Synthetic Biologics, Inc.
Form 10-K
March 30, 2012

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2011

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)
3985 Research Park Drive, Suite 200 Ann Arbor, MI	48108
(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 AMEX

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, 2011, was approximately $16,266,000 based on $0.86, the price at which the registrant's common stock was last sold on that date.

As of March 26, 2012, the issuer had 32,701,984 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. (formerly Adeona Pharmaceuticals, Inc.) and its subsidiaries.

Item 1. ***Business***

We are a biotechnology company focused on the development of synthetic DNA-based therapeutics and innovative disease-modifying medicines for serious illnesses. Our initial synthetic biologic product candidate is intended to treat pulmonary arterial hypertension (PAH), a serious life-threatening lung disease, by locally delivering therapeutic DNA to the lungs of PAH patients and controlling long-term expression of such DNA via an oral daily pill. We also intend to expand new and existing collaborations in the area of DNA-based therapeutics. In addition, we have several small molecule clinical-stage programs, the majority of which are being funded, or partially funded, by grants, charitable organizations and corporate partners. In this area we are developing, or have partnered the development of, product candidates to treat relapsing-remitting multiple sclerosis (MS), cognitive dysfunction in MS, fibromyalgia and amyotrophic lateral sclerosis (ALS).

Product Pipeline:

Synthetic Biologics:

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Our initial synthetic biologic product candidate is intended to treat PAH, a serious life-threatening lung disease. This product is designed to deliver DNA that encodes a therapeutic protein called prostacyclin synthase (PGIS) locally to the pulmonary arteries of PAH patients via a single procedure, and, via an oral daily pill, control the long-term local expression of such therapeutic protein. We are developing this initial product candidate pursuant a global exclusive channel collaboration that we entered into with the private synthetic biology company Intrexon Corporation (Intrexon) in November 2011. As part of this collaboration, we have access to Intrexon's UltraVector® platform and RheoSwitch Therapeutic System® for this product application. We anticipate that by continuously producing and delivering prostacyclin directly where it is needed, in the pulmonary arteries of PAH patients, this product candidate may overcome the dose limiting side effects of systemic prostacyclin treatments for PAH, a mainstay of PAH treatment. According to GlobalData, the global market for PAH treatments is estimated to exceed $3.6 billion by 2015.

(UltraVector® and RheoSwitch Therapeutic System® are registered trademarks of Intrexon Corporation)

Funded/Small Molecule Clinical Programs:

- Trimesta™ (oral estriol) is being developed as an oral once-daily treatment for relapsing-remitting MS in women. Patient enrollment of 164 patients is complete in this randomized, double-blind, placebo-controlled Phase II clinical trial being conducted at 15 centers in the U.S. Patients are being dosed and monitored for two years. This clinical 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. According to various reports, sales of oral disease-modifying therapies for MS, of which Trimesta™, if and when approved, would be in such class, are anticipated to grow from $500 million in 2010 to $5 billion annually by 2017.

- Trimesta™ (oral estriol) is also being developed for the treatment of cognitive dysfunction in female MS patients. In January 2012, patient enrollment began in a randomized, double-blind, placebo-controlled Phase II clinical trial being conducted at University of California, Los Angeles (UCLA). 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.

- Effirma™ (flupirtine) is being developed for the treatment of fibromyalgia. On May 6, 2010, we entered into a sublicense agreement with Meda AB, a multi-billion dollar international pharmaceutical company, covering all of our patents' rights on the use of flupirtine for fibromyalgia in the U.S., Canada and Japan. According to Meda's 2010 Annual Report, flupirtine for fibromyalgia is currently in Phase II development. 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. 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.

- AEN-100 (gastroretentive zinc acetate) is being developed under an investigator-initiated Investigational New Drug (IND) application for the treatment of ALS, also known as Lou Gehrig's disease. We intend to sponsor a multi-center, double-blind, placebo-controlled, adaptively designed Phase II/III clinical trial in ALS patients. It is anticipated that the clinical trial will comprise two phases. The first phase of the trial is anticipated to enroll at least 65 patients randomized to receive either AEN-100 or placebo for a period of six months at which time the average change in functional rating between the groups will be compared via an interim analysis conducted on a blinded basis. Should the interim analysis meet the threshold criteria in favor of the treatment group, the second phase of the study will be initiated and will seek to enroll approximately 50 additional subjects to receive treatment for nine months. This study is intended to be conducted by PNA Center for Neurological Research (PNA) which previously sponsored and completed a successful pilot Phase I/II study of oral zinc therapy for ALS. Separately, PNA intends to conduct a Phase I study of AEN-100 in normal volunteers prior to initiating the Phase II/III clinical trial in ALS patients. We have committed to support approximately $400,000 to PNA for the first phase of the Phase II/III clinical trial, payable based upon study enrollment and milestones. There is only one approved therapy for ALS, the efficacy of which is considered to be marginal. Based on an estimated annual price of $10,000 per ALS patient, we estimate that the total market potential in the U.S. is $300 million.

