Synthetic Biologics, Inc.
Form 10-K
March 16, 2015

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

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

For the fiscal year ended December 31, 2014

OR

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

For the transition period from to

Commission File Number: 1-12584

SYNTHETIC BIOLOGICS, INC.

(Name of small business issuer in its charter)

Nevada (State or other jurisdiction of incorporation or organization)	**13-3808303** *(IRS Employer Identification Number)*
155 Gibbs Street, Suite 412 Rockville, MD (Address of principal executive offices)	20850 *(Zip Code)*
617 Detroit Street, Suite 100 Ann Arbor, MI (Mailing address)	48104 *(Zip Code)*

Registrant s telephone number, including area code: (734) 332-7800

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

(Title of Class)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	**NYSE MKT**

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

None

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained

herein, and will not be contained, to the best of issuer s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

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

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

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

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

The aggregate market value of the registrant s common stock held by non-affiliates of the registrant as of June 30, 2014, was approximately $79.4 million based on $1.72, the price at which the registrant s common stock was last sold on that date.

As of March 10, 2015, the issuer had 72,725,987 shares of common stock outstanding.

Documents incorporated by reference: Portions of the registrant s Proxy Statement for its 2015 Annual Meeting of Stockholders are incorporated by reference in Part III of this Annual Report on Form 10-K where indicated. Such Proxy Statement will be filed with the Securities and Exchange Commission within 120 days of the registrant s fiscal year ended December 31, 2014.

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

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PART I

Forward-Looking Statements

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

Item 1. ***Business***

We are a clinical-stage biotechnology company developing pathogen-specific therapies for serious infections and diseases, with a focus on protecting the microbiome. We are developing an oral biologic to protect the gut microbiome (gastrointestinal (GI) microflora) from intravenous (IV) antibiotics for the prevention of C. difficile infection, an oral statin treatment to reduce the impact of methane producing organisms on irritable bowel syndrome with constipation (IBS-C) and a monoclonal antibody combination for the treatment of Pertussis. In addition, we are developing a Phase 2 oral estriol drug for the treatment of relapsing-remitting multiple sclerosis (MS) and cognitive dysfunction in MS.

Product Pipeline:

Summary of Pathogen-Specific Therapy Programs:

***C. difficile* infections (CDI):** We are in clinical development of a novel second-generation oral enzyme candidate, SYN-004, for co-administration with commonly used IV beta-lactam antibiotics, intended to protect the microbiome and prevent the development of and severe effects from CDI. CDIs are a leading type of hospital acquired infection (HAI) and are frequently associated with IV antibiotic treatment. Designed to be given orally and co-administered with certain IV beta-lactam antibiotics (e.g., penicillins and cephalosporins), SYN-004 is intended to protect the gut while the IV antibiotics fight the primary infection. SYN-004 is believed to not only have a similar profile to its first-generation predecessor, which demonstrated protection of the microbiome (gut flora) during treatment with certain penicillins, but also has the potential to act against a broader spectrum of IV beta-lactam antibiotics. Beta-lactam antibiotics are a mainstay in hospital infection management and

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include the commonly used penicillin and cephalosporin classes of antibiotics. SYN-004 s target market is significant and represented by annual U.S. hospitals purchases of approximately 118 million doses of IV beta-lactam antibiotics which are administered to approximately 14 million patients.* Currently there are no approved treatments designed to protect the gut microbiome from the damaging effects of IV antibiotics. This worldwide market could represent a multi-billion dollar opportunity for us. In December 2014, the U.S. Patent and Trademark Office (USPTO) issued Patent No. 8,894,994 that has claims to compositions of matter and pharmaceutical compositions of beta-lactamases, including SYN-004, and carries a patent term to at least 2031. We also have an extensive patent estate on other aspects of this program which includes patent applications that could carry a term to at least 2035. In the fourth quarter of 2014, we initiated our randomized, double-blind placebo-controlled Phase 1a clinical trial, reported positive topline safety and tolerability results from the Phase 1a clinical trial, and initiated the Phase 1b clinical trial evaluating multiple ascending doses of SYN-004. In February 2015, we reported positive topline results from the Phase 1b clinical trial of escalating doses of oral SYN-004, with no safety or tolerability issues reported at dose levels and dose regimens both meeting and exceeding those expected to be studied in upcoming clinical trials. It is anticipated that the initiation of a Phase 2a clinical trial of SYN-004 and topline pharmacokinetics data from both of the SYN-004 Phase 1 clinical trials will be reported during the first quarter of 2015. The initiation of a Phase 2b proof-of-concept clinical trial is expected in the second half of 2015, with Phase 2b topline data anticipated during the second half of 2015.

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

IBS-C: In December 2013, through our majority-owned subsidiary, Synthetic Biomics, Inc., we entered into a worldwide exclusive license agreement with Cedars-Sinai Medical Center (CSMC) for the right to develop products for therapeutic and prophylactic treatments of acute and chronic diseases, including the development of SYN-010 to target IBS-C. An investigational team led by Mark Pimentel, M.D., at CSMC discovered that SYN-010 may reduce the production of methane gas by certain gastrointestinal (GI) microorganisms. Methane produced by these organisms is perceived as an underlying cause of pain, bloating, and constipation associated with IBS-C, and may contribute to the pathology of other diseases. SYN-010 is a modified release formulation of a statin being designed to reduce the impact of methane producing organisms on IBS-C. A 505(b)(2) regulatory pathway is anticipated for the development of SYN-010. We licensed an extensive intellectual property portfolio from CSMS including granted use patents and pending patent applications for SYN-010. Additional worldwide patent filings having composition of matter claims, which were recently filed by CSMC and licensed to us, could extend patent protection of SYN-010 to 2035. Based on guidance from the members on our IBS clinical advisory board, we plan to file an Investigational New Drug (IND) application with the U.S. FDA to support the initiation of Phase 2 clinical trials in the second quarter of 2015, with Phase 2 topline data anticipated during the second half of 2015.

Pertussis: In December 2012, in collaboration with Intrexon Corporation (NYSE: XON) (Intrexon), we initiated development of a monoclonal antibody (mAb) therapy for the treatment of Pertussis infections, more commonly known as whooping cough. Combining two mAbs, SYN-005 is designed to target and neutralize pertussis toxin as a prophylaxis for high-risk newborns and in order to reduce the mortality rate in infected infants. To further the development of this potential therapy for Pertussis, we entered into an agreement with The University of Texas at Austin (UT) to license the rights to certain research and pending patents related to pertussis antibodies. We have patents pending on compositions and uses of SYN-005 and we have an issued U.S. patent on other pertussis mAbs from UT. According to the World Health Organization, each year, *B. pertussis* infection is estimated to cause up to 300,000 deaths worldwide, primarily among unvaccinated infants. Positive preclinical research findings for SYN-005 were reported in April 2014, and again in September 2014, for our proprietary mAb combination therapy for treating Pertussis, in non-human

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primate studies. In September 2014 we received a U.S. Orphan Drug designation for SYN-005 for the treatment of Pertussis. We intend to seek non-dilutive funding to support the clinical development of SYN-005 for prophylaxis and treatment of Pertussis, including the anticipated filing of an IND application in 2015 and the anticipated initiation of a Phase 1 clinical trial during the second half of 2015, with topline Phase 1 data expected during 2015.

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

Summary of Multiple Sclerosis Program:

Relapsing-Remitting MS: Patient follow-up is complete in the UCLA-led Phase 2, investigator-initiated, randomized (n = 158), double-blinded, placebo-controlled trial which evaluated our drug candidate, Trimesta, in women with relapsing-remitting MS at 16 sites across the U.S. In April 2014, the principal investigator presented positive Phase 2 topline efficacy and safety results. In September 2014, the lead principal investigator presented additional Phase 2 clinical outcome data, including more detailed results on improvements in cognitive and disability measures, at the 2014 Joint Americas and European Committees for Treatment and Research in Multiple Sclerosis Meeting (ACTRIMS-ECTRIMS) in Boston. The data as reported by the lead principal investigator for the UCLA-led Phase 2 study provided supportive data for the potential of Trimesta to have a novel dual mechanism of action for both the anti-inflammatory effects that improve relapse rate, and a neuroprotective effect that improves standard measures of disability and cognition. Further analyses of the magnetic resonance imaging (MRI) data are ongoing, with topline data expected from the principal investigator during the first half of 2015. This investigator-initiated Phase 2 clinical trial was supported by grants exceeding $8 million, awarded primarily by the National Multiple Sclerosis Society (NMSS) in partnership with the NMSS s Southern California chapter, and the National Institutes of Health. Annual worldwide sales of MS therapies are forecasted to be approximately $17.8 billion in 2019. We have licensed issued method of treatment patents in the U.S. for MS therapy with estriol and estriol combination therapies (including estriol with Copaxone®) from UCLA, and numerous new provisional patent applications have been filed based on the Phase 2 clinical results. We are engaging with the neurology community and potential strategic partners, as we determine next steps for Trimesta.

Cognitive Dysfunction in MS: Trimesta is also being developed for the treatment of cognitive dysfunction in female MS patients. This 12-month, UCLA-led, randomized, double-blind, placebo-controlled investigator-initiated Phase 2 clinical trial is being conducted at four sites in the United States. The primary endpoint is the effect on cognitive function as assessed by Paced Auditory Serial Addition Test (PASAT). Patient enrollment is ongoing. The majority of the costs of this trial are being funded by grants from foundations and charitable organizations through direct funding to the principal investigator 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 for this indication.

Since our inception in January 2001, our efforts and resources have been focused primarily on acquiring and developing our product candidates, our clinical trials, raising capital, manufacturing and recruiting personnel. 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 $101.0 million through September 30, 2014. 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.

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Recent Developments

On October 10, 2014, we sold a total of 14,059,616 units at a purchase price of $1.47 per unit, with each unit consisting of one share of our common stock, and one warrant to purchase 0.5 shares of common stock in a registered direct offering for gross proceeds of $20.7 million and net proceeds of $19.1 million.

Pipeline Programs and Therapeutic Areas

Pathogen-Specific Therapy Programs

We are developing pathogen-specific therapies for serious infections and diseases, with a focus on protecting the microbiome. Infectious disease outbreaks are increasing while intervention options are declining due to widespread multidrug-resistant bacteria, increasing numbers of immuno-compromised patients (e.g., the elderly and cancer patients), and the isolation of new pathogens. We are developing an oral biologic to protect the GI microflora from the effects of certain IV beta-lactam antibiotics for the prevention of CDI, an oral treatment to reduce the impact of methane producing organisms on IBS-C and a monoclonal antibody combination for the treatment of Pertussis.

Microbiome-Focused Therapies:

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

C. difficile:

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

CDI is a widespread and often drug resistant infectious disease, it is estimated that 1.1 million patients are infected with *C. diff* annually in the U.S.*, and it has been reported that 30,000 patients die with a *C. diff* infection each year. CDI has surpassed methicillin-resistant staphylococcus aureus (MRSA) as the most frequently acquired hospital infection. Controlling the spread of CDI has proven challenging, as the *C. difficile* spores are easily transferred to patients via normal contact with healthcare personnel and with inanimate objects. There is currently no vaccine or approved product for the prevention of *C. diff* infection.

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

C. difficile: Acquisition of Clinical-Stage Program

In November 2012, we acquired a series of oral beta-lactamase enzymes (P1A, P2A and P3A) and related assets targeting the prevention of CDI, the leading HAI that generally occurs secondary to treatment with IV antibiotics. The acquired assets include a pre-IND package for P3A (now referred to as SYN-004), Phase 1 and Phase 2 clinical data for P1A, manufacturing processes and data, and a portfolio of issued and pending U.S. and international patents intended to support an IND and Biologics License Application (BLA) with the FDA. Utilizing this portfolio of assets, we developed a proprietary, secondary generation oral beta-lactamase enzyme product candidate, SYN-004.

