Synthetic Biologics, Inc.
Form 10-K
March 31, 2014

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-K

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2013

OR

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES ACT OF 1934**

For the transition period from_____ to_____

Commission File Number: 1-12584

SYNTHETIC BIOLOGICS, INC.

(Name of small business issuer in its charter)

Nevada	**13-3808303**

(State or other jurisdiction of incorporation or organization) *(IRS Employer Identification Number)*

155 Gibbs Street, Suite 412
Rockville, MD **20850**
(Address of principal executive offices) *(Zip Code)*

Registrant's telephone number, including area code:

(734) 332-7800

Securities registered pursuant to Section 12(b) of the Act:	**Name of each exchange on which registered**
(Title of Class)	
Common Stock, $0.001 par value per share	**NYSE MKT**

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x

Indicate by check mark whether the issuer: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of issuer's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, if any, every interactive data file required to be submitted and posted pursuant to Rule 405 of Regulation S-T (section 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).Yes x No ¨

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated file, a non-accelerated file, or a smaller reporting company. See the definitions of "large accelerated filer, "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	¨	Accelerated filer	¨
Non-accelerated filer	¨	Smaller reporting company	x
(Do not check if a smaller reporting company)			

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No x

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant as of June 28, 2013, was approximately $47.1 million based on $1.72, the price at which the registrant's common stock was last sold on that date.

As of March 27, 2014, the issuer had 58,276,556 shares of common stock outstanding.

Documents incorporated by reference: None.

SYNTHETIC BIOLOGICS, INC.

FORM 10-K

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PART I

Forward-Looking Statements

Certain of the matters discussed within this report include forward-looking statements on our current expectations and projections about future events. In some cases you can identify forward-looking statements by terminology such as "may," "should," "potential," "continue," "expects," "anticipates," "intends," "plans," "believes," "estimates," and sim These statements are based on our current beliefs, expectations, and assumptions and are subject to a number of risks and uncertainties, many of which are difficult to predict and generally beyond our control, that could cause actual results to differ materially from those expressed, projected or implied in or by the forward-looking statements. Such risks and uncertainties include the risks noted under "Item 1A Risk Factors." We do not undertake any obligation to update any forward-looking statements. Unless the context requires otherwise, references to "we," "us," "our," and "Synthet Biologics," refer to Synthetic Biologics, Inc. and its subsidiaries.

Item 1. ***Business***

We are a biotechnology company focused on the development of novel anti-infective biologic and drug candidates targeting specific pathogens that cause serious infections and other diseases. We are developing an oral treatment to reduce the impact of methane producing organisms on constipation-predominant irritable bowel syndrome (C-IBS), an oral biologic to protect the gastrointestinal (GI) microflora from the effects of intravenous (IV) antibiotics for the prevention of *Clostridium difficile (C. diff)* infection, a series of monoclonal antibodies (mAbs) for the treatment of Pertussis and *Acinetobacter* infections, and a biologic targeted at the prevention and treatment of a root cause of a subset of IBS. In addition, we have two legacy programs. We are developing an oral estriol drug for the treatment of relapsing-remitting multiple sclerosis (MS) and cognitive dysfunction in MS. We have also partnered the development of a treatment for fibromyalgia.

Product Pipeline:

Summary of Pathogen-Specific Anti-Infective Biologic and Drug Programs:

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C-IBS: In December 2013, through our majority-owned subsidiary, Synthetic Biomics, Inc., we entered into a worldwide exclusive license agreement with Cedars-Sinai Medical Center (CSMC) for the right to develop products for therapeutic and prophylactic treatments for acute and chronic diseases. An investigational team led by Mark Pimentel, M.D. at CSMC has discovered that these products are intended to target the production of methane gas by certain pathogenic gastrointestinal (GI) microorganisms that are perceived as the underlying cause of gas, pain and constipation associated with C-IBS, as well as diseases such as obesity and type 2 diabetes. Initially we will focus on the development of an oral treatment to reduce the impact of methane producing organisms on C-IBS. We intend to initiate *in vivo*/pharmacokinetic/pharmacodynamic studies in the first half of 2014, and to initiate a Phase II clinical trial during the second half of 2014 under an Investigational New Drug application (IND).

***C. diff* infections:** We are in preclinical development of a novel second-generation oral enzyme drug candidate, SYN-004, for co-administration with commonly used IV antibiotics intended to prevent the development of severe effects of *C. diff* infections. *C. diff* infections are a leading cause of hospital acquired infections (HAIs), that generally occur secondary to treatment with IV antibiotics. Designed to be given orally to protect the gut while certain IV beta-lactam antibiotics (penicillins and cephalosporins) fight the primary infection, SYN-004 is believed to have a similar profile to its first-generation predecessor, which demonstrated favorable protection of the gut flora (microbiome) during treatment with certain penicillins, with the potentially added ability to act against a broader spectrum of IV beta-lactam antibiotics. Beta-lactam antibiotics are a mainstay in hospital infection management and include the commonly used penicillin and cephalosporin classes of antibiotics. Approximately 14.4 million patients are administered "SYN-004 target" IV beta-lactam antibiotics annually, representing an estimated target market for SYN-004 of 117.6 million beta-lactam doses purchased by U.S. hospitals. The addressable market for SYN-004 is significant. Currently there are no approved treatments designed to protect the microbiome from the damaging effects of IV antibiotics. This worldwide opportunity could represent a multi-billion dollar market.* We intend to initiate Phase Ia and Ib clinical trials during the second half of 2014.

* This information is an estimate derived from the use of information under license from the following IMS Health Incorporated information service: CDM Hospital database for full year 2012. IMS expressly reserves all rights, including rights of copying, distribution and republication.

Pertussis: In December 2012, in collaboration with Intrexon Corporation (NYSE: XON) (Intrexon), we initiated development of a mAb therapy for the treatment of Pertussis infections, more commonly known as whooping cough. We are developing a mAb therapy, SYN-005, designed to target and neutralize the pertussis toxin, in order to reduce the mortality rate in infants and potentially shorten the duration of chronic cough in afflicted adults. To further the development of this potential therapy for Pertussis, we entered into an agreement with The University of Texas at Austin to license the rights to certain research and pending patents related to pertussis antibodies. According to the World Health Organization, each year, *B. pertussis* infection causes an estimated 300,000 deaths worldwide, primarily among young, unvaccinated infants. As part of our IND-enabling studies, we initiated a pilot large animal study in the first quarter of 2014 utilizing the antibody combination in a non-human primate model. This model, in addition to the murine model, is supportive of the development of a pertussis therapeutic. We are currently planning a confirmatory follow-up large animal study, and expect to report topline results during the second quarter of 2014.

