

Synthetic Biologics, Inc.
Form 424B5
December 11, 2013

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities became effective under the Securities Act of 1933, as amended. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting an offer to buy these securities, in any jurisdiction where the offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(5)

Registration No. 333-189794

**PRELIMINARY PROSPECTUS SUPPLEMENT SUBJECT TO DATED DECEMBER 11,
COMPLETION 2013**

(To the Prospectus dated July 16, 2013)

Shares

Common Stock

We are offering _____ shares of our common stock, par value \$0.001 per share, pursuant to this prospectus supplement and the accompanying prospectus.

Our common stock is listed on the NYSE MKT under the symbol "SYN." On December 10, 2013, the closing price of our common stock was \$1.35 per share.

As of December , 2013, the aggregate market value of our outstanding common stock held by non-affiliates was approximately \$44,922,912, 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 \$1.64 based on the closing sale price of our common stock on October 22, 2013. We have not offered any securities during the past twelve months pursuant to General Instruction I.B.6 of Form S-3.

Our business and an investment in our common stock involve significant risks. See “Risk Factors” beginning on page S-7 of this prospectus supplement and on page 5 of the accompanying prospectus.

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.

	Per	
	Share	Total
Public offering price	\$	\$
Underwriting discount ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

⁽¹⁾ The underwriters will receive compensation in addition to the underwriting discount. See “Underwriting” beginning on page S-12 of this prospectus supplement for a description of compensation payable to the underwriters.

We have granted a 45-day option to the underwriters solely to cover over-allotments, if any.

The underwriters expect to deliver the shares against payment therefor on or about December , 2013.

Aegis Capital Corp

December , 2013

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PROSPECTUS

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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 underwriters that would permit a public offering of the common stock 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 common stock 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.

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 Quarterly Report on Form 10-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.

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 common stock. 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 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, C. diff) infections: We are in preclinical development with SYN-004, a novel second-generation oral enzyme drug candidate, for co-administration with commonly used IV antibiotics intended to prevent the development of severe effects of *C. diff* infections, the leading cause of hospital acquired infections, that generally occur secondary to treatment with intravenous 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 favorable protection of the gut flora (microbiome) during treatment with certain penicillins, with the potentially added ability 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. Roughly 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. While the final dosing regimen for SYN-004 is yet to be determined, the addressable market is extremely 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 potential multi-billion dollar market.* In October 2013, we initiated manufacturing of SYN-004 material to support our planned preclinical and clinical studies.

*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.

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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 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 United States. 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 United States, Canada and Japan. The

sublicense agreement provides that all ongoing and future development costs are to be 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 United States Food and Drug Administration ("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 United States Based on an estimated annual price of \$1,200 per fibromyalgia patient, we estimate that the total market potential in the United States is \$6 billion.

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

Recent Developments

On December 5, 2013, we, through our newly formed, majority owned subsidiary, Synthetic Biomics, Inc. (“SYN Biomics”), entered into a worldwide exclusive license agreement (the “CSMC License Agreement”) and option agreement (the “CSMC Option Agreement”) with Cedars-Sinai Medical Center (“CSMC”) for the right to develop, manufacture, use, and sell products for the human and veterinary therapeutic and prophylactic treatments for acute and chronic diseases discovered by an investigational team led by Mark Pimentel, M.D. at CSMC to be associated with pathogenic gastrointestinal microorganisms, including for example, irritable bowel syndrome (IBS), obesity and type 2 diabetes. The portfolio of intellectual property licensed to SYN Biomics under the License Agreement includes 9 issued U.S. patents, 1 issued European patent validated in 18 countries, 1 issued European patent validated in 3 countries, 2 issued Australian patents, and 1 issued Japanese patent as well as 13 pending U.S. and international patent applications for most fields of use and modalities (subject to certain agreed-upon exceptions); two pending U.S. patent applications are optioned to SYN Biomics under the Option Agreement.”

