

Synthetic Biologics, Inc.
Form 424B5
July 15, 2015

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. 333-203322

SUBJECT TO COMPLETION, DATED JULY 15, 2015

Preliminary Prospectus Supplement

(To Prospectus dated April 20, 2015)

Common Stock

We are offering _____ shares of our common stock pursuant to this prospectus supplement and the accompanying prospectus.

Our common stock is listed on the NYSE MKT under the symbol "SYN." On July 14, 2015, the closing price of our common stock was \$4.00 per share.

Investing in our common stock involve significant risks. See “Risk Factors” beginning on page S-5 of this prospectus supplement and on page 6 of the accompanying prospectus.

	Per Share	Total
Public Offering Price	\$	\$
Underwriting Discount ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

⁽¹⁾ See “Underwriting” beginning on page S-10 of this prospectus supplement for a description of compensation payable to the underwriters.

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.

We have granted the underwriters a 30-day option to purchase up to additional shares of common stock at the public offering price, less the underwriting discount, to cover over-allotments, if any.

The underwriters expect to deliver the shares against payment therefor on or about July , 2015.

Joint Book-Running Managers

William Blair RBC Capital Markets

BTIG

July , 2015

TABLE OF CONTENTS

	<u>Page</u>
PROSPECTUS SUPPLEMENT	
<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	ii
<u>INDUSTRY AND MARKET DATA</u>	ii
<u>PROSPECTUS SUPPLEMENT SUMMARY</u>	S-1
<u>THE OFFERING</u>	S-4
<u>RISK FACTORS</u>	S-5
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	S-6
<u>USE OF PROCEEDS</u>	S-7
<u>DIVIDEND POLICY</u>	S-7
<u>CAPITALIZATION</u>	S-8
<u>DILUTION</u>	S-9
<u>UNDERWRITING</u>	S-10
<u>LEGAL MATTERS</u>	S-13
<u>EXPERTS</u>	S-13
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	S-13
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	S-13
 <u>PROSPECTUS</u>	
<u>ABOUT THIS PROSPECTUS</u>	3
<u>PROSPECTUS SUMMARY</u>	3
<u>RISK FACTORS</u>	6
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	7
<u>USE OF PROCEEDS</u>	8
<u>DIVIDEND POLICY</u>	8
<u>DESCRIPTION OF CAPITAL STOCK</u>	9
<u>DESCRIPTION OF WARRANTS</u>	9
<u>DESCRIPTION OF UNITS</u>	10
<u>PLAN OF DISTRIBUTION</u>	11
<u>LEGAL MATTERS</u>	13
<u>EXPERTS</u>	13
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	13
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	13
<u>DISCLOSURE OF THE SECURITIES AND EXCHANGE COMMISSION POSITION ON</u>	
<u>INDEMNIFICATION FOR SECURITIES ACT LIABILITIES</u>	14

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.

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 microbiome-focused, clinical-stage company developing therapeutics to protect the microbiome while targeting pathogen-specific diseases. Our lead candidates in Phase 2 development include SYN-004 which is designed to protect the gut microbiome (gastrointestinal (GI) microflora) from the effects of certain commonly used intravenous (IV) antibiotics for the prevention of *C. difficile* infection and antibiotic-associated diarrhea (AAD), and SYN-010 which is intended to reduce the impact of methane producing organisms in the gut microbiome to treat the underlying cause of irritable bowel syndrome with constipation (IBS-C). In addition, we are developing a Phase 2 oral estriol drug, Trimesta, for the treatment of relapsing-remitting multiple sclerosis (MS) and cognitive dysfunction in MS, and a monoclonal antibody combination for the treatment of Pertussis in collaboration with Intrexon Corporation (NYSE:XON).