When co-administered with certain IV beta-lactam antibiotics, it is expected that SYN-004 can degrade the antibiotic that is excreted in the GI tract, thus preserving the natural balance of the patient s microflora,

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and preventing opportunistic infections including CDI. Beta-lactam antibiotics are a mainstay in hospital infection management and include the commonly used penicillin and cephalosporin classes of antibiotics. SYN-004 s target market is significant and represented by annual U.S. hospitals purchases of approximately 118 million doses of IV beta-lactam antibiotics which are administered to approximately 14 million patients.* Currently there are no approved treatments designed to protect the microbiome from the damaging effects of IV antibiotics. The worldwide market for SYN-004 could represent a multi-billion dollar opportunity for us.

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C. difficile: Oral Enzyme Background

Beta-lactamase enzymes have the ability to degrade beta-lactam antibiotics that may be excreted into the GI tract. P1A (the first generation candidate) showed acceptable safety and tolerability in a Phase 1 study. In addition, two Phase 2 clinical studies demonstrated that P1A had the ability to preserve GI microflora in hospitalized patients treated with IV ampicillin or the combination of piperacillin and tazobactam.

C. difficile: Preclinical and Clinical Development

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

In June 2014, we formed a Clinical Advisory Board (CAB) to support development of SYN-004. The CAB is comprised of industry leaders Mark Wilcox, M.D., (Chairman), Curtis Donskey, M.D., Ciarán Kelly, M.D. and Tom Louie, M.D., all of whom are providing expertise and guidance on each aspect of the *C. diff* clinical program.

In August 2014, we announced an agreement with Evonik Corporation for GMP manufacturing of our proprietary oral beta-lactamase enzyme, SYN-004. Evonik formulated and encapsulated enterically coated SYN-004 for oral delivery for use in our Phase 1a, 1b and planned Phase 2a clinical trials, using material generated by our API manufacturer FUJIFILM Diosynth Biotechnologies UK Limited. In January 2015, we entered into an agreement with Halo Pharmaceutical (Whippany, NJ) to formulate and encapsulate enterically coated SYN-004 for oral delivery for use in our planned Phase 2b and other future clinical trials, using material generated by our API manufacturer FUJIFILM Diosynth Biotechnologies UK Limited.

In December 2014, we initiated Phase 1a and 1b clinical trials of SYN-004, and also reported positive topline safety and tolerability results from the Phase 1a study. In February 2015, we reported positive topline results from the Phase 1b clinical trial of escalating doses of oral SYN-004, with no safety or tolerability issues reported at dose levels and dose regimens both meeting and exceeding those expected to be studied in upcoming clinical trials. It is anticipated that the initiation of a Phase 2a study of SYN-004 and topline pharmacokinetics data from both of the SYN-004 Phase 1 clinical trials will be reported during the first quarter of 2015. The initiation of a Phase 2b proof-of-concept clinical trial is expected in the second half of 2015, with Phase 2b topline data anticipated during the second half of 2015.

In March 2015, we announced that late-breaking preclinical results supporting the development of SYN-004, our candidate therapy designed to degrade IV antibiotics within the GI tract and maintain the natural balance of the gut

microbiome for the prevention of CDI, were accepted for poster presentation at Digestive Disease Week® (DDW) 2015 in Washington DC in May 2015. The late-breaking abstract title is *SYN-004, a Clinical Stage Oral Beta-Lactamase Therapy, Protects the Intestinal Microflora from Antibiotic-Mediated Damage in Humanized Pigs.*

C. difficile: Intellectual Property

In October 2014, the USPTO issued a Notice of Allowance for a composition of matter patent application that has claims to compositions of matter and pharmaceutical compositions of beta-lactamases, including SYN-004, and carries a patent term to at least 2031. This patent has since issued as U.S. Patent 8,894,994. In

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addition to this newly granted patent, we have numerous related granted and pending U.S. and international patent applications that are central to our intellectual property estate. Further, we continue to grow our intellectual property estate with new filings, many of which would expire in at least 2035, if granted.

IBS-C:

Irritable Bowel Syndrome (IBS) is a functional GI disorder characterized by gas, abdominal pain, bloating and diarrhea or constipation, or alternating episodes of both. According to reports published by The International Foundation for Functional Gastrointestinal Disorders (IFFGD), IBS affects an estimated 10 to 15 percent of the population, or as many as 40 million Americans. The illness affects both men and women; two-thirds of diagnosed sufferers are women. The onset of IBS can begin anytime from adolescence to adulthood. Four bowel patterns may be seen with IBS, including: IBS-C (constipation predominant), D-IBS (diarrhea predominant), M-IBS (mixed diarrhea and constipation) and A-IBS (alternating diarrhea and constipation). The development of SYN-010 is an oral treatment intended to reduce the impact of methane producing organisms on IBS-C.

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

IBS-C: Acquisition of Clinical-Stage Program

In December 2013, we entered into a worldwide exclusive license agreement with CSMC for the right to develop products for therapeutic and prophylactic treatments for acute and chronic diseases. We licensed from CSMC a portfolio of intellectual property comprised of several U.S. and international patents and pending patent applications for various fields of use, including IBS-C, obesity and diabetes. An investigational team led by Mark Pimentel, M.D. at CSMC has discovered that these products may reduce the production of methane gas by certain GI microorganisms. Methane produced by these microorganisms is perceived as the underlying cause of pain, bloating, and constipation associated with IBS-C, and may contribute to the pathology of other diseases. Initially we will focus on the development of SYN-010, an oral treatment being designed to reduce the impact of methane producing organisms on IBS-C.

IBS: Gas Producing Organisms Background

In the 1990 s, research showed that IBS patients (over a given time) produced five times more gas than did people without IBS. Since the only source of those gases was bacterial, the initial presumption was that IBS patients had excessive bacteria in the colon. Subsequent studies showed that IBS patients had excessive quantities of gas in the small bowel; these data were the catalyst for studying small bowel bacteria in IBS. Normally the small intestine contains a very small quantity of bacteria. In published studies, indirect measures of small bowel bacteria suggest that 84% of IBS sufferers have excessive quantities of bacteria typically found in the colon. The CSMC investigational team led by Dr. Pimentel is researching a recent theory that defines IBS as a bacterial disease. Gut microflora that should normally be confined to the large intestine inappropriately colonize the small intestine. This process is referred to as small intestine bacterial overgrowth (SIBO), which results in gas, bloating, abdominal pain and altered stool habits characterized by IBS.

IBS-C: Methane Producing Organisms Background

Further research by the CSMC investigational team led by Dr. Pimentel is focused on the IBS-C patient population. Extensive studies conducted by Dr. Pimentel and collaborators have shown that overproduction of methane gas is directly associated with bloating, pain and constipation in IBS-C patients. CSMC investigators have discovered that inhibiting intestinal methane production may reverse constipation associated with IBS-C, and can be beneficial in other major diseases such as obesity and type 2 diabetes.

IBS-C: Preclinical and Clinical Development

Efforts led by Dr. Pimentel included formulating and testing non-antibiotic FDA-approved oral drug candidates for ultimate product registration via potential expedited pathways. Such candidates are intended for the reduction or elimination of methane gas production within the intestines, with the goal of having little or no unintended impact on a patient s normal GI microflora.

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In April 2014, we formed a CAB to support development of SYN-010, and also announced that gastroenterologist and lead investigator for the IBS-C program, Dr. Mark Pimentel, is the Chair of the CAB. In October 2014, we announced the expansion of the IBS-C CAB to include William Chey, M.D., Gail M. Comer, M.D., Anthony J. Lembo, M.D., and, Philip Schoenfeld, M.D., MSEd, MSc.

In September 2014, we announced that our candidate, SYN-010, is a modified release formulation of a statin being designed to reduce the impact of methane producing organisms on IBS-C. A 505(b)(2) regulatory pathway is anticipated for the development of SYN-010.

Based on guidance from the members on our IBS CAB, we plan to file an IND application with the U.S. FDA to support the initiation of Phase 2 clinical trials in the second quarter of 2015, with Phase 2 topline data anticipated during the second half of 2015.

In February 2015, we announced that preclinical results supporting the development of SYN-010 (based on research performed at Cedars-Sinai Medical Center under the direction of Dr. Mark Pimentel), our candidate therapy to reduce the impact of methane producing organisms on IBS-C, were accepted for poster presentation at DDW 2015 in Washington DC in May 2015. The abstract title is *Lovastatin improves stool form in Methanobrevibacter smithii colonized rats with constipation.*

IBS-C: Intellectual Property

An extensive intellectual property portfolio including granted use patents and pending patent applications for SYN-010 has been licensed to us by CSMC. Additional worldwide patent filings, including composition of matter claims, among other claims, recently filed by CSMC and licensed to us could extend patent protection of SYN-010 to 2035.

Monoclonal Antibodies:

Monoclonal Antibodies for Infectious Diseases

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

Intrexon Collaboration: Monoclonal Antibodies for Infectious Diseases

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

** mAbLogix™ and LEAP® are trademarks of Intrexon Corporation.

Pertussis:

Bordetella pertussis (B. pertussis) is a gram-negative bacterium that infects the upper respiratory tract, causing uncontrollable and violent coughing. Antibiotic treatment does not have a major effect on the course of Pertussis, because while it can eliminate the *B. pertussis* bacteria from the respiratory tract, it does not neutralize the pertussis toxin. Infants with Pertussis often require hospitalization in pediatric intensive care units, frequently requiring mechanical ventilation. Pertussis in adults generally leads to a chronic cough referred to as the cough of 100 days. The incidence of Pertussis is increasing due to the declining effectiveness of the acellular vaccine introduced in the 1990s, exposure of unvaccinated and under-vaccinated

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individuals including infants who are not yet fully vaccinated, exposure of individuals whose immunity has diminished over time, as well as asymptomatic carriers.

According to the World Health Organization there are 50 million cases of whooping cough and *B. pertussis* infection that are estimated to cause up to 300,000 deaths each year worldwide, primarily among unvaccinated infants. Recent news reports throughout the U.S. indicate that the pertussis vaccine introduced in the 1990s does not provide long-term protection and, as a result, whooping cough cases have increased to a 60-year high.

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

In December 2012, we initiated mAb development for the treatment of Pertussis focusing on toxin neutralization pursuant to our August 2012 collaboration with Intrexon. Unlike antibiotics, we are developing a therapy comprising a combination of two mAbs, SYN-005, to target and neutralize the pertussis toxin as a prophylaxis for high-risk newborns and in order to reduce the mortality rate in infected infants.

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

Pertussis: Preclinical and Clinical Development

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

In April 2014, and again in September 2014, we received positive preclinical research findings for SYN-005, our proprietary mAb combination therapy for treating Pertussis (whooping cough), in three non-human primate studies (n = 19). In the latter two Pertussis studies in particular, SYN-005 rapidly blunted the rise in white blood cell count that is characteristic of the disease and accelerated its return to baseline.

In addition, during September 2014 we received U.S. Orphan Drug designation from the FDA for SYN-005 for the treatment of Pertussis.

We intend to seek non-dilutive funding to support the clinical development of SYN-005 for the prophylaxis and treatment of Pertussis, including the anticipated filing of an IND application in 2015, and the anticipated initiation of a Phase 1 clinical trial during the second half of 2015, with topline Phase 1 data expected during 2015.

In March 2015, we announced that preclinical results supporting the development of SYN-005, our mAb therapy candidate for the treatment of Pertussis, were accepted for two poster presentations at the European Congress of Clinical Microbiology and Infectious Diseases meeting (ECCMID) 2015 in Copenhagen, Denmark, in April 2015. The abstract titles are *Antibody Cocktail Effectively Treats Pertussis in a Baboon Disease Model* and *Spontaneous Identification of Bordetella bronchiseptica in a Baboon Colony: Potential Ramifications for Bordetella pertussis*

Modeling.

Pertussis: Intellectual Property

We have patents pending on compositions and uses of SYN-005 and we have an issued U.S. patent on other pertussis mAbs from UT.

