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With Restructuring Completed in January 2011, the New Coronado Biosciences, Inc. is an Immunotherapy Company with One Product Focused on Autoimmune Diseases and the Other Product Focused on Immunotherapy for Cancer

Healthcare  
Biotechnology  
(CNDO-NASDAQ)

Coronado Biosciences, Inc.

15 New England Executive Park  
Burlington, MA 01803  
Phone: 781-238-6621



**Dr. Bobby W. Sandage Jr., Ph.D.**  
President, CEO and Director

**BIO:**

Dr. Sandage has served as our president and chief executive officer since April 2011 and has over 30 years of experience in the pharmaceutical industry, most recently as the vice president and head of oncology research and development for Covidien Pharmaceuticals, a specialty pharmaceuticals company, a position he held from March 2010 until March 2011. From November 1991 to December 2009, Dr. Sandage held various positions at Indevus Pharmaceuticals, a specialty pharmaceuticals company,

including executive vice president of research and development and chief scientific officer, prior to the sale of the company to Endo Pharmaceuticals. Prior to joining Indevus Pharmaceuticals, from 1981 to 1991, Dr. Sandage held senior drug development positions at DuPont Merck Pharmaceutical Company, DuPont Critical Care (formerly American Critical Care) and Merrell Dow Pharmaceuticals. Dr. Sandage is currently a member of the board of directors of Gentium S.p.A., a pharmaceutical company. Dr. Sandage has also served as a member of the board of directors of Osteologix, Inc. and Genta Incorporated. Dr. Sandage has a B.S. in pharmacy from the University of Arkansas and a Ph.D. in clinical pharmacy from Purdue University.

**Company Profile:**

Coronado Biosciences, Inc. is engaged in the development of novel immunotherapy biologic agents. The Company's two principal pharmaceutical product candidates in clinical development are: CNDO-201, a biologic for the treatment of autoimmune diseases, such as Crohn's disease, ulcerative colitis and multiple sclerosis; and CNDO-109, a biologic that activates natural killer (NK) cells, for the treatment of acute myeloid leukemia (AML) and solid tumors. For more information, please visit [www.coronadobiosciences.com](http://www.coronadobiosciences.com).

**Interview conducted by:**  
**Bud Wayne, Editorial Executive**  
**CEOCFO Magazine.com**

**CEOCFO:** Dr. Sandage, would you give us a brief history of Coronado Biosciences, and the vision for the company?

**Dr. Sandage:** Coronado as it exists today is actually a combination of two different companies. Originally Coronado was formed as an oncology company with several compounds. Data from the NK (natural killer cells) program continued to get more interesting. This prompted the founder of the company, Dr. Lindsay Rosenwald to focus on the NK program. He had another company called Asphelia that focused on the treatment of autoimmune diseases again with several products in that company but TSO, their lead product, was the best by far. In late 2010, he decided to combine the companies and focus on immunotherapy, modulating the immune system with TSO and using the innate immune system with NK cells to treat cancer. The combining of the two companies was completed in January of 2011. The new Coronado is an immunotherapy company with one product focused on the treatment of autoimmune diseases and the other product focused on immunotherapy of cancer.

**CEOCFO:** Did these products come from the same technology?

**Dr. Sandage:** No. TSO was a discovery from the University of Iowa by Drs. Joel Weinstock, Elliott and Summers. It was originally licensed to a company in Germany called OvaMed. Coronado then licensed the rights for the use of TSO for all indications for North America, South America and Japan from OvaMed. The NK program comes out of the University College of London, where professor Dr. Mark Lowdell, the inventor is located. It was licensed directly from the University.

**CEOCFO:** Does Coronado Biosciences own both of these 100% right now?

**Dr. Sandage:** As I mentioned we have licensed worldwide rights for all indications from the University College of London, for which we owe a single digit royalty on net sales. Again as I mentioned, TSO is licensed from OvaMed, who has the original license from the University of Iowa. We have the rights for all indications in just for North America, South America, and Japan. We pay OvaMed a royalty of 4% of net sales and they in turn pay the University of Iowa 4%. We purchase TSO from OvaMed, our exclusive manufacturer. In addition, OvaMed has a partner in Europe. Their partner in Europe, the Dr. Falk Pharma company licensed just the gastrointestinal indications. I am not sure of the details of their business arrangement. However, I would like to point out that we just signed a three-way agreement with OvaMed and the Dr. Falk Pharma company. Coronado, Dr. Falk Pharma and OvaMed have agreed to enter into a Collaboration Agreement under which Falk will grant Coronado exclusive rights and licenses under certain Falk patent rights, pre-clinical data and clinical data from Falk's clinical trials of TSO in Crohn's disease, including an ongoing Phase II clinical trial, for use in North America, South America and Japan. Coronado will grant Falk exclusive rights and licenses to Company data from planned clinical trials of TSO in Crohn's disease for use in European studies. The hope is that it will accelerate both of our programs and reduce the overall cost for the programs going forward.

