships for any of its products. Any failure to achieve one or more of these milestones as planned would have a material adverse effect on its business, financial condition, and results of operations.

If the Company fails to attract and retain key employees, the development and commercialization of its products may be adversely affected.

The Company depends on the key members of its scientific and management staff. If the Company loses any of these people, its ability to develop products and become profitable could suffer. The risk of being unable to retain key personnel may be increased because the Company has not executed long-term employment contracts with its employees, except for with its senior executives. The Company's future success will also depend in large part on its ability to attract and retain other highly qualified scientific and management personnel. The Company faces competition for personnel from other companies, academic institutions, government entities, and other organizations.

The Company may be unable to obtain or enforce patents to protect its technologies from other companies with competitive products, and patents of other companies could prevent it from manufacturing, developing, or marketing its products.*Patent Protection*

The patent positions of biotechnology companies are uncertain and involve complex legal and factual questions. There is no consistent policy regarding the breadth of claims set by the U.S. Patent and Trademark Office (nor by many other patent offices in the world) when it comes to companion animal and livestock patents. Allowable and patentable subject matter may differ between jurisdictions, as might the scope of patent protection obtainable. If a patent office allows broad claims, the number and cost of patent interference proceedings in the jurisdiction of the office may increase. The risk of infringement litigation may then increase for the same reason. If a jurisdiction narrows the claims allowed, the risk of infringement may decrease, but the value of the Company's rights under its patents, licenses, and patent applications may also decrease. The scope of the claims in a patent application can be significantly modified during prosecution before the patent is issued. As a result, the Company cannot know whether its pending applications will result in the issuance of patents or, if any patents are issued, whether they

will provide it with significant proprietary protection; they could be circumvented, invalidated, or found to be unenforceable.

Publication of discoveries in scientific or patent literature can often lag behind actual discoveries. As a result, patent applications filed in the U.S. generally will be published 18 months after the filing date unless the applicant certifies that the invention will not be the subject of a foreign patent application. In many other jurisdictions, such as Canada, patent applications are published 18 months from the priority date. The Company cannot assure shareholders that, even if published, the Company will be aware of all such literature. Accordingly, the Company cannot be certain that the named inventors of its products and processes were the first to invent that product or process or that the Company was the first to pursue patent coverage for its inventions.

Enforcement of Intellectual Property Rights

It can be complex and costly to protect the rights revealed in published patent applications. The Company's commercial success depends, in part, on its ability to maintain and enforce its proprietary rights, but outcomes here can be uncertain. If third parties engage in activities that infringe the Company's proprietary rights, management's focus will be diverted and the Company may incur significant costs in asserting its rights. The Company may not be successful in asserting its proprietary rights, which could result in its patents being held invalid or a court holding that the third party is not infringing—either of which would harm its competitive position. Others organizations may design around the Company's patented technology. The Company may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, European opposition proceedings, or other analogous proceedings in other parts of the world. These proceedings to determine priority of invention and the validity of patent rights granted or applied for could result in substantial cost and delay, even if the eventual outcome is favorable to the Company. The Company cannot assure shareholders that its pending patent applications, if issued, would be held valid or enforceable.

Trade Secrets

The Company also relies on trade secrets and know-how, as well as confidentiality provisions in its agreements with its collaborators, employees, and consultants to protect its intellectual property. However, the Company's counterparties may not comply with the terms of their agreements and the Company might be unable to adequately enforce its rights against these people or obtain adequate compensation for the damages caused by their unauthorized disclosure or use of trade secrets or know how. The Company's trade secrets or those of its collaborators may become known or may be independently discovered by others.

The Company is dependent on sole suppliers for its raw materials and finished goods.

Any disruption to the activities of such suppliers would adversely affect it. Due to the small volumes of active ingredients and finished goods that the Company currently orders, each of its products (OxC-beta™ active and premix, Oximunol™, and Vivamune™) are produced at a single site. Any disruption in its short-term supply for whatever reason will have a negative impact on its financial condition and results of operations. The Company outsources the production and distribution of its OxC-beta™-based products. If a labor disruption occurs at the production or distribution site, sales of its products would be adversely impacted and would have a negative impact on its financial condition and its operational results.