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Acinetobacter Infections:

Acinetobacter baumanii is a difficult to treat pathogen due to its rapid and well-established development of resistance to most antibiotics, making it a multidrug-resistant pathogen. In addition, as a biofilm-forming pathogen, *Acinetobacter baumanii* has the ability to survive up to twice as long as non-biofilm-forming pathogens. In the U.S., *Acinetobacter baumanii* has been reported to be the cause of up to 2.6% of hospital acquired infections, 1.3% of bloodstream infections and 7.0% of ICU respiratory tract infections, and more than half of the *Acinetobacter baumanii* isolates are multidrug-resistant. According to published articles, mortality rates associated with *Acinetobacter* infections as high as 43.0% are reported in hospitals and ICU settings. While *Acinetobacter baumanii* is a well-documented pathogen in the hospital setting, this pathogen also poses an increasing danger to wounded servicemen and women in military treatment centers and to those treated in trauma centers following natural disasters.

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

Acinetobacter: Intrexon Collaboration

In September 2012, we initiated a mAb discovery and development program for *Acinetobacter* infections pursuant to our August 2012 collaboration with Intrexon. This program is in the discovery stage and the generation of a panel of antibodies is ongoing.

Multiple Sclerosis Program

Relapsing-Remitting MS:

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

There are nine FDA-approved therapies for the treatment of relapsing-remitting MS: Betaseron®, Rebif®, Avonex®, Copaxone®, Tysabri®, Gilenya®, Extavia®, Aubagio® and Tecfidera®. Many of these therapies provide only a modest benefit for patients with relapsing-remitting MS. All of these drugs except Gilenya®, Aubagio® and Tecfidera® require frequent (daily, weekly & monthly) injections (or infusions) on an ongoing basis and can be associated with unpleasant side effects (such as flu-like symptoms) and high rates of non-compliance among users. Despite the availability of therapies for the treatment of relapsing-remitting MS, the disease is highly underserved and exacts a heavy personal and economic toll. Annual worldwide sales of MS therapies have been forecasted to reach approximately $17.8 billion in 2019.

Relapsing-Remitting MS: Background

Research has shown that pregnant women with MS tend to experience a spontaneous reduction of disease symptoms during pregnancy, particularly in the third trimester. The PRIMS (Pregnancy In MS) study published in 1998, a landmark observational clinical study published in the *New England Journal of Medicine* followed 254 women with MS during 269 pregnancies and for up to one year after delivery. The PRIMS study demonstrated that relapse rates were significantly reduced by 71% ($p < 0.001$) through the third trimester of pregnancy compared to

pre-pregnancy-rates, and that relapse rates increased by 120% ($p < 0.001$) during the first three months after birth (post-partum) and then return to pre-pregnancy rates. It has been hypothesized that the female hormone, estriol, produced by the placenta during pregnancy, plays a role in fetal immune privilege , a process that prevents a mother s immune system from attacking and rejecting the fetus. The maternal levels of estriol increase linearly through the third trimester of pregnancy until birth, whereupon it abruptly returns to low circulating levels. The anti-autoimmune effects of estriol are thought to be responsible for the therapeutic effects experienced by MS patients during pregnancy.

Rhonda Voskuhl, M.D., Director, UCLA MS program, UCLA Department of Neurology, has published that plasma levels of estriol achieved during pregnancy have immunomodulatory effects. Dr. Voskuhl further postulated and tested in a pilot clinical study that oral doses of estriol may have a therapeutic benefit when administered to non-pregnant female MS patients.

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

Relapsing-Remitting MS: Clinical Development

Trimesta (oral estriol) is being developed as an adjunctive once-daily treatment for 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 MRI (an established neuroimaging measure of disease activity in MS). Over the next three months of treatment with Trimesta, the median total enhancing lesion volumes decreased by 79% ($p = 0.02$) and the number of lesions decreased by 82% ($p = 0.09$). They remained decreased during the next 3 months of treatment, with lesion volumes decreased by 82% ($p = 0.01$), and numbers decreased by 82% ($p = 0.02$). Following a six-month drug holiday during which the patients were not on any drug therapies, median lesion volumes and numbers returned to near baseline pretreatment levels. Trimesta therapy was reinitiated during a four-month retreatment phase of this clinical trial. The relapsing-remitting MS patients again demonstrated a decrease in enhancing lesion volumes of 88% ($p = 0.008$) and a decrease in the number of lesions by 48% ($p = 0.04$) compared with original baseline scores. The study was published by the principal investigator in Ann Neurol. 2002 Oct;52(4):421-8.

Patient follow-up is complete in the UCLA-led Phase 2, investigator-initiated, randomized (n = 158), double-blinded, placebo-controlled trial which evaluated our drug candidate, Trimesta, in women with relapsing-remitting MS at 16 sites across the U.S. Positive Phase 2 topline efficacy and safety results were presented in April 2014 by lead principal investigator, Dr. Rhonda Voskuhl of UCLA at the 66th American Academy of Neurology Annual Meeting. Dr. Voskuhl presented additional Phase 2 clinical outcome data, including more detailed results on improvements in cognitive and disability measures, at the 2014 Joint ACTRIMS-ECTRIMS in Boston in September 2014. The data as reported by Dr. Voskuhl for the UCLA-led Phase 2 study demonstrated the potential of Trimesta to have a novel dual mechanism of action for both the anti-inflammatory effects that improve relapse rate, and a neuroprotective effect that improves standard measures of disability and cognition.

Specifically, Dr. Voskuhl reported the following results:

(i) *Annualized relapse rate:* A 47% reduction in annualized relapse rate in the Trimesta+Copaxone® arm as compared to the placebo+Copaxone® arm (active control arm) at 12 months of therapy ($p = 0.02$), meeting the primary outcome of the trial. These improvements in annualized relapse rate were sustained during the 24 months of therapy. When compared to the placebo+Copaxone® arm at 24 months, the Trimesta+Copaxone® arm demonstrated a 32% lower relapse rate ($p = 0.11$).

(ii) *Cognitive disability:* Patients in the Trimesta+Copaxone® arm who had Paced Auditory Serial Addition Test (PASAT) scores lower than 55 before treatment (PASAT scale maximum of 60) experienced an approximately 12%, or 6 point, improvement in cognitive scores within 12 months of treatment ($p < 0.05$). This improvement from baseline was sustained throughout the 24 month study. In addition, a significantly larger proportion of patients in the Trimesta+Copaxone® arm demonstrated sustained improvement in cognition during the entire 24 month period, as approximately 33% of the patients showed sustained improvement of at least 3 points during this time period, compared to only about 21% in the placebo+ Copaxone® arm ($p < 0.05$).

(iii) *Physical disability:* Expanded Disability Status Scale (EDSS) scores in the Trimesta+Copaxone® arm significantly improved during 24 month follow-up by at least 0.5 point ($p = 0.03$) compared to the placebo+Copaxone® arm which experienced no change in EDSS scores. The between group difference showed a positive trend ($p = 0.25$). The 25 foot walk test showed a significant difference, while the patients in the Trimesta+Copaxone® arm were stable during the study, those

in the active control arm did worse. The between group difference ($p = 0.02$).
In addition, adjunctive oral Trimesta plus injectable standard of care Copaxone® demonstrated a strong safety profile and was well tolerated by women in the study. Further analyses of the MRI data are ongoing,

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with topline data expected from the principal investigator during the first half of 2015. We are engaging with the neurology community and potential strategic partners, as we determine next steps for Trimesta.

This investigator-initiated Phase 2 clinical trial was supported by grants exceeding $8 million, awarded primarily by the NMSS in partnership with the NMSS s Southern California chapter, and the National Institutes of Health.

Relapsing-Remitting MS: Intellectual Property

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

In April 2013, we announced that the USPTO issued U.S. Patent No. 8,372,826 entitled, *Estriol Therapy for Multiple Sclerosis and Other Autoimmune Diseases*, to the Regents of the University of California which includes claims to the use of our drug candidate, Trimesta, in combination with glatiramer acetate injection (Copaxone®). According to Teva Pharmaceutical Industries Ltd. s Form 20-F for the year ended December 31, 2014, filed with the SEC on February 9, 2015, Copaxone® continued to be the leading MS therapy in the U.S, and globally, with approximately $4.2 billion in global net revenues. Currently marketed exclusively by Teva Pharmaceutical Industries Ltd., U.S. Orange Book patents on Copaxone® expired in May 2014 and, subject to further judicial review, in September 2015.

Through our wholly owned subsidiary, we hold the exclusive worldwide license to issued U.S. Patents 8,895,539, 8,658,627, 8,372,826 and 6,936,599, as well as pending patents for MS and other autoimmune diseases covering the uses of our drug candidate, Trimesta. Numerous new provisional patent applications have been filed based on the Phase 2 clinical results.

Cognitive Dysfunction in MS:

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

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

Cognitive Dysfunction in MS: Background

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

expressed as a mean percent change from baseline.

Cognitive Dysfunction in MS: Clinical Development

Our Trimesta drug candidate is also being developed for the treatment of cognitive dysfunction in female MS patients. This randomized, double-blind, placebo-controlled Phase 2 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 four clinical sites in the United States, including UCLA. Up to 64 patients between the ages of 18 and 50 will be randomized 1:1 into the

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treatment and placebo groups. Investigators will administer either oral Trimesta or a matching placebo, in addition to an FDA-approved MS treatment, including Copaxone®, Avonex®, Betaseron®, Extavia®, Rebif®, Gilenya®, Aubagio® and Tecfidera®. 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 pledged to equally support this new clinical trial, and we will also provide Trimesta drug supply. The trial also received contributions from several other supporters. Patient recruitment and enrollment into this trial is ongoing.

Intellectual Property

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

Cedars-Sinai Medical Center License Agreement

On December 5, 2013, through our newly formed, majority owned subsidiary, Synthetic Biomics, Inc. (SYN Biomics), we entered into a worldwide exclusive license agreement (the CSMC License Agreement) for the right to develop, manufacture, use, and sell products for the human and veterinary therapeutic and prophylactic treatments for acute and chronic diseases. An investigational team lead by Dr. Mark Pimentel at CSMC has discovered that these products are intended to target certain pathogenic GI microorganisms that are perceived as an underlying cause of diseases such as IBS-C, obesity and type 2 diabetes. The portfolio of intellectual property licensed to SYN Biomics under the CSMC License Agreement includes nine issued U.S. patents, 30 issued patents in various European countries, three issued Australian patents, one Canadian patent and one issued Japanese patent as well as several pending U.S. and international patent applications for most fields of use and modalities (subject to certain agreed-upon exceptions. On December 5, 2013, we also entered into an option agreement with CSMC, which expired unexercised on December 31, 2014.

Under the terms of the CSMC License Agreement we issued 291,569 unregistered shares of our common stock to CSMC, as payment of an initial license fee and patent reimbursement fees of $150,000 and $220,000, respectively. The parties also entered into a Stock Purchase Agreement with respect to such stock issuance and other issuances of unregistered shares of our common stock that may be issued to CSMC in lieu of cash, including license fees, milestone payments, expense reimbursements and option fees under the CSMC License Agreement. The CSMC License Agreement also provides that commencing on the second anniversary of the CSMC License Agreement, SYN Biomics will pay an annual maintenance fee, which payment shall be creditable against annual royalty payments owed under the CSMC License Agreement. In addition to royalty payments which are a percentage of Net Sales (as defined in the CSMC License Agreement) of Licensed Products (as defined in the CSMC License Agreement) and Licensed Technology products (as defined in the CSMC License Agreement), SYN Biomics is obligated to pay CMSC a percentage of any non-royalty sublicense revenues, as well as additional consideration upon the achievement of the following milestones (the first two of which are payable in cash or unregistered shares of our stock at our option): (i) successful Phase 1 trial completion of the first Licensed Product or first Licensed Technology Product; (ii) successful Phase 2 trial completion of the first Licensed Product or first Licensed Technology Product; (iii) initiation of Phase 3 dosing for each additional indication of a Licensed Product or Licensed Technology Product; (iv) successful Phase 3 trial completion for each Licensed Product and each Licensed Technology Product; (v) the FDA s acceptance of a New

Drug Application for each Licensed Product and each Licensed Technology Product; (vi) regulatory approval for each Licensed Product and each Licensed Technology Product; and (vii) the first commercial sale of each Licensed Product and each Licensed Technology Product. The stock issuances are subject to prior approval of the NYSE MKT, LLC.

