Synthetic Biologics, Inc.
Form 424B5
October 10, 2014

Filed Pursuant to Rule 424(b)(5)

Registration No. 333-189794

Prospectus Supplement

(To Prospectus dated July 16, 2013)

14,059,616 Units Each Consisting of

One Share of Common Stock

and

A Warrant to purchase 0.5 shares of Common Stock

We are offering 14,059,616 units pursuant to this prospectus supplement, with each unit consisting of one share of our common stock together with warrants to purchase 0.5 shares of common stock. The common stock and warrants will be sold together as a unit with a per unit purchase price of $1.47. The exercise price of the warrants issued in the offering as part of such unit will be $1.75 and the warrants will be exercisable beginning on the closing date for a term of five years. The shares of common stock and warrants will be issued separately but can only be purchased together in this offering.

Our common stock is listed on the NYSE MKT under the symbol "SYN." On October 9, 2014, the closing price of our common stock was $1.41 per share. We do not intend to apply for listing of the warrants on any national securities exchange or for inclusion of the warrants in any automated quotation system. The warrants will be issued in physical form.

Our business and an investment in our common stock involve significant risks. See "Risk Factors" beginning on page S-5 of this prospectus supplement and on page 5 of the accompanying prospectus.

	Per Share and Accompanying Warrant	**Total**
Public offering price	$ 1.47	$20,667,636
Placement agent fees[(1)]	$ 0.1029	$1,446,734
Proceeds, before expenses, to us[(2)]	$ 1.3671	$19,220,902

(1) See "Plan of Distribution" for a description of the compensation payable to the placement agent.

(2) The proceeds shown exclude proceeds that we may receive upon exercise of the warrants.

We have engaged William Blair & Company, L.L.C. as sole placement agent in this offering to use its best efforts to solicit offers to purchase the units in this offering. The sole placement agent is not purchasing or selling any units pursuant to this prospectus supplement or the accompanying prospectus, nor are we requiring any minimum purchase or sale of any specific number of units.

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

William Blair

Sole Placement Agent

The date of this prospectus supplement is October 10, 2014

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement that we filed with the Securities and Exchange Commission (the "SEC") using a "shelf" registration process and consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, gives more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts of this document combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated into each by reference include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents we have referred you to in the section of this prospectus supplement and the accompanying prospectus entitled "Where You Can Find More Information."

You should rely only on this prospectus supplement, the accompanying prospectus and any free writing prospectus we may provide to you in connection with this offering and the information incorporated or deemed to be incorporated by reference therein. We have not authorized anyone to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. We are not offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

No action has been or will be taken in any jurisdiction by us or the placement agent that would permit a public offering of the common stock or warrant or the possession or distribution of this prospectus supplement and the accompanying prospectus in any jurisdiction, other than in the United States. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the units and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus

do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

INDUSTRY AND MARKET DATA

We obtained the industry and market data in this prospectus supplement from our own research as well as from industry and general publications, surveys and studies conducted by third parties. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the industry in which we operate is necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in “Risk Factors” and elsewhere in this prospectus supplement. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

PROSPECTUS SUPPLEMENT SUMMARY

The items in the following summary are described in more detail elsewhere in this prospectus supplement and in the documents incorporated by reference herein. This summary provides an overview of selected information and does not contain all the information you should consider before investing in our securities. Therefore, you should read the entire prospectus supplement and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the "Risk Factors" section and other documents or information included or incorporated by reference in this prospectus supplement before making any investment decision.

Our Business

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

Product Pipeline:

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

- ***C. difficile* infections (CDI):** We are in preclinical development of a novel second-generation oral enzyme candidate, SYN-004, for co-administration with commonly used IV beta-lactam antibiotics intended to prevent the development of and severe effects from *C. difficile* infections (CDI). CDIs are a leading type of hospital acquired infections (HAIs) that generally occur secondary to treatment with IV antibiotics. Designed to be given orally to protect the gut while certain IV beta-lactam antibiotics (penicillins and cephalosporins) fight the primary infection, SYN-004 is believed to have a similar profile to its first-generation predecessor, which demonstrated protection of the gut flora (microbiome) during treatment with certain penicillins, with 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. Approximately 14.4 million patients are administered "SYN-004 target" IV beta-lactam antibiotics annually representing an estimated target market for SYN-004 of 117.6 million beta-lactam doses purchased by U.S. hospitals. The addressable market for SYN-004 is significant. Currently there are no approved treatments designed to protect the microbiome from the damaging effects of IV antibiotics. This worldwide opportunity could represent a multi-billion dollar market.* We have a patent pending for SYN-004 on compositions of matter and methods of use with coverage through at least 2031. We remain on schedule to file an Investigational New Drug (IND) application for SYN-004, and intend to initiate Phase 1a and 1b clinical studies in the fourth quarter of 2014. Preliminary Phase 1 topline data is expected by year-end 2014, and a Phase 2a trial of SYN-004 is planned to begin in the first half of 2015, followed by the initiation of a Phase 2b clinical trial in the second half of 2015. Clinical manufacturing of SYN-004 in accordance with GMP guidelines has commenced, and completion of manufacturing for Phase 1 and 2 trials is expected during the second half of 2014.

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

- **C-IBS:** In December 2013, through our majority-owned subsidiary, Synthetic Biomics, Inc., we entered into a worldwide exclusive license agreement with Cedars-Sinai Medical Center (CSMC) for the right to develop products for therapeutic and prophylactic treatments for acute and chronic diseases, including the development of SYN-010 to target C-IBS. 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 gastrointestinal (GI) microorganisms. Methane produced by these organisms is perceived as an underlying cause of bloating, pain and constipation associated with C-IBS, and may contribute to the pathology of other diseases. 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 C-IBS. A 505(b)(2) regulatory pathway is anticipated for the development of SYN-010. An extensive portfolio of granted use patents and pending patent applications for SYN-010 have been licensed to us by CSMC. 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 complete a Phase 1 pharmacokinetics/pharmacodynamics trial of SYN-010 in the first half of 2015. We also expect to file an IND with the U.S. FDA in the first quarter of 2015, followed by the initiation of a Phase 2 clinical trial, also in the first half of 2015, with Phase 2 data anticipated during the first 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. We are developing a mAb therapy, SYN-005, designed to target and neutralize pertussis toxin, in order to reduce the mortality rate in 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 causes an estimated 300,000 deaths worldwide, primarily among young, 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. We intend to seek non-dilutive funding to support the clinical development of SYN-005 for the treatment of Pertussis. Based on positive non-human primate and murine model findings, we intend to file an IND application in 2015 to support a Phase 1 clinical trial expected to initiate during the second half of 2015, with topline Phase 1 data expected during 2015. This is expected to be followed by the initiation of a Phase 2/3 trial during 2016. In addition, in September 2014 we have received a U.S. Orphan Drug designation for SYN-005 for the treatment of Pertussis.