***Acinetobacter* infections:** In September 2012, in collaboration with Intrexon, we initiated efforts to develop a mAb therapy for the treatment of *Acinetobacter* infections. Many strains of *Acinetobacter* are multidrug-resistant and pose an increasing global threat to hospitalized patients, wounded military personnel and those affected by natural disasters. A treatment for *Acinetobacter* infections represents a billion dollar market opportunity. The generation of a panel of antibodies is ongoing.

IBS: In December 2013, in collaboration with Intrexon, and partially utilizing the intellectual property optioned from CSMC, we announced we intend to develop biologic approaches targeted at the prevention, and acute and chronic treatment of a subset of IBS pathologies specifically caused by auto-antibodies.

Summary of Multiple Sclerosis Program:

Trimesta™ (oral estriol) is being developed as an oral once-daily treatment for relapsing-remitting MS in women. Patient enrollment is complete in this two-year, randomized, double-blind, placebo-controlled Phase II clinical trial being conducted at 15 centers in the United States. The primary endpoint is relapse rate at two years. This investigator-initiated trial evaluating our drug candidate, Trimesta™, is supported by grants awarded to the University of California, Los Angeles (UCLA) exceeding $8.0 million, which should be sufficient to fund the trial through completion. Annual worldwide sales of current MS therapies are estimated at $14.1 billion. Top-line results are scheduled to be presented at the American Academy of Neurology's Annual Meeting in April 2014 by the lead principal investigator, Rhonda Voskuhl, MD.

- Trimesta is also being developed for the treatment of cognitive dysfunction in female MS patients. This 12-month randomized, double-blind, placebo-controlled Phase II clinical trial is being conducted at UCLA. The primary endpoint is the effect on cognitive function as assessed by Paced Auditory Serial Addition Test (PASAT). Patient enrollment is ongoing. The majority of the costs of this trial are being funded by grants from foundations and charitable organizations and we have pledged approximately $500,000 to UCLA to partially fund this trial payable over three years. An estimated 50-65% of MS patients are expected to develop disabilities due to cognitive dysfunction and there is currently no approved treatment.

Summary of Fibromyalgia Program:

Effirma™ (flupirtine) is being developed for the treatment of fibromyalgia by Meda AB (Meda), a multi-billion dollar international pharmaceutical company. On May 6, 2010, we entered into a sublicense agreement with Meda covering all of our patents' rights on the use of flupirtine for fibromyalgia in the United States, Canada and Japan. The sublicense agreement provides that all ongoing and future development costs are to be borne by Meda and we are entitled to receive certain payments if milestones are achieved and royalties on sales. According to Meda's 2012 Year-End Report filed in February 2013, Meda has received the go-ahead from the United States Food and Drug Administration (FDA) to conduct a Phase II proof of concept study for the treatment of fibromyalgia. Meda also announced that the randomized, double-blind, placebo and active-controlled study of patients with fibromyalgia will be conducted at 25 clinics in the United States Based on an estimated annual price of $1,200 per fibromyalgia patient, we estimate that the total market potential in the United States is $6.0 billion.

Pipeline Programs and Therapeutic Areas

Pathogen-Specific Anti-Infective Biologic and Drug Programs

We are a biotechnology company focused on the development of novel anti-infective biologic and drug candidates targeting specific pathogens that cause serious infections and other diseases. Infectious disease outbreaks are increasing while intervention options are declining due to widespread multidrug-resistant bacteria, increasing numbers of immuno-compromised patients (e.g., the elderly and cancer patients), and the isolation of new pathogens. We are developing an oral treatment to reduce the impact of methane producing organisms on C-IBS, an oral biologic to protect the gastrointestinal microflora from the effects of IV antibiotics for the prevention of *C. diff* infection, a series of monoclonal antibodies for the treatment of Pertussis and *Acinetobacter* infections, and a biologic targeted at the prevention and treatment of a root cause of a subset of IBS.

Several of our programs are focused on protecting the microbiome, or our gut flora, which is home to millions of bacteria, composed of a natural balance of both "good" beneficial bacteria and "bad" pathogenic bacteria. When that natural balance of all of these bacteria is disrupted, a person's health is compromised.

C-IBS:

Irritable Bowel Syndrome (IBS) is a functional GI disorder characterized by gas, abdominal pain, bloating and diarrhea or constipation, or alternating episodes of both. According to reports published by The International Foundation for Functional Gastrointestinal Disorders (IFFGD), IBS affects an estimated 10 to 15 percent of the

population, or as many as 40 million Americans. The illness affects both men and women; two-thirds of diagnosed sufferers are women. The onset of IBS can begin anytime from adolescence to adulthood. Four bowel patterns may be seen with IBS, including: C-IBS (constipation predominant), D-IBS (diarrhea predominant), M-IBS (mixed diarrhea and constipation) and A-IBS (alternating diarrhea and constipation).

It has been reported that one-third of all IBS patients have C-IBS. Current FDA-approved therapies for the treatment of C-IBS include AMITIZA® (lubiprostone) and LINZESS® (linaclotide). Prescription and over-the-counter laxatives are also used by C-IBS patients for symptomatic relief. According to GlobalData, sales of approved drugs to treat C-IBS in seven major markets are projected to reach $1.3 billion by 2018.

C-IBS: Acquisition of Clinical-Stage Program

In December 2013, we entered into a worldwide exclusive license agreement with CSMC for the right to develop products for therapeutic and prophylactic treatments for acute and chronic diseases. We licensed and optioned from CSMC a portfolio of intellectual property comprised of several U.S. and international patents and pending patent applications for various fields of use, including C-IBS, obesity and diabetes. An investigational team led by Mark Pimentel, M.D. at CSMC has discovered that these products are intended to target the production of methane gas by certain pathogenic gastrointestinal microorganisms that are perceived as the underlying cause of gas, pain and constipation associated with C-IBS, as well as diseases such as obesity and type 2 diabetes. Initially we will focus on the development of an oral treatment to reduce the impact of methane producing organisms on C-IBS.

IBS: Gas Producing Organisms Background

In the 1990’s, research showed that IBS patients (over a given time) produced five times more gas than did people without IBS. Since the only source of those gases was bacterial, the initial presumption was that IBS patients had excessive bacteria in the colon. Subsequent studies showed that IBS patients had excessive quantities of gas in the small bowel; these data were the catalyst for studying small bowel bacteria in IBS. Normally the small intestine contains a very small quantity of bacteria. In published studies, indirect measures of small bowel bacteria suggest that 84% of IBS sufferers have excessive quantities of bacteria typically found in the colon.