Product Pipeline:

Summary of Pathogen-Specific Therapy Programs:

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

beta-lactam antibiotics. Beta-lactam antibiotics are a mainstay in hospital infection management and include the commonly used penicillin and cephalosporin classes of antibiotics. SYN-004's target market is significant and represented by annual U.S. hospitals purchases of approximately 118 million doses of IV beta-lactam antibiotics which are administered to approximately 14 million patients.* Currently there are no approved treatments designed to protect the gut microbiome from the damaging effects of IV antibiotics. This worldwide market could represent a multi-billion dollar opportunity for us. In November 2014, the U.S. Patent and Trademark Office (USPTO) issued Patent No. 8,894,994 that has claims to compositions of matter and pharmaceutical compositions of beta-lactamases, including SYN-004, and carries a patent term to at least 2031. We also have an extensive patent estate on other aspects of this program which includes patent applications that could carry a term to at least 2035. In the fourth quarter of 2014, we initiated our randomized, double-blind placebo-controlled Phase 1a clinical trial, reported positive topline safety and tolerability results from the Phase 1a clinical trial, and initiated the Phase 1b clinical trial evaluating multiple ascending doses of SYN-004. In February 2015, we reported positive topline results from the Phase 1b clinical trial of escalating doses of oral SYN-004, with no safety or tolerability issues reported at dose levels and dose regimens both meeting and exceeding those expected to be studied in upcoming clinical trials. In March 2015, we reported positive pharmacokinetics data from both Phase 1 clinical trials, with supportive evidence that SYN-004 should have no effect on the IV antibiotic in the bloodstream, allowing the antibiotic to fight the primary infection. In March 2015, we also initiated a Phase 2a clinical trial to evaluate the GI antibiotic-degrading effects and the safety of SYN-004. In June 2015, the first participant was dosed in a second Phase 2a clinical trial of SYN-004, to evaluate the GI antibiotic-degrading effects and the safety of SYN-004, in the presence of the proton pump inhibitor (PPI), esomeprazole. Topline data is expected from the first Phase 2a clinical trial during the third quarter of 2015, and from the second Phase 2a clinical trial during the second half of 2015. In July 2015, we reported data from the first four of 12 expected participants in the first Phase 2a open-label clinical trial; the data showed that SYN-004 degraded IV ceftriaxone in the chyme of the four healthy participants with functioning ileostomies without affecting the ceftriaxone in the bloodstream. The initiation of a Phase 2b proof-of-concept clinical trial of SYN-004 is expected in the third quarter of 2015. This randomized, placebo-controlled clinical trial is expected to enroll approximately 370 patients at up to 75 global clinical sites. Phase 2b interim results are anticipated during the second half of 2015. The initiation of pivotal Phase 3 clinical trial(s) are anticipated during 2016.

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

IBS-C: In December 2013, through our majority-owned subsidiary, Synthetic Biomics, Inc., we entered into a worldwide exclusive license agreement with Cedars-Sinai Medical Center (CSMC) for the right to develop products for therapeutic and prophylactic treatments of acute and chronic diseases, including the development of SYN-010 to target IBS-C. SYN-010 is our proprietary modified-release formulation of the classic statin, lovastatin, that is intended to reduce methane-production by certain microorganisms (*M. smithii*) in the gut while minimizing disruption to the microbiome. SYN-010 is intended to act primarily in the intestinal lumen while avoiding systemic absorption, thereby targeting the cause of IBS-C, not just the symptoms. An investigational team led by Mark Pimentel, M.D. at CSMC discovered that SYN-010 may reduce the production of methane gas by certain gastrointestinal (GI) microorganisms. Methane produced by these organisms is perceived as an underlying cause of pain, bloating, and constipation associated with IBS-C, and may contribute to the pathology of other diseases. In May 2015, preclinical results were presented in a poster at Digestive Disease Week® (DDW) 2015 demonstrating that lovastatin prevented proliferation of methanogens in the small intestines of rats with minimal impact on remaining microbiome. In his practice, Dr. Pimentel translated the use of statins to reduce methane in humans by evaluating commercial lovastatin formulations in select IBS-C patients, demonstrating that lovastatin prevented methane production by methanogens in human stool. Using stringent disease diagnosis criteria to ensure market relevance and a population most likely to receive a diagnosis and prescription drug treatment, there are an estimated 40.7 million cases of IBS reported in the U.S., Europe and Japan, and it has been reported that up to 20 percent of all IBS patients have IBS-C. The estimated global sales for IBS therapeutics for 2015 are \$669.3 million, and global sales are expected to be greater than \$1.5 billion in 2023*. A 505(b)(2) regulatory pathway is anticipated for the development of SYN-010. We licensed an intellectual property portfolio from CSMC including granted use patents and pending patent applications for SYN-010. Additional worldwide patent filings having composition of matter claims, which were recently filed by CSMC and licensed to us, could extend patent protection of SYN-010 to 2035. Our Investigational New Drug (IND) application was submitted to the U.S. Food and Drug Administration (FDA) in May 2015. In June 2015, we initiated our first Phase 2 placebo-controlled clinical trial of SYN-010. This clinical trial is expected to enroll approximately 60 patients who will be randomly assigned in a 1:1:1 ratio to one of three groups, including two different SYN-010 dose groups and a placebo group. Patients are scheduled to receive single oral doses of SYN-010 each day for 28 days. The primary objective of this clinical trial is to evaluate the change from baseline in breath methane, as determined by a lactulose breath test, in methane-positive patients with IBS-C after seven days of treatment with one of two formulations of SYN-010 compared with placebo. Secondary endpoints include Improvement in the number of complete spontaneous bowel movements (CSBM) per week, and improvement in abdominal pain and bloating per standard scales required per U.S. Food and Drug Administration (FDA) guidance. We anticipate reporting topline results from the first Phase 2 clinical trial during the second half of 2015. We also anticipate initiating the second Phase 2 “SYN-010 only” clinical trial during the second half of 2015, with topline results from this trial expected during the first half of 2016. The primary endpoint of the second Phase 2 is to evaluate the ability of SYN-010 to sustain the reduction in breath methane levels, and secondary endpoints include evaluating pain, bloating and CSBM. The initiation of pivotal Phase 3 clinical trial(s) are anticipated during 2016.

