

Synthetic Biologics, Inc.
Form POS AM
July 12, 2012

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

POST-EFFECTIVE AMENDMENT NO. 1 TO FORM S-3

ON

FORM S-1

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

SYNTHETIC BIOLOGICS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Nevada

(State or Other Jurisdiction of Incorporation or Organization)

2834

(Primary Standard Industrial Classification Code Number)

13-3808303

(I.R.S. Employer Identification No.)

617 Detroit Street, Suite 100

Ann Arbor, MI 48104

(734) 332-7800

(Address and telephone number of principal executive offices)

Copy to:

Leslie Marlow, Esq.

Hank Gracin, Esq.

Gracin & Marlow, LLP

The Chrysler Building

405 Lexington Avenue, 26th Floor

New York, New York 10174

(212) 907-6457

(Name, address and telephone number of agent for service)

Approximate Date of Proposed Sale to the Public: From time to time after the date this registration statement becomes effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Edgar Filing: Synthetic Biologics, Inc. - Form POS AM

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>

(Do not check if a smaller reporting company)

EXPLANATORY NOTE

The Registrant filed a registration statement on Form S-3 (Registration No. 333-166750) (the “Original Registration Statement”) declared effective by the Securities and Exchange Commission on June 14, 2010, which registered shares of common stock of the Registrant. This Post-Effective Amendment No. 1 to Form S-3 on Form S-1 Registration Statement is being filed to amend the Original Registration Statement into a registration statement on Form S-1 to maintain the registration of certain securities previously registered on the Original Registration Statement. On June 12, 2012, Synthetic Biologics, Inc. (the “Company”) was notified by the Securities and Exchange Commission (“SEC”) staff that under its guidelines it was unable to grant a waiver request for the Company’s continued use of its existing Form S-3 because of the failure of Berman & Company, P.A. (“Berman & Co.”) to follow proper partner rotation procedures that resulted in the Company’s Annual Report on Form 10-K for the year ended December 31, 2011 being deemed to be filed late. Consequently, the Registrant is no longer eligible to use Form S-3 in connection with the current offering. The Registrant is filing this Post-Effective Amendment No.1 to Form S-3 on Form S-1 to amend the Original Registration Statement into a registration statement on Form S-1 to (i) continue the registration of: (a) 94,391 shares of common stock issuable upon exercise of the warrants originally issued in the April 2011 offering subject to the April 11, 2011 Prospectus Supplement, and exchanged for warrants issued in July 2011 and (b) 18,182 shares of common stock issuable upon exercise of the warrants issued in the July 2010 offering subject to the July 2, 2010 Prospectus Supplement, all previously registered on the Original Registration Statement, and (ii) remove from registration the unsold portion of securities registered under the Original Registration Statement. All filing fees payable in connection with the registration of these securities were previously paid in connection with the filing of the original registration statement.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

THE INFORMATION CONTAINED IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. THESE SECURITIES MAY NOT BE SOLD UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS DECLARED EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL THESE SECURITIES AND IT IS NOT SOLICITING AN OFFER TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

SUBJECT TO COMPLETION, DATED JULY 12, 2012

PRELIMINARY PROSPECTUS

SYNTHETIC BIOLOGICS, INC.

112,573 Shares of Common Stock

This prospectus covers the sale of up to:

- 94,391 shares of common stock issuable upon the exercise of warrants sold in our April 11, 2011 offering which were exchanged for warrants issued in July 2011 and may be exercised at a price of \$1.00 per share, and
- 18,182 shares of common stock issuable upon the exercise of warrants sold in our July 2, 2010 offering which may be exercised at a price of \$1.32 per share.

Our common stock became eligible for trading on the NYSE Amex October 16, 2008. Our common stock is eligible for quotation on the NYSE Amex under the symbol "SYN". The closing price of our stock on July 11, 2012 was \$2.01.

Investing in our securities involves a high degree of risk. See "Risk Factors" beginning on page 4 of this prospectus for more information.