**CEOCFO:** Could you give us a brief description of the technology, what it is and why you are finding it effective, first for the CNDO-201 with the TSO for autoimmune diseases and then for CNDO-109 which is for the NK (natural killer cells) that activates them?

**Dr. Sandage:** Let's start with CNDO-201, we call it TSO. It stands for *Trichuris suis ova* or more commonly known as pig whipworm eggs. It is an intestinal helminth or intestinal parasite. The idea of using a helminth as a therapeutic agent is based on what is known as the "hygiene hypothesis". This concept was developed by the group at the University of Iowa. As I mentioned earlier, Dr. Weinstock and his colleagues are all gastroenterologists and treat many patients with Crohn's disease and ulcerative colitis. Like many of their colleagues, they were trying to understand why there

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**- Dr. Bobby W. Sandage Jr., Ph.D.**

has been a dramatic explosion in the number of patients with Crohn's disease and ulcerative colitis. They had observed that not only were these autoimmune GI diseases were on the increase but all autoimmune diseases were increasing at a dramatic rate in the industrialized world primarily, North America and Europe. They developed this idea that instead of something from the outside like an environmental factor was causing this rise in incidence of autoimmune diseases that maybe it was something now missing from these patients. So their hypothesis, the "hygiene hypothesis", simply states that because we are so clean, in other words very

good hygiene practices, that we never get exposed to helminths that we might lack a key immune regulatory factor. In fact, if you look at other parts of the world where the incidence of autoimmune disease is very low and steady, it overlaps where natural intestinal helminth infections are common.

They first tested their hypothesis in animals. They showed that they could effectively prevent and treat models of gastrointestinal autoimmune diseases such as Crohn's disease and ulcerative colitis by exposing an animal to the helminths. They then moved on to human clinical trials. There are several very important factors to consider when trying to determine which helminth could be used as a therapeutic immune-modulating agent. The most important feature is that the helminth not be a human pathogen, in other words, that it not invade or cause disease in humans. It turns out that *Trichuris suis*, the pig whipworm is the ideal choice. This particular helminth elicits the desired -immune-modulating response but it doesn't produce human infections. It colonizes the GI tract briefly but is not systemically invasive. In humans it fails to fully mature and is harmlessly shed after a couple of weeks. The eggs or ova must incubate in the

soil for 2-3 weeks before they are infective preventing direct host-to-host transmission and the ova or eggs are very stable and can stand up to the rigors of pharmaceutical grade processing. Finally, they were based in Iowa, where they knew that the pig farmers were exposed to these eggs almost on a daily basis and they had never observed a case of a human being infected with the pig whipworm. The first study they conducted was in patients with Crohn's disease. They observed after 24 weeks of treatment with 2500 TSO taken orally every 3 weeks that over 72% of the patients were considered to be in complete clinical remission. It was very dra-

matic effect and it is as good as any of the current treatments that are on the market for treating Crohn's disease. They then went on to conduct another trial but this time it was a double-blind, placebo-controlled trial in 54 patients with ulcerative colitis. They observed statistically significantly more patients responding to TSO when compared to the placebo treated patients. It was very well tolerated in both studies.

We now know a lot more about the mechanism of how these helminths may work to modulate the immune system in patients with autoimmune diseases. In simplest terms, in the long list of 100 autoimmune disease, such as ulcerative colitis or Crohn's disease or multiple sclerosis or Type 1 diabetes, or rheumatoid arthritis, there is one common feature they all have an excess activity from their T-helper-1 (TH1) cells producing an excess of proinflammatory cytokines. For example, these patients typically have elevated levels of interleukin II and interferon gamma. When you expose an animal or a human to a helminth, the body's natural reaction is to reject it, but over the years, the helminths have figured out a way to live in the intestines. It is the perfect environment for them. So they respond to this reaction from the host by up regulating what is known as the T-helper-2 cell cytokines. This action automatically down regulates the action of the TH1 cells. The effect from this action is an immunomodulation and a related improvement in the patient's autoimmune symptoms. That is what in fact they were able to observe in the studies of patients with Crohn's disease and ulcerative colitis. In addition, the first study has been published showing that TSO has a beneficial effect in multiple sclerosis. This study also demonstrated immunomodulation and a rebalancing of the TH-1 and TH-2 system.

