Synthetic Biologics, Inc.
Form 10-K
April 16, 2013

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, 2012

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 30, 2012, was approximately $44,969,000 based on $1.98, the price at which the registrant's common stock was last sold on that date.

As of March 27, 2013, the issuer had 44,654,414 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

Most 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 simila 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 biologics for the prevention and treatment of serious infectious diseases. We are developing an oral enzyme for the prevention of *C. difficile* infections, and a series of monoclonal antibody therapies for the treatment of Pertussis and *Acinetobacter* infections. In addition, we are developing a drug candidate for the treatment of relapsing-remitting multiple sclerosis and cognitive dysfunction in multiple sclerosis, and have partnered the development of a treatment for fibromyalgia.

Product Pipeline:

Summary of Infectious Disease Programs:

- ***Clostridium difficile (C. difficile)*** **infections:** In November 2012, we acquired a series of oral beta-lactamase enzymes (P1A, P2A and P3A) and related assets targeting the prevention *of C. difficile* infections (CDI), the leading cause of hospital acquired infections (HAI), that generally occurs secondary to treatment with intravenous antibiotics. The acquired assets include a pre-Investigational New Drug (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 Biologic 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 IPSAT P3A. When co-administered with certain intravenous beta-lactam antibiotics, it is expected that SYN-004 can degrade the antibiotic that is excreted in the gastrointestinal (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. According to GlobalData, an estimated 8.7 million Americans were administered intravenous beta-lactam antibiotics in 2011.

- **Pertussis:** In December 2012, in collaboration with Intrexon Corporation (Intrexon), we initiated development of a monoclonal antibody (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 294,000 deaths worldwide, primarily among young, unvaccinated children.

- ***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 multi-billion dollar market opportunity.

Summary of Multiple Sclerosis Program:

- Trimesta™ (oral estriol) is being developed as an oral once-daily treatment for relapsing-remitting multiple sclerosis (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 U.S. The primary endpoint is relapse rate at two years, with top-line results expected in 1H 2014. This trial is supported by grants exceeding $8 million, which should be sufficient to fund the trial through completion. Current sales of injectable disease-modifying therapies for MS are estimated at $8.9 billion annually.

- 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 being conducted at University of California, Los Angeles (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 U.S., Canada and Japan. The sublicense agreement provides that all ongoing and future development costs are to 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 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. 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.

To prioritize our focus on the development of product candidates for the prevention and treatment of serious infectious diseases, we do not intend to pursue further development of our previously announced program for pulmonary arterial hypertension. However, we are currently in discussions with Intrexon to substitute this program with an alternate program better suited to our current objectives and focus.

In order to further prioritize our focus, we have elected to discontinue further development of AEN-100 for the treatment of amyotrophic lateral sclerosis. However, we are currently seeking development partners for our zinc-based intellectual property and assets including, AEN-100.

Pipeline Programs and Therapeutic Areas

Infectious Disease Programs

We are focused on the development of biologics for the prevention and treatment of serious infectious diseases. Infectious disease outbreaks are increasing while intervention options are declining due to widespread multidrug-resistant bacteria, increasing numbers of immuno-compromised patients (eg. the elderly and cancer patients), and the isolation of new pathogens. We are developing an oral enzyme for the prevention of *C. difficile* infections, and a series of monoclonal antibody therapies for the treatment of Pertussis and *Acinetobacter* infections.

***C. difficile Infections*:**

According to the Agency for Healthcare Research and Quality, aggregate costs associated with 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 (*C. difficile*-associated diarrhea (CDAD)), and in the most serious cases, pseudomembranous colitis (erosion of the lower GI tract) that can lead to death. CDI is a major, unintended risk associated with the prophylactic or therapeutic use of intravenous 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, resulting in more than 337,000 hospitalizations and 30,000 deaths in the U.S. during 2009, according to the U.S. Department of Health & Human Services. CDI has surpassed methicillin-resistant staphylococcus aureus (MRSA) as the most frequent infection acquired in the hospital. It has recently been reported by The Centers for Disease Control and Prevention that the current number of CDI cases may be as high as 500,000 annually in the U.S. 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.

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 CDI, the leading cause of HAIs, that generally occurs secondary to treatment with intravenous 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 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 IPSAT P3A. When co-administered with certain intravenous 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. According to GlobalData, an estimated 8.7 million Americans were administered intravenous beta-lactam antibiotics in 2011.

C. difficile: Oral Enzyme Background

We acquired a series of oral beta-lactamase enzymes (P1A, P2A and P3A). 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: Clinical Development

Compared to the first generation oral enzyme candidate, P1A, we believe that SYN-004 (formerly P3A) will have activity against a broader spectrum of beta-lactam antibiotics, including both penicillins and most cephalosporins. Due to the structural similarities between P1A and SYN-004 for the prevention of CDI, along with 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.

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 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)

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Pertussis (Whooping Cough):

Bordetella pertussis (B. pertussis) is a gram-negative bacterium that infects the upper respiratory tract, causing uncontrollable, 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 in association with 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, each year, *B. pertussis* infection causes an estimated 294,000 deaths worldwide, primarily among young, unvaccinated children. 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 are increasing 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 potentially shorten the duration of chronic cough in afflicted adults. SYN-005 is currently in preclinical studies.

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.

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 as high as 43% are reported in hospital 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 multi-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.

Multiple Sclerosis Program

Relapsing-Remitting MS in Women:

MS is a progressive neurological disease in which the body loses the ability to transmit messages along central nervous system nerve cells, 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 2.5 million people worldwide (approximately 400,000 patients in the U.S. of which approximately 70% 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 ten FDA-approved therapies for the treatment of relapsing-remitting MS: Betaseron®, Rebif®, Avonex®, Novantrone®, 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® 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.

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Current sales of injectable disease-modifying therapies for MS are estimated at $8.9 billion annually. According to various reports, sales of oral disease-modifying therapies for MS, such as Trimesta, if and when approved, are anticipated to grow from $500 million in 2010 to in excess of $5 billion annually by 2017.

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, a landmark 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. As of January 23, 2012, 164 patients have been enrolled and enrollment has been closed. The patients will be dosed and monitored for two years with the last patient scheduled to complete two years of therapy in January 2014.

With over $8 million in grant funding to date, the ongoing Trimesta clinical trial should be funded to its completion.

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 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 million upon the FDA's acceptance of the New Drug Application (NDA) for flupirtine for fibromyalgia and $10 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 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.

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.

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) thirty (30) months after the execution of the Prev Agreement, we have not initiated toxicology studies in non-rodent models or (ii) thirty six (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 thirty (30) and thirty six (36) month periods can be extended by us for an additional twelve (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 a second Exclusive Channel Collaboration Agreement (the "Second Channel Agreement") 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 Channel Agreement, 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 Channel Agreement, 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.

During the first 18 months, we may not terminate the Second Channel Agreement, except under limited circumstances. Following the first 18 months, we may voluntarily terminate the Second Channel Agreement upon 90 days written notice to Intrexon. Intrexon may also terminate the Second Channel Agreement if we elect not to pursue the development of a Program identified by Intrexon that is a "Superior Therapy" as defined in the Second Channel Agreement 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 Channel Agreement, subject to certain cure periods.

Upon termination of the Second Channel Agreement, 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 2 or Phase 3 clinical trial if such termination is by Intrexon due to a material breach by us of the Second Channel Agreement 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 Channel Agreement.

On October 16, 2012, we issued 3,552,210 shares of our Common Stock as consideration in connection with the Second Channel Agreement and the related Stock Issuance Agreement with Intrexon that we entered into on August 6, 2012 (the "Second Stock Issuance Agreement").

We also agreed upon the filing of an Investigational New Drug application with the U.S. Food and Drug Administration for a Synthetic Product, or alternatively the filing of the first equivalent regulatory filing with a foreign regulatory agency (both as applicable, the "IND Milestone Event"), to pay Intrexon either (i) two million dollars ($2M) in cash, or (ii) that number of shares of Common Stock (the "IND Milestone Shares") having a fair market value equaling two million dollars ($2M) where such fair market value is determined using published market data of the share price for Common Stock at the close of market on the business day immediately preceding the date of public announcement of attainment of the IND Milestone Event.

Upon the first to occur of either first commercial sale of a Synthetic Product in a country or the granting of the regulatory approval of that Synthetic Product (both as applicable, the "Approval Milestone Event"), we agreed to pay to Intrexon either (i) three million dollars ($3M) in cash, or (ii) that number of shares of Common Stock (the "Approval Milestone Shares") having a fair market value equaling three million dollars ($3M) where such fair market value is determined using published market data of the share price for Common Stock at the close of market on the business day immediately preceding the date of public announcement of attainment of the Approval Milestone Event.

We also agreed that we will pay an optional and varying fee whereby we remit a payment, in cash or equity at our sole discretion, to Intrexon calculated as a multiple of the number of targets in excess of three (3) total that we desire to elect (the "Field Expansion Fee"). The Field Expansion Fee must be paid completely in either Common Stock or cash, and will comprise either (i) two million dollars ($2M) in cash for each target in excess of three (3) total that we elect, or (ii) that number of shares of Common Stock (the "Field Expansion Fee Shares") having a fair market value equaling two million dollars ($2M) for each such target that we elect in excess of three where such fair market value is determined using published market data establishing the volume-weighted average price for a share of Common Stock over the thirty (30) day period immediately preceding the date of the Field Expansion Fee Closing.