* GlobalData, Irritable Bowel Syndrome - Global Drug Forecast and Market Analysis to 2023, December 2014

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

worldwide, primarily among unvaccinated infants. Positive preclinical research findings for SYN-005 were reported in April 2014, and again in September 2014, for our proprietary mAb combination therapy for treating Pertussis, in non-human primate studies. In September 2014 we received a U.S. Orphan Drug designation for SYN-005 for the treatment of Pertussis. In April 2015, positive preclinical findings were reported in poster two posters at ECCMID 2015 (European Congress of Clinical Microbiology and Infectious Diseases). We intend to seek non-dilutive funding to support preclinical and clinical development of SYN-005 for prophylaxis and treatment of Pertussis, including the anticipated filing of an IND application and the anticipated initiation of a Phase 1 clinical trial.

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

Summary of Multiple Sclerosis Program:

Relapsing-Remitting MS: We have licensed issued method of treatment patents in the U.S. for MS therapy with estriol and estriol combination therapies (including estriol with Copaxone®) from University of California, Los Angeles (UCLA). In April 2014, positive Phase 2 topline efficacy and safety results was presented by the lead principal investigator of the UCLA Phase 2 investigator initiated randomized (n=158) double-blinded placebo trial which evaluated our drug candidate, Trimesta, in woman with relapsing remitting MS at 16 sites in the U.S. In September 2014, the lead principal investigator presented additional Phase 2 clinical outcome data, including more detailed results on improvements in cognitive and disability measures, at the 2014 Joint Americas and European Committees for Treatment and Research in Multiple Sclerosis Meeting (ACTRIMS-ECTRIMS) in Boston. The data as reported by the lead principal investigator for the UCLA-led Phase 2 study supported the potential of Trimesta to have a novel dual mechanism of action for both the anti-inflammatory effects that improve relapse rate, and a neuroprotective effect that improves standard measures of disability and cognition. Numerous new provisional patent applications have been filed based on the Phase 2 clinical results. This investigator-initiated Phase 2 clinical trial was supported by grants exceeding \$8 million, awarded primarily by the National Multiple Sclerosis Society (NMSS) in partnership with the NMSS's Southern California chapter, and the National Institutes of Health. Annual worldwide sales of MS therapies are forecasted to be approximately \$17.8 billion in 2019. In June 2015, we were informed by UCLA that MRI analyses are ongoing to evaluate changes in the brain that correlate with improvements seen in clinical outcomes, and we expect to report topline MRI data 30 days following our receipt of this data from UCLA. We continue to engage the neurology community and potential strategic partners, as we determine next steps for Trimesta.