The CSMC investigational team led by Dr. Pimentel is researching a recent theory that defines IBS as a bacterial disease. Gut microflora that should normally be confined to the large intestine inappropriately colonize the small intestine. This process is referred to as small intestine bacterial overgrowth (SIBO), which results in gas, bloating, abdominal pain and altered stool habits characterized by IBS.

C-IBS: Methane Producing Organisms Background

Further research by the CSMC investigational team led by Dr. Pimentel is focused on the C-IBS patient population. The theory that defines this patient set is that the constipation associated with C-IBS is due to an infectious disease. Overgrowth of certain gut microflora may lead to overproduction of methane gas resulting in pain, bloating and constipation. CSMC investigators have discovered that inhibiting intestinal methane production may treat the underlying cause of major diseases, including constipation associated with C-IBS.

C-IBS: Preclinical and Clinical Development

Ongoing efforts led by Dr. Pimentel include formulating and testing non-antibiotic FDA-approved oral drug candidates for ultimate product registration via potential expedited pathways. Such candidates are intended for the specific elimination of methane gas production within the intestines, with the goal of having little or no unintended impact on a patient's normal intestinal microflora. Initially we will focus on the development of an oral treatment to reduce the impact of methane producing organisms on C-IBS.

We intend to initiate *in vivo*/pharmacokinetic/pharmacodynamic studies in the first half of 2014, and to initiate a Phase II clinical trial during the second half of 2014 under an IND.

***C. difficile*:**

According to the Agency for Healthcare Research and Quality, aggregate costs associated with *C. diff* infection (CDI)-related stays in the hospital were $8.2 billion in the U.S. during 2009. CDI is a rising global HAI problem in which the toxins produced by *C. difficile* bacteria result in diarrhea antibiotic-associated diarrhea (AAD), and in the most serious cases, pseudomembranous colitis (erosion of the lower GI tract) that can lead to death. The Centers for Disease Control and Prevention (CDC) recently identified *C. diff* as an “urgent public health threat,” particularly given its resistance to many drugs used to treat other infections. CDI is a major, unintended risk associated with the prophylactic or therapeutic use of IV antibiotics, which may alter the natural balance of microflora that normally protect the GI tract, leading to *C. difficile* overgrowth and infection. Other risk factors for CDI include hospitalization, prolonged length of stay, underlying illness, immune-compromising conditions including the administration of chemotherapy, and advanced age.

CDI is a widespread and often drug resistant infectious disease, and it is estimated that 1.1 million patients are infected with *C. diff* annually in the U.S.*, and it has been reported that 30,000 patients die with a *C. diff* infection

each year. CDI has surpassed methicillin-resistant staphylococcus aureus (MRSA) as the most frequent infection acquired in the hospital. Controlling the spread of CDI has proven challenging, as the *C. difficile* spores are easily transferred to patients via normal contact with healthcare personnel and other inanimate objects. There is currently no vaccine or approved product for the prevention of *C. diff* infection.

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C. difficile: Acquisition of Clinical-Stage Program

In November 2012, we acquired a series of oral beta-lactamase enzymes (P1A, P2A and P3A) and related assets targeting the prevention of CDI, the leading cause of HAIs that generally occurs secondary to treatment with IV antibiotics. The acquired assets include a pre-IND package for P3A (SYN-004), Phase I and Phase II clinical data for P1A, manufacturing processes and data, and a portfolio of issued and pending U.S. and international patents intended to support an IND and Biologics License Application (BLA) with the FDA. Utilizing this portfolio of assets, we intend to develop a proprietary oral beta-lactamase enzyme product candidate, SYN-004, previously known as P3A. When co-administered with certain IV beta-lactam antibiotics, it is expected that SYN-004 can degrade the antibiotic that is excreted in the GI tract, thus preserving the natural balance of the patient's microflora, and preventing opportunistic infections including CDI. Beta-lactam antibiotics are a mainstay in hospital infection management and include the commonly used penicillin and cephalosporin classes of antibiotics. Approximately 14.4 million patients are administered "SYN-004 target" IV beta-lactam antibiotics annually, representing an estimated target market for SYN-004 of 117.6 million beta-lactam doses purchased by U.S. hospitals. The addressable market is significant and currently there are no approved treatments designed to protect the microbiome from the damaging effects of IV antibiotics. This worldwide opportunity could represent a multi-billion dollar market.*

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C. difficile: Oral Enzyme Background

We acquired a series of oral beta-lactamase enzymes. Beta-lactamase enzymes have the ability to degrade beta-lactam antibiotics that may be excreted into the GI tract. P1A (the first generation candidate) showed acceptable safety and tolerability in a Phase I study. In addition, two Phase II clinical studies demonstrated that P1A had the ability to preserve GI microflora in hospitalized patients treated with intravenous ampicillin or the combination of piperacillin and tazobactam.

C. difficile: Preclinical and Clinical Development

Compared to the first generation oral enzyme candidate, P1A, we believe that the second generation candidate, SYN-004 (formerly P3A), will have activity against a broader spectrum of beta-lactam antibiotics, including both penicillins and certain cephalosporins. Due to the structural similarities between P1A and SYN-004, and based on previous discussions with the FDA, it is anticipated that certain preclinical data collected on P1A may be used in support of an IND for our new product candidate, SYN-004.

In October 2013, we initiated manufacturing of SYN-004 material to support our planned preclinical and clinical studies. We intend to initiate Phase Ia and Ib clinical trials during the second half of 2014.

Monoclonal Antibodies:

Monoclonal Antibodies for Infectious Diseases

Acting as the body's army, antibodies are proteins, generally found in the bloodstream, that provide immunity in detecting and destroying pathogens, such as viruses and bacteria and their associated toxins. MAbs can also be designed and produced as therapeutic agents, utilizing protein engineering and recombinant production technologies. The mAbs being developed under our collaboration with Intrexon are intended to supplement a patient's own immune system by providing the means to specifically and rapidly neutralize and/or clear specific pathogens and toxins of interest in a process known as “passive immunity”. Many pathogens that cause infectious diseases are innately resistant to, or over time have developed increased resistance to, antibiotics and other drugs.

Intrexon Collaboration: Monoclonal Antibodies for Infectious Diseases

In August 2012, we entered into a worldwide exclusive channel collaboration (“Second ECC”) with Intrexon through which we intend to develop a series of mAb therapies for the treatment of certain infectious diseases not adequately addressed by existing therapies. Utilizing Intrexon’s comprehensive suite of proprietary technologies, including the mAbLogix™ platform for rapid discovery of fully human mAbs and the LEAP™ cell processing station, our initial efforts will target three infectious disease indications.*** We also have the option to target an additional five infectious disease indications under this collaboration. To date, we have initiated development of a mAb therapy for the treatment of Pertussis and *Acinetobacter* infections.