In connection with the transactions contemplated by the Second Stock Issuance Agreement, and pursuant to the First Amendment to Registration Rights Agreement (the "First Amendment to Registration Rights Agreement") executed and delivered by the parties at the closing, we agreed to file a "resale" registration statement registering the resale of certain of the shares issued under the Second Stock Issuance Agreement. None of the shares to be issued under the Second Stock Issuance Agreement need to be registered until April 30, 2013. Under that agreement, we are obligated to use our reasonable best efforts to cause the "resale" registration statement to be declared effective as promptly as practicable after filing and to maintain the effectiveness of the registration statement until all securities therein are sold or are otherwise can be sold pursuant to Rule 144, without any restrictions.

DNA-Based Therapy Collaboration with Intrexon

On November 18, 2011, we entered into a Channel Agreement with Intrexon (the "Channel Agreement") that governs an "exclusive channel collaboration" arrangement in which we intend to use Intrexon's technology directed towards the production of prostaglandin synthase (PGIS), through the use of *in vivo* conditionally regulated embedded controllable bioreactors for the treatment of PAH. The Channel Agreement establishes committees comprised of our and Intrexon representatives that will govern activities related to the PAH program in the areas of project establishment, chemistry, manufacturing and controls, clinical and regulatory matters, commercialization efforts and intellectual property.

The Channel Agreement grants us a worldwide license to use specified patents and other intellectual property of Intrexon in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products involving the production of PGIS through the use of an *in vivo* conditionally regulated embedded controllable bioreactor for the treatment of PAH in humans. Such license is exclusive with respect to any clinical development, selling, offering for sale or other commercialization of Products, and otherwise is non-exclusive. We may not sublicense the rights described without Intrexon's written consent.

Under the Channel Agreement, and subject to certain exceptions, we are responsible for, among other things, the performance of the PAH program including the development, commercialization and certain aspects of manufacturing products. Among other things, Intrexon is responsible for the costs of establishing manufacturing capabilities and facilities for the bulk manufacture of products developed under the PAH program, certain other aspects of manufacturing, costs of discovery-stage research with respect to platform improvements and costs of filing, prosecution and maintenance of Intrexon's patents.

Subject to certain expense allocations and other offsets provided in the Channel Agreement, we will pay Intrexon 50% of the cumulative net quarterly profits derived from the sale of products, calculated on a product-by-product basis. We have likewise agreed to pay Intrexon 50% of quarterly revenue obtained from a sublicensor in the event of a sublicensing arrangement. During the first 18 months, neither we nor Intrexon may terminate the Channel Agreement, except under limited circumstances. Following the first 18 months, we may voluntarily terminate the Channel Agreement upon 90 days written notice to Intrexon. Following the first 18 months, Intrexon may also terminate the Channel Agreement if we elect not to pursue the development of a PAH program identified by Intrexon that is a "Superior Therapy" as defined in the Channel Agreement.

Upon termination of the Channel Agreement, we may continue to develop and commercialize any Product that, at the time of termination:

- 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 the subject of at least an ongoing Phase II clinical trial (in the case of a termination by Intrexon due to our uncured breach or a voluntary termination by us), or an ongoing Phase I clinical trial in the Field (as defined in the Channel Agreement) (in the case of a termination by us due to an Intrexon uncured breach or a termination by Intrexon following an unconsented assignment by us or our election not to pursue development of a Superior Therapy), or
- we have spent at least $4.5 million developing.

We will be obligated to pay 50% of net profits or revenue with respect to these “retained” products, which will survive termination of the Channel Agreement.

As consideration for execution of the Channel Agreement, we entered into a Stock Purchase Agreement with Intrexon (the “Stock Purchase Agreement”) pursuant to which we issued to Intrexon a number of shares of our common stock equal to 9.995% of the number of shares of our common stock issued and outstanding following and giving effect to such issuance (the “First Tranche”) at a purchase price equal to the $0.001 par value of such shares, which issuance was deemed paid in consideration for the execution and delivery of the Channel Agreement. We also agreed to issue additional shares of our common stock to Intrexon upon dosing of the first patient in a Phase II clinical trial sponsored by us in the U.S., or similar study as the parties may agree in a country other than the U.S. The program under this Channel Agreement is in the discovery stage.

Under the Stock Purchase Agreement, Intrexon is entitled, at its election, to:

(i) participate in our future securities offerings that constitute “Qualified Financings” and purchase securities equal to 19.99% of the number of shares of common stock or other securities sold in such offering. For this purpose, a “Qualified Financing” means a sale of our common stock or equity securities convertible into our common stock in a public or private offering, raising gross proceeds of at least $5 million, where the sale of shares is either registered under the Securities Act of 1933, as amended (the “Securities Act”), at the time of issuance or we agree to register the resale of such shares, and

(ii) without restriction, purchase an additional number of shares of our common stock in the open market, or otherwise, that do not exceed an additional 10% of the number of shares of common stock then issued and outstanding.

The Stock Purchase Agreement contains a standstill provision pursuant to which, among other things, Intrexon has agreed that, for a period of three years, subject to certain exceptions and unless invited in writing by us to do so, neither Intrexon nor its affiliates will, directly or indirectly: (i) effect or seek, initiate, offer or propose to effect, or cause or participate in any acquisition of our securities or assets; any tender or exchange offer, merger, consolidation or other business combination involving us; any recapitalization, restructuring, liquidation, dissolution or other extraordinary transaction with respect to us; or any "solicitation" of "proxies" or consents to vote any of our voting securities, or in any way advise or, assist any other person in doing so; (ii) form, join or in any way participate in a "group" with respect to any of our securities; (iii) otherwise act to seek to control or influence the management, Board of Directors or our policies; (iv) take any action reasonably expected to force us to make a public announcement regarding any such matters; or (v) enter into any agreements, discussions or arrangements with any third party with respect to any of the foregoing.

In connection with the transactions contemplated by the Stock Purchase Agreement, and pursuant to the Registration Rights Agreement executed and delivered by us to Intrexon, we agreed to file a "resale" registration statement registering the resale of the First Tranche Shares within 120 days of the closing date of such issuance. The registration statement registering such shares was declared effective on April 13, 2012, but is not currently valid due to certain issues regarding the failure of our prior auditor to follow proper partner rotation. Intrexon has agreed not to require us to file a post effective registration statement on Form S-1 with respect to the First Tranche Shares and instead has agreed to wait until we are once again S-3 eligible for registration of such shares.

McLean Hospital Exclusive License Agreement and Meda AB Sublicense Agreement

In 2005, as amended in 2007 and 2010, we entered into an exclusive license agreement with the McLean Hospital, a Harvard University teaching hospital, relating to U.S. Patent No. 6,610,324 and its foreign equivalents, entitled "Flupirtine in the treatment of fibromyalgia and related conditions." Pursuant to this agreement, we paid an upfront fee and back patent costs of approximately $62,000 and agreed to pay McLean royalties on net sales of oral flupirtine equal to 3.5% of net sales of oral flupirtine for indications covered by the issued patents, reduced to 1.75% if we have a license to other intellectual property covering those indications. In addition, we agreed to use our best efforts to commercialize oral flupirtine for the therapeutic uses embodied in the patent applications. Furthermore, we agreed to reimburse McLean Hospital all future patent costs and pay the following milestone payments: $150,000 upon the initiation of a pivotal Phase III clinical trial of oral flupirtine; $300,000 upon the filing of an NDA for oral flupirtine; and $600,000 upon FDA approval of oral flupirtine. The due diligence requirements of the exclusive license agreement were amended in April of 2010 and further amended by a Non-Disturbance Agreement that was signed with McLean Hospital, Meda and us. The agreement remains in effect until the later of (i) the date all issued patents and filed patent applications within the Patent Rights (as defined in the agreement) expire or are abandoned and (ii) one year after the last Commercial Sale (as defined in the agreement) for which royalty is due or ten years after expiration or abandonment date set forth in clause (i) above, whichever is earlier. We have the right to terminate the agreement at any time upon 90 days notice. In addition, McLean may terminate the agreement (i) upon 10 days notice for nonpayment unless payment is made within such 10 days, (ii) immediately upon written notice if we fail to maintain required insurance or become insolvent, make an assignment for the benefit of creditors or petition for bankruptcy is filed for or against us or (ii) if we, our affiliates or our sublicensees default in performance of their obligations under the agreement and such default is not cured within 60 days.

Effective May 6, 2010, we entered into a Sublicense Agreement with Meda AB of Sweden. Pursuant to this agreement, Meda has been granted an exclusive sublicense to all of our patents covering the use of oral flupirtine for fibromyalgia. These patents have been issued in the U.S. and are pending in Canada and Japan (the "Territory"). This agreement provides that Meda will assume all future development costs for the commercialization of oral flupirtine for fibromyalgia. As consideration for this sublicense, we received an up-front payment of $2.5 million upon execution of this agreement and are entitled to milestone payments of $5 million upon filing of an NDA with the FDA for oral flupirtine for fibromyalgia and $10 million upon marketing approval. This agreement also provides that we are entitled to receive royalties of 7% of net sales of oral flupirtine approved for the treatment of fibromyalgia covered by issued patent claims in the Territory. Pursuant to the terms of this agreement with our university licensor, we are obligated to share half of the royalties we receive with the university licensor, McLean Hospital, and we were obligated to pay them $375,000 upon receipt of an upfront payment, which we did pay in May 2010 when we received the payment from Meda. The agreement continues in effect country by country until the earlier of the expiration of the Royalty Period (as defined in the agreement) or the termination of the McLean license. Meda has the right to terminate the agreement at any time upon 90 days notice. In addition, a party may terminate the agreement upon 30 days notice if the other party breached material obligations and such breach is not cured within a period of time set forth in the agreement. The parties also have the right to terminate the agreement upon 60 days notice in the event of the filing by a party of a bankruptcy petition, the filing of an involuntary petition not dismissed within 60 days, a party proposes a written agreement of composition or extension of its debt, a party becomes Insolvent (as defined in the agreement), liquidates, dissolves, ceases to conduct business or makes an assignment for the benefit of creditors. Upon a termination, all licenses revert to us.