Cognitive Dysfunction in MS: Trimesta is also being developed for the treatment of cognitive dysfunction in female MS patients. This 12-month, UCLA-led, randomized, double-blind, placebo-controlled investigator-initiated Phase 2 clinical trial is being conducted at four sites in the United States. The primary endpoint is the effect on cognitive function as assessed by Paced Auditory Serial Addition Test (PASAT). Patient enrollment is ongoing. The majority of the costs of this trial are being funded by grants from foundations and charitable organizations through direct funding to the lead principal investigator and we have pledged approximately \$500,000 to UCLA to partially fund this trial, payable over three years. An estimated 50 - 65% of MS patients are expected to develop disabilities due to cognitive dysfunction and there is currently no approved treatment for this indication.

Since our inception in January 2001, our efforts and resources have been focused primarily on acquiring and developing our product candidates, our clinical trials, raising capital, manufacturing and recruiting personnel. To date, we have financed our operations primarily through public and private sales of our common stock, and we expect to continue to seek to obtain the required capital in a similar manner. We have incurred an accumulated deficit of \$113.4 million through March 31, 2015. We cannot provide any assurance that we will be able to achieve profitability on a sustained basis, if at all, obtain the required funding, obtain the required regulatory approvals, or complete additional corporate partnering or acquisition transactions.

Company History

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

Corporate Information

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

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

S-3

Edgar Filing: Synthetic Biologics, Inc. - Form 424B5

7,913,587 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of July 13, 2015 having a weighted-average exercise price of \$1.79 per share.

S-4

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, 2014, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, (the “Exchange Act”), each of which is incorporated by reference in this prospectus supplement in its entirety, together with other information in this prospectus supplement and the accompanying prospectus, and the information and documents incorporated by reference in this prospectus supplement, the accompanying 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, clinical trials 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; and intellectual property, however, we have no current commitments or obligations to do so. 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 the 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, representing the difference between our as adjusted net tangible book value per share as of March 31, 2015 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 73,179,305 shares of our common stock outstanding as of July 13, 2015. As of that date, stock options and warrants outstanding represented 15,381,349 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.

S-5

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

All forward-looking statements involve inherent risks and uncertainties, and there are or will be important factors that could cause actual results to differ materially from those indicated in these statements. We believe that these factors include, but are not limited to, those factors set forth under the caption “Risk Factors” in this prospectus supplement and in the accompanying prospectus and under the captions “Risk Factors,” “Business,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” in our most recent Annual Report on Form 10-K and our subsequent Quarterly Reports on 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.

USE OF PROCEEDS

We intend to use the net proceeds from this offering for general corporate purposes, which may include, among other things, payment of general and administrative expenses and accounts payable, increasing our working capital and funding research and development, clinical trials 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, and intellectual property, 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 currently do not plan to declare dividends on shares of our common stock in the foreseeable future. We expect to retain all future earnings, if any, for use in the operation and expansion of our business. The payment of cash dividends in the future, if any, will be at the discretion of our board of directors and will depend upon such factors as any other factors our board deems relevant.

S-7

CAPITALIZATION

The following table sets forth our capitalization as of March 31, 2015:

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

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, 2014 and in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015, and the other financial information included and incorporated by reference in this prospectus supplement.

	(in thousands)	
	As of March 31, 2015	
	Actual	As Adjusted
Cash and cash equivalents	\$ 12,409	\$
Stockholders’ equity (deficit):		
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 ⁽¹⁾ , 72,807,469 shares issued and 72,725,987 shares outstanding, actual ⁽²⁾ ; and shares issued and shares outstanding, as adjusted	\$ 73	\$
Additional paid-in capital	\$ 111,702	\$
Accumulated deficit	\$ (113,400)	\$
Total stockholders’ equity (deficit)	\$ (1,625)	\$
Total capitalization	\$ (1,625)	\$

On May 15, 2015, we filed a Certificate of Amendment to our Articles of Incorporation with the Secretary of State (1) of the State of Nevada that increased the authorized number of our shares of common stock from 100,000,000 shares to 250,000,000 shares.

(2) Outstanding shares of common stock as of March 31, 2015 excludes:

6,531,106 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of \$1.97 per share;

1,667,964 shares of common stock which were reserved for future equity awards that may be granted in the future under our equity incentive plans;

7,974,794 shares of our common stock reserved for issuance upon the exercise of outstanding warrants, each with a weighted-average exercise price of \$1.80 per share; and

the underwriters' option to purchase additional shares.