The CSMC License Agreement provides that we will issue to CSMC 291,569 unregistered shares of Company common stock, subject to approval by the NYSE MKT, LLC, or in the event such shares are not issued within 30 days, pay to CSMC in the form of cash, an initial license fee and patent reimbursement fee of \$150,000 and \$220,000, respectively. The parties also entered into a Stock Purchase Agreement with respect to such stock issuance and other issuances of our unregistered shares of common stock that may be issued to CSMC in lieu of cash, including license fees, milestone payments expense reimbursements and options fees under the CSMC License Agreement or CSMC Option Agreement. Any and all such stock issuances by us shall be subject to the prior approval of the NYSE MKT, LLC. The CSMC License Agreement also provides that commencing on the second anniversary of the CSMC License Agreement, SYN Biomics will pay an annual maintenance fee, which payment shall be creditable against annual royalty payments owed under the CSMC License Agreement. In addition to royalty payments which are a percentage of Net Sales (as defined in the CSMC License Agreement) of Licensed Products (as defined in the CSMC License Agreement) and Licensed Technology products (as defined in the CSMC License Agreement), SYN Biomics is obligated to pay CMSC a percentage of any non-royalty sublicense revenues as well as additional consideration upon the achievement of the following milestones (the first two of which are payable in cash or our unregistered shares of stock at our option): (i) successful Phase I trial completion of the first Licensed Product or first Licensed Technology Product; (ii) successful Phase II trial completion of the first Licensed Product or first Licensed Technology Product; (iii) initiation of Phase III dosing for each additional indication of a Licensed Product or Licensed Technology Product; (iv) successful Phase III trial completion for each Licensed Product and each Licensed Technology Product; (v) the FDA’s acceptance of a New Drug Application for each Licensed Product and each Licensed Technology Product; (vi) regulatory approval for each Licensed Product and each Licensed Technology Product; and (vii) the first commercial sale of each Licensed Product and each Licensed Technology Product. The stock issuances are subject to prior approval of the NYSE MKT, LLC. The CSMC License Agreement automatically terminates upon the

occurrence of certain events and SYN Biomics has the right to terminate the CSMC License Agreement without cause, upon 6 months notice to CSMC however, upon such termination, SYN Biomics is obligated to pay a termination fee with the amount of such fee reduced: (i) if such termination occurs after an IND submission to the FDA but prior to completion of a Phase II clinical trial; (ii) reduced further if such termination is after completion of Phase II clinical trial but prior to completion of a Phase II clinical trial; and (iii) reduced to zero if such termination occurs after completion of a Phase III clinical trial.

Prior to the execution of the License Agreement, we issued shares of common stock of SYN Biomics to each of CSMC and Mark Pimentel, M.D. (the primary inventor of the intellectual property), representing 11.5% and 8.5%, respectively, of the outstanding shares of SYN Biomics (the "SYN Biomics Shares"). The Stock Purchase Agreements for the SYN Biomics Shares provide for certain anti-dilution protection until such time as an aggregate of \$3,000,000 in proceeds from equity financings are received by SYN Biomics as well as a right, under certain circumstances in the event that the SYN Biomics Shares are not then freely tradeable, and subject to NYSE MKT, LLC approval, as of the 18 and 36 month anniversary date of the effective date of the Stock Purchase Agreements, for each of CSMC and the Mark Pimentel to exchange up to 50% of their SYN Biomics shares for unregistered shares of our common stock, with the rate of exchange based upon the relative contribution of the valuation of SYN Biomics to our public market valuation at the time of each exchange. The Stock Purchase Agreements also provide for tag-along rights in the event of the sale by us of our shares of SYN Biomics.

Pursuant to the terms of the CSMC Option Agreement, SYN Biomics has a period of six months to negotiate an exclusive license to develop, manufacture, use, and sell biologic products relating to the prevention, acute treatment and chronic treatment of irritable bowel syndrome or other indications utilized or derived from certain optioned patent applications pending completion of certain limited testing of technology embodied in the patents applications. The CSMC Option Agreement provides that, within 30 days of the execution of the CSMC Option Agreement, we are obligated to pay to CSMC a non-refundable option fee of 43,342 shares of our unregistered stock, or \$50,000 cash in the event such issuance is not approved by NYSE MKT, LLC. In addition, SYN Biomics has the right to extend the option period for an additional six months, for an additional non-refundable extension fee of \$25,000, payable in our unregistered shares of common stock having a market value of 110% of such amount, subject to approval of NYSE MKT, LLC, or in cash. At any time during the 6 or 12 month option period (if so extended) SYN Biomics has the right to exercise the option and negotiate an exclusive license to be optioned patent applications, which shall provide for (i) a \$50,000 license issue fee plus reimbursement of patent expenses incurred by CSMC prior to the exclusive license payable to CSMC in our unregistered shares of stock having a market value of 110% of such amount, subject to approval of the NYSE MKT, LLC, or in cash, (ii) the same milestone payments, royalties and sublicense fees as are payable under the CSMC License Agreement, and (iii) such other customary terms and conditions CSMC typically includes in its license agreements.