**CEO CFO:** Where is Coronado in its human trials?

**Dr. Sandage:** The previous studies in Crohn's disease, ulcerative colitis has provided phase 2 efficacy data. The multiple sclerosis trial also provided early phase 2 efficacy. These data provided us with a significant clinical

database that allowed us to open an IND with the FDA. We have initiated a phase 1, single dose, dose escalation study which we anticipate completing in the first quarter of 2012 and then hope to start our own Phase 2 Crohn's study some time in the second quarter of next year.

**CEO CFO:** Are there any other biotech companies that are trying this approach or are you the only one?

**Dr. Sandage:** No, not that we are aware. However, there are individual investigators that are studying the mechanisms of how other helminths might work for treating autoimmune disease. For example, there is a group in the U.K. that has been studying the mechanism of action of the hookworm. There are several problems with the hookworm. First, unlike TSO which is taken orally, the hookworm has to penetrate the skin to get into the gastrointestinal tract. Secondly, it is a human pathogen, so it actually causes disease in humans, whereas the pig whipworm does not. We don't think this application has any commercial utility. As I mentioned before, TSO is really the ideal product and we do not know of anyone else that it is doing any work regarding a commercial application and our patients are pretty broad. We actually cover a range of other helminths and a many autoimmune diseases.

**CEO CFO:** Are there any other products on the market that have been successful in Crohn's or is this an area that there is such a great need and nothing else has really worked that it has made a difference.

**Dr. Sandage:** There are other drugs on the market to treat Crohn's disease. However, the ones that are well tolerated have limited efficacy and the ones that work well have seriously toxicities, such as steroids and the TNF alpha Inhibitors or the monoclonal antibodies; drugs like Humira and Remicade®. They work, but because they are immunosuppressive agents, they can dramatically suppress the immune system. The patients and doctors worry about the development of serious infections and cancers. In addition, many patients are also faced with the real prospect of requiring abdominal surgery and

they end up with colostomy bags. It is a terrible disease, so there is clearly room for a safe, effective orally active product to help these patients.

**CEO CFO:** So this is clearly an area of unmet need?

**Dr. Sandage:** It clearly is an area of unmet need. Our KOLs, our key opinion leaders and thought leaders in this area believe that this has real potential. If the studies continue to show similar effects as has been observed then they believe TSO could eventually become first line therapy; especially because it is so easy to administer and it appears to be very safe. The side effects are limited to mild diarrhea and GI cramping that lasts for a few days. It occurs in about a third to one-half the patients and it seems to go away with continued dosing.

**CEO CFO:** What is the potential market size for Coronado's TSO product?

**Dr. Sandage:** We have not completed a large-scale market research study yet, but I will provide you two pieces of information. In a NIH survey conducted a few years ago, they found that 5% to 8% of the U.S. population, which is tens of millions of people, has an autoimmune disease. We do not know if it going to work in every autoimmune disease but we believe that it has enormous potential. The current size of ulcerative colitis, Crohn's disease and multiple sclerosis in market is about \$9 billion.

**CEO CFO:** Would you tell us about your NK (natural killer cells) technology, and where are you in the clinical studies?

**Dr. Sandage:** In your body there are a group of cells called natural killer cells and they make up about anywhere from 5% to 10% of your white blood cells. They are part of what is known as the innate immune system, so they are there for two reasons. One is that you have cells turning over in your body all the time and sometimes you get a mutant cell and the NK cells job is to identify that abnormal cell and kill it before it grows into a cancer. The other feature is it kills cells infected with a virus. However, what happens is that as you age, you get defects in the system,

either they do not work as well as they used to or the cancer gets a foothold and tricks the NK cells in not being able to recognize it. In other words, your NK cells lose their ability to recognize the aberrant cells or they just do not work as well as they once did. In simple, terms they just were not activated in a way to be effective any longer. A group at the National Cancer Institute in the early 1980's came up with a method to activate NK cells. They would separate the NK cells during an apheresis process. They then would incubate these isolated NK cells with Interleukin II (IL-2) outside the body and then infuse them back into the patient. These activated NK cells would then be able to kill aberrant cells again. One issue with this method was to keep the NK cells activated they had to infuse IL-2 in to the patient following reintroduction of the activated NK cells. Unfortunately, IL-2 can have significant toxicity. Since this initial discovery that activated NK cells can treat cancer, specifically minimal residue disease many researchers have been searching for a method to activate these NK cells outside the body without having to use IL-2. We now believe that Dr. Lowdell has discovered a method to activate NK cells without the use of IL-2 by using CDNO-109. Dr. Lowdell's discovery is a tumor cell line that when incubated with NK cells activate them without IL-2.