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Product Candidates and Medical Indications

Synthetic Biologic Products

We are engaged in the emerging field of synthetic biology directed for the purpose of developing new human therapeutic products. Synthetic biology in an emerging field that combines molecular biology and automation to design, optimize and construct new biological systems and functions. These technologies utilize a combination of automated processes including, DNA sequencing, computer-aided design, DNA synthesis, fabrication of modular transgenes and high throughput testing to create and optimize biologic products.

Our initial efforts in this area are being conducted in collaboration with Intrexon, and are directed towards the design, optimization and development of synthetic DNA-based therapeutic product candidates utilizing Intrexon's UltraVector® platform for the treatment of PAH. Synthetic DNA-based therapeutics comprise constructs of DNA that can be administered to patients via a single procedure. Once introduced, they are intended to continuously produce therapeutic proteins *in vivo* in a controllable and localized fashion for up to a period of years.

An important feature of our product candidates developed in collaboration with Intrexon may be the incorporation of Intrexon's RheoSwitch Therapeutic System®. Such system is intended to provide unprecedented control of therapeutic protein expression through the use of a highly specific orally available activating ligand that can be taken by patients on a daily basis as one or more pills. In this way, the levels of *in vivo* protein expression may be adjusted from time to time by treating physicians through simple dose adjustment of the oral activating ligand. Such system also provides an important safety mechanism not previously available in gene therapy clinical trials since in the absence of taking an oral pill, protein expression would not be expected to occur.

Pulmonary Arterial Hypertension (PAH)

Synthetic DNA-based Therapy

Disease

PAH is a progressive, disabling and life-threatening disorder characterized by abnormally high blood pressure (hypertension) in the pulmonary artery, the blood vessel that carries blood from the heart to the lungs. Hypertension occurs when most of the very small arteries throughout the lungs narrow in diameter, therefore constricting blood flow through the lungs. The constriction of blood flow causes the pressure to increase in the pulmonary artery and in the

right ventricle (the heart chamber that pumps blood into the pulmonary artery). Signs and symptoms of PAH take place when the increased pressure cannot overcome the constriction and there is insufficient blood flow to the body. Shortness of breath during exertion and fainting spells are the most common early symptoms of PAH. Despite current treatments, PAH generally has a very poor outcome and is associated with high rates of mortality within three to five years of diagnosis.

Synthetic DNA-based Therapeutic for PAH

Our initial synthetic DNA-based therapeutic product candidate is intended for the treatment of PAH, a serious life-threatening lung disease. This product candidate is designed to deliver DNA that encodes a therapeutic protein called PGIS locally to the pulmonary arteries of PAH patients via a single pulmonary catheter procedure and via an oral daily pill, control the long-term local expression of such therapeutic protein.

We are developing this initial product candidate in collaboration with Intrexon. Under the collaboration, we intend to utilize Intrexon's advanced transgene engineering platform for the controlled, precise and continuous *in vivo* cellular production of PGIS. PGIS is a specific effector enzyme that regulates the production of prostacyclin, a potent mediator of arterial dilation that also prevents smooth muscle proliferation and arterial wall thickening. PGIS expression is decreased in the lungs of PAH patients and deficiency in prostacyclin production is strongly implicated in PAH. We anticipate that by continuously producing and delivering prostacyclin directly where it is needed, in the pulmonary arteries of PAH patients via PGIS, this product candidate may overcome the dose limiting side effects of systemic prostacyclin-based treatments for PAH. While systemic prostacyclin-based treatments for PAH are currently a mainstay of PAH therapy, their considerable systemic side effects limit their dose and ultimate long-term utility.

The global market potential for the treatment of PAH is estimated to be up to $3.6 billion by 2015, according to GlobalData, Pulmonary Arterial Hypertension (PAH) – Drug Pipeline Analysis and Market Forecasts for 2016.