In collaboration with Intrexon Corporation, and partially utilizing the intellectual property optioned or licensed from CSMC described in the CSMC Option Agreement, we and SYN Biomics intend to develop biologic approaches for the prevention, and acute and chronic treatment of a subset of irritable bowel syndrome (IBS) pathologies specifically caused by auto-antibodies. During the option period, we, SYN Biomics and Intrexon will seek to create and test a variety of biologic candidates for the treatment of IBS. This biologic program has been selected as the third target under our exclusive channel collaboration with Intrexon Corporation dated August 6, 2012.

On July 3, 2013, we entered into a Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co. pursuant to which we may offer and sell shares of our common stock in an at-the-market public offering for up to \$15,000,000 of shares of our common stock from time to time through Cantor Fitzgerald & Co., acting as agent (the “ATM”). As of the date of this filing, we have not sold any shares under the ATM. We amended the Controlled Equity OfferingSM Sales Agreement on December 10, 2013 to limit our ability to sell shares of our common stock under such agreement to the lesser of \$15,000,000 or the amount that we can sell under General Instruction I.B.6 of Form S-3, if still applicable, after this offering. We will not use the ATM unless and until we file an updated prospectus supplement reflecting the number or dollar amount of shares which we may sell under the ATM after taking into account the foregoing amendment, but only if such amount is less than \$15,000,000.

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 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 is performing 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 United States 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 United States and for territories outside of the United States (as defined in the Prev Agreement); and (vi) upon BLA approval in the United States and upon approval in territories outside the United States. 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 after the execution of the Prev Agreement, we 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’s 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. During the three month period ended September 30, 2013, the note receivable and associated interest receivable were deemed uncollectible. Accordingly, we recorded bad debt expense of \$763,000.

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.

Corporate 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 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.

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

Common stock offered by us shares of common stock

Common stock to be outstanding after this offering shares of common stock

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, 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, and to fund possible investments in and acquisitions of complementary businesses or partnerships. See "Use of Proceeds" on page S-8.

Risk Factors See "Risk Factors" beginning on page S-7 of 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.

NYSE MKT symbol SYN

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

- based on 44,654,414 shares outstanding on December 10, 2013;

• assumes no exercise by the underwriters of their over-allotment option to purchase up to an additional shares to cover over-allotments, if any;

• excludes 3,879,580 shares of our common stock subject to options outstanding as of December 10, 2013 having a weighted-average exercise price of \$1.79 per share;

• excludes 4,107,321 shares of our common stock that have been reserved for issuance in connection with future grants under our stock option plans as of December 10, 2013; and

• excludes 1,632,501 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of December 10, 2013 having a weighted-average exercise price of \$1.99 per share.

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Unless otherwise stated, all information contained in this prospectus reflects an assumed public offering price of \$ per share, which was the closing price of our common stock on the NYSE MKT on December , 2013.

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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, 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, (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.

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, 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, and to fund possible investments in and acquisitions of complementary businesses or partnerships. 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 common stock 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 share 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 shares of common stock in this offering at a public offering price of \$ per share, after deducting the estimated underwriting discount and estimated offering expenses payable by us, you will experience immediate dilution of approximately

\$ per share (or immediate dilution of approximately \$ per share if the underwriters exercise in full their option to purchase additional shares in this offering), representing the difference between our as adjusted net tangible book value per share as of September 30, 2013 after giving effect to this offering and the public offering price. 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 44,654,414 shares of our common stock outstanding as of December 10, 2013. As of that date, stock options and warrants outstanding represented 5,512,081 shares of our common stock that could be issued in the future. 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.

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USE OF PROCEEDS

We estimate that the net proceeds of this offering, after deducting the underwriting discount and the estimated offering expenses payable by us, will be approximately \$ million (or approximately \$ million if the underwriters exercise the over-allotment option in full).

We intend to use the net proceeds, if any, from this offering 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.