S-8

DILUTION

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

Our net tangible book value on March 31, 2015 was approximately \$(1.6) million, or \$(0.02) 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 shares of common stock in this offering at the public offering price of \$ per share, and after deducting estimated offering commissions and expenses payable by us, our as adjusted net tangible book value as of March 31, 2015 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:

Public offering price per share	\$
Net tangible book value per share as of March 31, 2015	\$(0.02)
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 72,725,987 shares of our common stock outstanding as of March 31, 2015, which does not include the following, all as of March 31, 2015:

- 6,531,106 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of \$1.97 per share;
- 1,667,964 shares of common stock which were reserved for future equity awards that may be granted in the future under our equity incentive plans; and

- 7,974,794 shares of our common stock reserved for issuance upon the exercise of outstanding warrants, each with a weighted-average exercise price of \$1.80 per share.

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

If the underwriters exercise in full their option to purchase _____ additional shares of common stock at the public offering price of \$ _____ per share, the as adjusted net tangible book value after this offering would be \$ _____ per share, representing an increase in net tangible book value of \$ _____ per share to existing stockholders and immediate dilution in net tangible book value of \$ _____ per share to investors purchasing our common stock in this offering at the public offering price.

S-9

UNDERWRITING

The underwriters named below, for which William Blair & Company, L.L.C. and RBC Capital Markets, LLC are acting as representatives, have severally agreed, subject to the terms and conditions set forth in the underwriting agreement by and among the underwriters and us, to purchase from us, the respective number of shares of common stock set forth opposite each underwriter's name in the table below.

<u>Underwriter</u>	Number of Shares
William Blair & Company, L.L.C.	
RBC Capital Markets, LLC	
BTIG, LLC	
Total	

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

If the underwriters sell more shares than the total number set forth in the table above, the underwriters have an option to buy up to additional shares from us, on the same terms and conditions solely to cover over-allotments, if any. The underwriters may exercise that option for 30 days from the date of this prospectus supplement.

The following table shows the per share and total public offering price, underwriting discounts and commissions and proceeds, before expenses, to us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' over-allotment option.

	Per Share	Total	
		No Exercise	Full Exercise
Public offering price	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of

up to \$ _____ per share from the public offering price. After the offering, the underwriters may reduce the initial public offering price and concession to dealers. No such reduction will change the amount of proceeds received by us, as set forth on the cover page. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We and each of our executive officers and directors have agreed with the underwriters, subject to certain exceptions, not to (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant for the sale of, or otherwise dispose of or transfer any shares of common stock or any securities convertible into or exchangeable or exercisable for shares of common stock, whether now owned or subsequently acquired or with respect to which we have acquired the power of disposition, or (ii) cause to be filed, any registration statement under the Securities Act of 1933, as amended (the "Securities Act"), with respect to any of the foregoing, or (iii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the common stock, whether any such swap or transaction is to be settled by delivery of common stock or other securities, in cash or otherwise, during the period from the date of this prospectus supplement continuing through the date 90 days after the date of this prospectus supplement, except with the prior written consent of the representatives.

The 90-day restricted period described in the preceding paragraph may be extended if: (i) during the last 17 days of the 90-day restricted period: (a) we release earnings results, (b) announce material news, or (c) a material event relating to our business occurs, or (ii) before the expiration of the 90-day restricted period, we announce that we will release earnings results or become aware that material news or a material event will occur during the 16-day period following the last day of the 90-day restricted period, then in each case the 90-day restricted period may be extended by the underwriters by written notice to us, and the restrictions imposed shall continue to apply, until the expiration of the 18-day period beginning on the date of the earnings release or the announcement of material news or the occurrence of a material event relating to our business, as the case may be.

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

We estimate that the total expenses of the offering payable by us, excluding underwriting discounts and commissions, will be approximately \$100,000. We have also agreed to reimburse the underwriters for certain of their actual expenses reasonably incurred (including the reasonable fees and expenses of their counsel and any other independent experts) in an amount not to exceed \$75,000 as set forth in the underwriting agreement. In addition, pursuant to an engagement letter entered into by and between us and William Blair, dated September 19, 2014, if we, directly or indirectly, subject to certain exceptions, consummate a transaction in which we sell securities within 18 months following the termination of such engagement letter (which termination occurred on October 10, 2014, the date of the closing of a registered direct offering in which William Blair acted as our placement agent), then William Blair will be entitled to a fee of 7% of the total transaction consideration; provided, however, that William Blair has agreed to share such fee with the other underwriters in this offering.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act. If we are unable to provide this indemnification, we have agreed to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments of ours. The underwriters and their respective affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Short Sales, Stabilizing Transactions and Penalty Bids

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short

sales. Shorts sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares from us in the offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option granted to them by us. "Naked" short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own account, may have the effect of preventing or retarding a decline in the market price of the company's stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued at any time. These transactions may be effected on the NYSE MKT, in the over-the-counter market or otherwise.