Prior to the execution of the CSMC License Agreement, SYN Biomics issued shares of common stock of SYN Biomics to each of CSMC and Dr. Mark Pimentel (the primary inventor of the intellectual property), representing 11.5% and 8.5%, respectively, of the outstanding shares of SYN Biomics (the SYN Biomics

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

The CSMC License Agreement terminates: (i) automatically if SYN Biomics enters into a liquidating bankruptcy or other specified bankruptcy event or if the performance of any term, covenant, condition or provision of the CSMC License Agreement will jeopardize the licensure of CMSC, its participation in certain reimbursement programs, its full accreditation by the Joint Commission of Accreditation of Healthcare Organizations or any similar state organizations, its tax exempt status or is deemed illegal; (ii) upon 30 days notice from CMSC if SYN Biomics fails to make a payment or use commercially reasonable efforts to exploit the patent rights; (iii) upon 60 days notice from CMSC if SYN Biomics fails to cure any breach or default of any material obligations under the CSMC License Agreement; or (iv) upon 90 days notice from SYN Biomics if CMCS fails to cure any breach or default of any material obligations under the CSMC License Agreement. SYN Biomics also has the right to terminate the License Agreement without cause upon 6 months notice to CSMC; however, upon such termination, SYN Biomics is obligated to pay a termination fee with the amount of such fee reduced: (i) if such termination occurs after an IND submission to the FDA but prior to completion of a Phase 2 clinical trial, (ii) reduced further if such termination occurs after completion of Phase 2 clinical trial but prior to completion of a Phase 3 clinical trial; and (iii) reduced to zero if such termination occurs after completion of a Phase 3 clinical trial.

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

On December 19, 2012, we entered into a Patent License Agreement (the Texas License Agreement) with The University of Texas at Austin (the University) for the exclusive license of the right to use, develop, manufacture, market and commercialize certain research and patents related to pertussis antibodies developed in the lab of Dr. Jennifer A. Maynard, Associate Professor of Chemical Engineering. The Texas License Agreement provides that the University is entitled to payment of past patent expenses, an annual payment of $50,000 per year commencing on the effective date through December 31, 2014 and a $25,000 payment on December 31, 2015 and milestone payments of $50,000 upon commencement of Phase 1 Clinical Trials, $100,000 upon commencement of Phase 3 Clinical Trials, $250,000 upon NDA submission in the United States, $100,000 upon European Medicines Agency approval and $100,000 upon regulatory approval in an Asian country. In addition, the University is entitled to a running royalty upon Net Product Sales and Net Service Sales (as defined in the Texas License Agreement). The License Agreement terminates upon the expiration of the patent rights (as defined in the Texas License Agreement); provided, however that the Texas License Agreement is subject to early termination by us in our discretion and by the University for a breach of the Texas License Agreement by us.

In connection with the Texas License Agreement, we also entered into a Sponsored Research Agreement (the Sponsored Research Agreement) with the University pursuant to which the University will perform certain research work related to pertussis under the direction of Dr. Jennifer Maynard. All inventions conceived during such research shall be subject to the Texas License Agreement and we will obtain certain rights to patents and technology developed during the course of such research. The Sponsored Research Agreement may be renewed annually, in our sole discretion, after the first year for two additional one year terms with a fixed fee for the first year of $303,287. The Sponsored Research Agreement was renewed for the second and third years, at fixed fees of $316,438 and $328,758 respectively, all payable in quarterly installments. The Sponsored Research Agreement will expire on December 31,

2015; provided, however, the Sponsored Research Agreement is subject to early termination upon the written agreement of the parties, a default in the material obligations under the Sponsored Research Agreement which remain uncured for sixty days after receipt of notice, automatically upon our bankruptcy or insolvency and by us in our sole discretion at any time after the one year anniversary of the date of execution thereof upon no less than 90 days notice.

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Upon a termination after December 31, 2014 or due to a breach by the University, we shall only be responsible for all reasonable expenses that do not exceed the fixed annual amount and that are incurred by the University prior to the termination date for services performed prior to the termination date.

We have patents pending on compositions and uses of SYN-005 that are co-owned by us and UT and licensed to us, and we have an issued U.S. patent and patent applications on other Pertussis mAbs licensed from UT.

Oral Enzyme for C. difficile Program Acquisition Agreement

On November 8, 2012, we entered into an Asset Purchase Agreement (the Prev Agreement) with Prev ABR LLC (Prev), and subsequently closed the transaction on November 28, 2012. Pursuant to the Prev Agreement we acquired the *C. difficile* program assets of Prev, including pre-IND package for P3A (SYN-004), Phase 1 and Phase 2 clinical data for P1A, manufacturing processes and data, and a portfolio of issued and pending U.S. and international patents intended to support an IND and BLA with the FDA. Pursuant to the Prev Agreement, we paid Prev an initial cash payment of $100,000 upon execution of the Prev Agreement and at closing paid an additional cash payment of $135,000 and issued 625,000 unregistered shares of our common stock to Prev. In addition, upon the achievement of the milestones set forth below, Prev may be entitled to receive additional consideration payable 50% in cash and 50% in our stock, subject to Prev s option to receive the entire payment in shares of our stock: (i) upon commencement of an IND; (ii) upon commencement of a Phase 1 clinical trial; (iii) upon commencement of a Phase 2 clinical trial; (iv) upon commencement of a Phase 3 clinical trial; (v) upon Biologic License Application (BLA) filing in the U.S. and for territories outside of the U.S. (as defined in the Prev Agreement); and (vi) upon BLA approval in the U.S. and upon approval in territories outside the U.S. As of December 31, 2014, the first two milestones have been met, and at Prev s option, Prev elected to receive 212,843 shares of our common stock; such payments have been accrued. The future stock issuances are subject to prior approval of the NYSE MKT, LLC. No royalties are payable to Prev under the Prev Agreement.

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

Infectious Disease Collaboration with Intrexon

On August 6, 2012, we expanded our relationship with Intrexon and entered into the Second ECC with Intrexon that governs a channel collaboration arrangement in which we will use Intrexon s technology relating to the identification, design and production of human antibodies and DNA vectors for the development and commercialization of a series of monoclonal antibody therapies for the treatment of certain serious infectious diseases the (Program) for the treatment of up to eight specific target infectious disease indications (the Field). Our development efforts are targeting Pertussis and *Acinetobacter*. Such license is exclusive with respect to any clinical development, selling, offering for sale or other commercialization of our products within the Field (Synthetic Products), and otherwise is non-exclusive. We may not sublicense the rights described without Intrexon s written consent. Under the Second ECC, and subject to certain exceptions, we are responsible for, among other things, the performance of the Program including the development, commercialization and manufacturing of products.

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

We may voluntarily terminate the Second ECC upon 90 days written notice to Intrexon. Intrexon may also terminate the Second ECC if we elect not to pursue the development of a Program identified by Intrexon that is a Superior Therapy as defined in the Second ECC upon 60 days notice unless we remedy the

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circumstances giving rise to the termination during such notice period. Each party has the right to terminate the agreement upon 60 days notice if the other party commits a material breach of the Second ECC, subject to certain cure periods.

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

is being commercialized by us,
has received regulatory approval,
is a subject of an application for regulatory approval that is pending before the applicable regulatory authority,
is a subject of at least a Phase 2 or Phase 3 clinical trial if such termination is by Intrexon due to a material breach by us of the Second ECC or by us upon 60 days notice after the first 18 months.

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

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

We also agreed upon the filing of an IND application with the FDA for a Synthetic Product, or alternatively the filing of the first equivalent regulatory filing with a foreign regulatory agency (both as applicable, the IND Milestone Event), to pay Intrexon either (i) $2.0 million in cash, or (ii) that number of shares of Common Stock (the IND Milestone Shares) having a fair market value equaling $2.0 million where such fair market value is determined using published market data of the share price for Common Stock at the close of market on the business day immediately preceding the date of public announcement of attainment of the IND Milestone Event.

Upon the first to occur of either first commercial sale of a Synthetic Product in a country or the granting of the regulatory approval of that Synthetic Product (both as applicable, the Approval Milestone Event), we agreed to pay to Intrexon either (i) $3.0 million in cash, or (ii) that number of shares of Common Stock (the Approval Milestone Shares) having a fair market value equaling $3.0 million where such fair market value is determined using published market data of the share price for Common Stock at the close of market on the business day immediately preceding the date of public announcement of attainment of the Approval Milestone Event.

We also agreed that we will pay an optional and varying fee whereby we remit a payment, in cash or equity at our sole discretion, to Intrexon calculated as a multiple of the number of targets in excess of three total that we desire to elect (the Field Expansion Fee). The Field Expansion Fee must be paid completely in either Common Stock or cash, and will comprise either (i) $2.0 million in cash for each target in excess of three total that we elect, or (ii) that number of shares of Common Stock (the Field Expansion Fee Shares) having a fair market value equaling $2.0 million for each such target that we elect in excess of three where such fair market value is determined using published market data establishing the volume-weighted average price for a share of Common Stock over the 30 day period immediately preceding the date of the Field Expansion Fee Closing.

In connection with the transactions contemplated by the Second Stock Issuance Agreement, and pursuant to the First Amendment to Registration Rights Agreement (the First Amendment to Registration Rights Agreement) executed and delivered by the parties at the closing, we filed a resale registration statement registering the resale of certain of the shares issued under the Second Stock Issuance Agreement.

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. Effective May 6, 2010, we entered into a Sublicense Agreement with Meda AB of Sweden. Pursuant to this agreement, Meda

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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. Meda AB informed us that due to the decision of the European Medicines Agency (EMA) to limit the use of flupirtine for long-term pill and systemic use, it has postponed its planned fibromyalgia clinical trials in the U.S.

The Regents of University of California License Agreement

In July 2005, we were granted an exclusive worldwide license agreement with the Regents of the University of California (the Regents) relating to issued U.S. Patent Nos. 6,936,599, 8,372,826, 8,658,627 and 8,895,539 and pending patent applications covering the uses of the drug candidate Trimesta, which has been subsequently amended. Pursuant to this agreement, we paid an upfront license fee and reimbursed patent expenses totaling approximately $61,000 and agreed to pay a license fee of $25,000 during 2006. We also agreed to pay annual maintenance fees, milestone payments totaling $750,000 that are payable on filing an NDA, and on approval of an NDA with the FDA, an additional $750,000 payable upon the first achievement of $50.0 million in annual sales while covered by a validly issued U.S. patent as well as a 4% royalty on net sales of Trimesta covered by the licensed patents. We may be permitted to partially pay milestone payments in the form of equity. The duration of this agreement is from the effective date of July 11, 2005 until the last-to-expire patent in Regent s Patent Rights, or until the last patent application licensed under this agreement is abandoned and no patent in Regent s Patent Rights ever issues. We have the right to terminate this agreement at any time and termination will be effective 90 days after the effective date of the termination notice. The Regents may terminate the agreement with a written notice of default if we violate or fail to perform any material term or covenant of this agreement including failure within three years from the successful completion of the ongoing clinical trial of estriol for relapsing-remitting MS being conducted by Dr. Rhonda Voskuhl as principal investigator, to initiate a Phase 3 clinical trial, or within 17 years of the effective date of the agreement to complete the commercial sale of a product for human therapeutics for the treatment of autoimmune diseases, including MS. However, we have 60 days after the effective date of the notice of default to repair the default.

Numerous new provisional patent applications have been filed for Trimesta based on the Phase 2 clinical results.

Manufacturing

We utilize contract manufacturing firms to produce our investigational products Trimesta, SYN-004 and SYN-010 in accordance with current good manufacturing practices (cGMP) guidelines outlined by the FDA.

Research and Development

During the years ended December 31, 2014, 2013 and 2012, we incurred $14.5 million, $6.5 million and $12.3 million, respectively, in research and development expenses.

Government Regulation

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 primarily the FDA. 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 prescription drugs, 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.