DILUTION

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

Our net tangible book value on September 30, 2013 was approximately \$6.4 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 \$ million of common stock in this offering at an assumed offering price of \$ per share, which was the closing price of our common stock as reported on NYSE MKT on , 2013, and after deducting estimated offering commissions and expenses payable by us, our as adjusted net tangible book value as of September 30, 2013 would have been approximately \$ million, or \$ per share of common stock. This represents an immediate increase in net tangible book value of \$ per share to our existing stockholders and an immediate dilution in net tangible book value of \$ per share to investors participating in this offering. The following table illustrates this dilution per share to investors participating in this offering:

Assumed offering price per share	\$
Net tangible book value per share as of September 30, 2013	\$
Increase in net tangible book value per share attributable to new investors in offering	\$
As adjusted net tangible book value per share after giving effect to the offering	\$
Dilution per share to new investors	\$

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 shares of our common stock issued and outstanding as of September 30, 2013, which does not include the following, all as of September 30, 2013:

- 3,804,580 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of \$1.79 per share;

- 1,182,321 shares of common stock which were reserved for future equity awards that may be granted in the future under our equity incentive plans; and

- 1,632,501 shares of our common stock reserved for issuance upon the exercise of outstanding warrants, each with a weighted-average exercise price of \$1.99 per share.

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

The information above assumes that the underwriters do not exercise their over-allotment option. If the underwriters exercise their over-allotment option in full, the as adjusted net tangible book value will increase to \$ per share, representing an immediate increase in as adjusted net tangible book value of \$ per share to our existing stockholders and an immediate dilution in net tangible book value of \$ per share to investors participating in this offering.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain our future earnings, if any, for use in our business and therefore do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs.

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CAPITALIZATION

The following table sets forth our capitalization as of September 30, 2013:

• on an actual basis, without giving effect to this offering and the use of net proceeds as discussed in “Use of Proceeds;”

- on an as adjusted basis to reflect this offering and the use of net proceeds as discussed in “Use of Proceeds.”

This capitalization table should be read in conjunction with management's discussion and analysis of results of operations and our consolidated financial statements and related notes included in our annual report on Form 10-K for the year ended December 31, 2012 and in our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2013, June 30, 2013 and September 30, 2013, and the other financial information included and incorporated by reference in this prospectus supplement.

	(in thousands)	
	As of September 30, 2013	
	Actual	As Adjusted
Cash	\$ 5,145	
Stockholders' equity:		
Preferred stock, par value \$0.001, 10,000,000 shares authorized, none issued and outstanding	\$ -	
Common stock, par value \$0.001, 100,000,000 shares authorized, 44,735,896 issued and 44,654,414 shares outstanding, actual and shares issued and outstanding, as adjusted ⁽¹⁾	\$ 45	
Additional paid-in capital	\$ 83,358	
Accumulated deficit	\$ (77,034)
Total stockholders' equity	\$ 6,369	
Total capitalization	\$ 6,369	

(1) Outstanding shares of common stock as of September 30, 2013 excludes:

• 3,804,580 shares issuable upon the exercise of outstanding stock options with a weighted average exercise price of \$1.79 per share;

- 1,182,321 shares of common stock which were reserved for future equity awards that may be granted in the future under our equity incentive plans;

- 1,632,501 shares of common stock reserved for issuance upon the exercise of outstanding warrants, each with a weighted average exercise price of \$1.99 per share; and

- the underwriters' over-allotment option.

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UNDERWRITING

Aegis Capital Corp. is acting as the representative of the underwriters of the offering. We have entered into an underwriting agreement, dated December 11, 2013, with the representative. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to each underwriter named below and each underwriter named below has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

Underwriter	Number of Shares
Aegis Capital Corp.	
Total	

The underwriters are committed to purchase all the shares of common stock offered by us other than those covered by the option to purchase additional shares described below. The obligations of the underwriters may be terminated upon the occurrence of certain events specified in the underwriting agreement. Furthermore, pursuant to the underwriting agreement, the underwriters' obligations are subject to customary conditions, representations and warranties contained in the underwriting agreement, such as receipt by the underwriters of officers' certificates and legal opinions.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act of 1933, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

The underwriters propose to offer the shares offered by us to the public at the public offering price set forth on the cover of this prospectus supplement. In addition, the underwriters may offer some of the shares to other securities dealers at such price less a concession of \$ per share. After the initial offering, the public offering price and concession to dealers may be changed.