Notice to Non-U.S. Investors

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive, each of which we refer to as a relevant member state, with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state, or the relevant implementation date, an offer of securities described in this prospectus supplement may not be made to the public in that relevant member state other than: provided that no such offer of securities shall require us or the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an “offer of shares to the public” in relation to any shares of common stock in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the same may be varied in that member state by any measure implementing the Prospectus Directive in that member state and the expression “Prospectus Directive” means Directive 2003/71/EC and includes any relevant implementing measure in each relevant member state.

- 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;
- To any legal entity that has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- To fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of representatives for any such offer; or
- In any other circumstances that do not require the publication of a prospectus pursuant to Article 3 of the Prospectus Directive; provided that no such offer of securities shall require us or the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

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. Goodwin Procter LLP, New York, New York is acting as counsel for the underwriters in connection with this offering.

EXPERTS

The financial statements of Synthetic Biologics, Inc. as of December 31, 2014 and 2013 and for each of the three years ended in the period ended December 31, 2014 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2014 incorporated by reference in this Prospectus have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered 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

Edgar Filing: Synthetic Biologics, Inc. - Form 424B5

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, 2014 filed with the SEC on March 16, 2015 (File No. 001-12584);

· Our quarterly report on Form 10-Q for the quarter ended March 31, 2015 filed with the SEC on May 11, 2015 (File No. 001-12584).

· Our current reports on Form 8-K filed with the SEC on January 12, 2015, March 19, 2015, May 4, 2015, May 18, 2015, June 16, 2015, and July 9, 2015 (File No. 001-12584);

· Our definitive proxy statement on Schedule 14A filed with the SEC on April 13, 2015 (File No. 001-12584); and

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

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

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

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

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

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

617 Detroit Street, Suite 100
Ann Arbor, Michigan 48104

(734) 332-7800

PROSPECTUS

\$100,000,000

Common Stock

Warrants

Units

We may offer and sell up to \$100 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 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 traded on NYSE MKT under the symbol “SYN”. On April 7, 2015, the last reported sale price for the common stock was \$2.04 per share. We urge prospective purchasers of our common stock to obtain current information about the market prices of our common stock.

Our executive offices are located at 155 Gibbs Street, Suite 412, Rockville, Maryland 20850 and our administrative offices are located at 617 Detroit Street, Suite 100, Ann Arbor, Michigan 48104. Our telephone number is (734) 332-7800.

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

The date of this prospectus is April 20, 2015.

TABLE OF CONTENTS

	Page
<u>About this Prospectus</u>	3
<u>Prospectus Summary</u>	3
<u>Risk Factors</u>	6
<u>Special Note Regarding Forward-Looking Statements</u>	7
<u>Use of Proceeds</u>	8
<u>Dividend Policy</u>	8
<u>Description of Capital Stock</u>	9
<u>Description of Warrants</u>	9
<u>Description of Units</u>	10
<u>Plan of Distribution</u>	11
<u>Legal Matters</u>	13
<u>Experts</u>	13
<u>Where You Can Find More Information</u>	13
<u>Incorporation of Certain Documents by Reference</u>	13
<u>Disclosure of the Securities and Exchange Commission Position on Indemnification for Securities Act Liabilities</u>	14

The registration statement containing this prospectus, including the exhibits to the registration statement, provides additional information about us and the common stock offered under this prospectus. 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 not an offer or solicitation in respect to these securities in any jurisdiction in which such offer or solicitation would be unlawful. This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the “SEC”). The registration statement that contains this prospectus (including the exhibits to the registration statement) contains additional information about our company and the securities offered under this prospectus. That registration statement can be read at the SEC website or at the SEC’s offices listed under the heading “Where You Can Find More Information.” We have not authorized anyone else to provide you with different information or additional information. You should not assume that the information in this prospectus, or any supplement or amendment to this prospectus, is accurate at any date other than the date indicated on the cover page of such documents.