The Company is currently dependent on one technology.

The Company's main technology is related to fully oxidized carotenoids, which is incorporated in its three products. The failure of any of its products to achieve market penetration will have a negative impact on its financial condition and results of operations.

The Company's products and product candidates may infringe the intellectual property rights of others, or others may infringe on its intellectual property rights which could increase its costs.

The Company's success also depends on avoiding infringement of the proprietary technologies of others. In particular, there may be certain issued patents and patent applications claiming subject matter which the Company or its collaborators may be required to license in order to research, develop, or commercialize its product candidates. In addition, based on patents or other intellectual property rights, third parties may assert infringement or other intellectual property claims against the Company. An adverse outcome in these proceedings could subject Avivagen to significant liabilities to third parties, require disputed rights to be licensed from third-parties, or require it to cease or modify its use of the technology. The Company cannot assure shareholders that in the event that the Company is required to license a technology, a license under such patents and patent applications will be available on acceptable terms or at all. Further, the Company may incur substantial costs defending itself in lawsuits against charges of patent infringement or other unlawful use of another's proprietary technology. The Company may also need to bring claims against others who the Company believes are infringing its rights in order to become or remain competitive and successful.

If product liability claims are brought against the Company or it is unable to obtain or maintain product liability insurance, the Company may incur substantial liabilities that could reduce its financial resources.

The commercial use of products in companion animals and livestock involves significant exposure to product liability claims. The Company has obtained limited product liability insurance coverage; however, its insurance coverage may be insufficient to protect it against all product liability damages. Regardless of merit or eventual outcome, liability claims may result in decreased demand for a future product, injury to reputation, loss of revenue, costs of litigation, distraction of management, and substantial monetary awards to plaintiffs. Additionally, the Company may not have sufficient financial resources to complete development or commercialization of any of its products if the Company is required to pay a product liability claim, and its business and results of operations may be adversely affected as a result. Furthermore, insurance will not protect it against some of its own actions such as negligence.

The Company may be the subject of litigation.

From time to time, the Company may be the subject of litigation. Damages claimed under such litigation may be material or may be indeterminate. The outcome of such litigation may materially impact Avivagen's financial condition or results of operations. While the Company assesses the merits of each lawsuit and defends itself accordingly, it may be required to incur significant expenses or devote significant resources to defend against litigation. Third parties may own patents relating to competing product formulations. Liability for damages may arise from potential claims by these companies that the Company has infringed their proprietary technology and may delay the development and commercialization of Avivagen's products. Competitors in the animal healthcare industry could make such claims against the Company for strategic purposes. Defending patent litigation is time-consuming and costly and will negatively impact Avivagen's financial condition and results of operations.

The Company's major markets are outside of Canada and may expose it to political and legal risk.

The Company believes that its business opportunities lie primarily outside of Canada, including in the rest of North America, Asia, and South America. Operating in foreign countries provides further market opportunities but also exposes the Company to political risks, country risks, and currency risks in many forms. The forms of these risks can include tariff and non-tariff trade barriers, potential confiscation of goods or capital, and revolution, both violent and non-violent. Any political or legal disruption in its major markets will negatively impact its financial condition and results of operations.

The Company's competitors may be better capitalized and have more attractive product offerings than the Company does.

The Company competes with both large and small companies offering supplements that purport to help to maintain the health of companion and livestock animals. Such companies offer products that compete with the Company's and could be found preferable by customers due to their technical merits, by way of superior marketing resources or skills, or for other reasons. In addition, competitors may be better capitalized than the Company. The Company cannot assure shareholders that it will succeed in the face of such competition and its financial condition and results of operations will be significantly negatively impacted.

The Company's share price has been and may continue to be volatile and an investment in its common shares could suffer a decline in value.