Relapsing-Remitting Multiple Sclerosis (MS) in Women

Trimesta (oral estriol)

Disease

MS is a progressive neurological disease in which the body loses the ability to transmit messages along central nervous system nerve cells, leading to a loss of muscle control, paralysis, cognitive impairment and in some cases death. According to the National Multiple Sclerosis Society (NMSS), currently, more than 2.5 million people worldwide (approximately 400,000 patients in the U.S. of which 70% are estimated to be women) have been diagnosed with MS. Young adults, ages 20 to 50, and two to three times as many women than men are predominantly diagnosed with MS. According to the NMSS, approximately 85% of MS patients are initially diagnosed with the relapsing-remitting form, compared to 10-15% with other progressive forms.

There are currently eight Food & Drug Administration (FDA) approved therapies for the treatment of relapsing-remitting MS: Betaseron®, Rebif®, Avonex®, Novantrone®, Copaxone®, Tysabri®, Gilenya® and Extavia®. These therapies provide only a modest benefit for patients with relapsing-remitting MS and therefore serve to only delay progression of the disease. All of these drugs except Gilenya® 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), high rates of non-compliance among users, and eventual loss of efficacy due to the appearance of resistance in approximately 30% of patients. Despite the availability of multiple FDA-approved therapies for the treatment of relapsing-remitting MS, the disease is highly underserved and exacts a heavy economic toll.

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, of which Trimesta™, if and when approved, would be in such class, are anticipated to grow from $500 million in 2010 to in excess of $5 billion annually by 2017.

Background

It has been scientifically documented that pregnant women with certain autoimmune diseases 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 percent ($p < 0.001$) through the third trimester of pregnancy compared to pre-pregnancy-rates, and that relapse rates increased by 120 percent ($p < 0.001$) during the first three months after birth (post-partum) before returning 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 her fetus. Maternal levels of estriol increase in a linear fashion through the third trimester of pregnancy until birth, whereupon they abruptly return to low circulating levels. The anti-autoimmune effects of esteriol is 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 pregnancy levels of estriol have potent immunomodulatory effects. She further postulated and tested in pilot clinical studies 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.

Clinical Development

Our Trimesta (oral estriol) drug candidate is 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 measurement 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. The purpose of this clinical trial is to study 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 (Copaxone®) injections, an FDA-approved therapy for MS, to women between the ages of 18 to 50 who have been recently diagnosed with relapsing-remitting MS. The primary endpoint in this clinical trial being run under an investigator-initiated IND application, is relapse rates at two years. As of January 23, 2012, 164 patients have been enrolled in the clinical trial and the trial enrollment has been closed. The patients will be dosed and monitored for two years.

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

Cognitive Dysfunction in Multiple Sclerosis

Trimesta (oral estriol)

Disease

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 problems remembering things, finding the right words, concentrating on a task or something they are reading, or following a conversation. These are all cognitive symptoms of MS. Of those affected by MS, 50-65% have cognitive dysfunction issues. Despite the fact that most symptoms are mild to moderate, they can have a significant impact on a person's ability to normally function. The overall cognitive dysfunction can be described as a reduction in mental "sharpness."

The major areas of cognition that can be dysfunctional include what are termed 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 display these cognitive issues, and no two people will experience exactly the same types or severity of problems.

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 Paced Auditory Serial Addition Test (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.

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.

Fibromyalgia

Effirma (flupirtine)

Disease

Fibromyalgia is a chronic and debilitating condition characterized by widespread pain and stiffness throughout the body, often accompanied by severe fatigue, insomnia and mood symptoms. 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 this indication in the U.S. – Lyrica®, Cymbalta® and Savella®. Flupirtine is differentiated from these products in that it employs a unique mode of action.

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.

Clinical Development

Our Effirma (flupirtine) product candidate is for the treatment of fibromyalgia. 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 AB) and has been approved and is marketed by Meda AB 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.

Meda Corporate Partnership

On May 6, 2010, we entered into a sublicense agreement with Meda AB, a multi-billion dollar international pharmaceutical company, pursuant to which Meda AB assumed all future development costs and may commercialize flupirtine for 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 AB 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. According to Meda's 2010 Annual Report, flupirtine for fibromyalgia is currently in Phase II development.

