

Synthetic Biologics, Inc.  
Form 424B5  
November 15, 2016

**Filed Pursuant to Rule 424(b)(5)**

**Registration No. 333-206266**

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. 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 state or other jurisdiction where the offer or sale is not permitted.

**SUBJECT TO COMPLETION, DATED NOVEMBER 14, 2016**

**preliminary Prospectus Supplement**

**(To Prospectus dated August 18, 2015)**

**Shares of Common Stock**

**Warrants to Purchase                      Shares of Common Stock**

We are offering                      shares of our common stock and warrants to purchase up to                      shares of our common stock (and the shares of common stock issuable from time to time upon exercise of each of the warrants), pursuant to this prospectus supplement and the accompanying prospectus. The common stock and warrants will be sold in combination, with two warrants, each to purchase one share of common stock, for each one share of common stock sold. The purchase price for each share of common stock and accompanying warrants is \$                      .

Each warrant will be exercisable beginning on or after its date of issuance. One of the warrants (the Series A warrants) will have an exercise price of \$1.43 per share and be exercisable until the four year anniversary of the issuance date. The other warrants (the Series B warrants) will have an exercise price of \$1.72 per share and be exercisable until December 31, 2017.

Our common stock is listed on the NYSE MKT under the symbol “SYN.” On November 11, 2016, the closing price of our common stock was \$1.58 per share. There is no established public trading market for the warrants and we do not expect a market to develop. In addition, we do not intend to apply for listing of the warrants on any securities exchange or recognized trading system. The warrants will be issued in book-entry form pursuant to a warrant agreement between us and Corporate Stock Transfer, Inc., as warrant agent.

**Our business and an investment in our securities involves a high degree of risk. Before making an investment decision, please read the information under “Risk Factors” beginning on page S-6 of this prospectus supplement and under similar headings in the documents incorporated by reference into this prospectus supplement.**

	<b>Per Share and Accompanying Warrants</b>	<b>Total</b>
<b>Public offering price</b>	\$	\$
<b>Underwriting discounts and commissions <sup>(1)</sup></b>	\$	\$
<b>Proceeds, before expenses, to us</b>	\$	\$

<sup>(1)</sup> See “Underwriting” beginning on page S-14 of this prospectus supplement for a description of compensation payable to the underwriter.

One of our directors has indicated an interest in purchasing up to \$300,000 of shares of our common stock and warrants to purchase shares of our common stock in this offering. An indication of interest is not binding and the director may purchase some, none or all of the securities for which he has indicated an interest.

The underwriter expects to deliver the shares of common stock and accompanying warrants against payment on or about November , 2016. We have granted the underwriter an option for a period of 30 days to purchase up to additional shares of our common stock and warrants to purchase up to additional shares of our common stock. If the underwriter exercises the option in full, the total underwriting discounts and commissions payable by us will be \$ and the total proceeds to us, before expenses, will be \$ .

**Cantor Fitzgerald & Co.**

The date of this prospectus supplement is November , 2016

**TABLE OF CONTENTS**

	<b>Page</b>
<b>PROSPECTUS SUPPLEMENT</b>	
<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-5
<u>RISK FACTORS</u>	S-6
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	S-8
<u>USE OF PROCEEDS</u>	S-9
<u>DIVIDEND POLICY</u>	S-10
<u>DILUTION</u>	S-11
<u>DESCRIPTION OF THE SECURITIES WE ARE OFFERING</u>	S-12
<u>UNDERWRITING</u>	S-14
<u>LEGAL MATTERS</u>	S-18
<u>EXPERTS</u>	S-18
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	S-18
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	S-18
<b>PROSPECTUS</b>	
<u>ABOUT THIS PROSPECTUS</u>	1
<u>PROSPECTUS SUMMARY</u>	2
<u>RISK FACTORS</u>	7
<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>	11
<u>PLAN OF DISTRIBUTION</u>	13
<u>LEGAL MATTERS</u>	14
<u>EXPERTS</u>	14
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	15
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	15
<u>DISCLOSURE OF THE SECURITIES AND EXCHANGE COMMISSION POSITION ON</u>	15
<u>INDEMNIFICATION FOR SECURITIES ACT LIABILITIES</u>	15

## **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 dated August 18, 2015, including the documents incorporated by reference therein, provides 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 the information in this prospectus supplement. Any statement so modified will be deemed to constitute a part of this prospectus supplement only as so modified, and any statement so superseded will be deemed not to constitute a part of 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.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our

affairs.