Edgar Filing: Synthetic Biologics, Inc. - Form POS AM

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus or the prospectus to which it relates is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is July __, 2012.

TABLE OF CONTENTS

	Page
PROSPECTUS SUMMARY	1
RISK FACTORS	4
USE OF PROCEEDS	15
DILUTION	16
CAPITALIZATION	16
BUSINESS	17
MARKET PRICE OF COMMON STOCK AND OTHER STOCKHOLDER MATTERS	28
PLAN OF DISTRIBUTION	30
MANAGEMENT'S DISCUSSION AND ANALYSIS OR PLAN OF OPERATION	31
DIRECTORS, EXECUTIVE OFFICERS, PROMOTERS AND CONTROL PERSONS	37
EXECUTIVE COMPENSATION	41
SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT	44
CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS	46
DESCRIPTION OF SECURITIES	47
EXPERTS	49
DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES	50
LEGAL MATTERS	50
WHERE YOU CAN FIND MORE INFORMATION	50
INDEX TO FINANCIAL STATEMENTS	64
PART II	88

You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from that which is contained in this prospectus. This prospectus may be used only where it is legal to sell these securities. The information in this prospectus may only be accurate on the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of securities.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus; it does not contain all of the information you should consider before investing in our common stock. You should read the entire prospectus before making an investment decision. Throughout this prospectus, the terms “Synthetic Biologics, Inc.,” “we,” “us,” “our,” and “our company” refer to Synthetic Biologics, Inc., a Nevada corporation.

Company Overview

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:

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 2011 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.

Corporate Information

Our executive offices are located at 617 Detroit Street, Suite 100, Ann Arbor, Michigan 48104, and our telephone number is (734) 382-7800. Our website address is www.syntheticbiologics.com. The information on our website is not incorporated by reference into this prospectus, and you should not consider it part of this prospectus.

The Offering

Issuer Synthetic Biologics, Inc.

Securities offered	This prospectus covers the sale of up to: <ul style="list-style-type: none">• 94,391 shares of common stock issuable upon the exercise of warrants which may be exercised at a price of \$1.00 per share, and• 18,182 shares of common stock issuable upon the exercise of warrants which may be exercised at a price of \$1.32 per share.
Common stock to be outstanding after this offering	33,413,720 shares (assuming all the warrants are exercised)
Use of Proceeds	We will receive proceeds from the exercise of the warrants if the warrants are exercised for cash. See “Use of Proceeds”.

Risk Factors You should carefully read and consider the information set forth under “Risk Factors,” together with all of the other information set forth in this prospectus, before deciding to invest in shares of our common stock.

NYSE Amex symbol We list our common stock on the NYSE Amex under the symbol “SYN”.

The number of shares of common stock outstanding before and after the offering is based on 33,301,147 shares outstanding as of June 30, 2012 and excludes:

- 1,418,493 shares of common stock issuable upon the exercise of warrants with a weighted average exercise price of \$3.10 per share;
- 3,968,746 shares of common stock issuable upon the exercise of options with a weighted average exercise price of \$1.73 per share; and
- 1,349,821 shares of common stock reserved for future grants and awards under our equity incentive plans.

RISK FACTORS

Investing in our common stock involves a high degree of risk, and you should be able to bear the complete loss of your investment. You should carefully consider the risks described below, the other information in this prospectus and the documents incorporated by reference herein when evaluating our company and our business. If any of the following risks actually occur, our business could be harmed. In such case, the trading price of our common stock could decline and investors could lose all or a part of the money paid to buy our common stock.

RISKS RELATING TO OUR BUSINESS

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 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 March 31, 2012, our accumulated deficit totaled approximately \$53.1 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. Our recent loss of S-3 eligibility due to the failure of Berman & Company, P.A. to follow proper partner rotation procedures may also negatively affect our ability to raise capital. 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.

Edgar Filing: Synthetic Biologics, Inc. - Form POS AM

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.