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

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could result, among other things, in suspension of regulatory approval, recalls, suspension of production or injunctions, seizures, or civil or criminal sanctions. We cannot be certain that we or our present or future subcontractors will be able to comply with these regulations.

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

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

preclinical laboratory and animal tests;
submission of an IND, prior to commencing human clinical trials;
adequate and well-controlled human clinical trials to establish safety and efficacy for intended use;
submission to the FDA of a New Drug Application (NDA) or BLA; and
FDA review and approval of an NDA or BLA.

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

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

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

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

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

Phase 1: The drug is initially tested in healthy human subjects or patients for safety, dosage tolerance, absorption, metabolism, distribution, and excretion.

Phase 2: 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.

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Phase 3: When Phase 2 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 1, Phase 2, or Phase 3 testing of our product candidates within any specific time period, if at all. Furthermore, the FDA, an Institutional Review Board (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 cGMP requirements. The manufacturing process must conform to consistency and quality standards, and we must develop methods for testing the quality, purity, and potency of the final products. Appropriate packaging is selected and tested, and chemistry stability studies are conducted to demonstrate that the product does not undergo unacceptable deterioration over its shelf-life. Results of the foregoing are submitted to the FDA as part of a NDA (or BLA in case of biologic products) for marketing and commercial shipment approval. The FDA reviews each NDA or BLA submitted and may request additional information.

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

Submission of an NDA or BLA with clinical data requires payment of a substantial fee. In return, the FDA assigns a goal for review and decision on the application, in which the FDA may approve or deny the NDA or BLA, or issue a complete response letter outlining information needed to support approval, including a potential need for additional clinical data. Even if these data are submitted, the FDA may ultimately decide the NDA or BLA does not satisfy approval criteria. If the FDA approves the NDA or BLA, the product becomes available for marketing. Product approval may be withdrawn if regulatory compliance is not maintained or safety problems occur. The FDA may require post-marketing studies, also known as Phase 4 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.

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Competitive Environment

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

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

Our History

Our predecessor, Sheffield Pharmaceuticals, Inc., was incorporated in 1986, and in 2006 engaged in a reverse merger with Pipex Therapeutics, Inc., a publicly-traded 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 engaged in a merger with a wholly owned subsidiary for the purpose of reincorporating in the State of Nevada. After reprioritizing our focus and entering into our first collaboration with Intrexon, we amended our Articles of Incorporation to change our name to Synthetic Biologics, Inc. on February 15, 2012.

Employees

As of March 10, 2015, we employed approximately 23 individuals, 17 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.

Executive Officers

Name	Position	Age	Executive Officer Since
Jeffrey Riley	President and Chief Executive Officer	52	2012
C. Evan Ballantyne	Chief Financial Officer	55	2012

Jeffrey Riley. Mr. Riley, a member of the Synthetic Biologics Board of Directors since March 2010 and Chairman of the Board from November 2011 to May 2012, was appointed as the Company s President and Chief Executive Officer in February 2012. He has more than 20 years of experience in the biotechnology and pharmaceutical industries during which he negotiated numerous worldwide strategic corporate alliances, established joint ventures, and assisted in obtaining venture financings to support product development. Most recently, he served as Managing Director of 526 Ventures. Prior to this, he was a venture partner with QIC Bioventures Fund. Over his career, Mr. Riley held senior positions within the mergers & acquisitions and in country management groups at SmithKline Beecham and Pfizer,

and he served as CFO and VP Corporate Development for Nichols Institute Diagnostics, later acquired by Corning and spun out to Quest Diagnostics, Inc. Mr. Riley s education includes: a B.S. degree from Boise State University, coursework at UCSF/Berkeley in drug discovery/development and participation in a dual-degree graduate program, an M.B.A./M.I.M. sponsored by Arizona State University and the Thunderbird School of Global Management.

C. Evan Ballantyne. Mr. Ballantyne joined Synthetic Biologics as its Chief Financial Officer in February 2012. He also serves as the Company s Corporate Secretary and Treasurer. He brings more than 25 years of financial and operations experience to the Company. Most recently, Mr. Ballantyne served as Executive Vice President and Chief Financial Officer of Clinical Data, Inc., a publicly-traded biopharmaceutical company which was acquired by Forest Laboratories, Inc. for $1.3 billion. He has also served as Chief Financial Officer of a number of private medical technology companies, including Avedro and

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ZymeQuest. Earlier in his career, he served as Vice President and Chief Operating Officer for ACNielsen Europe Middle East & Africa and held the Chief Financial Officer position as well for two years, and began his career at the Dun & Bradstreet Corporation where he held several senior financial positions. Mr. Ballantyne earned a B.A. from the University of Western Ontario, and took a post-graduate degree in Business Administration with Honors from the University of Windsor.

Properties

Our principal executive offices are located at 155 Gibbs Street, Suite 412, Rockville, Maryland 20850. We also maintain an administrative and finance office located at 617 Detroit Street, Suite 100, Ann Arbor, Michigan 48104.

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.

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

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

RISKS RELATING TO OUR BUSINESS

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

With the exception of the three months ended June 30, 2010, we have experienced significant losses since inception and have a significant accumulated deficit. We expect to incur additional operating losses in the future and therefore expect our cumulative losses to increase. With the exception of the quarter ended June 30, 2010, and limited laboratory revenues from Adeona Clinical Laboratory, which we sold in March 2012, we have generated very minimal revenues. We do not expect to derive revenue from any source in the near future until we or our potential partners successfully commercialize our products. As of December 31, 2014, our accumulated deficit totaled approximately $101.0 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 funding, such as additional financing or grant funding, and additional financing may not be available on favorable terms, if at all. If we do not succeed in raising additional funds on acceptable terms, we may be unable to complete planned preclinical and clinical trials or obtain approval of our product candidates from the FDA and other regulatory authorities. In addition, we could be forced to delay, discontinue or curtail product development, forego sales and marketing efforts, and forego licensing in attractive business opportunities. Any additional sources of financing will likely involve the issuance of our equity or debt securities, which will have a dilutive effect on our stockholders.

We have not been able to sustain profitability.

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

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

We may experience negative cash flow for the foreseeable future as we fund our development and clinical programs 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.

We have not been able to sustain profitability.

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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.

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

We do not expect to generate any additional revenue from our sublicense with Meda AB due to recent developments in Europe.

On May 6, 2010, we entered into a sublicense agreement with Meda AB whereby we were given the right to receive certain milestone payments totaling $17.5 million (including an upfront payment of $2.5 million that was received in 2010), plus certain royalties on our flupirtine program. Meda AB informed us that due to the decision of the European

Medicines Agency (EMA) to limit the use of flupirtine for long-term pill and systemic use, it has postponed its planned fibromyalgia clinical trials in the U.S. Therefore, we do not expect that the various milestones set forth in the sublicense agreement will be achieved by Meda AB, or that Meda AB will develop flupirtine for fibromyalgia in the U.S., Canada or Japan and accordingly we do not expect receive any additional milestone payments or royalties on sales in connection with the sublicense agreement.

We do not expect to generate any additional revenue from our sublicense withMeda AB due to recent development

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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 Regents of the University of California relating to our Trimesta technology, and an exclusive license agreement with CSMC relating to our IBS-C program. 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 Second ECC with Intrexon provides that Intrexon may terminate the agreement if we do not perform certain specified requirements, including developing therapies considered superior. Our agreement with The University of Texas allows the University to terminate its agreement if we fail to comply with the terms of the agreement. Our agreement with Prev provides Prev with the right to the return of the assets if we do not perform certain requirements. Our agreement with CSMC allows CSMC to terminate its agreement if we fail to comply with the terms of the agreement.

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 the Second ECC arrangement with Intrexon and our agreements with Prev and CSMC.

Pursuant to the Second ECC with Intrexon, we are responsible for future research and development expenses of product candidates developed under our collaboration, the effect of which has and will continue to increase the level of our overall research and development expenses going forward. Our agreements with Prev and CSMC require that we initiate certain studies and file or have accepted an NDA within a certain amount of time, each of which are costly and will require additional expenditures. Although all manufacturing, preclinical studies and human clinical trials are expensive and difficult to design and implement, costs associated with the manufacturing, research and development of biologic product candidates are generally greater in comparison to small molecule product candidates. We have added additional personnel and expect to add additional personnel to support the Second ECC with Intrexon, and research and development of our candidates, SYN-004 and SYN-010. In addition, we have commenced manufacturing of SYN-004 material to support our planned preclinical and clinical studies which will require us to incur additional expenses.

Because our biologic programs are relatively new, we have only recently assumed development responsibility and costs associated with such programs. In addition, because development activities in collaboration with Intrexon are determined pursuant to joint steering committees comprised of Intrexon and ourselves and we have limited experience, future development costs associated with this program may be difficult to anticipate and exceed our expectations. Our actual cash requirements may vary materially from our current expectations for a number of other

factors that may include, but are not limited to, unanticipated technical challenges, changes in the focus and direction of our development activities or adjustments necessitated by changes in the competitive landscape in which we operate. If we are unable to continue to financially support such collaborations due to our own working capital constraints, we may be forced to delay our activities. If we are unable to obtain additional financing on terms acceptable to us or at all, we may be forced to seek licensing partners or discontinue development.

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

Companies that currently sell or are developing proprietary products for the prevention and treatment of *C. difficile* infection include: Actelion, Merck & Co., Merus, Pfizer and Sanofi. Companies that currently sell

We will incur additional expenses in connection with the Second ECCarrangement with Intrexon and our agreement

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or are developing proprietary products for IBS-C include: Ironwood Pharmaceuticals, Inc./Forest Laboratories, Synergy Pharmaceuticals, Takeda. Companies that currently sell or are developing proprietary products for Pertussis include: GlaxoSmithKline Pharmaceuticals, Mitsubishi and Sanofi. Companies that currently sell or are developing both generic and proprietary products to treat multiple sclerosis include: AB Science, AbbVie Inc., Acordia Therapeutics, Bayer Health Care, Biogen Idec, F. Hoffman-La Roche Ltd., Merck & Co., Neuron Biotech, Opexa Therapeutics, Inc., Pfizer Inc., Novartis AG, Receptos, Inc., Sanofi, and Teva Pharmaceuticals. Many of our competitors have significant financial and human resources. The infectious disease market is highly competitive with many generic and proprietary intravenous and oral formulations available to physicians and their patients. For our monoclonal antibodies, we currently do not expect to be able to deliver our infectious disease candidates via the oral route and may thus be limited to the in-patient and/or acute treatment setting. In addition, academic research centers may develop technologies that compete with our Trimesta, SYN-004, SYN-010 and SYN-005 technologies. Should clinicians or regulatory authorities view alternative therapeutic regiments as more effective than our products, this might delay or prevent us from obtaining regulatory approval for our products, or it might prevent us from obtaining favorable reimbursement rates from payers, such as Medicare, Medicaid, hospitals and private insurers.

We operate in a highly competitive environment.

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

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

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

Since we do not have composition of matter patent claims for estriol, others may obtain approvals for other uses of these products that are not covered by our issued or pending patents. For example, the active ingredients in Trimesta (oral estriol) have been approved for marketing in overseas countries for different uses. Other companies, including the original developers or licensees or affiliates may seek to develop Trimesta or its 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 estriol in various formulations or delivery systems that might adversely affect our ability 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 estriol for different applications than what we are developing. Many of these companies may have more resources than us. We cannot provide any assurances that our products will be FDA-approved prior to our competitors.

If a product containing our active ingredients is already marketed or if the FDA approves other products containing our active ingredients in the future to treat indications, physicians may elect to prescribe and substitute a competitor s

products to treat the diseases for which we are intending to commercialize; this is commonly referred to as off-label use. While under FDA regulations a competitor is not allowed to promote off-label uses of its product, the FDA does not regulate the practice of medicine and, as a result, cannot direct physicians to select certain products for their patients. Consequently, we might be limited in our ability to prevent off-label use of a competitor s product to treat the diseases we are intending to commercialize, even if we have issued method of use patents for that indication. If we are not able to obtain and enforce our patents, if any, or otherwise receive orphan drug protection, a competitor could develop and commercialize similar

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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 its active ingredients estriol. We rely on issued patent and pending patent applications for use of Trimesta to treat MS (issued U.S. Patent Nos. 6,936,599, 8,372,826 and 8,658,627) and various other therapeutic indications, which have been exclusively licensed to us.