A potential investor should consider an investment in the Company's common shares as risky. A potential investor should invest only if he or she can withstand a significant loss and wide fluctuations in the market value of the investment. Securities analysts pay only limited attention to the Company and the Company frequently experiences an imbalance between supply and demand for its common shares. The market price of its common shares has been highly volatile and may continue to be volatile. This leads to a heightened risk of securities litigation pertaining to such volatility.

Factors affecting its common share price include but are not limited to the following:

- its financial position and doubt as to whether the Company will be able to continue as a going concern;
- its ability to raise additional capital;
- the progress of its trials;
- its ability to maintain or obtain partnerships and collaborators to assist with the future development of its products;
- general market conditions;
- announcements of technological innovations or new product candidates by the Company, its collaborators, or its competitors;
- published reports by securities analysts;
- developments in patent or other intellectual property rights;
- the cash and short-term investments held the Company and its ability to secure future financing;
- public concern as to the safety and efficacy of products that the Company and its competitors develop; and
- the level of shareholder interest in the Company's common shares.

Future sales of common shares by the Company or by its existing shareholders could cause its share price to fall.

The issuance of common shares by the Company could result in significant dilution in the equity interest of existing shareholders and adversely affect the market price of its common shares. Sales by existing shareholders of a large number of its common shares in the public market and the issuance of shares issued in connection with strategic alliances, or the perception that such additional sales could occur, could cause the market price of its common shares to decline and have an undesirable impact on its ability to raise capital.

The Company is susceptible to stress in the global economy and therefore, its business may be affected by current and future global financial conditions.

The Company's operations, business, financial condition, and the trading price of its common shares could be materially adversely affected by the continuance of the high levels of volatility and market turmoil that have marked recent years. Furthermore, general economic conditions may have a great impact on the Company, including its ability to raise capital, its commercialization opportunities, and its ability to establish and maintain arrangements with others for research, manufacturing, product development, and sales.

There is no assurance that an active trading market in the Company's common shares will be sustained.

The Company's common shares are listed for trading on the TSX Venture Exchange. The Company cannot assure shareholders that an active trading market in its common shares on the stock exchange will be sustained or that the Company will be able to maintain its listing.

Key Points

- Avivagen Inc. (“Avivagen” or “the Company”) is a life sciences company developing products to replace the use of antibiotics in livestock feed, product candidates that may aid human health and wellness, and products to help companion animals (pets) achieve and maintain optimal health.
- Given that 80% of all antibiotics sold in the U.S. are for use in poultry and livestock for purposes that are not always related to treatment of disease, there is an unmet need to develop and commercialize products that can replace antibiotics in livestock feeds, as doing so could provide health and economic benefits to food producers and have a dramatic effect at curbing the rise of deadly, antibiotic-resistant bacteria strains.
- Avivagen believes its proprietary, non-antibiotic, hormone-free OxC-beta™ technology holds the key to balancing the food production industry’s need for the benefits of antibiotics with society’s need to preserve antibiotics for only medically necessary uses.
- Avivagen, the National Research Council of Canada, and other funding and research partners have invested over two decades and roughly \$30 million into extensive studies of OxC-beta™, ultimately finding that the improvement in animal health using OxC-beta™ is comparable to what occurs using antibiotics. The Company’s scientific studies have been published in four peer-reviewed journals: the *Canadian Journal of Chemistry*, *PLOS ONE*, the *American Journal of Veterinary Research*, and the *Journal of Agricultural and Food Chemistry*.
 - The biological effects of OxC-beta™ at stimulating the immune system are host-mediated, meaning there are no direct antibacterial effects and thus zero likelihood of creating antibiotic-resistant pathogens.
- OxC-beta™ Livestock is cleared for sale in the Philippines, where commercial sales started during 2016, Thailand, and Taiwan. Avivagen is also pursuing product registration and distribution agreements in other countries, including a joint venture recently established in China—the world’s top market for livestock feed.
- In April 2016, Avivagen authored a peer-reviewed article published in the *Journal of Agricultural and Food Chemistry* detailing a discovery that the bioactive component of OxC-beta™ occurs naturally in human foodstuffs. These findings are helping drive the Company’s human health platform, and are expected to favorably impact the ability of Avivagen to gain regulatory acceptance for its OxC-beta™ technology in humans given the inherent safety of its primary ingredient. New patent applications also stem from this discovery.
- The global animal feed additives market is projected to cross \$37 billion by early 2022 from \$28.6 billion in 2016, growing at a CAGR of over 5.3% over the forecast period.
- The rise of drug-resistant bacterial superbugs has been a concern of public health officials for years. In a worst case scenario case, the U.S. CDC reported in January 2017 that a woman with a bacterial infection that was resistant to all FDA-approved treatments had died after being infected with a drug-resistant bacterium, *Klebsiella pneumoniae*, that was resistant to all antibiotics available in the U.S.
- On January 3, 2017, the FDA announced that it had completed the implementation of Guidance for Industry #213 to transition antimicrobial drugs with importance in human medicine (medically important antimicrobials) that are used in the feed or drinking water of food-producing animals to veterinary oversight and eliminate the use of these products in animals for production (e.g., growth promotion) purposes. With these FDA Guidelines, some farmers, ranchers, veterinarians, and others may face challenges as they adjust to these changes, which is what Avivagen’s product has been developed to address.
- The Company is led by a skilled executive management team that combines scientific expertise (chemists, veterinary scientists, and biomedical researchers) with business acumen from the life sciences, pharmaceutical distribution, and corporate finance worlds.