***mAbLogix™ and LEAP™ are registered trademarks of Intrexon Corporation

Bordetella pertussis (B. pertussis) is a gram-negative bacterium that infects the upper respiratory tract, causing uncontrollable, and violent coughing. Antibiotic treatment does not have a major effect on the course of Pertussis, because while it can eliminate the *B. pertussis* bacteria from the respiratory tract, it does not neutralize the pertussis toxin. Infants with Pertussis often require hospitalization in pediatric intensive care units, frequently requiring mechanical ventilation. Pertussis in adults generally leads to a chronic cough referred to as the "cough of 100 days." The incidence of Pertussis is increasing due to a less effective acellular vaccine introduced in the 1990s, exposure of unvaccinated and under-vaccinated individuals including infants who are not yet fully vaccinated, exposure of individuals whose immunity has diminished over time, as well as asymptomatic carriers.

According to the World Health Organization there are 50 million cases of whooping cough and *B. pertussis* infection causes an estimated 300,000 deaths each year worldwide, primarily among young, unvaccinated infants. Recent news reports throughout the U.S. indicate that the pertussis vaccine introduced in the 1990s does not provide long-term protection and, as a result, whooping cough cases have increased to a 60-year high. There is no approved treatment for Pertussis, and antibiotic treatment does not have a major effect on the course of Pertussis, because while it can eliminate the *B. pertussis* bacteria from the respiratory tract, it does not neutralize the pertussis toxin.

Pertussis: Intrexon Collaboration and The University of Texas at Austin Agreement

In December 2012, we initiated mAb development for the treatment of Pertussis focusing on toxin neutralization pursuant to our August 2012 collaboration with Intrexon. Unlike antibiotics, we are developing a mAb therapy, SYN-005, to target and neutralize the pertussis toxin, in order to reduce the mortality rate in infants and shorten the duration of chronic cough in afflicted adults.

To further the development of this potential therapy for pertussis, we have entered into an agreement with The University of Texas at Austin to license the rights to certain research and pending patents related to pertussis antibodies. These research efforts are being conducted at the Cockrell School of Engineering in the laboratory of Assistant Professor, Jennifer A. Maynard, Ph.D., the Laurence E. McMakin, Jr. Centennial Faculty Fellow in the McKetta Department of Chemical Engineering. Dr. Maynard brings to the project her expertise in defining the key neutralizing epitopes of pertussis toxin to optimize the potential efficacy of antibody therapeutics.

Pertussis: Preclinical and Clinical Development

Working with our collaborator, Intrexon, and our academic collaborator, The University of Texas at Austin, we have established a combination of two humanized antibodies designed to neutralize pertussis toxin, a major cause of pertussis-mediated infant morbidity and mortality. Benchtop studies demonstrated high affinity binding to the toxin, as well as potent neutralization of the toxin. In addition, the antibodies were highly efficacious in a murine model of pertussis in which they completely mitigated elevations of the white blood cell count that is characteristic of the illness.

As part of our IND-enabling studies, we initiated a pilot large animal study in the first quarter of 2014 utilizing the antibody combination in a non-human primate model, which in addition to the murine model, is supportive of the development of a pertussis therapeutic. We are currently planning a confirmatory follow-up large animal study, and expect to report topline results during the second quarter of 2014.

Manufacturing of antibodies for nonclinical development is underway. We are filing patents to strengthen our intellectual property position around pertussis antibodies. In addition, we intend to file an orphan drug application for the pertussis indication.

Acinetobacter Infections:

Acinetobacter baumanii is a difficult to treat pathogen due to its rapid and well-established development of resistance to most antibiotics, making it a multidrug-resistant pathogen. In addition, as a biofilm-forming pathogen, *Acinetobacter baumanii* has the ability to survive up to twice as long as non-biofilm-forming pathogens. In the U.S., *Acinetobacter baumanii* has been reported to be the cause of up to 2.6% of hospital acquired infections, 1.3% of bloodstream infections and 7% of ICU respiratory tract infections, and more than half of the *Acinetobacter baumanii* isolates are multidrug-resistant. According to published articles, mortality rates associated with *Acinetobacter* infections as high as 43% are reported in hospitals and ICU settings. While *Acinetobacter baumanii* is a well-documented pathogen in the hospital setting, this pathogen also poses an increasing danger to wounded servicemen and women in military treatment centers and to those treated in trauma centers following natural disasters.

A treatment for *Acinetobacter* infections represents a billion dollar market opportunity.

Acinetobacter: Intrexon Collaboration

In August 2012, we initiated a mAb discovery and development program for *Acinetobacter* infections pursuant to our August 2012 collaboration with Intrexon. Discovery efforts for the development of a mAb are currently underway.

IBS:

Existing IBS therapies, which are primarily focused on supportive care, are unlikely to address the treatment needs of the patient population with auto-antibodies, an underlying immune-specific pathology. Through our collaboration with Intrexon, we intend to address the unmet medical need in these patients with personalized medicine and target the root causes of a subset of IBS-associated pathologies.

IBS: Intrexon Collaboration

In December 2013, in collaboration with Intrexon, and partially utilizing the intellectual property optioned from CSMC, we announced an intent to develop biologic approaches targeted at the prevention, and acute and chronic treatment of a subset of IBS pathologies specifically caused by auto-antibodies.

We intend to utilize intellectual property optioned from CSMC. According to an increasing body of recent work conducted by CSMC, a subset of IBS cases appear to be causally initiated by one or more encounters with acute infectious gastroenteritis, such as the foodborne illness*, Campylobacter jejuni*. CSMC has identified a novel autoimmune target for this subset of IBS cases because of the development of cross-reacting antibodies between a bacterial toxin and a protein important for controlling GI motility. This program is in the discovery stage.

Multiple Sclerosis Program

Relapsing-Remitting MS:

MS is a progressive neurological disease in which the body loses the ability to transmit messages along the central nervous system, leading to pain, loss of muscle control, paralysis, cognitive impairment and in some cases death. According to the National Multiple Sclerosis Society (NMSS), more than 2.3 million people worldwide (approximately 400,000 patients in the U.S. of which approximately 65% are women) have been diagnosed with MS. The diagnosis is typically made in young adults, ages 20 to 50. According to the NMSS, approximately 85% of MS patients are initially diagnosed with the relapsing-remitting form, and 10-15% with other progressive forms.

There are nine FDA-approved therapies for the treatment of relapsing-remitting MS: Betaseron®, Rebif®, Avonex®, Copaxone®, Tysabri®, Gilenya®, Extavia®, Aubagio® and Tecfidera™. Many of these therapies provide only a modest benefit for patients with relapsing-remitting MS. All of these drugs except Gilenya®, Aubagio® and Tecfidera™ require frequent (daily, weekly & monthly) injections (or infusions) on an ongoing basis and can be associated with unpleasant side effects (such as flu-like symptoms) and high rates of non-compliance among users. Despite the availability of therapies for the treatment of relapsing-remitting MS, the disease is highly underserved and exacts a heavy personal and economic toll. Annual worldwide sales of current MS therapies are estimated at $14.1 billion.