The patent positions of pharmaceutical companies are uncertain and may involve complex legal and factual questions. We may incur significant expenses 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 expenses and divert the attention of our management.

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

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

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

As of March 10, 2015, we employed approximately 23 individuals, 17 of whom are full-time employees. We have also engaged clinical consultants to advise us on our clinical programs and regulatory consultants to advise us on our dealings with the FDA and other foreign regulatory authorities. We have been and will be required to retain additional consultants and employees in order to fulfill our obligations under the Second ECC with Intrexon, our development obligations under our agreement with Prev and our agreement with CSMC. 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.

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

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

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

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

We rely on suppliers for the substance raw materials of our product candidates and third parties for certain manufacturing-related services to produce material that meets appropriate content, quality and stability standards and use in clinical trials of our products and, after approval, for commercial distribution. With the exception of FUJIFILM Diosynth Biotechnologies UK Limited, our manufacturer of API for SYN-004, and Evonik Corporation and Halo Pharmaceuticals, our SYN-004 drug product manufacturers, we have not yet established cGMP manufacturers for our biologic and drug candidates. To succeed, clinical trials require adequate supplies of study material, which may be difficult or uneconomical to procure or manufacture and there can be no assurance that we will successfully procure such study material. We and our suppliers and vendors may not be able to (i) produce our study material to appropriate standards for use in clinical studies, (ii) perform under any definitive manufacturing, supply or service agreements with us, or (iii) remain in business for a sufficient time to successfully produce and market our product candidates. If we do not maintain important manufacturing and service relationships, we may fail to find a replacement supplier or required vendor or develop our own manufacturing capabilities which could delay or impair our ability to obtain regulatory approval for our products and substantially increase our costs or deplete profit margins, if any. If we do find replacement manufacturers and vendors, we may not be able to enter into agreements with them on terms and conditions favorable to us and, there could be a substantial delay before a new facility could be qualified and registered with the FDA and foreign regulatory authorities.

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.

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

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

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

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

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

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

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

We are also highly dependent on government and private grants to fund certain of our clinical trials for our product candidates. For example, the lead principal investigator to Trimesta (oral estriol) received grants totaling over $8.0 million, predominantly from the Southern California Chapter of the NMSS and the National Institutes of Health which funded a majority of the Phase 2 clinical trial in relapsing-remitting MS for women. Although we believe that funding will be available to complete future trials, if sufficient funding is not available we may not be able to complete further clinical trials and commercialize estriol. 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.

With respect to our product candidates in collaboration with Intrexon, we are dependent upon Intrexon s synthetic biology facilities and capabilities as we have no such facilities and capabilities of our own. We are also reliant on their vectors, monoclonal antibody discovery, production cell line development and know-how.

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With respect to our product candidate for Pertussis in collaboration with University of Texas at Austin, we are dependent on its research laboratories as we have no such facilities or capabilities of our own. 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 monoclonal antibody field is particularly complex, constantly evolving and highly fragmented. 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.

Our principal stockholder has the ability to influence the vote on matters submitted to our stockholders and subsequent sales by such stockholder could adversely affect the market for our stock.

Through Intrexon Corporation and NRM VII Holdings I, LLC, Randal J. Kirk indirectly, beneficially owns approximately 12.3 million shares of our common stock as of December 31, 2014. As a result, he will be able to exert influence over issues submitted to our stockholders, including the election of our Board of Directors and the vote on issues. The sale of a number of shares by our principal stockholder could have an adverse effect on the market for our stock and our share price.

We will seek to raise additional funds in the future, which may be dilutive tostockholders or impose operational restr

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Holders of our warrants issued in our October 2014 offering have no rights as common stockholders until they exercise their warrants and acquire our common stock and limited liquidity for the warrants.

Until the holders of the warrants we issued in our October 2014 offering acquire shares of our common stock by exercising their warrants, the holders have no rights as a stockholder with respect to the shares of common stock underlying their warrants. Upon exercise of the warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

Because there is no established public trading market for the warrants we issued, the liquidity of the warrants is limited. We do no expect a market to develop, nor do we intend to apply to list the warrants on any securities exchange. Upon exercise of the warrants, our stockholders will experience dilution.

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

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

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

We cannot assure you that we will be able to maintain the continued listing standards of the NYSE MKT. The NYSE MKT requires companies to meet certain continued listing criteria including certain minimum stockholders equity as outlined in the NYSE MKT Exchange Company Guide. We may not be able to maintain such minimum stockholders equity and/or issue additional equity securities in exchange for cash or other assets, if available, to maintain certain minimum stockholders equity required by the NYSE MKT. If we are delisted from the NYSE MKT then our common stock will trade, if at all, only on the over-the-counter market, such as the OTC Bulletin Board securities market, and then only if one or more registered broker-dealer market makers comply with quotation requirements. In addition, delisting of our common stock could depress our stock price, substantially limit liquidity of our common stock and materially adversely affect our ability to raise capital on terms acceptable to us, or at all. Delisting from the NYSE MKT could also have other negative results, including the potential loss of confidence by suppliers and employees, the loss of institutional investor interest and fewer business development opportunities. In order to remain listed on NYSE MKT, we are required to maintain a minimum stockholders equity of $6.0 million.

Our principal stockholder has the ability to influence the vote on matterssubmitted to our stockholders and subsequ

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.

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

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

Stockholders may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share paid by existing stockholders, thereby subjecting such stockholders to dilution. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by existing stockholders, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by existing stockholders.

We do not intend to pay dividends in the foreseeable future.

We have never paid cash dividends on our common stock. We currently intend to retain our future earnings, if any, to finance the operation and growth of our business and currently do not plan to pay any cash dividends in the foreseeable future. If we do not pay dividends, our common stock may be less valuable because a return on your investment will only occur if the market price of our common stock price appreciates.

Resales of our common stock in the public market by our stockholders may cause the market price of our common stock to fall.

We may issue common stock from time to time in connection with future offerings. Any issuance from time to time of new shares of our common stock, or our ability to issue shares of common stock in future offerings, could result in resales of our common stock by our current stockholders concerned about the potential dilution of their holdings. In turn, these resales could have the effect of depressing the market price for our common stock.

RISKS RELATED TO OUR INDUSTRY

If we do not obtain the necessary regulatory approvals in the U.S. and/or other countries we will not be able to sell our product candidates.

We cannot assure you that we will receive the approvals necessary to commercialize any of our product candidates or any product candidates we acquire or develop in the future. We will need FDA approval to commercialize our product candidates in the U.S. and approvals from the FDA-equivalent regulatory authorities in foreign jurisdictions to commercialize our product candidates in those jurisdictions. We will be required to conduct clinical trials that will be

costly. We cannot predict whether our clinical trials will demonstrate the safety and efficacy of our product candidates or if the results of any clinical trials will be sufficient to advance to the next phase of development or for approval from the FDA. We also cannot predict whether our research and clinical approaches will result in drugs or therapeutics that the FDA considers safe and effective for the proposed indications. The FDA has substantial discretion in the drug approval process. The approval process may be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals may prevent or delay commercialization of, and our ability to derive product revenues from, our product candidates; and diminish any competitive advantages that we may otherwise believe that we hold.

Even if we comply with all FDA requests, the FDA may ultimately reject one or more of our NDAs or BLAs. We may never obtain regulatory clearance for any of our product candidates. Failure to obtain FDA

If we do not obtain the necessary regulatory approvals in the U.S. and/or othercountries we will not be able to sell o

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approval of any of our product candidates will severely undermine our business by leaving us without a saleable product, and therefore without any source of revenues, until another product candidate can be developed. There is no guarantee that we will ever be able to develop or acquire another product candidate.

In addition, the FDA may require us to conduct additional pre-clinical and clinical testing or to perform post-marketing studies, as a condition to granting marketing approval of a product. The results generated after approval could result in loss of marketing approval, changes in product labeling, and/or new or increased concerns about the side effects or efficacy of a product. The FDA has significant post-market authority, including the explicit authority to require post-market studies and clinical trials, labeling changes based on new safety information, and compliance with FDA-approved risk evaluation and mitigation strategies. The FDA s exercise of its authority has in some cases resulted, and in the future could result, in delays or increased costs during product development, clinical trials and regulatory review, increased costs to comply with additional post-approval regulatory requirements and potential restrictions on sales of approved products.

In foreign jurisdictions, we must also receive approval from the appropriate regulatory authorities before we can commercialize any products, which can be time consuming and costly. Foreign regulatory approval processes generally include all of the risks associated with the FDA approval procedures described above. There can be no assurance that we will receive the approvals necessary to commercialize our product candidate for sale outside the United States.

If the FDA approves any of our product candidates, the labeling, manufacturing, packaging, adverse event reporting, storage, advertising, promotion and record-keeping for our products will be subject to ongoing FDA requirements and continued regulatory oversight and review. Our drug manufacturers and subcontractors that we retain will comply with FDA and other regulations. We may also be subject to additional FDA post-marketing obligations. If we are not able to maintain regulatory compliance, we may not be permitted to market our product candidates and/or may be subject to product recalls, seizures, suspension of regulatory approval, suspension of production, injunctions or civil or criminal sanctions. The subsequent discovery of previously unknown problems with any marketed product, including adverse events of unanticipated severity or frequency, may result in restrictions on the marketing of the product, and could include withdrawal of the product from the market.

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

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

submitting significantly less clinical data outside the ANDA context. Such applications, known as 505(b)(2) NDAs or paper NDAs, may rely on clinical investigations not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use and are subject to the ANDA notification procedures described above.

The law also permits restoration of a portion of a product s patent term that is lost during clinical development and NDA review, and provides statutory protection, known as exclusivity, against FDA approval or acceptance of certain competitor applications. Restoration can return up to five years of patent term for a patent covering a new product or its use to compensate for time lost during product development and

We do not have a guarantee of patent term restoration and marketing exclusivity of the ingredients for our drugs ev

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

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

None.

Item 2. ***Properties***

We currently rent approximately 1,200 square feet of office space in Rockville, Maryland for monthly rent of $3,628, and we rent approximately 1,600 square feet of office space in Ann Arbor, Michigan for monthly rent of $2,900. We are currently negotiating a lease agreement for new office space in Rockville, Maryland.

Item 3. ***Legal Proceedings***

None.

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

Not applicable.

We do not have a guarantee of patent term restoration and marketing exclusivity of the ingredients for our drugs ev

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PART II

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

Our common stock has traded on the NYSE MKT, LLC 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, 2014 and December 31, 2013. These quotations represent inter-dealer prices, without retail mark-up, markdown, or commission, and may not represent actual transactions. The last price of our common stock as reported on the NYSE MKT on March 10, 2015 was $2.94 per share. As of March 10, 2015, 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, 2014		
Fourth quarter	$ 1.77	$ 1.37
Third quarter	$ 2.62	$ 1.36
Second quarter	$ 3.09	$ 1.16
First quarter	$ 3.45	$ 1.61
YEAR ENDED DECEMBER 31, 2013		
Fourth quarter	$ 1.85	$ 1.00
Third quarter	$ 1.71	$ 1.42
Second quarter	$ 1.83	$ 1.38
First quarter	$ 2.00	$ 1.65

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.

Stock Performance Graph

Set forth below is a line graph comparing changes in the cumulative total return on Synthetic Biologics common stock, a major market index (the NASDAQ Composite Index), and a sub-index (the NASDAQ Biotechnology Index). The graph assumes investments of $100 on December 31, 2009 in our common stock and in each of the indices, including the reinvestment of dividends.

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	12/31/2009	12/31/2010	12/31/2011	12/31/2012	12/31/2013	12/31/2014
Synthetic Biologics, Inc.	100.00	223.21	225.00	314.29	273.21	260.71
NASDAQ Composite	100.00	117.43	118.27	138.47	196.27	223.17
NASDAQ Biotechnology	100.00	106.62	122.01	166.55	286.43	378.29

Equity Compensation Plan Information

See Item 12 Executive compensation for equity compensation plan information.