- ***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 is ongoing.

- **IBS:** In December 2013, in collaboration with Intrexon, and partially utilizing the intellectual property optioned from CSMC, we announced an intent to develop biologic approaches targeted at the prevention, and acute and chronic treatment of a subset of IBS pathologies specifically caused by auto-antibodies. This program is in the early discovery stage, and we are still evaluating the option.

Summary of Multiple Sclerosis Program:

Relapsing-Remitting MS: Patient follow-up is complete in the 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 the University of California, Los Angeles (UCLA) David Geffen School of Medicine 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 Americas and European Committees for Treatment and Research in Multiple Sclerosis Meeting (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 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).

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
(iii) 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, with topline data expected during the first quarter of 2015. This investigator-initiated clinical trial is 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 $17.8 billion in 2019. We have licensed from UCLA issued method of treatment patents in the U.S. for MS therapy with estriol and estriol combination therapies (including estriol with Copaxone®), and four new provisional patent applications have been filed based on these recent 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 randomized, double-blind, placebo-controlled Phase 2 clinical trial is being conducted at four sites in the United States, including UCLA. The primary endpoint is the effect on cognitive function as assessed by Paced Auditory Serial Addition Test (PASAT). Patient enrollment is ongoing. The majority of the costs of this trial are being funded by grants from foundations and charitable organizations and we have pledged approximately $500,000 to UCLA to partially fund this trial, payable over three years. An estimated 50-65% of MS patients are expected to develop disabilities due to cognitive dysfunction and there is currently no approved treatment for this indication.

Company History

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

Corporate Information

Our executive offices are located at 155 Gibbs Street, Suite 412, Rockville, Maryland 20850. We also maintain administrative and finance office in Ann Arbor, Michigan. Our telephone number is (732) 332-7800, and our website address is www.syntheticbiologics.com. The information contained on our website is not part of, and should not be construed as being incorporated by reference into this prospectus supplement.

As used in this prospectus supplement, unless the context otherwise requires, references to “Synthetic,” “we,” “us,” “our,” and similar references refer to Synthetic Biologics, Inc.

THE OFFERING

Common Stock offered by us	14,059,616 shares.
Warrants offered by us	Warrants to purchase up to 7,029,808 shares of common stock at an exercise price of $1.75 per share, subject to adjustment. The warrants will be exercisable at any time after the closing date for a term of five years. The shares of common stock and warrants comprising the units are immediately separable and will be issued separately, but will be purchased together in this offering. We are also registering the shares of common stock issuable upon conversion of the warrants and exercise of the warrants.
Public Offering Price	$1.47 per unit.
Common stock to be outstanding after this offering	72,513,144 shares of common stock or 79,542,952 shares if the warrants sold in this offering are exercised in full.
Use of Proceeds	We intend to use the net proceeds from this offering, if any, for general corporate purposes, which may include, among other things, funding research and development, and clinical trials of our pipeline programs. In addition, we may use a portion of the net proceeds for licensing or acquiring intellectual property to incorporate into our pipeline programs. See “Use of Proceeds” on page S-8.
Risk Factors	See “Risk Factors” beginning on page S-5 of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement and page 5 of the accompanying prospectus for a discussion of factors you should read and consider carefully before investing in our common stock and warrants.

NYSE MKT symbol “SYN”

Except as otherwise indicated, all information in this prospectus supplement:

- is based on 58,453,528 shares outstanding on October 9, 2014;

- excludes 5,786,106 shares of our common stock subject to options outstanding as of October 9, 2014 having a weighted-average exercise price of $2.03 per share;

- excludes 2,194,212 shares of our common stock that have been reserved for issuance in connection with future grants under our stock incentive plans as of October 9, 2014;

- excludes 944,986,shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of October 9, 2014 (other than those covered by this prospectus supplement) having a weighted-average exercise price of $2.16 per share; and

- excludes shares of our common stock that may be issuable upon exercise of the warrants covered by this prospectus supplement.

RISK FACTORS

You should consider carefully the risks discussed under the section captioned "Risk Factors" contained in our annual report on Form 10-K for the year ended December 31, 2013, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, (the "Exchange Act"), each of which is incorporated by reference in this prospectus supplement in its entirety, together with other information in this prospectus supplement and the prospectus, and the information and documents incorporated by reference in this prospectus supplement, the prospectus, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our securities. If any of these events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment.

Additional Risks Relating to the Offering

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of proceeds from this offering. The net proceeds from this offering will be used for general corporate purposes, which may include, among other things, funding research and development, and clinical trials for our pipeline programs. In addition, we may use a portion of the net proceeds for licensing or acquiring intellectual property to incorporate into our pipeline programs. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our common stock.

If you purchase units sold in this offering, you will experience immediate dilution in your investment. You will experience further dilution if we issue additional equity securities in future fundraising transactions and if shares of our common stock underlying our significant number of outstanding warrants and options are purchased by the holders thereof.

The portion of the public offering price per unit in this offering attributable to our common stock exceeds the net tangible book value per share of our common stock outstanding prior to this offering. Assuming we sell all of the units in this offering at the public offering price of $1.47 per unit, after deducting the estimated placement agent commission and estimated offering expenses payable by us, you will experience immediate dilution of approximately $1.10 per share, representing the difference between our as adjusted net tangible book value per share as of June 30, 2014 after giving effect to this offering and the public offering price without giving effect to the potential exercise of

the warrants being offered by this prospectus supplement. See the section entitled “Dilution” below for a more detailed illustration of the dilution you would incur if you participate in this offering.

If in the future we issue additional common stock, or securities convertible into or exchangeable or exercisable for common stock, our stockholders, including investors who purchase shares offered under this prospectus supplement, will experience additional dilution, and any such issuances may result in downward pressure on the price of our common stock.