Amyotrophic Lateral Sclerosis (ALS)

AEN-100 (gastroretentive zinc acetate)

Disease

ALS, also known as Lou Gehrig's Disease, is a devastating progressive neurodegenerative disease that affects the motor nerve cells in the brain and the spinal cords. It is estimated that as many as 30,000 Americans may have the disease at any given time. The progressive degeneration of the motor neurons in ALS eventually leads to the death of the patient. Motor neurons reach from the brain to the spinal cord and from the spinal cord to the muscles throughout the body. When motor neurons die, the ability of the brain to initiate and control muscle movement is lost. With voluntary muscle action progressively affected, patients in the later stages of the disease may become totally paralyzed. While non-invasive ventilation and gastrostomy tubes prolong life by 6-12 months, the average lifespan from time of symptom onset is 2-5 years. Currently, RILUTEK® is the only FDA-approved drug for ALS. RILUTEK is a N-methyl d-aspartate (NMDA) receptor antagonist and has been shown to prolong life in patients with ALS by 3 months. Presently, there is no cure for ALS.

Based on an estimated annual price of $10,000 per ALS patient, we estimate that the total market potential in the U.S. is $300 million.

Background

Clinical investigators at the PNA cite multiple lines of scientific research that suggest a potential benefit of zinc therapy for ALS patients, including:

- The use of zinc therapy for ALS patients is supported in animal models of ALS. Approximately 2% of ALS diagnoses are associated with a mutation in the copper/zinc superoxide dismutase (SOD1) gene. In ALS mutant

SOD1 animal models, zinc supplementation has been shown to delay death.

- Genetic mutations affecting the ability of a protein known as copper/zinc SOD1 to properly bind zinc are associated with the familial form of ALS, which shares many of the same features as the more prevalent sporadic form of ALS.

- Zinc is an important modifier of glutamate toxicity, a neurotransmitter linked to cell death in ALS patients.

Clinical Development

Preparations are underway to evaluate the safety and efficacy of our proprietary drug candidate, AEN-100, a gastroretentive, sustained-release zinc-based tablet, in a multi-center, double-blind, placebo-controlled clinical trial in ALS patients intended to be conducted under an investigator-initiated IND application. Manufacturing of AEN-100 study material has been completed and stability studies are ongoing.

We intend to provide the study material and support a multi-center, double-blind, placebo-controlled, adaptively designed Phase II/III clinical trial in ALS patients to be conducted by PNA. It is anticipated that the Phase II/III clinical trial will comprise two phases. The first phase of the trial is anticipated to enroll at least 65 patients randomized to receive either AEN-100 or placebo for a period of six months at which time the average change in functional rating between the groups will be compared via an interim analysis conducted on a blinded basis. Should the interim analysis meet the threshold criteria in favor of the treatment group the second phase of the study will be initiated and seek to enroll up to a total of 114 patients, inclusive of the 65 subjects from the first phase who continue to meet eligibility criteria at such time, to receive treatment for nine months.

In November 2011, PNA reported top-line results from its pilot Phase I/II open label, three month safety study of oral high dose zinc therapy in ALS. The clinical study met its primary outcome as no safety issues related to zinc therapy were observed. In addition, an average decrease in the monthly rate of disease progression was observed in the ALS patients on zinc therapy, compared to published historical controls, as well as compared to the average monthly rate of disease progression of the subjects prior to enrollment in the study. AEN-100 is not the same zinc formulation untilized by PNA in its previously completed Phase I/II safety study of zinc for ALS, and PNA intends to conduct a Phase I study of AEN-100 in normal volunteers prior to initiating the Phase II/III clinical trial in ALS patients.

We have committed to support approximately $400,000 to PNA for the first phase of the Phase II/III clinical trial, payable based upon study enrollment and completion milestones.

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.

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 (Regents) relating to issued U.S. Patent No. 6,936,599 and pending patent applications covering the uses of the drug candidate Trimesta (oral esteriol). 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, 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. However, we have 60 days after the effective date of the notice of default to repair the default.

The Intrexon Collaboration

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 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 byus), 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 partial consideration for execution of the Channel Agreement, we entered into a Stock Purchase Agreement with Intrexon 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 partial 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.

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 a Registration Rights Agreement that was executed and delivered by the parties at the First Tranche closing, we agreed to file a "resale" registration statement (the "Registration Statement") registering the resale of the First Tranche shares within 120 days of the First Tranche closing.