We have granted the underwriters an over-allotment option. This option, which is exercisable for up to forty-five (45) days after the date of this prospectus, permits the underwriters to purchase a maximum of _____ additional shares from us. If the underwriters exercise all or part of this option, they will purchase shares covered by the option at the public

offering price that appears on the cover page of this prospectus supplement, less the underwriting discount. If this option is exercised in full, the total price to the public will be approximately \$ and the total proceeds to us, before expenses, will be approximately \$.

Discounts and Commissions. The following table shows the public offering price, underwriting discount and proceeds, before expenses, to us. The information assumes either no exercise or full exercise by the underwriters of their option.

	Per Share	Total Without Option	Total With Option
Public offering price	\$	\$	\$
Underwriting discount (6.5%)	\$	\$	\$
Non-accountable expense allowance (1%) ⁽¹⁾	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

(1) The expense allowance of 1% is not payable with respect to the shares sold upon exercise of the underwriters' over-allotment option.

Griffin Securities, Inc. ("Griffin") is acting as a financial advisor in connection with this offering and will be paid fees out of the underwriting commission of up to a maximum of \$140,000; provided, however, that Griffin's compensation will be reduced pro rata to the extent the aggregate gross proceeds to us in the offering are less than \$10 million (*i.e.*, Griffin shall be entitled to receive 21.54% of the aggregate underwriting discount or spread); provided, further, however, that Griffin's compensation shall be reduced by its pro rata portion (*i.e.*, 21.54%) of the underwriters' reasonably incurred expenses of the offering, including, but not limited to, the reasonable fees and expenses of counsel to the underwriters in an amount not to exceed \$10,000. In August 2012, as amended in December 2012, we entered into an agreement with Griffin, terminable by either party upon thirty (30) days prior written notice, pursuant to which Griffin acts as an advisor to us and is paid a monthly fee of \$10,000 for such services.

We have paid an expense deposit of \$25,000 to the representative, which will be applied against the accountable expenses that will be paid by us to the representative in connection with this offering. The underwriting agreement provides that in the event the offering is terminated, the \$25,000 expense deposit paid to the representative will be returned to us to the extent that offering expenses are not actually incurred by the representative.

We have agreed to pay certain of the underwriters' expenses relating to the offering, including (a) all fees incurred in clearing this offering with FINRA; (b) all fees, expenses and disbursements relating to the registration, qualification or exemption of securities offered under the securities laws of such foreign jurisdictions as the underwriters may reasonably designate; (c) the fees and expenses of counsel to the underwriters not to exceed \$25,000; (d) \$21,775 for the underwriters' use of Ipreo's book-building, prospectus tracking and compliance software for this offering; and (e) up to \$10,000 of the representative's actual accountable road show expenses for the offering. The total of any advanced payments will be refundable to the extent not actually incurred in compliance with FINRA Rule 5110(f)(2)(C).

We estimate that the total expenses of the offering payable by us, excluding the underwriting discount and expense reimbursement, will be approximately \$100,000.

Discretionary Accounts. The underwriters do not intend to confirm sales of the securities offered hereby to any accounts over which they have discretionary authority.

Lock-Up Agreements. Each of our directors and executive officers, subject to certain exceptions, have agreed with the underwriter not to dispose of or hedge any of our shares of common stock or securities convertible into or exercisable or exchangeable for common stock for ninety (90) days after the date of this prospectus supplement without first obtaining the written consent of Aegis Capital Corp., other than the issuance of common stock pursuant to the valid exercises, vesting or settlements of options, warrants or rights outstanding on the date hereof.

Any of the securities subject to the lock-up agreement may be released in whole or part from the terms thereof only upon the approval of the representative; provided, however, that we must announce any such release through a major news service and such release will only be effective two business days after the publication date of such press release.

Electronic Offer, Sale and Distribution Shares. A prospectus supplement in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectus supplements electronically. The representative may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus supplement in electronic format, the information on these websites is not part of this prospectus

supplement or the registration statement of which this prospectus supplement forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees; however, except as disclosed in this prospectus supplement, we have no present arrangements with any of the underwriters for any further services.

Stabilization. In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

Stabilizing transactions permit bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the shares while the offering is in progress.

Overallotment transactions involve sales by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase pursuant to their option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares pursuant to their option to purchase additional shares. The underwriters may close out any short position by exercising their option to purchase additional shares and/or purchasing shares in the open market.