In addition, we have a significant number of outstanding securities convertible into, or allowing the purchase of our Common Stock. Investors will be subject to increased dilution upon the exercise of outstanding stock options and warrants. There were 58,453,528 shares of our common stock outstanding as of October 9, 2014. As of that date, stock options and warrants outstanding represented 6,276,092 shares of our common stock that could be issued in the future (not including the warrants being offered by this prospectus supplement). Most of the outstanding shares of our common stock, as well as the vast majority of the shares of our common stock that may be issued under our outstanding options and warrants, are not restricted from trading. Also, the issuance of additional shares as a result of such conversion or purchase, or their subsequent sale, could adversely affect the price of our common stock.

There is no public market for the warrants to purchase common stock being offered by this prospectus supplement.

There is no established public trading market for the warrants being offered by this prospectus supplement, and we do not expect a market to develop. In addition, we do not intend to apply to list the warrants on any securities exchange. Without an active market, the liquidity of the warrants will be limited.

Holders of our warrants will have no rights as a common stockholder until such holders exercise their warrants and acquire our common stock.

Until holders of warrants acquire shares of our common stock upon exercise of the warrants, holders of warrants will have no rights with respect to the shares of our common stock underlying such warrants. Upon exercise of the warrants, the holders thereof 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.

The warrants included in this offering may not have any value.

Each warrant has an exercise price of $1.75 per share of common stock, subject to adjustment, will be exercisable at any time and from time to time after the closing date, and will expire five years from the closing date. In the event our common stock price does not exceed the exercise price of the warrants during the period when the warrants are exercisable, the warrants may not have any value.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements contained or incorporated by reference in this prospectus supplement or in the accompanying prospectus may include forward-looking statements that reflect our current views with respect to our ongoing and planned clinical trials, business strategy, business plan, financial performance and other future events. These statements include forward-looking statements both with respect to us, specifically, and the biotechnology sector, in general. We make these statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements that include the words “expect,” “intend,” “plan,” “believe,” “project,” “estimate,” “may,” “should,” “
“will” and similar statements of a future or forward-looking nature identify forward-looking statements for purposes of the federal securities laws or otherwise.

All forward-looking statements involve inherent risks and uncertainties, and there are or will be important factors that could cause actual results to differ materially from those indicated in these statements. We believe that these factors include, but are not limited to, those factors set forth under the caption “Risk Factors” in this prospectus supplement and in the accompanying prospectus and under the captions “Risk Factors,” “Business,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” in our most recent Annual Report on Form 10-K and our subsequent Quarterly Reports on Form10-Q, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus supplement and the accompanying prospectus. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

If one or more of these or other risks or uncertainties materializes, or if our underlying assumptions prove to be incorrect, actual results may vary materially from what we anticipate. All subsequent written and oral forward-looking statements attributable to us or individuals acting on our behalf are expressly qualified in their entirety by this Note. Before purchasing any shares of common stock, you should consider carefully all of the factors set forth or referred to in this prospectus supplement and in the accompanying prospectus that could cause actual results to differ.

DESCRIPTION OF SECURITIES WE ARE OFFERING

In this offering, we are offering for sale units, with each unit consisting of one share of common stock and a warrant to purchase 0.5 shares of common stock. The shares of common stock and warrants comprising the units are immediately separable and will be issued separately, but will be purchased together in this offering. We are also registering the shares of common stock issuable upon exercise of the warrants.

These securities are being issued pursuant to a securities purchase agreement between each of the investors and us. You should review the securities purchase agreement, and the form of warrant, each filed as exhibits to a Current Report on Form 8-K filed with the Securities and Exchange Commission (SEC) in connection with this offering, for a complete description of the terms and conditions applicable to the warrants. The following brief summary of the material terms and provisions of the common stock and the warrants is subject to, and qualified in its entirety by the form of warrant.

Common Stock

The material terms and provisions of our common stock and each other class of our securities that qualifies or limits our common stock are described under the caption “Description of Capital Stock” starting on page 6 of the accompanying prospectus. As of October 9, 2014, there are 58,453,528 shares of common stock issued and outstanding.

Warrants

Exercisability. Each warrant will be exercisable at any time after the closing date for a term of five years. The warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and payment in full for the number of shares of our common stock purchased upon such exercise, except in the case of a cashless exercise as discussed below.

Cashless Exercise. The holder may exercise the warrant on a cashless basis. When exercised on a cashless basis, a portion of the warrant is cancelled in payment of the purchase price payable in respect of the number of shares of our common stock purchasable upon such exercise.

Exercise Price. Each warrant represents the right to purchase up to one half of a share of common stock at an exercise price of $1.75 per share. The exercise price per share is subject to adjustment for stock dividends, distributions, subdivisions, combinations, or reclassifications. Subject to limited exceptions, a holder of warrants will not have the right to exercise any portion of the warrant to the extent that, after giving effect to the exercise, the holder, together with its affiliates, would beneficially own in excess of 4.99% or 9.99%, depending on the holder's initial election, of the number of shares of our common stock outstanding immediately after giving effect to its exercise. The holder may elect to increase or decrease this beneficial ownership limitation to any other percentage, but not in excess of 19.9% of the total number of issued and outstanding shares of common stock (including for such purpose the shares of common stock issuable upon such exercise), provided that any such increase or decrease will not be effective until 61 days after such written notice is delivered.

Fundamental Transactions. In the event we effect certain mergers, consolidations, sales of substantially all of our assets, tender or exchange offers, reclassification or share exchange in which our common stock is effectively converted into or exchanged for other securities, cash or property, we consummate a business combination in which another person acquires 50% of the outstanding shares of our common stock, or any person or group becomes the beneficial owner of 50% of the aggregate ordinary voting power represented by our issued and outstanding common stock (a "Fundamental Transaction"), then, upon any subsequent exercise of the warrants, the holders of warrants will have the right to receive any shares of the acquiring corporation or other consideration it would have been entitled to receive if it had been a holder of the number of shares of common stock then issuable upon exercise in full of the warrants. Except in connection with a Fundamental Transaction in which the consideration for each share of common stock is at least 300% of the exercise price of the warrant, we or the successor entity will, at the holder's option, purchase the unexercised portion of the warrant from the holder (i) in the case of all cash transaction or a transaction in which the consideration consists partially of cash or securities of a successor entity to the extent of the percentage of the cash consideration, for an amount of cash equal to equal to the Black-Scholes value of the remaining unexercised portion of the warrant on the date of the consummation of the transaction and (ii) in the case of any other Fundamental Transaction or in a transaction in which the consideration consists partially of cash or securities of a successor entity to the extent the consideration is represented by securities, for a number of shares of common stock equal to the Black Scholes value of the portion of the warrant subject to redemption divided by 95% of the closing sale price of the common stock on the day preceding the date on which the Fundamental Transaction is consummated.