Relapsing-Remitting MS: Background

Research has shown that pregnant women with MS tend to experience a spontaneous reduction of disease symptoms during pregnancy, particularly in the third trimester. The PRIMS (Pregnancy In MS) study published in 1998, a landmark observational clinical study published in the *New England Journal of Medicine* followed 254 women with MS during 269 pregnancies and for up to one year after delivery. The PRIMS study demonstrated that relapse rates were significantly reduced by 71% ($p < 0.001$) through the third trimester of pregnancy compared to pre-pregnancy-rates, and that relapse rates increased by 120% ($p < 0.001$) during the first three months after birth (post-partum) and then return to pre-pregnancy rates. It has been hypothesized that the female hormone, estriol, produced by the placenta during pregnancy, plays a role in “fetal immune privilege”, a process that prevents a mother’s immune system from attacking and rejecting the fetus. The maternal levels of estriol increase linearly through the third trimester of pregnancy until birth, whereupon it abruptly returns to low circulating levels. The anti-autoimmune effects of estriol are thought to be responsible for the therapeutic effects of pregnancy on MS.

Rhonda Voskuhl, M.D., Director, UCLA MS program, UCLA Department of Neurology, has found that plasma levels of estriol achieved during pregnancy have potent immunomodulatory effects. She further postulated and tested in a pilot clinical study that oral doses of estriol may have a therapeutic benefit when administered to non-pregnant female MS patients by, in essence, mimicking the spontaneous reduction in relapse rates seen in MS patients during pregnancy.

Estriol has been approved and marketed for over 40 years throughout Europe and Asia for the oral treatment of post-menopausal symptoms. It has never been approved by the U.S. FDA for any indication.

Relapsing-Remitting MS: Clinical Development

Trimesta (oral estriol) is being developed for the treatment of relapsing-remitting MS in women. An investigator-initiated, 10-patient, 22-month, single-agent, crossover clinical trial to study the therapeutic effects of 8 mg. of oral Trimesta taken daily in non-pregnant female relapsing-remitting MS patients was completed in the U.S. The total volume and number of gadolinium-enhancing lesions were measured by brain magnetic resonance imaging (an established neuroimaging measure of disease activity in MS). Over the next three months of treatment with Trimesta, the median total enhancing lesion volumes decreased by 79% ($p = 0.02$) and the number of lesions decreased by 82% ($p = 0.09$). They remained decreased during the next 3 months of treatment, with lesion volumes decreased by 82% ($p = 0.01$), and numbers decreased by 82% ($p =0.02$). Following a six-month drug holiday during which the patients were not on any drug therapies, median lesion volumes and numbers returned to near baseline pretreatment levels. Trimesta therapy was reinitiated during a four-month retreatment phase of this clinical trial. The relapsing-remitting MS patients again demonstrated a decrease in enhancing lesion volumes of 88% ($p = 0.008$) and a decrease in the number of lesions by 48% ($p = 0.04$) compared with original baseline scores.

A Phase II randomized, double-blind, placebo-controlled clinical trial is currently underway at 15 centers in the U.S. under the direction of Lead Principal Investigator, Dr. Rhonda Voskuhl. The purpose of this clinical trial is to evaluate whether 8 mg of oral Trimesta taken daily over a two year period will reduce the rate of relapses in a large population of female patients with relapsing-remitting MS. Investigators are administering either Trimesta or matching placebo, in addition to a standard of care, glatiramer acetate injections (Copaxone®), an FDA-approved therapy for MS, to women between the ages of 18 to 50 who have been recently diagnosed with relapsing-remitting MS. Relapse rates at two years is the primary endpoint in this clinical trial being run under an investigator-initiated IND.

Patients in this Phase II relapsing-remitting MS trial completed their final 24-month visit during January 2014. Dr. Rhonda Voskuhl is scheduled to present topline results at the American Academy of Neurology's 66th Annual Meeting in Philadelphia at the end of April 2014.

With over $8 million in grant funding awarded to UCLA to date, from organizations such as the National Institutes for Health and the National Multiple Sclerosis Society, the ongoing Trimesta clinical trial should be funded to its completion.

Relapsing-Remitting MS: Patents

In March 2014, we announced that the U.S. Patent & Trademark Office issued U.S. Patent No. 8,658,627 entitled, *Pregnancy Hormone Combination for Treatment of Autoimmune Diseases*, to the Regents of the University of California. The patent includes claims to the use of our drug candidate, Trimesta™ (oral estriol), in conjunction with a gestagen for the treatment of multiple sclerosis (MS) and other autoimmune diseases. The patent also includes a claim for the administration of Trimesta™, a gestagen and a third standard of care MS agent, such as glatiramer acetate injection (Copaxone®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®) or sphingosine-1-phosphate receptor modulator (Gilenya®).

In April 2013, we announced that the U.S. Patent & Trademark Office issued U.S. Patent No. 8,372,826 entitled, *Estriol Therapy for Multiple Sclerosis and Other Autoimmune Diseases*, to the Regents of the University of California which includes claims to the use of our drug candidate, Trimesta™ (oral estriol), in combination with glatiramer acetate injection (Copaxone®). According to Teva Pharmaceutical Industries Ltd.'s Form 20-F for the year ended December 31, 2012, filed with the SEC on February 12, 2013. Copaxone® is the number one selling drug for multiple sclerosis with approximately $4 billion in annual sales. Currently marketed exclusively by Teva Pharmaceutical Industries Ltd., Copaxone® is expected to face generic competition as certain patent terms begin to expire in 2014.

Through our wholly owned subsidiary, we hold the exclusive worldwide license to issued U.S. Patents 8,658,627, 8,372,826 and 6,936,599 and pending patents for multiple sclerosis and other autoimmune diseases covering the uses of our drug candidate, Trimesta™.

Cognitive Dysfunction in MS:

According to the NMSS and the Multiple Sclerosis Society of Canada publication, *Hold that Thought! Cognition and MS*, it is fairly common for people with MS to complain of cognitive difficulties, such as remembering things, finding the right words and the ability to concentrate. Among MS patients, 50-65% have some degree of cognitive dysfunction.

The major areas of cognition that may be affected include complex attention and executive functions. Complex attention involves multitasking, the speed with which information can be processed, learning and memory, and perceptual skills; executive functions include problem solving, organizational skills, the ability to plan, and word finding. Just as the nature, frequency, and severity of MS-related physical problems can widely vary, not all people with MS will have cognitive dysfunction, and no two people will experience exactly the same type or severity.