The Regents of University of California License Agreement

In July 2005, we were granted an exclusive worldwide license agreement with the Regents of the University of California (the "Regents") relating to issued U.S. Patent No. 6,936,599 and pending patent applications covering the uses of the drug candidate Trimesta (oral estriol), which has been subsequently amended. Pursuant to this agreement, we paid an upfront license fee and reimbursed patent expenses totaling approximately $61,000 and agreed to pay a license fee of $25,000 during 2006. We also agreed to pay annual maintenance fees, milestone payments totaling $750,000 that are payable on filing an NDA, and on approval of an NDA with the FDA, an additional $750,000 payable upon the first achievement of $50,000,000 in annual sales while covered by a validly issued U.S. patent as well as royalties on net sales of Trimesta covered by the licensed patents. We may be permitted to partially pay milestone payments in the form of equity. The duration of this agreement is from the effective date of July 11, 2005 until the last-to-expire patent in Regent's Patent Rights, or until the last patent application licensed under this agreement is abandoned and no patent in Regent's Patent Rights ever issues. We have the right to terminate this agreement at any time and termination will be effective 90 days after the effective date of the termination notice. The Regents may terminate the agreement with a written notice of default if we violate or fail to perform any material term or covenant of this agreement including failure within three years from the successful completion of the ongoing clinical trial of estriol for relapsing-remitting MS being conducted by Dr. Rhonda Voskuhl as principal investigator, to initiate a Phase III clinical trial, or within 17 years of the effective date of the agreement to complete the commercial sale of a product for human therapeutics for the treatment of autoimmune diseases, including MS. However, we have 60 days after the effective date of the notice of default to repair the default.

AEN-100 – Gastroretentive Zinc Acetate

AEN-100 is the subject of U.S. and international patent pending applications. On October 26, 2011, we received a final rejection letter with regard to U.S. patent application Ser. No. 11/621,962. On February 15, 2012, we filed a Request for Continued Examination.

Manufacturing

We utilize contract manufacturing firms to produce our investigational product Trimesta in accordance with “current good manufacturing processes” (cGMP) guidelines outlined by the FDA.

Research and Development

During the years ended December 31, 2012 and 2011, we incurred $12.3 million and $3.3 million, respectively, in research and development expenses.

Competitive Environment

The pharmaceutical and biotechnology industries are characterized by rapidly evolving technology and intense competition. Our competitors include major multi-national pharmaceutical companies and biotechnology companies developing both generic and proprietary therapies to treat serious diseases. Many of these companies are well-established and possess technical, human, research and development, financial, and sales and marketing resources significantly greater than ours. In addition, many of our potential competitors have formed strategic collaborations, partnerships and other types of joint ventures with larger, well established industry competitors that afford these companies potential research and development and commercialization advantages in the therapeutic areas we are currently pursuing.

Academic research centers, governmental agencies and other public and private research organizations are also conducting and financing research activities which may produce products directly competitive to those being developed by us. In addition, many of these competitors may be able to obtain patent protection, obtain FDA and other regulatory approvals and begin commercial sales of their products before us.

Our History

Our predecessor, Sheffield Pharmaceuticals, Inc. was incorporated in 1986, and in 2006 engaged in a reverse merger with Pipex Therapeutics, Inc., a Delaware corporation formed in 2001. After the merger, we changed our name to Pipex Pharmaceuticals, Inc., and in October 2008 we changed our name to Adeona Pharmaceuticals, Inc. On October 15, 2009, we reincorporated in the State of Nevada. After reprioritizing our focus on the emerging area of synthetic biologics and entering into our first collaboration with Intrexon, we amended our Articles of Incorporation to change our name to Synthetic Biologics, Inc. on February 15, 2012.

Employees

As of March 27, 2013, we employed approximately fourteen individuals, eight of whom are full-time employees. A significant number of our management and professional employees have had prior experience with pharmaceutical, biotechnology or medical product companies. None of our employees are covered by collective bargaining agreements, and management considers relations with our employees to be good.

Properties

Our principal executive offices are located at 155 Gibbs Street, Suite 412, Rockville, Maryland 20850. We also maintain an administrative and finance office in Ann Arbor, Michigan.

Available Information

Additional information about Synthetic Biologics is contained at our website, www.syntheticbiologics.com. Information on our website is not incorporated by reference into this report. We make available on our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K as soon as reasonably practicable after those reports are filed with the SEC. The following Corporate Governance documents are also posted on our website: Code of Conduct, Code of Ethics for Financial Management and the Charters for the Audit Committee, Compensation Committee and Nominations Committee of the Board of Directors. Our phone number is (734) 332-7800 and our facsimile number is (734) 332-7878.

Item 1A. ***Risk Factors***

Investing in our common stock involves a high degree of risk. In addition to the risks related to our business set forth in this Form 10-K and the other information included and incorporated by reference in this Form 10-K, you should carefully consider the risks described below before purchasing our common stock. Additional risks, uncertainties and other factors not presently known to us or that we currently deem immaterial may also impair our business operations.

RISKS RELATING TO OUR BUSINESS

We will need to raise additional capital to operate our business.

With the exception of the three months ended June 30, 2010, we have experienced significant losses since inception and have a significant accumulated deficit. We expect to incur additional operating losses in the future and therefore our cumulative losses to increase. To date, other than the licensing fee we received from Meda AB for the development and commercialization of Effirma (flupirtine) for fibromyalgia in the U.S., Canada and Japan and limited laboratory revenues from Adeona Clinical Laboratory, which we sold in March 2012, we have generated very minimal revenues. Inasmuch as our sole source of revenue (with the exception of the Meda licensing fee) has been our laboratory revenue and our laboratory was sold recently, we do not expect to derive revenue from any source in the near future until we or our partners successfully commercialize our products. As of December 31, 2012, our accumulated deficit totaled approximately $68.9 million on a consolidated basis. Until such time as we receive approval from the FDA and other regulatory authorities for our product candidates, we will not be permitted to sell our products and therefore will not have product revenues from the sale of products. For the foreseeable future we will have to fund all of our operations and capital expenditures from equity and debt offerings, cash on hand, licensing fees and grants. If our current cash, cash equivalents and short-term investments are not sufficient to sustain our operations, we will need to seek additional sources of financing and such additional financing may not be available on favorable terms, if at all. If we do not succeed in raising additional funds on acceptable terms, we may be unable to complete planned preclinical and clinical trials or obtain approval of our product candidates from the FDA and other regulatory authorities. In addition, we could be forced to delay, discontinue or curtail product development, forego sales and marketing efforts, and forego licensing in attractive business opportunities. Any additional sources of financing will likely involve the issuance of our equity or debt securities, which will have a dilutive effect on our stockholders.

We have not been able to sustain profitability.

Other than with respect to the three months ended June 30, 2010, we have a history of losses and we have incurred and continue to incur substantial losses and negative operating cash flow. Even if we succeed in developing and commercializing one or more of our product candidates, we may still incur substantial losses for the foreseeable future and may not sustain profitability. We also expect to continue to incur significant operating and capital expenditures and anticipate that our expenses will substantially increase in the foreseeable future as we do the following:

continue to undertake preclinical development and clinical trials for our product candidates;
expand our research activities with Intrexon relating to monoclonal antibodies for infectious diseases;
seek regulatory approvals for our product candidates;
develop our product candidates for commercialization;
implement additional internal systems and infrastructure;
lease additional or alternative office facilities; and
hire additional personnel, including members of our management team.

We may experience negative cash flow for the foreseeable future as we fund our technology development with capital expenditures. As a result, we will need to generate significant revenues in order to achieve and maintain profitability. We may not be able to generate these revenues or achieve profitability in the future. Our failure to achieve or maintain profitability could negatively impact the value of our common stock and underlying securities.

Our research and development efforts may not succeed in developing commercially successful products and technologies, which may limit our ability to achieve profitability.

We must continue to explore opportunities that may lead to new products and technologies. To accomplish this, we must commit substantial efforts, funds, and other resources to research and development. A high rate of failure is inherent in the research and development of new products and technologies. Any such expenditures that we make will be made without any assurance that our efforts will be successful. Failure can occur at any point in the process, including after significant funds have been invested.

Regardless of whether our clinical trials are deemed to be successful, promising new product candidates may fail to reach the market or may only have limited commercial success because of efficacy or safety concerns, failure to achieve positive clinical outcomes, inability to obtain necessary regulatory approvals or satisfy regulatory criteria, limited scope of approved uses, excessive costs to manufacture, the failure to establish or maintain intellectual property rights, or infringement of the intellectual property rights of others. Even if we successfully develop new products or enhancements, they may be quickly rendered obsolete by changing customer preferences, changing industry standards, or competitors' innovations. Innovations may not be quickly accepted in the marketplace because of, among other things, entrenched patterns of clinical practice or uncertainty over third-party reimbursement. We cannot state with certainty when or whether any of our products under development will be launched, whether we will be able to develop, license, or otherwise acquire drug candidates or products, or whether any products will be commercially successful. Failure to launch successful new products or new indications for existing products may cause our products to become obsolete, which may limit our ability to achieve profitability.