Transferability. Subject to applicable laws and restrictions, a holder may transfer a warrant upon surrender of the warrant to us with a completed and signed assignment in the form attached to the warrant. The transferring holder will be responsible for any tax that liability that may arise as a result of the transfer.

Exchange Listing. There is no established public trading market for the warrants, and we do not expect a market to develop. In addition, we do not intend to apply for listing of the warrants on any securities exchange or recognized trading system.

Rights as Stockholder. Except as set forth in the warrant, the holder of a warrant, solely in such holder's capacity as a holder of a warrant, will not be entitled to vote, to receive dividends, or to any of the other rights of our stockholders.

Amendments and Waivers. The provisions of each warrant may be modified or amended or the provisions thereof waived with the written consent of us and the holder.

USE OF PROCEEDS

We estimate that the net proceeds of this offering, after deducting the placement agent's fees and the estimated offering expenses payable by us, will be approximately $18.9 million excluding proceeds, if any, from the exercise of the warrants issued in this offering.

We intend to use the net proceeds from this offering, if any, for general corporate purposes, which may include, among other things, funding research and development, and clinical trials of our pipeline programs. In addition, we may use a portion of the net proceeds for licensing or acquiring intellectual property to incorporate into our pipeline programs.

The amounts and timing of our actual expenditures will depend on numerous factors, including our development and commercialization efforts, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities.

DIVIDEND POLICY

We currently do not plan to declare dividends on shares of our common stock in the foreseeable future. We expect to retain all future earnings, if any, for use in the operation and expansion of our business. The payment of cash dividends in the future, if any, will be at the discretion of our board of directors and will depend upon such factors as any other factors our board deems relevant.

DILUTION

If you invest in the units your interest will be diluted immediately to the extent of the difference between the offering price and the adjusted net tangible book value per share of our common stock contained in the units after this offering.

Our net tangible book value on June 30, 2014 was approximately $8.1 million, or $0.14 per share. "Net tangible book value" is total assets minus the sum of liabilities and intangible assets. "Net tangible book value per share" is net tangible book value divided by the total number of shares outstanding.

After giving effect to the sale of 14,059,616 units in this offering at the public offering price of $1.47 per unit, and after deducting estimated offering commissions and expenses payable by us, our as adjusted net tangible book value as of June 30, 2014 would have been approximately $27.0 million, or $0.37 per share of common stock without giving effect to the potential exercise of the warrants being offered by this prospectus supplement. This represents an immediate increase in net tangible book value of $0.23 per share to our existing stockholders and an immediate dilution in net tangible book value of $1.10 per share to investors participating in this offering. The following table illustrates this dilution per share to investors participating in this offering:

Public offering price per unit		$1.47
Net tangible book value per share as of June 30, 2014	$0.14	
Increase in net tangible book value per share attributable to new investors in offering	$0.23	
As adjusted net tangible book value per share after giving effect to the offering		$0.37
Dilution per share to new investors		$1.10

The above illustration of dilution per share to investors participating in this offering assumes no exercise of outstanding options to purchase our common stock or outstanding warrants to purchase shares of our common stock.

The above discussion and table are based on 58,453,528 shares of our common stock issued and outstanding as of June 30, 2014, which does not include the following, all as of June 30, 2014:

- 5,331,106 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of $2.05 per share;
- 2,649,212 shares of common stock which that have been reserved for issuance in connection with future grants under our stock incentive plans; and

- 944,986 shares of our common stock reserved for issuance upon the exercise of outstanding warrants (not including the warrants issued in this offering), each with a weighted-average exercise price of $2.16 per share.

To the extent that any of these outstanding options or warrants are exercised, there will be further dilution to new investors.

PLAN OF DISTRIBUTION

We have entered into a placement agency agreement, dated as of October 10, 2014, with William Blair & Company, L.L.C. Subject to the terms and conditions contained in the placement agency agreement, William Blair & Company, L.L.C. has agreed to act as the sole placement agent in connection with the sale of the units. There is no required minimum number of securities it is required to arrange the purchase or sale of or dollar amount of the securities, but it has agreed to use its best efforts to solicit purchasers for the securities being offered in this offering. There is no required minimum number of securities that must be sold as a condition to completion of the offering.

We will enter into a subscription agreement directly with investors in connection with this offering, and we will only sell to investors who have entered into the subscription agreement. Our obligation to issue and sell the units to investors is subject to the conditions set forth in the subscription agreement, which may be waived by us in our discretion. An investor's obligation to purchase the units is subject to conditions set forth in the subscription agreement, which may be waived by the investor.

Unless investors instruct us otherwise, we will deliver the shares of common stock being issued to the investors electronically upon receipt of investor funds for the purchase of the common stock offered pursuant to this prospectus supplement. We expect to deliver the shares of our common stock being offered pursuant to this prospectus supplement and the warrants on or about October 15, 2014. The warrants will be issued and delivered in physical form.

We have agreed to pay William Blair & Company, L.L.C. our sole placement agent, placement agent commissions and fees in an amount equal to 7.0% of the aggregate proceeds of this offering. In addition, we have agreed to reimburse the placement agent for its reasonable, out-of-pocket expenses incurred in connection with this offering in an amount not to exceed $125,000. The following table shows the estimated per unit and total cash fees we will pay to the placement agent in connection with the sale of the units offered pursuant to this prospectus supplement and the accompanying prospectus.

Per unit	$0.1029
Total	$1,446,734

However, because there is no minimum offering amount required as a condition to closing of this offering, the actual total offering commissions, if any, may be substantially less than the total offering amounts set forth above. We estimate the total expenses of this offering excluding the placement agent commission and expense reimbursement will be approximately $200,000.

The placement agent has informed us that it will not engage in over-allotment, stabilizing transactions or syndicate covering transactions in connection with this offering.