Cognitive Dysfunction in MS: Background

In the investigator-initiated, 10-patient, 22-month, single-agent, crossover clinical trial conducted by Dr. Rhonda Voskuhl, a statistically significant 14% improvement from baseline in the PASAT cognitive testing scores ($p = 0.04$) was observed in relapsing-remitting MS patients after six months of Trimesta therapy. PASAT is a routine cognitive test performed in patients with a wide variety of neuropsychological disorders such as MS. The PASAT scores are expressed as a mean percent change from baseline.

Cognitive Dysfunction in MS: Clinical Development

Our Trimesta (oral estriol) drug candidate is also being developed for the treatment of cognitive dysfunction in female MS patients. This randomized, double-blind, placebo-controlled Phase II clinical trial to evaluate Trimesta's potential neuroprotective and therapeutic effect on cognitive dysfunction in female MS patients is currently enrolling relapsing-remitting or secondary-progressive female MS patients at UCLA. Up to 64 patients between the ages of 18 and 50 will be randomized 1:1 into the treatment and placebo groups. Dr. Voskuhl will administer either oral Trimesta or a matching placebo, in addition to any FDA-approved MS treatment. Each patient will be dosed and monitored for one year after being enrolled. The primary endpoint in this clinical trial being run under an investigator-initiated IND application is expected to be improvement in PASAT cognitive testing scores versus matching placebo. We and a private foundation have pledged to equally support this new clinical trial, and we will also provide Trimesta drug supply. The trial also received contributions from several other supporters. Patient recruitment and enrollment into this trial is ongoing.

Fibromyalgia Program

Fibromyalgia is a chronic and debilitating condition characterized by widespread pain and stiffness throughout the body, often accompanied by severe fatigue, insomnia and alterations in mood. According to the National Fibromyalgia Association, fibromyalgia affects an estimated 3-6% of the population worldwide, including an estimated 10 million people in the U.S. There are presently three FDA products approved for the treatment of fibromyalgia - Lyrica®, Cymbalta® and Savella®.

Based on an estimated annual price of $1,200 per fibromyalgia patient, we estimate that the total market potential in the U.S. is $6 billion.

Fibromyalgia: *Meda Corporate Partnership*

On May 6, 2010, we entered into a sublicense agreement with Meda, a multi-billion dollar international pharmaceutical company, pursuant to which Meda assumed all future development costs and may commercialize flupirtine, a molecular entity with a unique mode of action for the treatment of fibromyalgia in the U.S. As consideration for such sublicense, we received an up-front payment of $2.5 million and are entitled to milestone payments of $5.0 million upon the FDA's acceptance of the New Drug Application (NDA) for flupirtine for fibromyalgia and $10.0 million upon FDA approval of such NDA. Pursuant to the sublicense agreement, we will also receive a 7% royalty on net sales of flupirtine for fibromyalgia in the U.S., Canada and Japan, with such royalties being shared equally with our licensor, McLean Hospital, a Harvard teaching hospital.

Flupirtine is approved and marketed by Meda and its distributors in Europe and other countries for indications other than fibromyalgia and has been prescribed to millions of patients worldwide. We believe that such substantial human experience with flupirtine should greatly assist the FDA in its evaluation of the safety of flupirtine upon review of an NDA of flupirtine for fibromyalgia.

Fibromyalgia: *Clinical Development*

Our Effirma (flupirtine) drug candidate for the treatment of fibromyalgia, has been partnered to Meda (see "Fibromyalgia: Meda Corporate Partnership" section above). Effirma is a selective neuronal potassium channel opener that also has N-methyl-D-aspartic (NMDA) receptor antagonist properties. Effirma is a non-opioid, non-NSAID, non-steroidal, analgesic. Preclinical data and clinical experience suggest that Effirma should also be effective for neuropathic pain since it acts in the central nervous system via a mechanism of action distinguishable from most marketed analgesics. Effirma is especially attractive because it operates through non-opiate pain pathways, exhibits no known abuse potential, and lacks withdrawal effects. In addition, no tolerance to its antinocioceptive effects has been observed. One common link between neuroprotection, nocioception and Effirma may be the N-methyl-D-aspartic acid

glutamate system, a major receptor subtype for the excitotoxic neurotransmitter, glutamate. Effirma has strong inhibitory actions on N-methyl-D-aspartic acid-mediated neurotransmission. Flupirtine was originally developed by Asta Medica (subsequently acquired by Meda) and has been approved and is marketed by Meda in Europe since 1984, as well as other countries, for the treatment of pain. It has never been approved by the FDA for any indication.

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According to Meda's 2012 Year-End Report filed in February 2013, Meda has received the go-ahead from the FDA to conduct a Phase II proof of concept study for the treatment of fibromyalgia. Meda also announced that the randomized, double-blind, placebo and active-controlled study of patients with fibromyalgia will be conducted at 25 clinics in the U.S.

Intellectual Property

Our goal is to (a) obtain, maintain, and enforce patent protection for our products, formulations, processes, methods, and other proprietary technologies, (b) preserve our trade secrets, and (c) operate without infringing on the proprietary rights of other parties, worldwide. We seek, where appropriate, the broadest intellectual property protection for product candidates, proprietary information, and proprietary technology through a combination of contractual arrangements and patents. Below is a description of our license and development agreements relating to our product candidates.

Cedars-Sinai Medical Center License and Options Agreements

On December 5, 2013, through our newly formed, majority owned subsidiary, Synthetic Biomics, Inc. ("SYN Biomics"), we entered into a worldwide exclusive license agreement (the "CSMC License Agreement") and option agreement (the "CSMC Option Agreement") with CSMC for the right to develop, manufacture, use, and sell products for the human and veterinary therapeutic and prophylactic treatments for acute and chronic diseases. An investigational team lead by Mark Pimentel, M.D. at CSMC has discovered that these products are intended to target certain pathogenic GI microorganisms that are perceived as an underlying cause of diseases such as C-IBS, obesity and type 2 diabetes. The portfolio of intellectual property licensed to SYN Biomics under the CSMC License Agreement includes nine issued U.S. patents, one issued European patent validated in 18 countries, one issued European patent validated in three countries, two issued Australian patents, and one issued Japanese patent as well as 15 pending U.S. and international patent applications for most fields of use and modalities (subject to certain agreed-upon exceptions); two pending U.S. patent applications are optioned to SYN Biomics under the CSMC Option Agreement.