The technology on which our channel partnering arrangements with Intrexon is based on early stage technology.

We have an exclusive channel collaboration arrangement with Intrexon that contemplates the use of Intrexon’s transgene engineering platform technology and regulatory control technology for the *in vivo* cellular production of PGIS, a specific effector enzyme that regulates the production of prostacyclin. Such technologies have a limited history of use in the design and development of human therapeutic product candidates and may therefore involve unanticipated risks or delays.

On August 8, 2012, we announced an additional exclusive channel collaboration with Intrexon relating to the design, production, testing and commercialization of monoclonal antibodies for the treatment of certain infectious diseases. Although monoclonal antibody therapeutics are well established in the biotechnology and pharmaceutical sectors, their use for the treatment of infectious disease is extremely limited. In order for monoclonal antibodies to be effective for infectious diseases, they must not only properly target the organism of interest (or its toxins), but may also need to overcome defenses and forms of resistance of such organisms. To accomplish this may require the use of more than one specific monoclonal antibody, and mixtures of different monoclonal antibodies, which may create additional unforeseen complications, including increased manufacturing complexity and expense. In order to be competitive, monoclonal antibodies will be required to be produced at a low enough cost of goods in order to be profitably marketed. We have very limited development and manufacturing experience in the field of monoclonal antibodies and infectious disease. We cannot assure that any monoclonal antibody candidates will provide satisfactory in vitro and in vivo nonclinical results sufficient to warrant the expense of cGMP manufacture and clinical testing in human clinical trials.

DNA-based therapy has not yet been proven to be successful.

The FDA has not yet approved any human DNA-based therapy product for sale. The field of DNA-based therapy, also referred to as gene therapy or gene transfer, is experimental and has not yet proven successful in many clinical trials. Clinical trials with DNA-based therapy have encountered a multitude of significant technical problems in the past, including, unintended integration with host DNA, poor levels of protein expression, transient protein expression, viral overload, immune reactions to either viral capsids utilized to deliver DNA, DNA itself, proteins expressed or cells transfected with DNA. There can be no assurance that our preclinical animals studies or human clinical trials will be successful or that we will receive the regulatory approvals necessary to initiate such studies. To the extent that we utilize viral constructs or other systems to deliver our DNA-based therapies and the same or similar delivery systems demonstrate unanticipated and/or unacceptable side effects in preclinical or clinical trials conducted by ourselves or others we may be forced to, or elect to, discontinue development of such product candidates. We do not intend to pursue further development of our previously announced program for pulmonary arterial hypertension. However, we are currently in discussions with Intrexon to substitute this program with an alternate program better suited to our current objectives and focus.

We may not generate additional revenue from our relationships with our corporate collaborators.

On May 6, 2010, we entered into a sublicense agreement with Meda AB whereby we may receive milestone payments totaling $17.5 million (including an upfront payment of $2.5 million that has already been received), plus royalties on our flupirtine program. There can be no assurance that Meda AB will successfully develop flupirtine for fibromyalgia in the U.S., Canada or Japan that would allow us to receive such additional $15 million in milestone payments and royalties on sales in connection with such agreement. The successful achievement of the various milestones set forth in the sublicense agreement is not within our control and we will be dependent upon Meda AB for achievement of such milestones. 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. There can be no assurance that Meda will initiate or successfully complete such planned study.

We have experienced several management changes.

We have had significant changes in management in the past few years. Jeffrey Riley was appointed Chief Executive Officer and President on February 3, 2012. Effective February 6, 2012, C. Evan Ballantyne was appointed Chief Financial Officer. James S. Kuo, M.D., served as Chief Executive Officer and President from February 6, 2010 until February 3, 2012. Changes in our key positions, as well as additions of new personnel and departures of existing personnel, can be disruptive, might lead to additional departures of existing personnel and could have a material adverse effect on our business, operating results, financial results and internal controls over financial reporting.

We may not be able to retain rights licensed to us by others to commercialize key products and may not be able to establish or maintain the relationships we need to develop, manufacture, and market our products.

In addition to our own patent applications, we also currently rely on licensing agreements with third party patent holders/licensors for our products. We have an exclusive license agreement with the McLean Hospital relating to the use of flupirtine to treat fibromyalgia which was sublicensed to Meda AB and an exclusive license agreement with the Regents of the University of California relating to our Trimesta technology. Each of these agreements requires us or our sublicensee to use our best efforts to commercialize each of the technologies as well as meet certain diligence requirements and timelines in order to keep the license agreement in effect. In the event we or our sublicensee are not able to meet our diligence requirements, we may not be able to retain the rights granted under our agreements or renegotiate our arrangement with these institutions on reasonable terms, or at all. Furthermore, we currently have very limited product development capabilities, and limited marketing or sales capabilities. For us to research, develop, and test our product candidates, we would need to contract with outside researchers, in most cases those parties that did the original research and from whom we have licensed the technologies. Our exclusive channel collaboration agreements with Intrexon provide that Intrexon may terminate each such agreement if we do not perform certain specified requirements, including developing therapies considered superior. Our agreement with The University of Texas allows the Universtiy to terminate its agreement if we fail to comply with the terms of the agreement. Our agreement with Prev provides Prev with the right to the return of the assets if we do not perform certain requirements.

We can give no assurances that any of our issued patents licensed to us or any of our other patent applications will provide us with significant proprietary protection or be of commercial benefit to us. Furthermore, the issuance of a patent is not conclusive as to its validity or enforceability, nor does the issuance of a patent provide the patent holder with freedom to operate without infringing the patent rights of others.

We will incur additional expenses in connection with our exclusive channel collaboration arrangements with Intrexon and Prev.

Pursuant to our exclusive channel collaborations with Intrexon, we are responsible for future research and development expenses of product candidates developed under each such collaboration, the effect of which has and will continue to increase the level of our overall research and development expenses going forward. Our agreement with Prev requires that we initiate certain studies and file an NDA within a certain amount of time, each of which are costly and will require additional expenditures. Although all manufacturing, preclinical studies and human clinical trials are expensive and difficult to design and implement, costs associated with the manufacturing, research and development of biologic product candidates are generally greater in comparison to small molecule product candidates. We have added additional personnel and expect to add additional personnel to support our exclusive channel collaborations with Intrexon, and research and development of our biologic candidate, SYN-004.

Because our biologic programs are relatively new, we have only recently assumed development responsibility and costs associated with such programs. In addition, because development activities in collaboration with Intrexon are determined pursuant to a joint steering committees comprised of Intrexon and ourselves and we have limited experience, future development costs associated this program may be difficult to anticipate and exceed our expectations. Our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, unanticipated technical challenges, changes in the focus and direction of our development activities or adjustments necessitated by changes in the competitive landscape in which we operate. If we are unable to continue to financially support such collaborations due to our own working capital constraints, we may be forced to delay our activities. If we are unable to obtain additional financing on terms acceptable to us or at all, we may be forced to seek licensing partners or discontinue development.

Developments by competitors may render our products or technologies obsolete or non-competitive.

Companies that currently sell or are developing both generic and proprietary products to treat multiple sclerosis include: Abbott Biotherapeutics Corporation, Bayer Health Care, Biogen Idec, Genzyme, GlaxoSmithKline Pharmaceuticals, Merck & Co., Pfizer, Novartis, Sanofi and Teva Pharmaceuticals. Companies that currently sell or are developing both generic and proprietary products to treat infectious diseases include: MedImmune, Pfizer, Cubist, Optimer Pharmaceuticals, Symphogen, Merus, GlaxoSmithKline Pharmaceuticals and Merck & Co.. Many of our competitors have significant financial and human resources. The infectious disease market is highly competitive with many generic and proprietary intravenous and oral formulations available to physicians and their patients. For our monoclonal antibodies, we currently do not expect to be able to deliver our infectious disease candidates via the oral route and may thus be limited to the in-patient and/or acute treatment setting. In addition, academic research centers may develop technologies that compete with our Trimesta and flupirtine technologies. Should clinicians or regulatory authorities view these therapeutic regiments as more effective than our products, this might delay or prevent us from obtaining regulatory approval for our products, or it might prevent us from obtaining favorable reimbursement rates from payers, such as Medicare, Medicaid, hospitals and private insurers.

We operate in a highly competitive environment.

The pharmaceutical and biotechnology industries, including the monoclonal antibody industry, are characterized by rapidly evolving technology and intense competition. Our competitors include major multi-national pharmaceutical companies and biotechnology companies developing both generic and proprietary therapies to treat serious diseases. Many of these companies are well-established and possess technical, human, research and development, financial, and sales and marketing resources significantly greater than ours. In addition, many of our potential competitors have formed strategic collaborations, partnerships and other types of joint ventures with larger, well established industry competitors that afford these companies potential research and development and commercialization advantages in the therapeutic areas we are currently pursuing.

Academic research centers, governmental agencies and other public and private research organizations are also conducting and financing research activities which may produce products directly competitive to those being developed by us. In addition, many of these competitors may be able to obtain patent protection, obtain FDA and other regulatory approvals and begin commercial sales of their products before us.

Competitors could develop and/or gain FDA approval of our product candidates for a different indication.