- Avivagen's intellectual property encompasses six patent families, with protections globally as far out as 2036.
- At January 31, 2017 (Avivagen's Q1), Avivagen held cash and cash equivalents of over C\$5.4 million, up from C\$5.1 million on October 31, 2016. At October 31, 2016 (Avivagen's fiscal year end), the Company held cash and cash equivalents of over C\$5.1 million, up from C\$632,247 on October 31, 2015. The increase in cash is primarily due to raising C\$6,694,703 in financing activities during the year, which were offset by C\$2,752,498 in operating losses.

Glossary

Antibiotic Growth Promoters (AGPs)—Also known as ‘growth promotants’, these substances, as the name indicates, are antibiotics that are used in feed continuously at a low level to improve growth and feed conversion.

Antibiotic Resistance—Happens when microorganisms (such as bacteria, fungi, viruses, and parasites) change when they are exposed to antimicrobial drugs (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics). Microorganisms that develop antimicrobial resistance are sometimes referred to as “superbugs.” As a result, the medicines become ineffective and infections persist in the body, increasing the risk of spread to others.

Antimicrobial Resistance (AMR)—See *antibiotic resistance*.

Aquaculture—The rearing of aquatic animals or the cultivation of aquatic plants for food.

Bovine Respiratory Disease Complex (BRDC)—A general term for respiratory disease in cattle caused by a range of factors, singly or in combination. A major cause of economic losses, BRD affects the lower respiratory tract/lungs (pneumonia) or upper respiratory tract (rhinitis, tracheitis, bronchitis).

Broiler Poultry—Chickens bred and raised specifically for meat production, as opposed to “layers,” which are chickens bred and raised specifically to lay eggs.

Carotenoids—Any of a group of red and yellow pigments, chemically similar to carotene, found in plants and in some animal fats. They give color to plants, fruits, and vegetables, such as ripe tomatoes and autumn leaves.

CD14 (Cluster of Differentiation 14)—A human gene that encodes proteins that are a key component of the innate immune system.

Dairy Ruminants—Cows raised mainly for their milk, especially cows of a dairy breed.

Deuterated—To introduce deuterium into (a chemical compound) and/or molecules where the ordinary isotope of hydrogen has been replaced with deuterium.

Enterotoxigenic *E. coli* (ETEC)—A type of *Escherichia coli* and one of the leading bacterial causes of diarrhea in the developing world, as well as the most common cause of travelers’ diarrhea.

Heifer—a young female cow that has not borne a calf.

Lycopene—A red carotenoid pigment present in tomatoes and many berries and fruits.

Methicillin-Resistant *Staphylococcus Aureus* (MRSA)—A bacterium responsible for several difficult-to-treat infections in humans.

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