When you are diagnosed with cancer, whatever cancer it is, your doctor will treat you with either chemotherapy or radiation or both and hopefully that treatment will put you into remission. If you are really lucky you stay in remission for a long time, however, most people relapse. Many experts believe that the relapse is due to what is known as "minimal residual disease" or MRD. MRD are the cancer cells that remain after your cancer treatment, the resistant cells. These resistance cells then get a foothold and are believed to be the cause of many relapses. Activated NK cells are specifically designed to kill these remaining cells. The first study to test this hypothesis with CNDO1-109 was recently presented at the international meeting of the American Society of Hematology. Dr. Lowdell and his col-

leagues studied 8 patients with acute myelogenous leukemia (AML). AML accounts for 90% of all new adult leukemias have a survival rate as low as 15% in five years. In addition, there have not been any new therapies for AML in the past 25 years. One of the hallmarks of AML is each subsequent remission is shorter than the previous remission. For example, a second remission is always shorter than the first remission and so on. In Dr. Lowdell's study the patients received their standard cancer therapy and then two to three days later they were infused with activated NK cells from a donor and followed for the length of the current remission which was then compared to the length of the previous remission. In 3 of 5 patients, they observed a longer remission than the previous one, something that is never seen in AML patients. The investigators treated one patient that was in partial relapse. Following treatment with activated NK cells the patient achieved a complete remission. Although it is a small set of patients, these activated NK cells demonstrated dramatic results. We are in the final steps required to completing our IND for submission to the FDA in the first quarter of 2012. We then hope to initiate a Phase 1/2 dose escalation trial in the United States starting some shortly after the IND submission.

**CEOCFO:** Going forward will this be like an adjuvant or something you are doing in conjunction with other chemotherapies or will this be a stand-alone product?

**Dr. Sandage:** It is not technically an adjuvant, but this therapy is not designed to be used alone. It is anticipated that the patient will be treated with the prescribed chemotherapy and then treated with the activated NK cells. Because of the nature of the NK cell treatment we think it might have utility in many cancers and in fact have laboratory data showing efficacy in multiple myeloma, ovarian cancer, breast cancer and prostate cancer.

**CEOCFO:** How is Coronado Biosciences situated financially to move your products into the trials and will you have to raise funds at this point or are you ok?

**Dr. Sandage:** We took a very unusual route to becoming public. Traditionally companies do IPOs or reverse mergers to get their companies public. We had completed three private rounds and raised \$65 million to-date. The last round was completed in late June for \$26 million. We had had evaluated various routes to get the company public. In the end we decided to go public through a self-registration process. We first filed a Form-10 and after approval by the SEC became a public reporting company in the middle of September. Then a potential market maker filed a Form-211 to allow us to list on the OTC Bulletin Board. At the same time we filed an S-1 to register all of our private shares. The S-1 went effective and we started trading on the OTC Bulletin Board, in the middle of November. On that same day we submitted our application to NASDAQ. Four weeks later we were approved by NASDAQ and started trading on Monday, December 19, 2011. As of the end of September we had \$27 million should take us toward the end of 2012. Therefore, we are in a very good position going into 2012. The programs are making significant progress, we are a NASDAQ listed company and we executing on our plan.

**CEOCFO:** Do you spend much time out doing road shows to reach investors?

**Dr. Sandage:** Yes we do! Again, because we did not do a traditional IPO with a banker assisting with the roadshow, we are doing it ourselves. It is up to us to make sure people hear and understand the story, the potential of the products and the plans for the company. Therefore, we are spending a lot of time on the road meeting with buy-side, sell-side organizations, individual investors and brokers. Just a few weeks ago the first analyst initiated coverage of the company.

**CEOCFO:** In closing, why should potential investors consider Coronado Biosciences?

**Dr. Sandage:** I think the best way to sum up Coronado Biosciences, as a potential investment is to review the value proposition. We have two biologics, which are inherently more

valuable than a small molecule because of lack of multiple potential generic competitors. Both products address huge unmet medical need markets, one for autoimmune disease potentially addressing up to 5% to 8% of the U.S. population and immunotherapy for cancer. The mechanisms

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