PROSPECTUS SUMMARY

Our Business

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

Product Pipeline:

Summary of Pathogen-Specific Therapy Programs:

***C. difficile* infections (CDI):** We are in clinical development of a novel second-generation oral enzyme candidate, SYN-004, for co-administration with commonly used IV beta-lactam antibiotics, intended to protect the microbiome and prevent the development of and severe effects from CDI. CDIs are a leading type of hospital acquired infection (HAI) and are frequently associated with IV antibiotic treatment. Designed to be given orally and co-administered with certain IV beta-lactam antibiotics (e.g., penicillins and cephalosporins), SYN-004 is intended to protect the gut

while the IV antibiotics fight the primary infection. SYN-004 is believed to not only have a similar profile to its first-generation predecessor, which demonstrated protection of the microbiome (gut flora) during treatment with certain penicillins, but also has the potential to act against a broader spectrum of IV beta-lactam antibiotics. Beta-lactam antibiotics are a mainstay in hospital infection management and include the commonly used penicillin and cephalosporin classes of antibiotics. SYN-004's target market is significant and represented by annual U.S. hospitals purchases of approximately 118 million doses of IV beta-lactam antibiotics which are administered to approximately 14 million patients.* Currently there are no approved treatments designed to protect the gut microbiome from the damaging effects of IV antibiotics. This worldwide market could represent a multi-billion dollar opportunity for us. In December 2014, the U.S. Patent and Trademark Office (USPTO) issued Patent No. 8,894,994 that has claims to compositions of matter and pharmaceutical compositions of beta-lactamases, including SYN-004, and carries a patent term to at least 2031. We also have an extensive patent estate on other aspects of this program which includes patent applications that could carry a term to at least 2035. In the fourth quarter of 2014, we initiated our randomized, double-blind placebo-controlled Phase 1a clinical trial, reported positive topline safety and tolerability results from the Phase 1a clinical trial, and initiated the Phase 1b clinical trial evaluating multiple ascending doses of SYN-004. In February 2015, we reported positive topline results from the Phase 1b clinical trial of escalating doses of oral SYN-004, with no safety or tolerability issues reported at dose levels and dose regimens both meeting and exceeding those expected to be studied in upcoming clinical trials. In March 2015, we reported positive pharmacokinetics data from both Phase 1 clinical trials, with supportive evidence that SYN-004 should have no effect on the IV antibiotic in the bloodstream, allowing the antibiotic to fight the primary infection. We also initiated a Phase 2a clinical trial to evaluate the GI antibiotic-degrading effects and the safety of SYN-004. The initiation of a Phase 2b proof-of-concept clinical trial is expected in the second half of 2015, with Phase 2b topline data anticipated during the second half of 2015.

Pertussis: In December 2012, in collaboration with Intrexon Corporation (NYSE: XON) (Intrexon), we initiated development of a monoclonal antibody (mAb) therapy for the treatment of Pertussis infections, more commonly known as whooping cough. Combining two mAbs, SYN-005 is designed to target and neutralize pertussis toxin as a prophylaxis for high-risk newborns and in order to reduce the mortality rate in infected infants. To further the development of this potential therapy for Pertussis, we entered into an agreement with The University of Texas at Austin (UT) to license the rights to certain research and pending patents related to pertussis antibodies. We have patents pending on compositions and uses of SYN-005 and we have an issued U.S. patent on other pertussis mAbs from UT. According to the World Health Organization, each year, *B. pertussis* infection is estimated to cause up to 300,000 deaths worldwide, primarily among unvaccinated infants. Positive preclinical research findings for SYN-005 were reported in April 2014, and again in September 2014, for our proprietary mAb combination therapy for treating Pertussis, in non-human primate studies. In September 2014 we received a U.S. Orphan Drug designation for SYN-005 for the treatment of Pertussis. We intend to seek non-dilutive funding to support preclinical and clinical development of SYN-005 for prophylaxis and treatment of Pertussis, including the anticipated filing of an IND application in 2015 and the anticipated initiation of a Phase 1 clinical trial during the second half of 2015, with topline Phase 1 data expected during 2015.