The placement agency agreement provides that the obligations of the placement agent are subject to certain conditions precedent, including the absence of any material adverse changes in our business and the receipt of certain certificates, opinions and letters from us, our counsels and our auditors.

We have agreed to indemnify the placement agent and specified other persons against certain civil liabilities, including liabilities under the Securities Act or the Exchange Act, and to contribute to payments that the placement agent may be required to make in respect of such liabilities.

Our officers and directors have signed lock-up agreements, pursuant to which they have agreed to not, directly or indirectly, offer, sell, agree to sell or otherwise transfer or dispose of any shares of our common stock or any securities convertible into or exchangeable for shares of our common stock, without the prior written consent of the placement agent for a period of 90 days after the date of this prospectus.

Our common stock is traded on the NYSE MKT under the symbol “SYN.”

The placement agent may distribute this prospectus supplement and the accompanying prospectus electronically.

The placement agency agreement will be included as an exhibit to a Current Report on Form 8-K that we will file with the SEC and that will be incorporated by reference into the registration statement of which this prospectus supplement forms a part.

The placement agent or its affiliates may in the future provide investment banking, commercial banking and/or other services to us from time to time, for which they may in the future receive customary fees and expenses.

LEGAL MATTERS

Parsons Behle & Latimer, Reno, Nevada will pass upon certain legal matters relating to the issuance and sale of the common stock offered hereby on behalf of Synthetic Biologics, Inc. and the common stock issuable upon exercise of the warrants. Gracin & Marlow, LLP, New York, New York will pass upon certain legal matters relating to the issuance and sale of the warrants offered hereby on behalf of Synthetic Biologics, Inc. Goodwin Procter LLP, New York, New York is acting as counsel for the placement agent in connection with this offering.

EXPERTS

The financial statements as of December 31, 2013 and 2012 and for each of the two years in the period ended December 31, 2013 incorporated by reference in this Prospectus have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus supplement forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

We file reports, proxy statements and other information with the SEC under the Exchange Act. You may read and copy this information from the Public Reference Room of the SEC, 100 F Street, N.E., Room 1580, Washington, D.C. 20549, at prescribed rates. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is *www.sec.gov*.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus supplement. The information incorporated by reference is considered to be part of this prospectus supplement, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this prospectus supplement and the termination of the offering however, we are not incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed "filed" with the SEC, or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K:

Our annual report on Form 10-K for the fiscal year ended December 31, 2013 filed with the SEC on March 30, 2014(File No. 001-12584);

Our quarterly report on Form 10-Q for the quarters ended March 31, 2014 filed with the SEC on May 15, 2014 and June 30, 2014 filed with the SEC on August 14, 2014(File No. 001-12584).

Our current reports on Form 8-K filed with the SEC on February 26, 2014, April 2, 2014, April 21, 2014, April 22, 2014, May 15, 2014 and June 13, 2014 (File No. 001-12584);

Our definitive proxy statement on Schedule 14A filed with the SEC on June 10, 2014 (File No. 001-12584); and

The description of our common stock set forth in our registration statement on Form 8-A12B, filed with the SEC on June 20, 2007 (File No. 000-12584).

In addition, all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed in such forms that are related to such items unless such Form 8-K expressly provides to the contrary) subsequently filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, as amended, before the date our offering is terminated or completed are deemed to be incorporated by reference into, and to be a part of, this prospectus supplement.

Any statement contained in this prospectus supplement or in a document incorporated or deemed to be incorporated by reference into this prospectus supplement will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus supplement modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to Synthetic Biologics, Inc. 617 Detroit Street, Suite 100, Ann Arbor, Michigan 48104, (734) 332-7800.

You should rely only on information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus supplement or the accompanying prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

You may obtain, free of charge, a copy of any of these documents (other than exhibits to these documents unless the exhibits are specifically incorporated by reference into these documents or referred to in this prospectus supplement) by writing or calling us at the following address and telephone number:

617 Detroit Street, Suite 100
Ann Arbor, Michigan 48104

(734) 332-7800

PROSPECTUS

$50,000,000

Common Stock

Warrants

Units

We may offer and sell up to $50 million in the aggregate of the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus (which includes, but is not limited to, the sales agreement prospectus) that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more placement agents, dealers and agents, or directly to purchasers, or through a combination of these methods. If any placement agents, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled “About this Prospectus” and “Plan of Distribution” for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the

offering of such securities.

This prospectus may not be used to sell securities unless it is accompanied by a prospectus supplement.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" ON PAGE 6 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on the NYSE MKT under the symbol "SYN." On July 1, 2013, the last reported sale price of our common stock on the NYSE MKT was $1.67 per share.

As of July 2, 2013, the aggregate market value of our outstanding common stock held by non-affiliates was approximately $45,744,673, based on 44,654,414 shares of outstanding common stock, of which approximately 17,262,394 shares are held by affiliates, and a per share price of $1.67 based on the closing sale price of our common stock on July 1, 2013. We have not offered any securities during the past twelve months pursuant to General Instruction I.B.6 of Form S-3.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is July 16, 2013

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You should rely only on the information we have provided or incorporated by reference in this prospectus or in any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus or in any prospectus supplement. This prospectus and any prospectus supplement is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information contained in this prospectus and in any prospectus supplement is accurate only as of their respective dates and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any prospective supplement or any sale of securities. The registration statement, including the exhibits and the documents incorporated herein by reference, can be read on the Securities and Exchange Commission website or at the Securities and Exchange Commission offices mentioned under the heading “Where You Can Find More Information.”

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, using a "shelf" registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings up to a total dollar amount of $50 million of securities from time to time as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus (which term includes, as applicable, the sales agreement prospectus filed with the registration statement of which this prospectus forms a part) that contains specific information about the securities being offered and sold and the specific terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you should rely on the prospectus supplement. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement, together with the additional information described under the heading "Where You Can Find More Information" and "Incorporation of Certain Information by Reference."

You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate as of the date on its respective cover, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates.

Unless otherwise stated or the context otherwise requires, references in this prospectus to "Synthetic," the "Company," "we," "our" and "us" refer to Synthetic Biologics, Inc., a Nevada corporation and its consolidated subsidiaries, unless otherwise specified. When we refer to "you," we mean the holders of the applicable series of securities.