Syndicate covering transactions involve purchases of shares in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of their option to purchase additional shares. If the underwriters sell more shares than could be covered by exercise of the option to purchase additional shares and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.

Penalty bids permit the representative to reclaim a selling concession from a syndicate member when the shares originally sold by that syndicate member are purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our shares or common stock or preventing or retarding a decline in the market price of our shares or common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on the NYSE MKT, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive market making. In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the NYSE MKT in accordance with Rule 103 of Regulation M under the Exchange Act, during a period before the commencement of offers or sales of the shares and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Offer restrictions outside the United States

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in

which such an offer or a solicitation is unlawful.

Australia

This prospectus supplement is not a disclosure document under Chapter 6D of the Australian Corporations Act, has not been lodged with the Australian Securities and Investments Commission and does not purport to include the information required of a disclosure document under Chapter 6D of the Australian Corporations Act. Accordingly, (i) the offer of the common stock under this prospectus supplement is only made to persons to whom it is lawful to offer the common stock without disclosure under Chapter 6D of the Australian Corporations Act under one or more exemptions set out in section 708 of the Australian Corporations Act, (ii) this prospectus is made available in Australia only to those persons as set forth in clause (i) above, and (iii) the offeree must be sent a notice stating in substance that by accepting this offer, the offeree represents that the offeree is such a person as set forth in clause (i) above, and, unless permitted under the Australian Corporations Act, agrees not to sell or offer for sale within Australia any of the common stock sold to the offeree within twelve (12) months after its transfer to the offeree under this prospectus supplement.

China

The information in this document does not constitute a public offer of the common stock, whether by way of sale or subscription, in the People's Republic of China (excluding, for purposes of this paragraph, Hong Kong Special Administrative Region, Macau Special Administrative Region and Taiwan). The common stock may not be offered or sold directly or indirectly in the PRC to legal or natural persons other than directly to “qualified domestic institutional investors.”

European Economic Area-Belgium, Germany, Luxembourg and Netherlands

The information in this document has been prepared on the basis that all offers of common stock will be made pursuant to an exemption under the Directive 2003/71/EC (“Prospectus Directive”), as implemented in Member States of the European Economic Area (each, a “Relevant Member State”), from the requirement to produce a prospectus for offers of securities.

An offer to the public of common stock has not been made, and may not be made, in a Relevant Member State except pursuant to one of the following exemptions under the Prospectus Directive as implemented in that Relevant Member State:

- (a) to legal entities that are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;

- (b) to any legal entity that has two or more of (i) an average of at least 250 employees during its last fiscal year; (ii) a total balance sheet of more than €43,000,000 (as shown on its last annual unconsolidated or consolidated financial statements) and (iii) an annual net turnover of more than €50,000,000 (as shown on its last annual unconsolidated or consolidated financial statements);

- (c) to fewer than 100 natural or legal persons (other than qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive) subject to obtaining the prior consent of the Company or any underwriter for any such offer; or

- (d) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of common stock shall result in a requirement for the publication by the Company of a prospectus pursuant to Article 3 of the Prospectus Directive.

France

This document is not being distributed in the context of a public offering of financial securities (*offre au public de titres financiers*) in France within the meaning of Article L.411-1 of the French Monetary and Financial Code (*Code monétaire et financier*) and Articles 211-1 et seq. of the General Regulation of the French *Autorité des marchés*

financiers (“AMF”). The common stock has not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France.

This document and any other offering material relating to the common stock have not been, and will not be, submitted to the AMF for approval in France and, accordingly, may not be distributed or caused to be distributed, directly or indirectly, to the public in France.

Such offers, sales and distributions have been and shall only be made in France to (i) qualified investors (*investisseurs qualifiés*) acting for their own account, as defined in and in accordance with Articles L.411-2-II-2° and D.411-1 to D.411-3, D. 744-1, D.754-1 and D.764-1 of the French Monetary and Financial Code and any implementing regulation and/or (ii) a restricted number of non-qualified investors (*cercle restreint d'investisseurs*) acting for their own account, as defined in and in accordance with Articles L.411-2-II-2° and D.411-4, D.744-1, D.754-1 and D.764-1 of the French Monetary and Financial Code and any implementing regulation.

Pursuant to Article 211-3 of the General Regulation of the AMF, investors in France are informed that the common stock cannot be distributed (directly or indirectly) to the public by the investors otherwise than in accordance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 to L.621-8-3 of the French Monetary and Financial Code.