Since we do not have composition of matter patent claims for flupirtine and estriol, others may obtain approvals for other uses of these products that are not covered by our issued or pending patents. For example, the active ingredients in both Effirma (flurpirtine) and Trimesta (oral estriol) have been approved for marketing in overseas countries for different uses. Other companies, including the original developers or licensees or affiliates may seek to develop Effirma or Trimesta or their respective active ingredient(s) for other uses in the U.S. or any country we are seeking approval for. We cannot provide any assurances that any other company may obtain FDA approval for products that contain flupirtine and estriol in various formulations or delivery systems that might adversely affect our ability or the ability of Meda to develop and market these products in the U.S. We are aware that other companies have intellectual property protection using the active ingredients and have conducted clinical trials of flupirtine and estriol for different applications than what we are developing. Many of these companies may have more resources than us. We cannot provide any assurances that our products will be FDA-approved prior to our competitors.

If a product containing our active ingredients is already marketed or if the FDA approves other products containing our active ingredients in the future to treat indications, physicians may elect to prescribe and substitute a competitor's products to treat the diseases for which we are intending to commercialize; this is commonly referred to as "off-label" use. While under FDA regulations a competitor is not allowed to promote off-label uses of its product, the FDA does not regulate the practice of medicine and, as a result, cannot direct physicians to select certain products for their patients. Consequently, we might be limited in our ability to prevent off-label use of a competitor's product to treat the diseases we are intending to commercialize, even if we have issued method of use patents for that indication. If we are not able to obtain and enforce our patents, if any, or otherwise receive orphan drug protection in the case of ALS, a competitor could develop and commercialize similar products for the same indications that we are pursuing. We cannot provide any assurances that a competitor will not obtain FDA approval for a product that contains the same active ingredients as our products.

We rely on method patents and patent applications and various regulatory exclusivities to protect some of our product candidates and our ability to compete may be limited or eliminated if we are not able to protect our products.

Our competitiveness may be adversely affected if we are unable to protect our proprietary technologies. We do not have composition of matter patents for Trimesta or Effirma, or their respective active ingredients estriol and flupirtine. We rely on issued patent and pending patent applications for use of Trimesta to treat MS (issued U.S. Patent Nos.

6,936,599 and 8,372,826) and various other therapeutic indications, which have been exclusively licensed to us. We have exclusively licensed an issued patent for the treatment of fibromyalgia with flupirtine, which we have sublicensed to Meda AB.

Our AEN-100 drug candidate (gastroretentive zinc acetate) is the subject of U.S. and international pending patent applications, such as published U.S. patent application Ser. No. 11/621,962 and corresponding international applications that claim priority to January 10, 2006 as well as additional patent applications. On October 26, 2011, we received a final rejection letter with regard to U.S. patent application Ser. No. 11/621,962. On February 15, 2012, we filed a Request for Continued Examination. Our inability to obtain patent protection could hinder our partnering efforts.

The patent positions of pharmaceutical companies are uncertain and may involve complex legal and factual questions. We may incur significant expense in protecting our intellectual property and defending or assessing claims with respect to intellectual property owned by others. Any patent or other infringement litigation by or against us could cause us to incur significant expense and divert the attention of our management.

Others may file patent applications or obtain patents on similar technologies or compounds that compete with our products. We cannot predict how broad the claims in any such patents or applications will be, and whether they will be allowed. Once claims have been issued, we cannot predict how they will be construed or enforced. We may infringe intellectual property rights of others without being aware of it. If another party claims we are infringing their technology, we could have to defend an expensive and time consuming lawsuit, pay a large sum if we are found to be infringing, or be prohibited from selling or licensing our products unless we obtain a license or redesign our product, which may not be possible.

We also rely on trade secrets and proprietary know-how to develop and maintain our competitive position. Some of our current or former employees, consultants, scientific advisors, current or prospective corporate collaborators, may unintentionally or willfully disclose our confidential information to competitors or use our proprietary technology for their own benefit. Furthermore, enforcing a claim alleging the infringement of our trade secrets would be expensive and difficult to prove, making the outcome uncertain. Our competitors may also independently develop similar knowledge, methods, and know-how or gain access to our proprietary information through some other means.

We may fail to retain or recruit necessary personnel, and we may be unable to secure the services of consultants.

As of March 27, 2013, we employed approximately fourteen individuals, eight of whom are full-time employees. We have also engaged clinical consultants to advise us on our clinical programs and regulatory consultants to advise us on our dealings with the FDA and other foreign regulatory authorities. We have been and will be required to retain additional consultants and employees in order to fulfill our obligations under our exclusive channel collaborations with Intrexon and our development obligations under our agreement with Prev. Our future performance will depend in part on our ability to successfully integrate newly hired officers into our management team and our ability to develop an effective working relationship among senior management.

Certain of our directors, scientific advisors, and consultants serve as officers, directors, scientific advisors, or consultants of other biopharmaceutical or biotechnology companies that might be developing competitive products to ours. Other than corporate opportunities, none of our directors are obligated under any agreement or understanding with us to make any additional products or technologies available to us. Similarly, we can give no assurances, and we do not expect and stockholders should not expect, that any biomedical or pharmaceutical product or technology identified by any of our directors or affiliates in the future would be made available to us other than corporate opportunities. We can give no assurances that any such other companies will not have interests that are in conflict with our interests.

Losing key personnel or failing to recruit necessary additional personnel would impede our ability to attain our development objectives. There is intense competition for qualified personnel in the drug and biologic development areas, and we may not be able to attract and retain the qualified personnel we would need to develop our business.

We rely on independent organizations, advisors, and consultants to perform certain services for us, including handling substantially all aspects of regulatory approval, clinical management, manufacturing, marketing, and sales. We expect that this will continue to be the case. Such services may not always be available to us on a timely basis when we need them.

If the parties we depend on for supplying substance raw materials for our product candidates and certain manufacturing-related services do not timely supply these products and services in sufficient quality or quantity, it may delay or impair our ability to develop, manufacture and market our product candidates.

We rely on suppliers for the substance raw materials of our product candidates and third parties for certain manufacturing-related services to produce material that meets appropriate content, quality and stability standards and use in clinical trials of our products and, after approval, for commercial distribution. We have not yet established cGMP manufacturers for our biologic and drug candidates. To succeed, clinical trials require adequate supplies of

study material, which may be difficult or uneconomical to procure or manufacture. We and our suppliers and vendors may not be able to (i) produce our study material to appropriate standards for use in clinical studies, (ii) perform under any definitive manufacturing, supply or service agreements with us, or (iii) remain in business for a sufficient time to successfully produce and market our product candidates. If we do not maintain important manufacturing and service relationships, we may fail to find a replacement supplier or required vendor or develop our own manufacturing capabilities which could delay or impair our ability to obtain regulatory approval for our products and substantially increase our costs or deplete profit margins, if any. If we do find replacement manufacturers and vendors, we may not be able to enter into agreements with them on terms and conditions favorable to us and, there could be a substantial delay before a new facility could be qualified and registered with the FDA and foreign regulatory authorities.

If successful large-scale manufacturing of DNA-based products is not possible, we or our collaborators may be unable to manufacture enough of our product candidates to achieve regulatory approval or market our DNA-based products.

Few companies to date have demonstrated successful large-scale manufacturing of DNA-based products, including those that have had significantly more resources than us and it is anticipated that significant challenges will be faced in the scale-up of our manufacturing process for commercial production. There are a limited number of contract manufacturers qualified to perform large-scale manufacturing of DNA-based products. We or our collaborators may be unable to manufacture commercial-scale quantities of DNA-based products or receive appropriate government approvals on a timely basis or at all. Failure to successfully manufacture or obtain appropriate government approvals on a timely basis or at all would prevent us from achieving our business objectives.

Clinical trials are very expensive, time-consuming, and difficult to design and implement.

Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process is also time-consuming. We estimate that clinical trials of our product candidates would take at least several years to complete. Furthermore, failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon or repeat clinical trials. Commencement and completion of clinical trials may be delayed by several factors, including:

obtaining an IND application with the FDA to commence clinical trials;
identification of, and acceptable arrangements with, one or more clinical sites;
obtaining IRB approval to commence clinical trials;
unforeseen safety issues;
determination of dosing;
lack of effectiveness during clinical trials;
slower than expected rates of patient recruitment;
inability to monitor patients adequately during or after treatment;
inability or unwillingness of medical investigators to follow our clinical protocols; and

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unwillingness of the FDA or IRBs to permit the clinical trials to be initiated.

In addition, we, IRBs or the FDA may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if IRBs or the FDA finds deficiencies in our submissions or conduct of our trials.

The results of our clinical trials may not support our product candidate claims and the results of preclinical studies and completed clinical trials are not necessarily predictive of future results.

To date, long-term safety and efficacy have not yet been demonstrated in clinical trials for any of our product candidates. Favorable results in our early studies or trials may not be repeated in later studies or trials. Even if our clinical trials are initiated and completed as planned, we cannot be certain that the results will support our product candidate claims. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. Furthermore, success of our predecessor with P1A, does not ensure success of SYN-004. We cannot be sure that the results of later clinical trials would replicate the results of prior clinical trials and preclinical testing nor that they would satisfy the requirements of the FDA or other regulatory agencies. Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. Any such failure could cause us or our sublicensee to abandon a product candidate and might delay development of other product candidates. Preclinical and clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals or commercialization. Any delay in, or termination of, our clinical trials would delay our obtaining FDA approval for the affected product candidate and, ultimately, our ability to commercialize that product candidate.

We depend on third parties, including researchers and sublicensees, who are not under our control.