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 2011 Annual Report, flupirtine for fibromyalgia is 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. 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 additional personnel to support our exclusive channel collaboration with Intrexon.

Because our collaboration with Intrexon is relatively new, we have only recently assumed development responsibility and costs associated with such program. In addition, because development activities are determined pursuant to a joint steering committee 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 collaboration 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 serious diseases include: Actelion Pharmaceuticals, Bayer Health Care, Biogen Idec, Eli Lilly & Co., Genzyme, GlaxoSmithKline Pharmaceuticals, Merck & Co., Pfizer, Novartis, Teva Pharmaceuticals and United Therapeutics. Many of our competitors have significant financial and human resources. The pulmonary arterial hypertension market is highly competitive and several different product classes currently compete in this space, including prostacyclin-based therapies, endothelin receptor antagonists and phosphodiesterase type 5 inhibitors. Prostacyclin-based therapies for PAH are available in a number of delivery formats, including intravenous, subcutaneous and inhaled routes and an oral prostacyclin-based product candidate is currently under NDA review in the U.S. In addition, academic research centers may develop technologies that compete with our Trimesta, sustained-release zinc preparation - AEN-100, and flupirtine technologies. Should clinicians or regulatory authorities view these therapeutic regimens 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 and private insurers.

We operate in a highly 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.

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

Since we do not have composition of matter patent claims for flupirtine, estriol or zinc acetate, 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 (flurpiratine) and Trimesta (oral estriol) have been approved for marketing in overseas countries for different uses and an oral immediate release form of zinc is approved in the U.S. and Europe for the treatment of Wilson's disease. 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 flurpiratine, estriol or zinc 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 flurpiratine, estriol and zinc 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 No. 6,936,599) 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.

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 June 30, 2012, we had nine employees. We have also engaged regulatory consultants to advise us on our dealings with the FDA and other foreign regulatory authorities and have been and will be required to retain additional consultants and employees in order to fulfill our obligations under our exclusive channel collaboration with Intrexon. 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-development field, 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 our drug substance raw materials and certain manufacturing-related services do not timely supply these products and services, it may delay or impair our ability to develop, manufacture and market our products.

We rely on suppliers for our drug substance raw materials 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. Our AEN-100 product candidate has limited stability data to date and is the subject of ongoing stability studies. To succeed, clinical trials require adequate supplies of drug substance and drug product, which may be difficult or uneconomical to procure or manufacture. We and our suppliers and vendors may not be able to (i) produce our drug substance or drug product 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

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 diagnostic 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 Phase II clinical trials does not ensure that later Phase II or Phase III clinical trials will be successful. We cannot be sure that the results of later clinical trials would replicate the results of prior clinical trials and preclinical testing. In particular, the limited results that we have obtained for our diagnostic tests may not predict results from studies in larger numbers of subjects drawn from more diverse populations over a longer period of time. 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 a collaboration agreement for the development of another product candidate, we depend upon our sublicensee and independent investigators and scientific collaborators, such as universities and medical institutions or private physician scientists, 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 at our expense 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 physician-sponsored IND applications, not corporate-sponsored INDs. Generally, we have experienced difficulty in collecting data generated from these physician-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.

Our AEN-100 program for ALS is reliant on the investigator-initiated IND of PNA as well as their clinical trial capabilities. Although the planned Phase II/III clinical trial that we intend to conduct with PNA has received regulatory approval to proceed, such clinical trial is still the subject of further protocol development and IRB approval, either of which may alter the anticipated timing and budget of such clinical trial. In addition, because AEN-100 is not the same zinc formulation utilized by PNA in its previously completed Phase I/II safety study of zinc for ALS, 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. The IRB approval process is ongoing for the planned Phase I study of AEN-100 and the planned Phase II/III clinical trial in ALS patients. Such Phase I study of AEN-100 may produce unanticipated and unacceptable safety, tolerability or bioavailability results that may substantially delay initiation of the planned Phase II/III clinical trial in ALS patients.