Under the terms of the CSMC License Agreement we issued 291,569 unregistered shares of our common stock to CSMC, as payment of an initial license fee and patent reimbursement fees of $150,000 and $220,000, respectively. The parties also entered into a Stock Purchase Agreement with respect to such stock issuance and other issuances of unregistered shares of our common stock that may be issued to CSMC in lieu of cash, including license fees, milestone payments, expense reimbursements and option fees under the CSMC License Agreement or CSMC Option Agreement. Any and all such stock issuances by us shall be subject to the prior approval of the NYSE MKT, LLC. The CSMC License Agreement also provides that commencing on the second anniversary of the CSMC License Agreement, SYN Biomics will pay an annual maintenance fee, which payment shall be creditable against annual royalty payments owed under the CSMC License Agreement. In addition to royalty payments which are a percentage

of Net Sales (as defined in the CSMC License Agreement) of Licensed Products (as defined in the CSMC License Agreement) and Licensed Technology products (as defined in the CSMC License Agreement), SYN Biomics is obligated to pay CMSC a percentage of any non-royalty sublicense revenues, as well as additional consideration upon the achievement of the following milestones (the first two of which are payable in cash or unregistered shares of our stock at our option): (i) successful Phase I trial completion of the first Licensed Product or first Licensed Technology Product; (ii) successful Phase II trial completion of the first Licensed Product or first Licensed Technology Product; (iii) initiation of Phase III dosing for each additional indication of a Licensed Product or Licensed Technology Product; (iv) successful Phase III trial completion for each Licensed Product and each Licensed Technology Product; (v) the FDA's acceptance of a New Drug Application for each Licensed Product and each Licensed Technology Product; (vi) regulatory approval for each Licensed Product and each Licensed Technology Product; and (vii) the first commercial sale of each Licensed Product and each Licensed Technology Product. The stock issuances are subject to prior approval of the NYSE MKT, LLC.

Prior to the execution of the CSMC License Agreement, SYN Biomics issued shares of common stock of SYN Biomics to each of CSMC and Mark Pimentel, M.D. (the primary inventor of the intellectual property), representing 11.5% and 8.5%, respectively, of the outstanding shares of SYN Biomics (the "SYN Biomics Shares"). The Stock Purchase Agreements for the SYN Biomics Shares provide for certain anti-dilution protection until such time as an aggregate of $3.0 million in proceeds from equity financings are received by SYN Biomics as well as a right, under certain circumstances in the event that the SYN Biomics Shares are not then freely tradeable, and subject to NYSE MKT, LLC approval, as of the 18 and 36 month anniversary date of the effective date of the Stock Purchase Agreements, for each of CSMC and the Dr. Pimentel to exchange up to 50% of their SYN Biomics shares for unregistered shares of our common stock, with the rate of exchange based upon the relative contribution of the valuation of SYN Biomics to the public market valuation of us at the time of each exchange. The Stock Purchase Agreements also provide for tag-along rights in the event of the sale by us of our shares of SYN Biomics.

The CSMC License Agreement terminates: (i) automatically if SYN Biomics enters into a liquidating bankruptcy or other specified bankruptcy event or if the performance of any term, covenant, condition or provision of the CSMC License Agreement will jeopardize the licensure of CMSC, its participation in certain reimbursement programs, its full accreditation by the Joint Commission of Accreditation of Healthcare Organizations or any similar state organizations, its tax exempt status or is deemed illegal; (ii) upon 30 days notice from CMSC if SYN Biomics fails to make a payment or use commercially reasonable efforts to exploit the patent rights; (iii) upon 60 days notice from CMSC if SYN Biomics fails to cure any breach or default of any material obligations under the CSMC License Agreement; or (iv) upon 90 days notice from SYN Biomics if CMCS fails to cure any breach or default of any material obligations under the CSMC License Agreement. SYN Biomics also has the right to terminate the License Agreement without cause upon 6 months notice to CSMC; however, upon such termination, SYN Biomics is obligated to pay a termination fee with the amount of such fee reduced: (i) if such termination occurs after an IND submission to the FDA but prior to completion of a Phase II clinical trial, (ii) reduced further if such termination occurs after completion of Phase II clinical trial but prior to completion of a Phase III clinical trial; and (iii) reduced to zero if such termination occurs after completion of a Phase III clinical trial.

Pursuant to the terms of the CSMC Option Agreement, SYN Biomics has a period of six months to negotiate an exclusive license to develop, manufacture, use, and sell biologic products relating to the prevention, acute treatment and chronic treatment of irritable bowel syndrome or other indications utilized or derived from certain optioned patent applications, pending completion of certain limited testing of technology embodied in the patent applications. Under terms of the CSMC Option Agreement we issued 43,342 shares of our unregistered stock to CSMC, as payment of a non-refundable option fee of $55,000. In addition, SYN Biomics has the right to extend the option period for an additional six months, for an additional non-refundable extension fee of $25,000, payable in unregistered shares of our common stock having a market value of 110% of such amount, subject to approval of NYSE MKT, LLC, or in cash. At any time during the 6 or 12 month option period (if so extended) SYN Biomics has the right to exercise the option and negotiate an exclusive license to the optioned patent applications, which shall provide for: (i) a $50,000 license issue fee plus reimbursement of patent expenses incurred by CSMC prior to the exclusive license, payable to CSMC in unregistered shares of our stock having a market value of 110% of such amount, subject to approval of the NYSE MKT, LLC, or in cash, (ii) the same milestone payments, royalties and sublicense fees as are payable under the CSMC License Agreement dated December 5, 2013 for separately licensed intellectual property, and (iii) such other customary terms and conditions CSMC typically includes in its license agreements.

In collaboration with Intrexon, and partially utilizing the intellectual property optioned and/or licensed from CSMC described in the CSMC Option Agreement, we intend to develop biologic approaches for the prevention, acute and chronic treatment of a subset of IBS pathologies specifically caused by auto-antibodies. During the option period, SYN Biomics, we and Intrexon will seek to create and test a variety of biologic candidates for the treatment of a subset of IBS cases. This biologic program has been selected as the third target under our Second ECC with Intrexon dated August 6, 2012 (see "*Infectious Disease Collaboration with Intrexon" below).*

The University of Texas at Austin License Agreement and Sponsored Research Agreement

On December 19, 2012, we entered into a Patent License Agreement (the "Texas License Agreement") with The University of Texas at Austin (the "University") for the exclusive license of the right to use, develop, manufacture, market and commercialize certain research and patents related to pertussis antibodies developed in the lab of Dr. Jennifer A. Maynard, Assistant Professor of Chemical Engineering. The Texas License Agreement provides that the University is entitled to payment of past patent expenses, an annual payment of $50,000 per year commencing on the effective date through December 31, 2014 and a $25,000 payment on December 31, 2015 and milestone payments of $50,000 upon commencement of Phase I Clinical Trials, $100,000 upon commencement of Phase III Clinical Trials, $250,000 upon NDA submission in the United States, $100,000 upon European Medicines Agency approval and $100,000 upon regulatory approval in an Asian country. In addition, the University is entitled to a running royalty upon Net Product Sales and Net Service Sales (as defined in the Texas License Agreement). The License Agreement terminates upon the expiration of the patent rights (as defined in the Texas License Agreement); provided, however that the Texas License Agreement is subject to early termination by us in our discretion and by the University for a breach of the Texas License Agreement by us.