Since we have in-licensed some of our product candidates, have sublicensed a product candidate and have collaboration agreements for the development of other product candidates, we depend upon our sublicensee and independent investigators and scientific collaborators, such as universities and medical institutions or private physician scientists, to advise us and to conduct our preclinical and clinical trials under agreements with us. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs or the timing of their procurement of clinical-trial data or their compliance with applicable regulatory guidelines. Should any of these scientific inventors/advisors or those of our sublicensee become disabled or die unexpectedly, or should they fail to comply with applicable regulatory guidelines, we or our sublicensee may be forced to scale back or terminate development of that program. They may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking those programs ourselves. Failing to devote sufficient time and resources to our drug-development programs, or substandard performance and failure to comply with regulatory guidelines, could result in delay of any FDA applications and our commercialization of the drug candidate involved.

These collaborators may also have relationships with other commercial entities, some of which may compete with us. Our collaborators assisting our competitors could harm our competitive position. For example, we are highly dependent on scientific collaborators for our Trimesta development program. Specifically, all of the clinical trials have been conducted under investigator-sponsored IND applications, not corporate-sponsored INDs. We have sometimes experienced difficulty in collecting data generated from these investigator-sponsored clinical trials for our programs. We cannot provide any assurances that we will not experience any additional delays in the future.

We are also highly dependent on government and private grants to fund certain of our clinical trials for our product candidates. For example, Trimesta (oral estriol) has received grants totaling over $8 million, predominantly from the Southern California Chapter of the NMSS and the National Institutes of Health which funds a majority of the ongoing clinical trial in relapsing-remitting MS for women. Although we believe that the grant funding received to date is sufficient to complete the current clinical trial based upon current cost estimates, if we experience any additional unanticipated costs or require further clinical trials, and our scientific collaborator is unable to maintain or receive additional grants, we might be forced to scale back or terminate the development of this product candidate. We will also need to cross reference our IND with the inventor/IND holder for this program should we elect to file our own corporate IND for our Trimesta (oral estriol) program. The on-going and future development and commercialization of Effirma (flupirtine) for fibromyalgia is the responsibility of Meda AB and no assurance can be given that Meda will gain the FDA’s acceptance of the NDA or obtain NDA approval from the FDA of flupirtine for fibromyalgia.

With respect to our product candidates in collaboration with Intrexon, we are dependent upon Intrexon’s synthetic biology facilities and capabilities as we have no such facilities and capabilities of our own. We are also reliant on their vector engineering platform, gene expression switch technology, monoclonal antibody discovery, production cell line development and know-how. If any of the foregoing were to become inaccessible or terminated, it would be difficult for us to develop and commercialize our synthetic biologic product candidates.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, as well as costs associated with lawsuits.

If any other person files patent applications, or is issued patents, claiming technology also claimed by us in pending applications, we may be required to participate in interference proceedings in the U.S. Patent and Trademark Office to determine priority of invention. We, or our licensors, may also need to participate in interference proceedings involving our issued patents and pending applications of another entity.

The intellectual property environment in the area of DNA-based therapeutics is particularly complex, constantly evolving and highly fragmented. Other companies and institutions have issued patents and have filed or will file patent applications that may issue into patents that cover or attempt to cover genes, vectors, cell lines, and methods of making and using DNA and DNA-based therapy products used in, or similar to our product candidate, and technologies. The same is true of the monoclonal antibody field in terms of methods of producing monoclonal antibodies for human use. We have not conducted freedom-to-use patent searches on all aspects of our product candidates or potential product candidates, and we may be unaware of relevant patents and patent applications of third parties. In addition, the freedom-to-use patent searches that have been conducted may not have identified all relevant issued patents or pending patents. We cannot provide assurance that our proposed products in this area will not ultimately be held to infringe one or more valid claims owned by third parties which may exist or come to exist in the future or that in such case we will be able to obtain a license from such parties on acceptable terms.

We cannot guarantee that the practice of our technologies will not conflict with the rights of others. In some foreign jurisdictions, we could become involved in opposition proceedings, either by opposing the validity of another's foreign patent or by persons opposing the validity of our foreign patents.

We may also face frivolous litigation or lawsuits from various competitors or from litigious securities attorneys. The cost to us of any litigation or other proceeding relating to these areas, even if deemed frivolous or resolved in our favor, could be substantial and could distract management from our business. Uncertainties resulting from initiation and continuation of any litigation could have a material adverse effect on our ability to continue our operations.

If we infringe the rights of others we could be prevented from selling products or forced to pay damages.

If our products, methods, processes, and other technologies are found to infringe the proprietary rights of other parties, we could be required to pay damages, or we may be required to cease using the technology or to license rights from the prevailing party. Any prevailing party may be unwilling to offer us a license on commercially acceptable terms.

RISKS RELATING TO OUR STOCK

We will seek to raise additional funds in the future, which may be dilutive to stockholders or impose operational restrictions.

We expect to seek to raise additional capital in the future to help fund development of our proposed products. If we raise additional capital through the issuance of equity or of debt securities, the percentage ownership of our current

stockholders will be reduced. We may also enter into strategic transactions, issue equity as part of license issue fees to our licensors, compensate consultants or settle outstanding payables using equity that may be dilutive. Our stockholders may experience additional dilution in net book value per share and any additional equity securities may have rights, preferences and privileges senior to those of the holders of our common stock.

We are substantially controlled by our current officers, directors, and principal stockholders.

Currently, our directors, executive officers, and principal stockholders beneficially own a substantial number of shares of our common stock. As a result, they will be able to exert substantial influence over the election of our Board of Directors and the vote on issues submitted to our stockholders. Our executive officers and directors beneficially owned approximately 8.9 million shares of our common stock, including stock options and warrants exercisable within 60 days of March 27, 2013. Randal J. Kirk indirectly beneficially owns approximately 9.8 million shares of our common stock. Our executive officers, directors and principal stockholders together beneficially owned approximately 18.7 million shares of our common stock, including the stock options and warrants exercisable within 60 days of March 27, 2013. Because our common stock has from time to time been “thinly traded”, the sale of a substantial number of shares by our executive officers, directors and principal stockholders would have an adverse effect on the market for our stock and our share price.

Our shares of common stock are from time to time thinly traded, so stockholders may be unable to sell at or near ask prices or at all if they need to sell shares to raise money or otherwise desire to liquidate their shares.

Our common stock has from time to time been “thinly-traded,” meaning that the number of persons interested in purchasing our common stock at or near ask prices at any given time may be relatively small or non-existent. This situation is attributable to a number of factors, including the fact that we are a small company that is relatively unknown to stock analysts, stock brokers, institutional investors and others in the investment community that generate or influence sales volume, and that even if we came to the attention of such persons, they tend to be risk-averse and would be reluctant to follow an unproven company such as ours or purchase or recommend the purchase of our shares until such time as we became more seasoned and viable. As a consequence, there may be periods of several days or more when trading activity in our shares is minimal or non-existent, as compared to a seasoned issuer which has a large and steady volume of trading activity that will generally support continuous sales without an adverse effect on share price. We cannot give stockholders any assurance that a broader or more active public trading market for our common shares will develop or be sustained, or that current trading levels will be sustained.

We cannot assure you that the common stock will be liquid or that it will remain listed on the NYSE MKT.

We cannot assure you that we will be able to maintain the continued listing standards of the NYSE MKT (formerly the NYSE Amex and the American Stock Exchange). The NYSE MKT requires companies to meet certain continued listing criteria including certain minimum stockholders' equity and equity prices per share as outlined in the NYSE MKT Exchange Company Guide. We may not be able to maintain such minimum stockholders' equity or prices per share or may be required to effect a reverse stock split to maintain such minimum prices and/or issue additional equity securities in exchange for cash or other assets, if available, to maintain certain minimum stockholders' equity required by the NYSE MKT. If we are delisted from the NYSE MKT then our common stock will trade, if at all, only on the over-the-counter market, such as the OTC Bulletin Board securities market, and then only if one or more registered broker-dealer market makers comply with quotation requirements. In addition, delisting of our common stock could depress our stock price, substantially limit liquidity of our common stock and materially adversely affect our ability to raise capital on terms acceptable to us, or at all. Delisting from the NYSE MKT could also have other negative results, including the potential loss of confidence by suppliers and employees, the loss of institutional investor interest and fewer business development opportunities. In order to remain listed on NYSE MKT, we are required to maintain a minimum stockholders’ equity of $6 million.

There may be issuances of shares of preferred stock in the future.

Although we currently do not have preferred shares outstanding, the Board of Directors could authorize the issuance of a series of preferred stock that would grant holders preferred rights to our assets upon liquidation, the right to receive dividends before dividends would be declared to common stockholders, and the right to the redemption of such shares, possibly together with a premium, prior to the redemption of the common stock. To the extent that we do issue preferred stock, the rights of holders of common stock could be impaired thereby, including without limitation, with respect to liquidation.

Our failure to fulfill all of our registration requirements may cause us to suffer liquidated damages, which may be very costly.

Pursuant to the terms of the registration rights agreement that we entered into with Intrexon and an affiliated entity, we are required to file a registration statement with respect to securities issued to them within a certain time period and maintain the effectiveness of such registration statement. The failure to do so could result in the payment of damages by us. There can be no assurance as to when the registration statement will be declared effective or that we will be able to maintain the effectiveness of any registration statement, and therefore there can be no assurance that we will not incur damages with respect to such agreements.

RISKS RELATED TO OUR INDUSTRY

We are subject to government regulation, compliance with which can be costly and difficult.