With respect to our synthetic biologic product candidates, 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 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. 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 June 30, 2012. Our executive officers, directors and principal stockholders together beneficially owned approximately 12 million shares of our common stock, including the stock options and warrants exercisable within 60 days of June 30, 2012. 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 Amex.

We cannot assure you that we will be able to maintain the continued listing standards of the NYSE Amex (formerly the American Stock Exchange). The NYSE Amex requires companies to meet certain continued listing criteria including certain minimum stockholders' equity and equity prices per share as outlined in the NYSE Amex 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 Amex. If we are delisted from the NYSE Amex 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 Amex 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 Amex, 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.

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, medical foods, conventional foods, homeopathic OTC drugs, 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.

We intend to develop our zinc candidate, AEN-100, as a drug and intend to file an IND with the FDA in order to conduct necessary clinical trials to support new medical claims and ultimately file one or more NDA with respect to such products which would subject us to time, expense and uncertainty associated with achieving approval of such NDA by the FDA.

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;

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 a qualified investigator in accordance with good clinical practice (GCP) regulations, which include informed consent requirements. An independent IRB at each medical center reviews and approves and monitors the study, and is periodically informed of the study's progress, adverse events and changes in research. Progress reports are submitted annually to the FDA and more frequently if 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. The process may be significantly extended by requests for additional information or clarification regarding information already provided. As part of this review, the FDA may refer the application to an appropriate 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 physicians prescription. 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 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.

USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately \$118,391 if all of the warrants are exercised.

We intend to use the net proceeds from this offering to fund research and development and for working capital and general corporate purposes.

Pending use of the net proceeds of this offering, we intend to invest such net proceeds in short-term, interest-bearing investment grade securities.

DILUTION

Our net tangible book value as of March 31, 2012 was \$7.9 million or \$0.24 per share of common stock. Net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of common stock outstanding. After giving effect to our sale in this offering of 94,391 warrants to purchase common stock at an exercise price of \$1.00 per share and 18,182 warrants to purchase common stock at an exercise price of \$1.32, our net tangible book value as of March 31, 2012 would have been \$8 million, or \$0.24 per share. The following table illustrates this calculation.

Offering price per share of common stock (weighted average price)	\$1.05
Net tangible book value per share as of March 31, 2012	\$0.24
Increase per share attributable to this offering	\$0.00
As adjusted tangible book value per share after this offering	\$0.24
Dilution per share to new investors in this offering	\$0.81

The number of shares of common stock outstanding used for existing stockholders in the table and calculations above is based on 32,776,127 outstanding as of March 31, 2012 and excludes:

- 2,414,922 shares of common stock issuable upon the exercise of warrants outstanding at March 31, 2012 with a weighted average exercise price of \$2.36 per share;
- 3,843,465 shares of common stock issuable upon the exercise of options outstanding at March 31, 2012 with a weighted average exercise price of \$1.79 per share; and
- 1,349,821 shares of common stock reserved for future grants and awards under our equity incentive plans as of March 31, 2012.

CAPITALIZATION

The following table sets forth our capitalization as of March 31, 2012:

- on an actual basis; and

- on a pro forma basis to give effect to:

the issuance of 112,573 warrants to purchase common stock and our receipt of \$118,391 in cash proceeds from that issuance

You should read the information in this table together with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and the accompanying notes.

	March 31, 2012	
	Actual	Pro forma
	(Unaudited)	
Cash and cash equivalents	\$6,802	\$6,920
Stockholders’ equity:		
Common stock, \$.001 par value: 100,000,000 shares authorized, 32,970,182 shares issued and outstanding, actual; 32,888,700 shares issued and outstanding, pro forma	\$33	\$33
Additional paid-in capital	60,946	61,064
Accumulated deficit	(53,073)	(53,073)
Total stockholders’ equity	7,906	8,024
Total capitalization	\$7,906	\$8,024

The number of shares of common stock outstanding used for existing stockholders is based on 32,776,127 shares outstanding as of March 31, 2012 and excludes:

- 2,414,922 shares of common stock issuable upon the exercise of warrants outstanding at March 31, 2012 with a weighted average exercise price of \$2.36 per share;
- 3,843,465 shares of common stock issuable upon the exercise of options outstanding at March 31, 2012 with a weighted average exercise price of \$1.79 per share; and

BUSINESS

History

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 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 MS, cognitive dysfunction in MS, fibromyalgia and ALS.