PROSPECTUS SUMMARY

The items in the following summary are described in more detail elsewhere in this prospectus and in the documents incorporated by reference herein. This summary provides an overview of selected information and does not contain all the information you should consider before investing in our common stock. Therefore, you should read the entire prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the "Risk Factors" section and other documents or information included or incorporated by reference in this prospectus before making any investment decision.

Our Business

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

Product Pipeline:

Summary of Infectious Disease Programs:

- ***Clostridium difficile (C. difficile)*** **infections:** In November 2012, we acquired a series of oral beta-lactamase enzymes (P1A, P2A and P3A) and related assets targeting the prevention *of C. difficile* infections (CDI), the leading cause of hospital acquired infections (HAI), that generally occurs secondary to treatment with intravenous antibiotics. The acquired assets include a pre-Investigational New Drug (IND) package for P3A (SYN-004), Phase I and Phase II clinical data for P1A, manufacturing processes and data, and a portfolio of issued and pending U.S. and international patents intended to support an IND and Biologic License Application (BLA) with the FDA. Utilizing this portfolio of assets, we intend to develop a proprietary oral beta-lactamase enzyme product candidate, SYN-004, previously known as IPSAT P3A. When co-administered with certain intravenous beta-lactam antibiotics, it is expected that SYN-004 can degrade the antibiotic that is excreted in the gastrointestinal (GI) tract, thus preserving the natural balance of the patient's microflora, and preventing opportunistic infections including CDI. Beta-lactam antibiotics are a mainstay in hospital infection management and include the commonly used penicillin and

cephalosporin classes of antibiotics. In 2012, 15 million Americans were administered beta-lactam antibiotics.*

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

Pertussis: In December 2012, in collaboration with Intrexon, we initiated development of a monoclonal antibody (mAb) therapy for the treatment of Pertussis infections, more commonly known as whooping cough. We are developing a mAb therapy, SYN-005, designed to target and neutralize the pertussis toxin, in order to reduce the mortality rate in infants and potentially shorten the duration of chronic cough in afflicted adults. To further the development of this potential therapy for Pertussis, we entered into an agreement with The University of Texas at Austin to license the rights to certain research and pending patents related to pertussis antibodies. According to the World Health Organization, each year, *B. pertussis* infection causes an estimated 300,000 deaths worldwide, primarily among young, unvaccinated infants.

- ***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.

Summary of Multiple Sclerosis Program:

- Trimesta ™ (oral estriol) is being developed as an oral once-daily treatment for relapsing-remitting multiple sclerosis (MS) in women. Patient enrollment is complete in this two-year, randomized, double-blind, placebo-controlled Phase II clinical trial being conducted at 15 centers in the U.S. The primary endpoint is relapse rate at two years, with top-line results expected in 1H 2014. This trial is supported by grants exceeding $8 million, which should be sufficient to fund the trial through completion. Annual worldwide sales of current MS therapies are estimated at $14.1 billion.

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

Summary of Fibromyalgia Program:

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

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

Recent Developments

On December 19, 2012, we entered into a Patent License Agreement (the "License Agreement") with The University of Texas at Austin (the "University") for the exclusive license of the right to use, develop, manufacture, market and commercialize certain research and patents related to Pertussis (more commonly known as whooping cough) antibodies developed in the lab of Dr. Jennifer A. Maynard, Assistant Professor of Chemical Engineering. In connection with the License Agreement, we and the University also entered into a Sponsored Research Agreement pursuant to which the University will perform certain research work related to pertussis under the direction of Dr. Jennifer Maynard and we will obtain certain rights to patents and technology developed during the course of such research.

On November 28, 2012, a closing was held for the transaction contemplated by the Asset Purchase Agreement (the "Prev Agreement") we entered into with Prev ABR LLC ("Prev"), pursuant to which we acquired the *C. diff* program assets of Prev, including pre-Investigational New Drug (IND) package, Phase I and Phase II clinical data, manufacturing process data and all issued and pending U.S. and international patents. Pursuant to the Prev Agreement, we paid Prev an initial cash payment of $100,000 upon execution of the Prev Agreement and at closing paid an additional cash payment of $135,000 and issued 625,000 unregistered shares of our common stock to Prev. In addition, upon the achievement of the milestones set forth below, Prev may be entitled to receive additional consideration payable 50% in cash and 50% in our stock, subject to Prev's option to receive the entire payment in shares of our stock, with the exception of the first milestone payments to be paid in cash: (i) upon commencement of an IND; (ii) upon commencement of a Phase I clinical trial; (iii) upon commencement of a Phase II clinical trial; (iv) upon commencement of a Phase III clinical trial; (v) upon Biologic License Application (BLA) filing in the U.S. and for territories outside of the U.S. (as defined in the Prev Agreement); and (vi) upon BLA approval in the U.S. and upon approval in territories outside the-U.S. The future stock issuances are subject to prior approval of the NYSE MKT, LLC. No royalties are payable to Prev under the Prev Agreement. The Prev Agreement also provides that Prev has a right to the return to it of all assets acquired by us under the Prev Agreement if on or prior to the date that is (i) thirty (30) months after the execution of the Prev Agreement, we have not initiated toxicology studies in non-rodent models or (ii) thirty six (36) months have not filed an IND under the program related to the assets and such failure is not due to action or inaction of Prev or breach of its representations or warranties or covenants or if there is a change of control as defined in the Prev Agreement and after such change of control the assets are not further developed; provided however that such thirty (30) and thirty six (36) month periods can be extended by us for an additional twelve (12) months upon payment of a cash milestone payment.

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

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

On August 6, 2012, we expanded our relationship with Intrexon and entered into a Second Channel Agreement with Intrexon (the "Second Channel Agreement") that governs an "exclusive channel collaboration" arrangement in which we will use Intrexon's technology relating to the identification, design and production of human antibodies and DNA vectors for the development and commercialization of a series of monoclonal antibody therapies for the treatment of certain serious infectious diseases (the "Program"). The Second Channel Agreement establishes committees comprised of our and Intrexon representatives that will govern activities related to the Program in the areas of project establishment, chemistry, manufacturing and controls, clinical and regulatory matters, commercialization efforts and intellectual property. On October 16, 2012, a closing was held for the transaction contemplated by the Second Channel Agreement. Pursuant to the terms of a Stock Issuance Agreement with Intrexon (the "Second Stock Purchase Agreement"), we issued 3,552,210 shares of our common stock, $0.001 par value, which issuance is also deemed paid in consideration for the execution and delivery of the Second Channel Agreement, dated August 6, 2012, between ourselves and Intrexon. We registered the shares issued to Intrexon in accordance with the First Amendment to Registration Rights Agreement.