AEN-100 – Gastroretentive Zinc Acetate

We intend to file for orphan drug designation in the U.S. and Europe for AEN-100 (gastroretentive, sustained-release zinc-based tablets) for the treatment of ALS. ALS qualifies as an "orphan disease" in that it affects less than 200,000 people in the U.S. Orphan drug designation provides for seven years of market exclusivity following approval in the U.S. and ten years of market exclusivity following approval in Europe. AEN-100, is also the subject of U.S. and international patent pending applications that may provide exclusivity beyond the expiration of orphan drug exclusivity, such as published U.S. patent application Ser. No. 11/621,962 and corresponding international applications that claim priority to January 10, 2006, and 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.

Manufacturing

We utilize contract manufacturing firms to produce our investigational products AEN-100 and Trimesta in accordance with "current good manufacturing processes" (cGMP) guidelines outlined by the FDA.

Research and Development

During the years ended December 31, 2011 and 2010, we spent $3.3 million and $1.6 million, respectively, on research and development.

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.

In the general area of commercial products for the treatment of serious diseases, we potentially compete with a variety of companies, most of whom are pharmaceutical or biotechnology companies. These include: Actelion Pharmaceuticals, Bayer Health Care, Biogen Idec, Eli Lilly & Co., Genzyme, GlaxoSmithKline Pharmaceuticals, Merck & Co., Pfizer, Novartis, Teva Pharmaceuticals and United Therapeutics.

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 a collaboration with Intrexon, on February 15, 2012, we amended our Articles of Incorporation to change our name to Synthetic Biologics, Inc.

Recent Events

On February 15, 2012, upon stockholder approval, we amended our Articles of Incorporation to change our name to Synthetic Biologics, Inc. Our common stock continues trade on the NYSE Amex stock exchange, currently under the symbol “SYN”. Prior to this time and since October 16, 2008, our name was Adeona Pharmaceuticals, Inc. and we traded on the NYSE Amex stock exchange under the symbol “AEN”. We are incorporated in the State of Nevada.

On March 8, 2012, we entered into a Membership Interest Purchase Agreement, and certain related agreements, pursuant to which we sold all of our interest in Adeona Clinical Laboratory, LLC (the “Lab”) to Hartlab, LLC, an entity controlled by the Lab’s former owner, in consideration for (i) the immediate assignment of the Lab’s outstanding accounts receivable up through the date of closing, plus (ii) $700,000 payable pursuant to the terms of a two-year non-recourse promissory note secured by all of the assets of the Lab.

During the period from January 1, 2012 through March 26, 2012, 1,120,121 warrants were exercised for gross proceeds of $1.4 million.

Employees

As of March 26, 2012, we employed approximately eight individuals, seven 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 3985 Research Park Drive, Suite 200, Ann Arbor, Michigan 48108 and we also maintain executive offices in Rockville, Maryland.

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.

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

With the exception of the quarter 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 of and commercialization of Effirma (flupirtine) for fibromyalgia in the U.S., Canada and Japan and limited laboratory revenues from Adeona Clinical Laboratory, which we have recently sold, 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, 2011, our accumulated deficit totaled approximately $51.9 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 discontinue 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 quarter 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;

- 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.

We have a limited operating history on which investors can base an investment decision.

We have not yet demonstrated our ability to perform the functions necessary for the successful commercialization of any of our product candidates. We have only recently entered into the emerging field of synthetic biology, and there can be no assurance that we will be successful in commercializing any products in such field. The successful commercialization of our product candidates will require us to perform a variety of functions, including:

- continuing to undertake preclinical development and clinical trials;
- participating in regulatory approval processes;
- formulating and manufacturing products; and
- conducting sales and marketing activities.

Our operations have been limited to organizing and staffing our company, acquiring, developing, and securing our proprietary technology, and undertaking preclinical and clinical trials of our principal product candidates. These operations provide a limited basis for you to assess our ability to commercialize our product candidates and the advisability of investing in our securities.

The technology on which our channel partnering arrangement with Intrexon is based on early stage technology in the field of synthetic DNA-based therapy.

Our exclusive channel collaboration arrangement with Intrexon 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.

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 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 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 2010 Annual Report, flupirtine for fibromyalgia is currently in Phase II development.

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; Mr. Riley remains Chairman of our Board. 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. Max Lyon served as Chief Executive Officer, President and director from June 26, 2009 until February 6, 2010. 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 agreement with Intrexon provides that Intrexon may terminate such agreement if we do not perform certain specified requirements, including developing therapies considered superior.

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 arrangement with Intrexon.

Pursuant to our exclusive channel collaboration with Intrexon, we are responsible for future research and development expenses of product candidates developed under such collaboration, the effect of which we expect will increase the level of our overall research and development expenses going forward. 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 additio