Product Pipeline:

Synthetic Biologics:

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 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 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 2011 Annual Report, flupirtine for fibromyalgia is 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 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 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 study, 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.

On November 18, 2011, we entered into a Channel Agreement with Intrexon 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.

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.

On December 21, 2011, we announced that the Board of Directors had taken several actions to prioritize our focus on our entry into the emerging field of synthetic biology. In connection with the change in business focus 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 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) Seven Hundred Thousand Dollars (\$700,000) payable pursuant to the terms of a two-year non-recourse promissory note secured by all of the assets of the Lab.

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. We continue to maintain our principal executive offices in Ann Arbor, MI, and are currently located at 617 Detroit Street, Suite 100, Ann Arbor, MI 48104.

Effective as of June 30, 2010, we emerged from a “Development-Stage Entity” as defined by Financial Accounting Standards Board Accounting Standards Codification (FASB ASC) 915-10. On May 6, 2010, we entered into a sublicense agreement with Meda AB of Sweden. This agreement provides that Meda AB will assume all future development costs for the commercialization of oral flupirtine for fibromyalgia. 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 filing of an NDA with the FDA of oral flupirtine for fibromyalgia and \$10 million upon marketing approval, plus royalties. We consider the agreement with Meda AB to be an indication that we have commenced our principal operations and therefore are not required to report as a development-stage entity.

To date, we have financed our operations primarily through public and private sales of our common stock, and we expect to continue to seek to obtain the required capital in a similar manner. We have incurred an accumulated deficit of \$53.1 million through March 31, 2012. We cannot provide any assurance that we will be able to achieve profitability on a sustained basis, if at all, obtain the required funding, obtain the required regulatory approvals, or complete additional corporate partnering or acquisition transactions.

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 is 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 prostacyclin synthase (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 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 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 antinociceptive effects has been observed. One common link between neuroprotection, nociception 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 2011 Annual Report, flupirtine for fibromyalgia is 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 an 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 utilized 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 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 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.

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.

Employees

As of June 30, 2012, we employed approximately nine 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 617 Detroit Street, Suite 100, Ann Arbor, Michigan 48104 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.

MARKET PRICE OF COMMON STOCK AND OTHER STOCKHOLDER MATTERS

Our common stock has traded on the NYSE Amex 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, 2011 and December 31, 2010. 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 Amex on July 11, 2012 was \$2.01 per share. As of June 30, 2012, there were approximately 349 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		
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
---------------	--------	--------

YEAR ENDED DECEMBER 31, 2010

Fourth quarter	\$1.40	\$0.70
Third quarter	\$1.19	\$0.77
Second quarter	\$2.70	\$1.03
First quarter	\$2.58	\$0.57

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 11 – Executive compensation for equity compensation plan information.

PLAN OF DISTRIBUTION

We will deliver the shares of common stock being issued to the purchasers electronically upon receipt of purchaser funds for the exercise of the warrants, if any, offered pursuant to this prospectus. We have agreed to indemnify the holders of the securities offered in this offering against some civil liabilities, including liabilities under the Securities Act and the Exchange Act. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons, we have been advised that in the opinion of the SEC this indemnification is against public policy as expressed in the Securities Act and is therefore, unenforceable.

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, 2011 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 synthetic DNA-based therapeutics and innovative disease-modifying medicines for serious illnesses. Our initial synthetic biologic product candidate is intended to treat PAH,