Recent Sales of Unregistered Securities

All sales of unregistered securities during the year ended December 31, 2014 have been previously disclosed in our filings with the Securities and Exchange Commission.

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

The following table sets forth our selected consolidated financial data for the periods and as of the dates indicated. You should read the following selected consolidated financial data in conjunction with our audited consolidated financial statements and the related notes thereto included elsewhere in this Annual Report and the Management s Discussion and Analysis of Financial Condition and Results of Operations section of this Annual Report.

The consolidated statement of operations data for the years ended December 31, 2014, 2013 and 2012, and the consolidated balance sheet data as of December 31, 2014, 2013 and 2012, are derived from our audited consolidated financial statements included elsewhere in this Annual Report. Our audited consolidated financial statements have been prepared in U.S. dollars in accordance with U.S. GAAP.

Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our results for any interim period are not necessarily indicative of results to be expected for a full fiscal year.

	For the years ended December 31,				
	2014	2013	2012	2011	2010
	(in thousands, except per share data)				
Consolidated Statement of Operations Data:					
Revenues:					
License revenue, net	$	$	$	$	$2,125
Grant revenue					489
Total Revenues					2,614
Operating Costs and Expenses:					
General and administrative	6,013	5,832	5,012	2,588	2,117
Research and development	14,489	6,507	12,287	3,340	1,580
Total Operating Costs and Expenses	20,502	12,339	17,299	5,928	3,697
Loss from Operations	(20,502)	(12,339)	(17,299)	(5,928)	(1,083)
Other Income (Expense):					
Change in fair value of warrant liability	620			(1,734)	
Impairment loss on equipment					(121)
Other income (expense)	95	(12)	(18)	22	9
Interest income	3	33	33	14	
Total Other Income (Expense)	718	21	15	(1,698)	(112)
Loss from Continuing Operations	(19,784)	(12,318)	(17,284)	(7,626)	(1,195)
Income (Loss) from Discontinued Operations			216	(523)	(516)
Net Loss	(19,784)	(12,318)	(17,068)	(8,149)	(1,711)
Net Loss Attributable to Non-controlling Interest		(1)			

Net Loss Attributable to Synthetic Biologics, Inc. and Subsidiaries	$(19,784)	$(12,317)	$(17,068)	$(8,149)	$(1,711)
Net Income (Loss) Per Share Basic and Dilutive					
Continuing operations	$(0.32)	$(0.27)	$(0.50)	$(0.27)	$(0.06)
Discontinued operations			0.01	(0.02)	(0.02)
Net Income (Loss) Per Share Attributable to Synthetic Synthetic Biologics, Inc. and Subsidiaries	$(0.32)	$(0.27)	$(0.49)	$(0.29)	$(0.08)
Weighted average number of shares outstanding during the period Basic and Dilutive	61,945,356	45,667,813	34,896,592	27,710,428	22,393,568

	As of December 31,				
	2014	2013	2012	2011	2010
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$17,525	$14,625	$9,954	$6,678	$2,649
Working capital	9,485	15,189	12,068	6,705	3,045
Total assets	19,144	16,257	13,423	7,476	4,111
Accumulated deficit	(101,042)	(81,258)	(68,941)	(51,873)	(43,724)
Total stockholders' equity	9,556	15,230	13,028	7,059	3,579

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

The following discussion of our financial condition and results of operations should be read in conjunction with the audited financial statements and notes thereto for the year ended December 31, 2014 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 clinical-stage biotechnology company developing pathogen-specific therapies for serious infections and diseases, with a focus on protecting the microbiome. We are developing an oral biologic to protect the gut microbiome (gastrointestinal (GI) microflora) from intravenous (IV) antibiotics for the prevention of *C. difficile* infection, an oral statin treatment to reduce the impact of methane producing organisms on irritable bowel syndrome with constipation (IBS-C) and a monoclonal antibody combination for the treatment of Pertussis. In addition, we are developing a Phase 2 oral estriol drug for the treatment of relapsing-remitting multiple sclerosis (MS) and cognitive dysfunction in MS.

Product Pipeline:

Summary of Pathogen-Specific Therapy Programs:

C. difficile infections (CDI): We are in clinical development of a novel second-generation oral enzyme candidate, SYN-004, for co-administration with commonly used IV beta-lactam antibiotics, intended to protect the microbiome and prevent the development of and severe effects from CDI. CDIs are a leading type of hospital acquired infection (HAI) and are frequently associated with IV antibiotic treatment. Designed to be given orally and co-administered with certain IV beta-lactam antibiotics (e.g., penicillins and cephalosporins), SYN-004 is intended to protect the gut while the IV antibiotics fight the primary infection. SYN-004 is believed to not only have a similar profile to its first-generation predecessor, which demonstrated protection of the microbiome (gut flora) during treatment with certain penicillins, but also has the potential to act against a broader spectrum of IV beta-lactam antibiotics. Beta-lactam antibiotics are a mainstay in hospital infection management and include the commonly used penicillin and cephalosporin classes of antibiotics. SYN-004 s target market is significant and represented by annual U.S. hospitals purchases of approximately 118 million doses of IV beta-lactam antibiotics which are administered to approximately 14 million

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patients.* Currently there are no approved treatments designed to protect the gut microbiome from the damaging effects of IV antibiotics. This worldwide market could represent a multi-billion dollar opportunity for us. In December 2014, the U.S. Patent and Trademark Office (USPTO) issued Patent No. 8,894,994 that has claims to compositions of matter and pharmaceutical compositions of beta-lactamases, including SYN-004, and carries a patent term to at least 2031. We also have an extensive patent estate on other aspects of this program which includes patent applications that could carry a term to at least 2035. In the fourth quarter of 2014, we initiated our randomized, double-blind placebo-controlled Phase 1a clinical trial, reported positive topline safety and tolerability results from the Phase 1a clinical trial, and initiated the Phase 1b clinical trial evaluating multiple ascending doses of SYN-004. In February 2015, we reported positive topline results from the Phase 1b clinical trial of escalating doses of oral SYN-004, with no safety or tolerability issues reported at dose levels and dose regimens both meeting and exceeding those expected to be studied in upcoming clinical trials. It is anticipated that the initiation of a Phase 2a clinical trial of SYN-004 and topline pharmacokinetics data from both of the SYN-004 Phase 1 clinical trials will be reported during the first quarter of 2015. The initiation of a Phase 2b proof-of-concept clinical trial is expected in the second half of 2015, with Phase 2b topline data anticipated during the second half of 2015.

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

IBS-C: In December 2013, through our majority-owned subsidiary, Synthetic Biomics, Inc., we entered into a worldwide exclusive license agreement with Cedars-Sinai Medical Center (CSMC) for the right to develop products for therapeutic and prophylactic treatments of acute and chronic diseases, including the development of SYN-010 to target IBS-C. An investigational team led by Mark Pimentel, M.D., at CSMC discovered that SYN-010 may reduce the production of methane gas by certain gastrointestinal (GI) microorganisms. Methane produced by these organisms is perceived as an underlying cause of pain, bloating, and constipation associated with IBS-C, and may contribute to the pathology of other diseases. SYN-010 is a modified release formulation of a statin being designed to reduce the impact of methane producing organisms on IBS-C. A 505(b)(2) regulatory pathway is anticipated for the development of SYN-010. We licensed an extensive intellectual property portfolio from CSMS including granted use patents and pending patent applications for SYN-010. Additional worldwide patent filings having composition of matter claims, which were recently filed by CSMC and licensed to us, could extend patent protection of SYN-010 to 2035. Based on guidance from the members on our IBS clinical advisory board, we plan to file an Investigational New Drug (IND) application with the U.S. FDA to support the initiation of Phase 2 clinical trials in the second quarter of 2015, with Phase 2 topline data anticipated during the second half of 2015.

Pertussis: In December 2012, in collaboration with Intrexon Corporation (NYSE: XON) (Intrexon), we initiated development of a monoclonal antibody (mAb) therapy for the treatment of Pertussis infections, more commonly known as whooping cough. Combining two mAbs, SYN-005 is designed to target and neutralize pertussis toxin as a prophylaxis for high-risk newborns and in order to reduce the mortality rate in infected infants. To further the development of this potential therapy for Pertussis, we entered into an agreement with The University of Texas at Austin (UT) to license the rights to certain research and pending patents related to pertussis antibodies. We have patents pending on compositions and uses of SYN-005 and we have an issued U.S. patent on other pertussis mAbs from UT. According to the World Health Organization, each year, *B. pertussis* infection is estimated to cause up to 300,000 deaths worldwide, primarily among unvaccinated infants. Positive preclinical research findings for SYN-005 were reported in April 2014, and again in September 2014, for our proprietary mAb combination therapy for treating Pertussis, in non-human primate studies. In September 2014, we received a U.S. Orphan Drug designation for SYN-005 for the treatment of Pertussis. We intend to seek non-dilutive funding to support the clinical development of SYN-005 for prophylaxis and treatment of Pertussis, including the anticipated filing

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of an IND application in 2015 and the anticipated initiation of a Phase 1 clinical trial during the second half of 2015, with topline Phase 1 data expected during 2015.

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

Summary of Multiple Sclerosis Program:

Relapsing-Remitting MS: Patient follow-up is complete in the UCLA-led Phase 2, investigator-initiated, randomized (n=158), double-blinded, placebo-controlled trial which evaluated our drug candidate, Trimesta, in women with relapsing-remitting MS at 16 sites across the U.S. In April 2014, the principal investigator presented positive Phase 2 topline efficacy and safety results. In September 2014, the lead principal investigator presented additional Phase 2 clinical outcome data, including more detailed results on improvements in cognitive and disability measures, at the 2014 Joint Americas and European Committees for Treatment and Research in Multiple Sclerosis Meeting (ACTRIMS-ECTRIMS) in Boston. The data as reported by the lead principal investigator for the UCLA-led Phase 2 study provided supportive data for the potential of Trimesta to have a novel dual mechanism of action for both the anti-inflammatory effects that improve relapse rate, and a neuroprotective effect that improves standard measures of disability and cognition. Further analyses of the MRI data are ongoing, with topline data expected from the principal investigator during the first half of 2015. This investigator-initiated Phase 2 clinical trial was supported by grants exceeding $8 million, awarded primarily by the NMSS in partnership with the NMSS s Southern California chapter, and the National Institutes of Health. Annual worldwide sales of MS therapies are forecasted to be approximately $17.8 billion in 2019. We have licensed issued method of treatment patents in the U.S. for MS therapy with estriol and estriol combination therapies (including estriol with Copaxone®) from UCLA, and numerous new provisional patent applications have been filed based on the Phase 2 clinical results. We are engaging with the neurology community and potential strategic partners, as we determine next steps for Trimesta.

Cognitive Dysfunction in MS: Trimesta is also being developed for the treatment of cognitive dysfunction in female MS patients. This 12-month, UCLA-led, randomized, double-blind, placebo-controlled investigator-initiated Phase 2 clinical trial is being conducted at four sites in the United States. The primary endpoint is the effect on cognitive function as assessed by Paced Auditory Serial Addition Test (PASAT). Patient enrollment is ongoing. The majority of the costs of this trial are being funded by grants from foundations and charitable organizations through direct funding to the principal investigator 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 for this indication.

Recent Developments

On October 10, 2014, we sold a total of 14,059,616 units at a purchase price of $1.47 per unit, with each unit consisting of one share of our common stock, and one warrant to purchase 0.5 shares of common stock in a registered direct offering for gross proceeds of $20.7 million and net proceeds of $19.1 million.

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 $101.0 million through December 31, 2014. 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.

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Critical Accounting Policies

The preparation of our consolidated financial statements in accordance with U.S. generally accepted accounting principles (GAAP) requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, net revenues and expenses, and related disclosures. We believe our estimates and assumptions are reasonable; however, actual results and the timing of the recognition of such amounts could differ from these estimates.