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

On December 21, 2011, we announced that the Board of Directors had taken several actions to prioritize our focus on our entry into the emerging field of synthetic biology. In connection with the change in business focus on March 8, 2012, we entered into a Membership Interest Purchase Agreement, and certain related agreements, pursuant to which we sold all of our interest in the Adeona Clinical Laboratory (the "Lab") to Hartlab, LLC, an entity controlled by the Lab's former owner, in consideration for (i) the immediate assignment of the Lab's outstanding accounts receivable up through the date of closing, plus (ii) Seven Hundred Thousand Dollars ($700,000) payable pursuant to the terms of a two-year non-recourse promissory note secured by all of the assets of the Lab.

On November 18, 2011, we entered into a Stock Purchase Agreement with Intrexon pursuant to which we issued to Intrexon 3,123,558 shares of our common stock at a purchase price equal to the $0.001 par value of such shares, which issuance was deemed paid in consideration for the execution and delivery of the channel agreement which was entered into on November 18, 2011 and terminated on April 16, 2013. We also agreed to an equity participation right in future securities offerings.

Company Information

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

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

THE OFFERING

We may offer shares of our common stock, warrants to purchase any of such securities, either individually or in combination, and/or units consisting of some or all of such securities for total gross proceeds of up to $50 million, from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities being offered. Below is a summary of the securities we may offer under this prospectus (together with the applicable prospectus supplement).

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We may sell the securities directly to investors or to or through agents, placement agents or dealers. We, and our agents or placement agents, reserve the right to accept or reject all or part of any proposed purchase of securities. Each prospectus supplement will set forth the names of any placement agents, dealers or agents involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

RISK FACTORS THAT MAY AFFECT FUTURE RESULTS

You should consider carefully the risks discussed under the section captioned "Risk Factors" contained in our annual report on Form 10-K for the year ended December 31, 2012 and in our subsequent quarterly reports on Form 10-Q, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, each of which is incorporated by reference in this prospectus in its entirety, together with other information in this prospectus, and the information and documents incorporated by reference in this prospectus, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. If any of these events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents incorporated by reference in it, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. These statements may be made directly in this document or they may be made part of this document by reference to other documents filed with the SEC, which is known as "incorporation by reference." You can find many (but not all) of these statements by looking for words such as "approximates," "believes," "expects," "anticipates," "estimates," "intends," "plans," "would," "could," "may" or other similar expressions in this prospectus or the documents incorporated by reference.

We caution investors that any forward-looking statements presented in this prospectus or the documents incorporated by reference, or those which we may make orally or in writing from time to time, are based on our beliefs and assumptions, as well as information currently available to us. Such statements are based on assumptions and the actual outcome will be affected by known and unknown risks, trends, uncertainties and factors that are beyond our control or ability to predict. Although we believe that our assumptions are reasonable, they are not guarantees of future performance and some will inevitably prove to be incorrect. As a result, our actual future results can be expected to differ from our expectations, and those differences may be material. Accordingly, investors should use caution in relying on past forward-looking statements, which are based on known results and trends at the time they are made, to anticipate future results or trends.

Some of the risks and uncertainties that may cause our actual results, performance or achievements to differ materially from those expressed or implied by forward-looking statements include the following:

- a failure to continue to undertake preclinical development and clinical trials for our product candidates;
- a failure to expand our research activities with Intrexon relating to monoclonal antibodies for infectious diseases;
- a failure of our product candidates to be demonstrably safe and effective;
- a failure to obtain regulatory approval for our products or to comply with ongoing regulatory requirements;
- a lack of acceptance of our product candidates in the marketplace;
- a failure by us to become or remain profitable;
- an inability by us to obtain the capital necessary to fund our research and development activities; and
- a loss of any of our key scientists or management personnel.

This prospectus and all subsequent written and oral forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We do not undertake any obligation to release publicly any revisions to our forward-looking statements to reflect events or circumstances after the dates that such statements are made.

For more information on the uncertainty of forward-looking statements, see “Risk Factors” in our Annual Reports on Form 10-K and our Quarterly Reports on Form 10-Q and any applicable prospectus supplement.

USE OF PROCEEDS

We intend to use the net proceeds, if any, from the sales of securities offered by this prospectus for general corporate purposes, which may include, among other things, increasing our working capital and funding research and development, and capital expenditures. In addition, we may use a portion of the net proceeds for licensing or acquiring intellectual property to incorporate into our products and product candidates or our research and development programs. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products; however, we have no current commitments or obligations to do so.

The amounts and timing of our actual expenditures will depend on numerous factors, including our development and commercialization efforts, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities.

DIVIDEND POLICY

We have never paid cash dividends on our common stock. Moreover, we do not anticipate paying periodic cash dividends on our common stock for the foreseeable future. We intend to use all available cash and liquid assets in the operation and growth of our business. Any future determination about the payment of dividends will be made at the discretion of our board of directors and will depend upon our earnings, if any, capital requirements, operating and financial conditions and on such other factors as our board of directors deems relevant.

DESCRIPTION OF CAPITAL STOCK

Authorized Capital

Our authorized capital consists of 100 million shares of common stock, par value $0.001 per share, and 10 million shares of preferred stock, par value $0.001 per share. As of July 2, 2013, 44,654,414 shares of common stock and no shares of preferred stock were outstanding.

Common Stock

We may issue shares of our common stock from time to time. Holders of shares of common stock have the right to cast one vote for each share of common stock in their name on the books of our company, whether represented in person or by proxy, on all matters submitted to a vote of holders of common stock, including election of directors. There is no right to cumulative voting in election of directors. Except where a greater requirement is provided by statute, by our articles of incorporation, or by our bylaws, the presence, in person or by proxy duly authorized, of the one or more holders of a majority of the outstanding shares of our common stock constitutes a quorum for the transaction of business. The vote by the holders of a majority of outstanding shares is required to effect certain fundamental corporate changes such as liquidation, merger, or amendment of our articles of incorporation. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock.