In the U.S., the formulation, manufacturing, packaging, storing, labeling, promotion, advertising, distribution and sale of our products are subject to regulation by various governmental agencies, including (1) the FDA, (2) the Federal Trade Commission, or FTC, (3) the Consumer Product Safety Commission, or CPSC, (4) the U.S. Department of Agriculture, or USDA. Our proposed activities may also be regulated by various agencies of the states, localities and foreign countries in which our proposed products may be manufactured, distributed and sold. The FDA, in particular, regulates the formulation, manufacture and labeling of over-the-counter, or OTC drugs, prescription drugs, conventional foods, dietary supplements, and cosmetics such as those that we intend to distribute. FDA regulations require us and our suppliers to meet relevant cGMP regulations for the preparation, packing, labeling, and storage of all drugs and foods.

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing FDA regulation, including record-keeping requirements, reporting of adverse experiences, submitting periodic reports, drug sampling and distribution requirements, manufacturing or labeling changes, record-keeping requirements, and compliance with FDA promotion and advertising requirements. Drug manufacturers and their subcontractors are required to register their facilities with the FDA and state agencies, and are subject to periodic unannounced inspections for GMP compliance, imposing procedural and documentation requirements upon us and third-party manufacturers. Failure to comply with these regulations could result, among other things, in suspension of regulatory approval, recalls, suspension of production or injunctions, seizures, or civil or criminal sanctions. We cannot be certain that we or our present or future subcontractors will be able to comply with these regulations.

The FDA regulates prescription drug labeling and promotion activities. The FDA actively enforces regulations prohibiting the marketing of products for unapproved uses. The FDA permits the promotion of drugs for unapproved uses in certain circumstances, subject to stringent requirements. We and our product candidates are subject to a variety of state laws and regulations which may hinder our ability to market our products. Whether or not FDA approval has been obtained, approval by foreign regulatory authorities must be obtained prior to commencing clinical trials, and sales and marketing efforts in those countries. These approval procedures vary in complexity from country to country, and the processes may be longer or shorter than that required for FDA approval. We may incur significant costs to comply with these laws and regulations now or in the future.

The FDA, comparable foreign regulators and state and local pharmacy regulators impose substantial requirements upon clinical development, manufacture and marketing of pharmaceutical products. These and other entities regulate research and development and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising, and promotion of our products. The drug approval process required by the FDA under the Food, Drug, and Cosmetic Act generally involves:

preclinical laboratory and animal tests;
submission of an IND, prior to commencing human clinical trials;
adequate and well-controlled human clinical trials to establish safety and efficacy for intended use;

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submission to the FDA of an NDA or Biologics License Application (BLA); and
FDA review and approval of an NDA or BLA.

The testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that any approval will be granted on a timely basis, if at all.

Preclinical tests include laboratory evaluation of the product candidate, its chemistry, formulation and stability, and animal studies to assess potential safety and efficacy. Certain preclinical tests must be conducted in compliance with good laboratory practice regulations. Violations of these regulations can, in some cases, lead to invalidation of the studies, requiring them to be replicated. In some cases, long-term preclinical studies are conducted concurrently with clinical studies.

We will submit the preclinical test results, together with manufacturing information and analytical data, to the FDA as part of an IND, which must become effective before we begin human clinical trials. The IND automatically becomes effective 30 days after filing, unless the FDA raises questions about conduct of the trials outlined in the IND and imposes a clinical hold, in which case, the IND sponsor and FDA must resolve the matters before clinical trials can begin. It is possible that our submission may not result in FDA authorization to commence clinical trials.

Clinical trials must be supervised by qualified investigators in accordance with good clinical practice (GCP) regulations, which include informed consent requirements. Each study must be approved and monitored by the appropriate IRBs which are periodically informed of the study's progress, adverse events and changes in research. Annual updates are submitted to the FDA and more frequently if certain serious adverse events occur.

Human clinical trials of drug candidates typically have three sequential phases that may overlap:

Phase I: The drug is initially tested in healthy human subjects or patients for safety, dosage tolerance, absorption, metabolism, distribution, and excretion.

Phase II: The drug is studied in a limited patient population to identify possible adverse effects and safety risks, determine efficacy for specific diseases and establish dosage tolerance and optimal dosage.

Phase III: When Phase II evaluations demonstrate that a dosage range is effective with an acceptable safety profile, Phase III trials to further evaluate dosage, clinical efficacy and safety, are undertaken in an expanded patient

population, often at geographically dispersed sites.

We cannot be certain that we will successfully complete Phase I, Phase II, or Phase III testing of our product candidates within any specific time period, if at all. Furthermore, the FDA, an IRB or the IND sponsor may suspend clinical trials at any time on various grounds, including a finding that subjects or patients are exposed to unacceptable health risk. Concurrent with these trials and studies, we also develop chemistry and physical characteristics data and finalize a manufacturing process in accordance with good manufacturing practice (GMP) requirements. The manufacturing process must conform to consistency and quality standards, and we must develop methods for testing the quality, purity, and potency of the final products. Appropriate packaging is selected and tested, and chemistry stability studies are conducted to demonstrate that the product does not undergo unacceptable deterioration over its shelf-life. Results of the foregoing are submitted to the FDA as part of a NDA (or BLA in case of biologic products) for marketing and commercial shipment approval. The FDA reviews each NDA or BLA submitted and may request additional information.

Once the FDA accepts the NDA or BLA for filing, it begins its in-depth review. The FDA has substantial discretion in the approval process and may disagree with our interpretation of the data submitted or identify new concerns. The process may be significantly extended by requests for new information or clarification of information already submitted. As part of this review, the FDA may refer the application to an advisory committee, typically a panel of clinicians. Manufacturing establishments often are inspected prior to NDA or BLA approval to assure compliance with GMPs and with manufacturing commitments made in the application.

Submission of an NDA or BLA with clinical data requires payment of a fee. In return, the FDA assigns a goal of ten months for issuing its “complete response,” in which the FDA may approve or deny the NDA or BLA, or require additional clinical data. Even if these data are submitted, the FDA may ultimately decide the NDA or BLA does not satisfy approval criteria. If the FDA approves the NDA or BLA, the product becomes available for marketing. Product approval may be withdrawn if regulatory compliance is not maintained or safety problems occur. The FDA may require post-marketing studies, also known as phase IV studies, as a condition of approval, and requires surveillance programs to monitor approved products that have been commercialized. The agency has the power to require changes in labeling or prohibit further marketing based on the results of post-marketing surveillance.

Satisfaction of these and other regulatory requirements typically takes several years, and the actual time required may vary substantially based upon the type, complexity and novelty of the product. Government regulation may delay or prevent marketing of potential products for a considerable period of time and impose costly procedures on our activities. We cannot be certain that the FDA or other regulatory agencies will approve any of our products on a timely basis, if at all. Success in preclinical or early-stage clinical trials does not assure success in later-stage clinical trials. Data obtained from preclinical and clinical activities are not always conclusive and may be susceptible to varying interpretations that could delay, limit or prevent regulatory approval. Even if a product receives regulatory approval, the approval may be significantly limited to specific indications or uses.

Even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delays in obtaining, or failures to obtain regulatory approvals would have a material adverse effect on our business.

The FDA's policies may change, and additional government regulations may be enacted which could prevent or delay regulatory approval of our potential products. Increased attention to the containment of health care costs worldwide could result in new government regulations materially adverse to our business. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the U.S. or abroad.

We do not have a guarantee of patent term restoration and marketing exclusivity of the ingredients for our drugs even if we are granted FDA approval of our products.

The U.S. Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman) permits the FDA to approve Abbreviated New Drug Applications (ANDAs) for generic versions of innovator drugs, as well as NDAs with less original clinical data, and provides patent restoration and exclusivity protections to innovator drug manufacturers. The ANDA process permits competitor companies to obtain marketing approval for drugs with the same active ingredient and for the same uses as innovator drugs, but does not require the conduct and submission of clinical studies demonstrating safety and efficacy. As a result, a competitor could copy any of our drugs and only need to submit data demonstrating that the copy is bioequivalent to gain marketing approval from the FDA. Hatch-Waxman requires a competitor that submits an ANDA, or otherwise relies on safety and efficacy data for one of our drugs, to notify us and/or our business partners of potential infringement of our patent rights. We and/or our business partners may sue the company for patent infringement, which would result in a 30-month stay of approval of the competitor's application. The discovery, trial and appeals process in such suits can take several years. If the litigation is resolved in favor of the generic applicant or the challenged patent expires during the 30-month period, the stay is lifted and the FDA may approve the application. Hatch-Waxman also allows competitors to market copies of innovator products by submitting significantly less clinical data outside the ANDA context. Such applications, known as "505(b)(2) NDAs" or "paper NDAs," may rely on clinical investigations not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use and are subject to the ANDA notification procedures described above.

The law also permits restoration of a portion of a product's patent term that is lost during clinical development and NDA review, and provides statutory protection, known as exclusivity, against FDA approval or acceptance of certain competitor applications. Restoration can return up to five years of patent term for a patent covering a new product or its use to compensate for time lost during product development and regulatory review. The restoration period is generally one-half the time between the effective date of an IND and submission of an NDA, plus the time between NDA submission and its approval (subject to the five-year limit), and no extension can extend total patent life beyond 14 years after the drug approval date. Applications for patent term extension are subject to U.S. Patent and Trademark Office (USPTO) approval, in conjunction with FDA. Approval of these applications takes at least nine months, and there can be no guarantee that it will be given at all.