There are accounting policies that we believe are significant to the presentation of our consolidated financial statements. The most significant accounting policies relate to stock-based compensation, revenue recognition and accounts receivable.

Stock-Based Compensation

Calculating stock-based compensation expense requires the input of highly subjective assumptions. We apply the Black-Scholes option pricing model to determine the fair value of our stock options. Inherent in this model are assumptions related to expected stock-price volatility, option life, risk-free interest rate and dividend yield. We estimate the volatility of our common stock at the date of grant based on historical volatility. We estimate the expected life of our option using the contractual term of the option. The risk-free interest rate is based on the U.S. Treasury zero-coupon yield curve on the grant date for a maturity similar to the expected life of the options. The dividend rate is based on our historical rate, which we anticipate to remain at zero. The assumptions used in calculating the fair value of stock options represent our best estimates, however these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and different assumptions are used, the stock-based compensation expense could be materially different in the future. In addition, we are required to estimate the expected forfeiture rate and only recognize expense for those stock options expected to vest over the service period.

Revenue Recognition

We record revenue when all of the following have occurred: (1) persuasive evidence of an arrangement exists, (2) the service is completed without further obligation, (3) the sales price to the customer is fixed or determinable, and (4) collectability is reasonably assured. We recognize milestone payments or upfront payments that have no contingencies as revenue when payment is received.

License Revenues

Our licensing agreements may contain multiple elements, such as non-refundable up-front fees, payments related to the achievement of particular milestones and royalties. Fees associated with substantive at risk performance-based milestones are recognized as revenue upon completion of the scientific or regulatory event specified in the agreement. When we have substantive continuing performance obligations under an arrangement, revenue is recognized over the performance period of the obligations using a time-based proportional performance approach. Under the time-based method, revenue is recognized over the arrangement s estimated performance period based on the elapsed time compared to the total estimated performance period. Revenue recognized at any point in time is limited to the amount of non-contingent payments received or due. When we have no substantive continuing performance obligations under an arrangement, we recognize revenue as the related fees become due.

Revenues from royalties on third-party sales of licensed technologies are generally recognized in accordance with the contract terms when the royalties can be reliably determined and collectability is reasonably assured.

Research and Development Costs

We expense research and development costs associated with developmental products not yet approved by the FDA to research and development expense as incurred. Research and development costs consist primarily of license fees (including upfront payments), milestone payments, manufacturing costs, salaries, stock-based compensation and related personnel costs, fees paid to consultants and outside service providers for laboratory development, legal expenses resulting from intellectual property prosecution and other expenses relating to the design, development, testing and enhancement of our product candidates.

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Results of Operations

Year Ended December 31, 2014, 2013 and 2012

General and Administrative Expenses

General and administrative expenses increased to $6.0 million for the year ended December 31, 2014, from $5.8 million for the year ended December 31, 2013. This increase of 3% is primarily the result of supplemental compensation granted by our Board of Directors to our executive officers and increased stock-based compensation expense during the year ended December 31, 2014, which was offset by the decrease of bad debt expense of $763,000 associated with the determination that the note receivable and interest receivable from the sale of Adeona Clinical Laboratory was uncollectible for the year ended December 31, 2013. *See Note 3 Discontinued Operations of Adeona Clinical Laboratory and Note Receivable*. The charge relating to stock-based compensation expense was $1.6 million for the year ended December 31, 2014, compared to $1.3 million for the year ended December 31, 2013.

General and administrative expenses increased to $5.8 million for the year ended December 31, 2013, from $5.0 million for the year ended December 31, 2012. This increase of 16% is primarily the result of bad debt expense of $763,000 associated with the determination that the note receivable and interest receivable from the sale of Adeona Clinical Laboratory is uncollectible. *See Note 3 Discontinued Operations of Adeona Clinical Laboratory and Note Receivable*. The charge relating to stock-based compensation expense was $1.3 million for the year ended December 31, 2013, compared to $1.5 million for the year ended December 31, 2012.

Research and Development Expenses

Research and development expenses increased to $14.5 million for the year ended December 31, 2014, from $6.5 million for the year ended December 31, 2013. This increase of 123% is primarily the result of increased program costs associated with expanded clinical development, manufacturing and research activities within our pathogen-specific microbiome-focused pipeline, including our *C. diff*, IBS-C and Pertussis programs. Research and development expenses also include a charge relating to non-cash stock-based compensation expense of $803,000 for the year ended December 31, 2014, compared to $375,000 for the year ended December 31, 2013.

Research and development expenses decreased to $6.5 million for the year ended December 31, 2013, from $12.3 million for the year ended December 31, 2012. This decrease of 47% is primarily the result of recording the fair value ($7.8 million) of the common stock issued to Intrexon as consideration for the Exclusive Channel Collaboration Agreement and the fair value ($1.2 million) of the common stock issued for the acquisition of the *C. diff* program assets of Prev ABR LLC for the year ended December 31, 2012. These were non-cash charges. The decrease in research and development costs for the year ended December 31, 2013 was off-set by increases in additional employee costs and increases in program costs associated with our infectious disease programs. The charge relating to share-based compensation expense was $375,000 for the year ended December 31, 2013, compared to $400,000 for the year ended December 31, 2012.

Other Income

Other income was $718,000 for the year ended December 31, 2014, compared to other income of $21,000 for the year ended December 31, 2013. The increase in other income is primarily due to non-cash income of $620,000 from the change in fair value of warrants for the year ended December 31, 2014. The decrease in value was primarily due to the decline in our stock price and the reduction in the time to maturity. There was no non-cash income or expense relating

to fair value warrants for the year ended December 31, 2013.

Other income was $21,000 for the year ended December 31, 2013, compared to other income of $15,000 for the year ended December 31, 2012.

Loss from Continuing Operations

Our loss from continuing operations for the year ended December 31, 2014, was $19.8 million, or $0.32 per common share, compared to $12.3 million, or $0.27 per common share for the year ended December 31, 2013.

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Our loss from continuing operations for the year ended December 31, 2013, was $12.3 million, or $0.27 per common share, compared to $17.3 million, or $0.50 per common share for the year ended December 31, 2012.

Income (Loss) from Discontinued Operations

There was no income or loss from discontinued operations for the years ended December 31, 2014 and 2013. Our income from discontinued operations was $216,000, or $0.01 per common share for the year ended December 31, 2012. 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. This resulted in the classification of the Lab as discontinued operations. *See Note 3 Discontinued Operations of Adeona Clinical Laboratory and Note Receivable* for summarized statement of operations data for the years ended December 31, 2014, 2013 and 2012.

Liquidity and Capital Resources

We have financed our operations since inception primarily through proceeds from equity financings, corporate partnering license fees, laboratory revenues and miscellaneous equipment sales.

Our cash totaled $17.5 million as of December 31, 2014, an increase of $2.9 million from December 31, 2013. During the year ended December 31, 2014, the primary use of cash was for working capital requirements and operating activities which resulted in a net loss of $19.8 million for the year ended December 31, 2014.

On October 10, 2014, we sold a total of 14,059,616 units at a purchase price of $1.47, with each unit consisting of one share of our common stock, and a warrant to purchase 0.5 shares of common stock in a registered direct offering for gross proceeds of $20.7 million and net proceeds of $19.1 million.

Our continued operations will primarily depend on our ability to raise additional capital from various sources including equity and debt financings, as well as, license fees from potential corporate partners, joint ventures and grant funding. Such additional funds may not become available on acceptable terms and there can be no assurance that any additional funding that we do obtain will be sufficient to meet our needs in the long term. We will continue to fund operations from cash on hand and through the similar sources of capital previously described. We can give no assurance that any additional capital that we are able to obtain will be sufficient to meet our needs.

Current and Future Financing Needs

We have incurred an accumulated deficit of $101.0 million through December 31, 2014. With the exception of the quarter ended June 30, 2010, we have incurred negative cash flow from operations since we started our business. We have spent, and expect to continue to spend, substantial amounts in connection with implementing our business strategy, including our planned product development efforts, our clinical trials, and our research and discovery efforts.

Based on our current plans, we believe that our cash will be sufficient to enable us to meet our planned operating needs for at least the next 12 months.

However, the actual amount of funds we will need to operate is subject to many factors, some of which are beyond our control. These factors include the following:

the progress of our research activities;
the number and scope of our research programs;

the progress of our preclinical and clinical development activities;
the progress of the development efforts of parties with whom we have entered into research and development agreements;
our ability to maintain current research and development licensing arrangements and to establish new research and development and licensing arrangements;
our ability to achieve our milestones under licensing arrangements;

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the costs involved in prosecuting and enforcing patent claims and other intellectual property rights; and
the costs and timing of regulatory approvals.

We have based our estimate on assumptions that may prove to be wrong. We may need to obtain additional funds sooner or in greater amounts than we currently anticipate. Potential sources of financing include strategic relationships, public or private sales of our shares or debt and other sources. We may seek to access the public or private equity markets when conditions are favorable due to our long-term capital requirements. We do not have any committed sources of financing at this time, and it is uncertain whether additional funding will be available when we need it on terms that will be acceptable to us, or at all. If we raise funds by selling additional shares of common stock or other securities convertible into common stock, the ownership interest of our existing stockholders will be diluted. If we are not able to obtain financing when needed, we may be unable to carry out our business plan. As a result, we may have to significantly limit our operations and our business, financial condition and results of operations would be materially harmed.

License and Contractual Agreement Obligations

Below is a table of our contractual obligations for the years 2015 through 2019 as of December 31, 2014 *(in thousands)*.

	Year ended December 31,					
	2015	2016	2017	2018	2019	Total
License Agreements	$ 60	$ 10	$ 10	$ 10	$ 10	$ 100
Sponsored Research Agreement	329					329
Lease Agreements	53				-	53
Total	$ 442	$ 10	$ 10	$ 10	$ 10	$ 482

Item 7A. ***Quantitative and Qualitative Disclosures About Market Risk***

As of December 31, 2014, our cash and cash equivalents consisted primarily of money market securities. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a sudden change in market interest rates or credit conditions on our securities portfolio.

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Item 8. ***Financial Statements and Supplemental Data***

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Report of Independent Registered Public Accounting Firm

Board of Directors and Stockholders
Synthetic Biologics, Inc.
Rockville, Maryland

We have audited the accompanying consolidated balance sheets of Synthetics Biologics, Inc. as of December 31, 2014 and 2013 and the related consolidated statements of operations, equity, and cash flows for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of Synthetic Biologics, Inc. s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Synthetic Biologics, Inc. at December 31, 2014 and 2013, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Synthetic Biologics, Inc. s internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control Integrated Framework (1992) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) and our report dated March 16, 2015 expressed an unqualified opinion thereon.

/s/ BDO USA, LLP

BDO USA, LLP

Troy, Michigan
March 16, 2015

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Synthetic Biologics, Inc. and Subsidiaries

Consolidated Balance Sheets
(In thousands except share amounts)

	December 31, 2014	December 31, 2013
Assets		
Current Assets		
Cash and cash equivalents	$17,525	$14,625
Prepaid expenses and other current assets	1,548	1,591
Total Current Assets	19,073	16,216
Property and equipment, net	65	37
Deposits and other assets	6	4
Total Assets	**$19,144**	**$16,257**
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$996	$142
Accrued expenses	1,298	882
Warrant liabilities	6,756	
Accrued employee benefits	538	3
Total Current Liabilities	9,588	1,027
Total Liabilities	9,588	1,027
Commitments and Contingencies		
Stockholders Equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, none issued and outstanding		
Common stock, $0.001 par value; 100,000,000 shares authorized, 72,594,626 issued and 72,513,144 outstanding and 58,295,808 issued and 58,214,326 outstanding	72	58
Additional paid-in capital	110,526	96,430
Accumulated deficit	(101,042)	(81,258)
Total Synthetic Biologics, Inc. and Subsidiaries Equity	9,556	15,230
Non-controlling interest		
Total Stockholders Equity	9,556	15,230
Total Liabilities and Stockholders Equity	**$19,144**	**$16,257**