There are no restrictions in our articles of incorporation or bylaws that prevent us from declaring dividends. We have not declared any dividends, and we do not plan to declare any dividends in the foreseeable future.

Holders of shares of our common stock are not entitled to preemptive or subscription or conversion rights, and no redemption or sinking fund provisions are applicable to our common stock. All outstanding shares of common stock are, and the shares of common stock sold in the offering will when issued be fully paid and non-assessable.

DESCRIPTION OF WARRANTS

Warrants

We may issue warrants for the purchase of common stock. We may issue warrants independently or in combination with common stock. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as any warrant agreements and warrant certificates that contain the terms of the warrants. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants also may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address

of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

The following description, together with the additional information that we include in any applicable prospectus supplement and in any related free writing prospectus that we may authorize to be distributed to you, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may be issued in one or more series. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement and in any related free writing prospectus that we may authorize to be distributed to you. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

The summary below and that contained in any prospectus supplement is qualified in its entirety by reference to all of the provisions of the warrant and/or the warrant agreement and warrant certificate, as applicable, applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the warrants that we may offer under this prospectus, as well as the complete warrant and/or the warrant agreement and warrant certificate, as applicable, that contains the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants being offered, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the number of warrants issued with each such security;
- the number of shares of common stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

a discussion of any material or special U.S. federal income tax considerations of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any:

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus supplement, we will, as soon as practicable, issue and deliver the securities purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

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Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A warrant agent may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

Governing Law

Unless we otherwise specify in the applicable prospectus supplement, the warrants and any warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

DESCRIPTION OF UNITS

Units

We may issue units consisting of any combination of our common stock and warrants. We will issue each unit so that the holder of the unit is also the holder of each security included in the unit. As a result, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

The summary below and that contained in any prospectus supplement is qualified in its entirety by reference to all of the provisions of the unit agreement and/or unit certificate, and depositary arrangements, if applicable. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the units that we may offer under this prospectus, as well as the complete unit agreement and/or unit certificate, and depositary arrangements, as applicable, that contain the terms of the units.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of unit agreement and/or unit certificate, and depositary

arrangements, as applicable, that contain the terms of the particular series of units we are offering, and any supplemental agreements, before the issuance of such units.

The applicable prospectus supplement, information incorporated by reference or free writing prospectus may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions for the issuance, payment, settlement, transfer, or exchange of the units or of the securities composing the units;
- whether the units will be issued in fully registered or global form; and
- any other terms of the units.

The applicable provisions described in this section, as well as those described under “Common Stock” and “Warrants” above, will apply to each unit and to each security included in each unit, respectively

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through placement agents or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

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Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If a placement agent is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the placement agent at the time of sale and the name of any placement agent will be provided in the prospectus supplement that the placement agent will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of securities for whom the placement agent may act as agent, may compensate the placement agent in the form of underwriting discounts or commissions. The placement agent may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the placement agents and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to placement agents, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by placement agents to participating dealers will be provided in the applicable prospectus supplement. Placement agents, dealers and agents participating in the distribution of the securities may be deemed to be placement agents within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify placement agents, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any common stock will be listed on the NYSE MKT, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons

may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

If indicated in the applicable prospectus supplement, placement agents or other persons acting as agents may be authorized to solicit offers by institutions or other suitable purchasers to purchase the securities at the public offering price set forth in the prospectus supplement, pursuant to delayed delivery contracts providing for payment and delivery on the date or dates stated in the prospectus supplement. These purchasers may include, among others, commercial and savings banks, insurance companies, pension funds, investment companies and educational and charitable institutions. Delayed delivery contracts will be subject to the condition that the purchase of the securities covered by the delayed delivery contracts will not at the time of delivery be prohibited under the laws of any jurisdiction in the United States to which the purchaser is subject. The placement agents and agents will not have any responsibility with respect to the validity or performance of these contracts.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be a placement agent and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The placement agents, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

LEGAL MATTERS

Gracin & Marlow, LLP, New York, New York will pass upon certain legal matters relating to the issuance and sale of the warrants and units offered hereby on behalf of Synthetic Biologics, Inc. and Parsons Behle & Latimer, Reno, Nevada will pass upon certain legal matters relating to the issuance and sale of the common stock and the common stock underlying the warrants offered hereby on behalf of Synthetic Biologics, Inc. Additional legal matters may be passed upon for us or any placement agents, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements as of December 31, 2012 and for the year ended December 31, 2012 incorporated by reference in this prospectus have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on authority of said firm as experts in auditing and accounting.

The financial statements as of December 31, 2011 and for the year ended December 31, 2011 incorporated by reference in this prospectus have been so incorporated in reliance on the report of Berman & Company, P.A. an independent registered public accounting firm, incorporated herein by reference, given on authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document we file at the SEC’s public reference room located at 100 F Street N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference room. Our public filings are also available to the public at the SEC’s web site at http://www.sec.gov.

This prospectus is part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act. This prospectus does not contain all of the information in the registration statement. We have omitted certain parts of the registration statement, as permitted by the rules and regulations of the SEC. You may inspect and copy the registration statement, including exhibits, at the SEC’s public reference room or Internet site.

Additional information about Synthetic Biologics. Inc. 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.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this prospectus and the termination of the offering, however, we are not incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed "filed" with the SEC, or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K:

Our annual report on Form 10-K for the fiscal year ended December 31, 2012 filed with the SEC on April 16, 2013;

Our quarterly report on Form 10-Q for the quarter ended March 31, 2013 filed with the SEC on May 15, 2013;

Our current report on Form 8-K filed with the SEC on April 19, 2013, and

The description of our common stock set forth in our registration statement on Form 8-A12B, filed with the SEC on June 20, 2007 (File No. 000-12584).

You may obtain, free of charge, a copy of any of these documents (other than exhibits to these documents unless the exhibits are specifically incorporated by reference into these documents or referred to in this prospectus) by writing or calling us at the following address and telephone number:

155 Gibbs Street, Ste. 412
Rockville, Maryland 20850

(734) 332-7800

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14,059,616 Units Each Consisting of

One Share of Common Stock

and

A Warrant to purchase 0.5 shares of Common Stock

PROSPECTUS SUPPLEMENT

William Blair

October 10, 2014

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