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

Summary of Multiple Sclerosis Program:

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

Cognitive Dysfunction in MS: Trimesta is also being developed for the treatment of cognitive dysfunction in female MS patients. This 12-month, UCLA-led, randomized, double-blind, placebo-controlled investigator-initiated Phase 2 clinical trial is being conducted at four sites in the United States. The primary endpoint is the effect on cognitive function as assessed by Paced Auditory Serial Addition Test (PASAT). Patient enrollment is ongoing. The majority of the costs of this trial are being funded by grants from foundations and charitable organizations through direct funding to the principal investigator and we have pledged approximately \$500,000 to UCLA to partially fund this trial, payable over three years. An estimated 50 – 65% of MS patients are expected to develop disabilities due to cognitive dysfunction and there is currently no approved treatment for this indication.

Since our inception in January 2001, our efforts and resources have been focused primarily on acquiring and developing our product candidates, our clinical trials, raising capital, manufacturing and recruiting personnel. To date, we have financed our operations primarily through public and private sales of our common stock, and we expect to continue to seek to obtain the required capital in a similar manner. We have incurred an accumulated deficit of \$101.0 million through December 31, 2014. We cannot provide any assurance that we will be able to achieve profitability on a sustained basis, if at all, obtain the required funding, obtain the required regulatory approvals, or complete additional corporate partnering or acquisition transactions.

Company History

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

Corporate Information

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

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

RISK FACTORS

An investment in our common stock involves a high degree of risk. You should consider carefully the risks discussed under the section captioned “Risk Factors” contained in our most recent annual report on Form 10-K 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements contained or incorporated by reference in this 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,” “anticipate,” “will” and similar statements of a 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 and under the captions “Risk Factors,” “Business,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” in our most recent Annual Report on Form 10-K and our subsequent Quarterly Reports on 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 that could cause actual results to differ.

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 clinical trials, 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, and/or 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 April 1, 2015, 72,725,987 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 our books, 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

As of April 1, 2015, we had issued and outstanding a total of 7,974,794 warrants to purchase our common stock outstanding at a weighted-average price of \$1.80.

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.

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 related to the issuance and sale of the warrants and units offered hereby on our behalf and Parsons Behle & Latimer, Reno, Nevada will pass upon certain legal matters relating to the issuance and sale of the common stock offered hereby on our behalf. Additional legal matters may be passed upon for us or any underwriters, dealers, of agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements of Synthetic Biologics, Inc. as of December 31, 2014 and 2013 and for each of the three years ended in the period ended December 31, 2014 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2014 incorporated by reference in this prospectus have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered 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 SEC. 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.

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

Edgar Filing: Synthetic Biologics, Inc. - Form 424B5

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 (other than any portions of any such documents that are not deemed “filed” under the Exchange Act in accordance with the Exchange Act and applicable SEC rules) 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:

Our annual report on Form 10-K for the fiscal year ended December 31, 2014 filed with the SEC on March 16, 2015 (File No. 001-12584);

Our current reports on Form 8-K filed with the SEC on January 12, 2015 (with respect to Item 5.02 of Form 8-K) and March 19, 2015 (File No. 001-12584) ;

Our preliminary proxy statement on Schedule 14A filed with the SEC on March 23, 2015 (File No. 001-12584); and

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

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: 617 Detroit Street, Suite 100, Ann Arbor, Michigan 48104, (734) 332-7800.

DISCLOSURE OF SECURITIES AND EXCHANGE COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Our amended and restated bylaws and Articles of Incorporation contain provisions that permit us to indemnify our directors and officers to the full extent permitted by Nevada law, and our Articles of Incorporation, as amended, contains provisions that eliminate the personal liability of our directors in each case for monetary damages to us or our stockholders for breach of their fiduciary duties, except to the extent that Nevada law prohibits indemnification or elimination of liability. These provisions do not limit or eliminate our rights or the rights of any stockholder to seek an injunction or any other non-monetary relief in the event of a breach of a director's or officer's fiduciary duty. In addition, these provisions apply only to claims against a director or officer arising out of his or her role as a director or officer and do not relieve a director or officer from liability if he or she engaged in willful misconduct or a knowing violation of the criminal law or any federal or state securities law.

The rights of indemnification provided in our amended and restated bylaws are not exclusive of any other rights that may be available under any insurance or other agreement, by vote of stockholders or disinterested directors or otherwise.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC this type of indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Shares

Common Stock

PROSPECTUS SUPPLEMENT

July , 2015

William Blair

RBC Capital Markets

BTIG

15