Ireland

The information in this document does not constitute a prospectus under any Irish laws or regulations and this document has not been filed with or approved by any Irish regulatory authority as the information has not been prepared in the context of a public offering of securities in Ireland within the meaning of the Irish Prospectus (Directive 2003/71/EC) Regulations 2005 (the “Prospectus Regulations”). The common stock has not been offered or sold, and will not be offered, sold or delivered directly or indirectly in Ireland by way of a public offering, except to (i) qualified investors as defined in Regulation 2(1) of the Prospectus Regulations and (ii) fewer than 100 natural or legal persons who are not qualified investors.

Israel

The common stock offered by this prospectus supplement has not been approved or disapproved by the Israeli Securities Authority, or "ISA," nor has such common stock been registered for sale in Israel. The shares may not be offered or sold, directly or indirectly, to the public in Israel, absent the publication of a prospectus. The ISA has not issued permits, approvals or licenses in connection with the offering or publishing the prospectus supplement; nor has it authenticated the details included herein, confirmed their reliability or completeness, or rendered an opinion as to the quality of the common stock being offered. Any resale in Israel, directly or indirectly, to the public of the common stock offered by this prospectus supplement is subject to restrictions on transferability and must be effected only in compliance with the Israeli securities laws and regulations.

Italy

The offering of the common stock in the Republic of Italy has not been authorized by the Italian Securities and Exchange Commission (*Commissione Nazionale per le Società e la Borsa*, "CONSOB") pursuant to the Italian securities legislation and, accordingly, no offering material relating to the common stock may be distributed in Italy and such securities may not be offered or sold in Italy in a public offer within the meaning of Article 1.1(t) of Legislative Decree No. 58 of 24 February 1998 ("Decree No. 58"), other than:

to Italian qualified investors, as defined in Article 100 of Decree no. 58 by reference to Article 34-ter of CONSOB Regulation no. 11971 of 14 May 1999 ("Regulation no. 11971") as amended ("Qualified Investors"); and

in other circumstances that are exempt from the rules on public offer pursuant to Article 100 of Decree No. 58 and Article 34-ter of Regulation No. 11971 as amended.

Any offer, sale or delivery of the common stock or distribution of any offer document relating to the common stock in Italy (excluding placements where a Qualified Investor solicits an offer from the issuer) under the paragraphs above must be:

made by investment firms, banks or financial intermediaries permitted to conduct such activities in Italy in accordance with Legislative Decree No. 385 of 1 September 1993 (as amended), Decree No. 58, CONSOB Regulation No. 16190 of 29 October 2007 and any other applicable laws; and

- in compliance with all relevant Italian securities, tax and exchange controls and any other applicable laws.

Any subsequent distribution of the common stock in Italy must be made in compliance with the public offer and prospectus requirement rules provided under Decree No. 58 and the Regulation No. 11971 as amended, unless an exception from those rules applies. Failure to comply with such rules may result in the sale of such common stock being declared null and void and in the liability of the entity transferring the common stock for any damages suffered by the investors.

Japan

The common stock have not been and will not be registered under Article 4, paragraph 1 of the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948), as amended (the “FIEL”) pursuant to an exemption from the registration requirements applicable to a private placement of securities to Qualified Institutional Investors (as defined in and in accordance with Article 2, paragraph 3 of the FIEL and the regulations promulgated thereunder). Accordingly, the common stock may not be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan other than Qualified Institutional Investors. Any Qualified Institutional Investor who acquires common stock may not resell them to any person in Japan that is not a Qualified Institutional Investor, and acquisition by any such person of common stock is conditional upon the execution of an agreement to that effect.

Portugal

This document is not being distributed in the context of a public offer of financial securities (*oferta pública de valores mobiliários*) in Portugal, within the meaning of Article 109 of the Portuguese Securities Code (*Código dos Valores Mobiliários*). The common stock has not been offered or sold and will not be offered or sold, directly or indirectly, to the public in Portugal. This document and any other offering material relating to the common stock have not been, and will not be, submitted to the Portuguese Securities Market Commission (*Comissão do Mercado de Valores Mobiliários*) for approval in Portugal and, accordingly, may not be distributed or caused to be distributed, directly or indirectly, to the public in Portugal, other than under circumstances that are deemed not to qualify as a public offer under the Portuguese Securities Code. Such offers, sales and distributions of common stock in Portugal are limited to persons who are “qualified investors” (as defined in the Portuguese Securities Code). Only such investors may receive this document and they may not distribute it or the information contained in it to any other person.