Hatch-Waxman also provides for differing periods of statutory protection for new drugs approved under an NDA. Among the types of exclusivity are those for a “new molecular entity” and those for a new formulation or indication for a previously-approved drug. If granted, marketing exclusivity for the types of products that we are developing, which include only drugs with innovative changes to previously-approved products using the same active ingredient, would prohibit the FDA from approving an ANDA or 505(b)(2) NDA relying on our safety and efficacy data for three years. This three-year exclusivity, however, covers only the innovation associated with the original NDA. It does not prohibit the FDA from approving applications for drugs with the same active ingredient but without our new innovative change. These marketing exclusivity protections do not prohibit the FDA from approving a full NDA, even if it contains the innovative change.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

We currently rent approximately 1,000 square feet of office space in Rockville, Maryland for monthly rent of $3,002, and we rent approximately 1,600 square feet of office space in Ann Arbor, Michigan for monthly rent of $2,633. We believe our current offices will be adequate for the foreseeable future.

Item 3. ***Legal Proceedings***

None.

Item 4. ***Mine Safety Disclosures***

Not applicable.

PART II

Item 5. ***Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchase of Equity Securities***

Our common stock has traded on the NYSE MKT under the symbol "SYN" since February 16, 2012. Prior to this time, our common stock traded under the symbol "AEN" since October 16, 2008. The following table states the range of the high and low sales prices of our common stock for each of the calendar quarters during the years ended December 31, 2012 and December 31, 2011. These quotations represent inter-dealer prices, without retail mark-up, markdown, or commission, and may not represent actual transactions. The last price of our common stock as reported on the NYSE MKT on March 27, 2013 was $1.75 per share. As of March 27, 2013, there were approximately 352 stockholders of record of our common stock. This number does not include beneficial owners from whom shares are held by nominees in street name.

	High	Low
YEAR ENDED DECEMBER 31, 2012		
Fourth quarter	$2.43	$1.60
Third quarter	$2.41	$1.80
Second quarter	$2.25	$1.51
First quarter	$2.80	$1.27
YEAR ENDED DECEMBER 31, 2011		
Fourth quarter	$1.42	$0.47
Third quarter	$0.91	$0.57
Second quarter	$2.13	$0.80
First quarter	$1.85	$1.04

Dividend Policy

We have never paid any cash dividends on our common stock to date, and do not anticipate paying such cash dividends in the foreseeable future. Whether we declare and pay dividends is determined by our Board of Directors at their discretion, subject to certain limitations imposed under Nevada corporate law. The timing, amount and form of dividends, if any, will depend on, among other things, our results of operations, financial condition, cash requirements and other factors deemed relevant by our Board of Directors.

Equity Compensation Plan Information

See Item 12 – Executive compensation for equity compensation plan information.

Recent Sales of Unregistered Securities

In September 26, 2012, we issued a performance warrant as compensation for a consulting agreement that we had entered into for a financial communications program. The performance warrant is exercisable for 250,000 shares of our common stock based on achievement of certain stock price milestones at an exercise price equal to the market price of our common stock on the date of execution of the agreement. Upon initiation of the program, 50,000 of the performance warrants vested. The warrant was issued in reliance on the exemption from registration afforded by Section 4(a)(2) of the Securities Act of 1933.

All other sales of unregistered securities have been previously reported.

Item 6. ***Selected Financial Data***

Not applicable because we are a smaller reporting company.

Item 7. ***Management's Discussion and Analysis of Financial Condition and Results of Operations***

The following discussion of our financial condition and results of operations should be read in conjunction with the audited financial statements and notes thereto for the year ended December 31, 2012 found in this report. In addition to historical information, the following discussion contains forward-looking statements that involve risks, uncertainties and assumptions. Where possible, we have tried to identify these forward looking statements by using words such as "anticipate," "believe," "intends," or similar expressions. Our actual results could differ materially from those anticipated by the forward-looking statements due to important factors and risks including, but not limited to, those set forth under "Risk Factors" in Part I, Item 1A of this Report.

Overview

We are a biotechnology company focused on the development of biologics for the prevention and treatment of serious infectious diseases. We are developing an oral enzyme for the prevention of *C. difficile* infections, and a series of monoclonal antibody therapies for the treatment of Pertussis and *Acinetobacter* infections. In addition, we are developing a drug candidate for the treatment of relapsing-remitting multiple sclerosis and cognitive dysfunction in multiple sclerosis, and have partnered the development of a treatment for fibromyalgia.

Product Pipeline:

Summary of Infectious Disease Programs:

- ***Clostridium difficile (C. difficile)*** **infections:** In November 2012, we acquired a series of oral beta-lactamase enzymes (P1A, P2A and P3A) and related assets targeting the prevention *of C. difficile* infections (CDI), the leading cause of hospital acquired infections (HAI), that generally occurs secondary to treatment with intravenous antibiotics. The acquired assets include a pre-Investigational New Drug (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 Biologic 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 IPSAT P3A. When co-administered with certain intravenous beta-lactam antibiotics, it is expected that SYN-004 can degrade the antibiotic that is excreted in the gastrointestinal (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. According to GlobalData, an estimated 8.7 million Americans were administered intravenous beta-lactam antibiotics in 2011.

Pertussis: In December 2012, in collaboration with Intrexon Corporation (Intrexon), we initiated development of a monoclonal antibody (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 294,000 deaths worldwide, primarily among young, unvaccinated children.

- ***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 multi-billion dollar market opportunity.

Summary of Multiple Sclerosis Program:

- Trimesta™ (oral estriol) is being developed as an oral once-daily treatment for relapsing-remitting multiple sclerosis (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 U.S. The primary endpoint is relapse rate at two years, with top-line results expected in 1H 2014. This trial is supported by grants exceeding $8 million, which should be sufficient to fund the trial through completion. Current sales of injectable disease-modifying therapies for MS are estimated at $8.9 billion annually.

- 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 University of California, Los Angeles (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 U.S., Canada and Japan. The sublicense agreement provides that all ongoing and future development costs are to 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 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. 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.

To prioritize our focus on the development of product candidates for the prevention and treatment of serious infectious diseases, we do not intend to pursue further development of our previously announced program for pulmonary arterial hypertension. However, we are currently in discussions with Intrexon to substitute this program with an alternate

program better suited to our current objectives and focus.

In order to further prioritize our focus, we have elected to discontinue further development of AEN-100 for the treatment of amyotrophic lateral sclerosis. However, we are currently seeking development partners for our zinc-based intellectual property and assets including, AEN-100.

Recent Developments

On December 19, 2012, we entered into a Patent License Agreement (the "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 (more commonly known as whooping cough) antibodies developed in the lab of Dr. Jennifer A. Maynard, Assistant Professor of Chemical Engineering. In connection with the License Agreement, we and the University also entered into a Sponsored Research Agreement 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.

On November 28, 2012, a closing was held for the transaction contemplated by the Asset Purchase Agreement (the "Prev Agreement") we entered into with Prev ABR LLC ("Prev"), pursuant to which we acquired the *C. diff* program assets of Prev, including pre-Investigational New Drug (IND) package, Phase I and Phase II clinical data, manufacturing process data and all issued and pending U.S. and international patents. 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) thirty (30) months after the execution of the Prev Agreement, we have not initiated toxicology studies in non-rodent models or (ii) thirty six (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 thirty (30) and thirty six (36) month periods can be extended by us for an additional twelve (12) months upon payment of a cash milestone payment.

On October 30, 2012, we completed a private placement (the "October 2012 Private Placement") with certain accredited investors, pursuant to which we sold an aggregate of 6,750,000 shares of our common stock at a price per share of $1.60 (the "Common Shares") for aggregate gross proceeds of $10.8 million and net proceeds of $10.1 million. In connection with the October 2012 Private Placement, we filed a registration statement with the SEC which was declared effective on December 20, 2012 for the resale of our common stock owned by certain of the purchasers in the October 2012 Private Placement. In connection with the October 2012 Private Placement, we also entered into an agreement with a certain purchaser that is an affiliate of Intrexon (the "Joinder Agreement") pursuant to which such purchaser agreed to be bound by the terms of and join Intrexon as a party to its registration rights agreement with us entered into in connection with the Second Channel Agreement.

Griffin Securities, Inc. ("Griffin") served as the placement agent for the October 2012 Private Placement. In consideration for services rendered by Griffin in the October 2012 Private Placement, we (i) paid to Griffin cash commissions equal to 6.0% of the gross proceeds received in the October 2012 Private Placement, (ii) issued to Griffin, or its designee, the Agent Warrants, which are five-year warrants to purchase 635,855 shares of our common stock with an exercise price of $1.60 per share; and (iii) reimbursed Griffin for its reasonable actual out-of-pocket expenses incurred in connection with the October 2012 Private Placement, including reasonable legal fees and disbursements. The common stock underlying the Agent Warrants was registered under the registration statement declared effective on December 20, 2012.

On August 6, 2012, we expanded our relationship with Intrexon and entered into a Second Channel Agreement with Intrexon (the "Second Channel Agreement") that governs an "exclusive 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"). The Second Channel Agreement establishes committees comprised of our and Intrexon representatives that will govern activities related to the Program in the areas of project establishment, chemistry, manufacturing and controls, clinical and regulatory matters, commercialization efforts and intellectual property. On October 16, 2012, a closing was held for the transaction contemplated by the Second Channel Agreement. Pursuant to the terms of a Stock Issuance Agreement with Intrexon (the "Second Stock Purchase Agreement"), we issued 3,552,210 shares of our common stock, $0.001 par value, which issuance is also deemed paid in consideration for the execution and delivery of the Second Channel Agreement, dated August 6, 2012, between ourselves and Intrexon. We also agreed to register the shares issued to Intrexon in accordance with the First Amendment to Registration Rights Agreement.