In connection with the Texas License Agreement, we also entered into a Sponsored Research Agreement (the "Sponsored Research Agreement") with the University pursuant to which the University will perform certain research work related to pertussis under the direction of Dr. Jennifer Maynard and we will obtain certain rights to patents and technology developed during the course of such research. All inventions conceived during such research shall be subject to the Texas License Agreement. The Sponsored Research Agreement may be renewed annually, in our sole discretion, after the first year for two additional one year terms with a fixed fee for the first year of $303,287 and for the second and third years, if renewed, a fixed fee of $316,438 and $328,758 respectively, all payable in quarterly installments. If renewed by us after the first year for the remaining two years, the research shall be performed from the effective date of the Sponsored Research Agreement until December 31, 2015; provided, however, the Sponsored Research Agreement is subject to early termination upon the written agreement of the parties, a default in the material obligations under the Sponsored Research Agreement which remain uncured for sixty days after receipt of notice, automatically upon our bankruptcy or insolvency and by us in our sole discretion at any time after the one year anniversary of the date of execution thereof upon no less than 90 days notice. Upon termination prior to December 31, 2014, we shall only be responsible for payment of expenses that do not exceed the fixed annual amount and are incurred prior to the termination date and non-cancellable expenses committed to be expended by the University prior to the termination date for the lesser of the remainder of their appointment in the case of salaries and December 31, 2014. Upon a termination after December 31, 2014 or due to a breach by the University, we shall only be responsible for all reasonable expenses that do not exceed the fixed annual amount and that are incurred by the University prior to the termination date for services performed prior to the termination date.

Oral Enzyme for C. difficile Program Acquisition Agreement

On November 8, 2012, we entered into an Asset Purchase Agreement (the "Prev Agreement") with Prev ABR LLC ("Prev"), and subsequently closed the transaction on November 28, 2012. Pursuant to the Prev Agreement we acquired the *C. difficile* program assets of Prev, including pre-IND package for P3A (SYN-004), Phase I and Phase II clinical data for P1A, manufacturing processes and data, and a portfolio of issued and pending U.S. and international patents intended to support an IND and BLA with the FDA. Pursuant to the Prev Agreement, we paid Prev an initial cash payment of $100,000 upon execution of the Prev Agreement and at closing paid an additional cash payment of $135,000 and issued 625,000 unregistered shares of our common stock to Prev. In addition, upon the achievement of the milestones set forth below, Prev may be entitled to receive additional consideration payable 50% in cash and 50% in our stock, subject to Prev's option to receive the entire payment in shares of our stock, with the exception of the first milestone payments to be paid in cash: (i) upon commencement of an IND; (ii) upon commencement of a Phase I clinical trial; (iii) upon commencement of a Phase II clinical trial; (iv) upon commencement of a Phase III clinical trial; (v) upon Biologic License Application (BLA) filing in the U.S. and for territories outside of the U.S. (as defined in the Prev Agreement); and (vi) upon BLA approval in the U.S. and upon approval in territories outside the U.S. The future stock issuances are subject to prior approval of the NYSE MKT, LLC. No royalties are payable to Prev under the Prev Agreement.

The Prev Agreement also provides that Prev has a right to the return to it of all assets acquired by us under the Prev Agreement if on or prior to the date that is (i) 30 months after the execution of the Prev Agreement, we have not initiated toxicology studies in non-rodent models or (ii) 36 months have not filed an IND under the program related to the assets and such failure is not due to action or inaction of Prev or breach of its representations or warranties or covenants or if there is a change of control as defined in the Prev Agreement and after such change of control the assets are not further developed; provided however that such 30 and 36 month periods can be extended by us for an additional 12 months upon payment of a cash milestone payment.

Infectious Disease Collaboration with Intrexon

On August 6, 2012, we expanded our relationship with Intrexon and entered into the Second ECC with Intrexon that governs a "channel collaboration" arrangement in which we will use Intrexon's technology relating to the identification, design and production of human antibodies and DNA vectors for the development and commercialization of a series of monoclonal antibody therapies for the treatment of certain serious infectious diseases the "Program") for the treatment of eight specific target infectious disease indications (the "Field"). Initially, our development efforts will target three infectious diseases within the Field. Within the first two years of the collaboration, we have the right to exchange our initial three targets on a one-for-one basis with any of the other five targeted infectious diseases in the Field at no additional cost. We also have the option, within such two year period, to choose to develop any or all of the other five target diseases in the Field, upon payment of the additional consideration described below. Such license is exclusive with respect to any clinical development, selling, offering for sale or other commercialization of our products within the Field ("Synthetic Products"), and otherwise is non-exclusive. We may not sublicense the rights described without Intrexon's written consent. Under the Second ECC, and subject to certain exceptions, we are

responsible for, among other things, the performance of the Program including the development, commercialization and manufacturing of products.

Subject to certain expense allocations and other offsets provided in the Second ECC, we will pay Intrexon royalties on annual net sales of the Synthetic Products, calculated on a Synthetic Product-by-Synthetic Product basis. We have likewise agreed to pay Intrexon a percentage of quarterly revenue obtained from a sublicensor in the event of a sublicensing arrangement.

We may voluntarily terminate the Second ECC upon 90 days written notice to Intrexon. Intrexon may also terminate the Second ECC if we elect not to pursue the development of a Program identified by Intrexon that is a "Superior Therapy" as defined in the Second ECC upon 60 days notice unless we remedy the circumstances giving rise to the termination during such notice period. Each party has the right to terminate the agreement upon 60 days notice if the other party commits a material breach of the Second ECC, subject to certain cure periods.

Upon termination of the Second ECC, we may continue to develop and commercialize any Synthetic Product that, at the time of termination satisfies one of the following:

- is being commercialized by us,
- has received regulatory approval,
- is a subject of an application for regulatory approval that is pending before the applicable regulatory authority,
- is a subject of at least a Phase II or Phase III clinical trial if such termination is by Intrexon due to a material breach by us of the Second ECC or by us upon 60 days notice after the first 18 months.

Our obligation to pay the royalties described above with respect to these "retained" products will survive termination of the Second ECC.

On October 16, 2012, we issued 3,552,210 shares of our Common Stock as consideratio