Sweden

This document has not been, and will not be, registered with or approved by Finansinspektionen (the Swedish Financial Supervisory Authority). Accordingly, this document may not be made available, nor may the common stock be offered for sale in Sweden, other than under circumstances that are deemed not to require a prospectus under the Swedish Financial Instruments Trading Act (1991:980) (Sw. lag (1991:980) *om handel med finansiella instrument*)). Any offering of common stock in Sweden is limited to persons who are “qualified investors” (as defined in the Financial Instruments Trading Act). Only such investors may receive this document and they may not distribute it or the information contained in it to any other person.

Switzerland

The common stock may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (“SIX”) or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering material relating to the common stock may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering material relating to the common stock have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of common stock will not be supervised by, the Swiss Financial Market Supervisory Authority.

This document is personal to the recipient only and not for general circulation in Switzerland.

United Arab Emirates

Neither this document nor the common stock has been approved, disapproved or passed on in any way by the Central Bank of the United Arab Emirates or any other governmental authority in the United Arab Emirates, nor has the Company received authorization or licensing from the Central Bank of the United Arab Emirates or any other governmental authority in the United Arab Emirates to market or sell the common stock within the United Arab Emirates. This document does not constitute and may not be used for the purpose of an offer or invitation. No services relating to the common stock, including the receipt of applications and/or the allotment or redemption of such shares,

may be rendered within the United Arab Emirates by the Company.

No offer or invitation to subscribe for common stock is valid or permitted in the Dubai International Financial Centre.

United Kingdom

Neither the information in this document nor any other document relating to the offer has been delivered for approval to the Financial Services Authority in the United Kingdom and no prospectus (within the meaning of section 85 of the Financial Services and Markets Act 2000, as amended (“FSMA”)) has been published or is intended to be published in respect of the common stock. This document is issued on a confidential basis to “qualified investors” (within the meaning of section 86(7) of FSMA) in the United Kingdom, and the common stock may not be offered or sold in the United Kingdom by means of this document, any accompanying letter or any other document, except in circumstances which do not require the publication of a prospectus pursuant to section 86(1) FSMA. This document should not be distributed, published or reproduced, in whole or in part, nor may its contents be disclosed by recipients to any other person in the United Kingdom.

Any invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) received in connection with the issue or sale of the common stock has only been communicated or caused to be communicated and will only be communicated or caused to be communicated in the United Kingdom in circumstances in which section 21(1) of FSMA does not apply to the Company.

In the United Kingdom, this document is being distributed only to, and is directed at, persons (i) who have professional experience in matters relating to investments falling within Article 19(5) (investment professionals) of the Financial Services and Markets Act 2000 (Financial Promotions) Order 2005 (“FPO”); (ii) who fall within the categories of persons referred to in Article 49(2)(a) to (d) (high net worth companies, unincorporated associations, etc.) of the FPO; or (iii) to whom it may otherwise be lawfully communicated (together “relevant persons”). The investments to which this document relates are available only to, and any invitation, offer or agreement to purchase will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

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. Certain legal matters in connection with this offering will be passed upon for the underwriters by Reed Smith LLP, New York, New York.

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 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, 2012 filed with the SEC on April 16, 2013;

Our quarterly reports on Form 10-Q for the quarters ended March 31, 2013, June 30, 2013 and September 30, 2013 filed with the SEC on May 15, 2013, August 14, 2013 and November 14, 2013, respectively;

Our current reports on Form 8-K filed with the SEC on April 19, 2013, October 15, 2013, October 25, 2013 and December 10, 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).

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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:

155 Gibbs Street, Ste. 412
Rockville, Maryland 20850

(734) 332-7800

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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 underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, 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).

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, 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 underwriters, 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 Securities Exchange Act of 1934 as amended, or 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 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.

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 underwriters 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.

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 an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter 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 underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters 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 underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters 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 underwriters, 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, underwriters 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 underwriters 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 an underwriter 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 underwriters, 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 underwriters, 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:

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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

Shares

Common Stock

PROSPECTUS SUPPLEMENT

Aegis Capital Corp

December , 2013