No action has been or will be taken in any jurisdiction by us or the underwriter 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 accompanying warrants. Therefore, you should read the entire prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the “Risk Factors” section and other documents or information included or incorporated by reference in this prospectus supplement and the accompanying prospectus before making any investment decision. Unless the context requires otherwise, references in this prospectus supplement to “Synthetic,” “the Company,” “we,” “us” and “our” refer to Synthetic Biologics, Inc.*

### **Our Business**

We are a clinical stage company developing therapeutics to protect the gut microbiome while targeting pathogen-specific diseases. Our lead candidates poised for Phase 3 development are: (1) SYN-010 which is intended to reduce the impact of methane-producing organisms in the gut microbiome to treat an underlying cause of irritable bowel syndrome with constipation (IBS-C), and (2) SYN-004 (ribaxamase) which is designed to protect the gut microbiome from the effects of certain commonly used intravenous (IV) beta-lactam antibiotics for the prevention of *C. difficile* infection (CDI), antibiotic-associated diarrhea (AAD) and the emergence of antibiotic-resistant organisms. In collaboration with Intrexon Corporation (“Intrexon”), we are also developing preclinical stage monoclonal antibody therapies for the prevention and treatment of pertussis, and novel discovery stage biotherapeutics for the treatment of phenylketonuria (PKU).

### *Product Pipeline:*

\* Two Phase 2 studies completed. Planning Phase 2b/3 pivotal trial

C–Cedars-Sinai Medical Center Collaboration

I-Intrexon Collaboration

T-The University of Texas at Austin Collaboration

S-1



## Summary of Clinical and Preclinical Programs

Therapeutic Area	Product Candidate	Status
Treatment of IBS-C	SYN-010 (oral modified-release lovastatin lactone)	<ul style="list-style-type: none"> <li>• Reported supportive topline data from two Phase 2 clinical trials (4Q 2015 &amp; 1Q 2016)</li> <li>• Received Type C meeting responses from U.S. Food and Drug Administration (the “FDA”) regarding late-stage aspects of clinical pathway (2Q 2016)</li> <li>• Presented detailed data supporting previously reported positive topline data from two Phase 2 clinical trials at Digestive Disease Week Conference 2016 (DDW) (May 2016)</li> <li>• Held End of Phase 2 meeting with FDA (July 2016)</li> <li>• Plan to initiate first Phase 2b/3 pivotal adaptive clinical trial (1Q 2017)</li> <li>• Collaboration with Cedars-Sinai Medical Center</li> </ul>
Prevention of CDI and AAD (Degrade IV beta-lactam antibiotics)	SYN-004 (ribaxamase) (oral enzyme)	<ul style="list-style-type: none"> <li>• Reported supportive Phase 1a/1b data (1Q 2015)</li> <li>• Initiated Phase 2b proof-of-concept clinical trial (3Q 2015)</li> <li>• Reported supportive topline data from first Phase 2a clinical trial (4Q 2015)</li> <li>• Reported supportive topline data from second Phase 2a clinical trial (2Q 2016)</li> <li>• Received USAN approval of the generic name “ribaxamase” for SYN -004 (July 2016)</li> <li>• Completed Enrollment of Phase 2b proof-of concept clinical trial (3Q 2016)</li> <li>• Awarded contract by the Centers for Disease Control and Prevention (CDC) (4Q 2016)</li> <li>• Plan to announce topline data from Phase 2b proof-of-concept clinical trial (1Q 2017)</li> </ul>

- Plan to initiate Phase 3 clinical trial(s) (end of 2017)

Prevention of  
CDI and

AAD SYN-007  
(Degradate oral (oral enzyme)  
beta-lactam  
antibiotics)

- Preclinical work ongoing to determine ability of SYN-007 to protect the gut microbiome and degrade oral beta-lactam antibiotics

Prevention  
and  
Treatment

of pertussis (monoclonal  
antibody  
therapies)

SYN-005

- Reported supportive preclinical research findings (2014)

- The University of Texas at Austin (“UT Austin”) received a grant from the Bill and Melinda Gates Foundation to support a preclinical study to evaluate the prophylactic capability of SYN-005 (4Q 2015)

- Collaborations with Intrexon and UT Austin

S-2

*Recent Developments*

*SYN-010*

On July 20, 2016, we participated in an End of Phase 2 meeting with the FDA. Following a review of data from the two Phase 2 clinical trials of SYN-010 conducted by us, a collaborative and positive discussion ensued with the FDA to determine the optimal pathway to advance SYN-010 into Phase 3 development. In accordance with guidance from the FDA, we plan to conduct a Phase 2b/3 adaptive design study for our first pivotal trial of SYN-010. In addition to IBS-C patients who present with high breath methane levels, further dose exploration will evaluate the potential efficacy of SYN-010 in IBS-C patients who may have low breath methane levels. We have submitted a study protocol design and corresponding statistical analysis plan to the FDA and are awaiting feedback on the protocol design from the FDA. The proposed Phase 2b/3 study design anticipates enrolling approximately 840 patients to be randomized in a 1:1:1 ratio to one of three treatment groups, including two different SYN-010 dose groups (21 mg and 42 mg) and a placebo group. Breath methane levels at screening will be used to ensure each treatment group has approximately the same ratio of high and low breath methane subjects. We anticipate initiating this clinical trial during the first quarter of 2017.

S-3

### *SYN-004*

In September 2016, we completed enrollment in our Phase 2b proof-of-concept clinical trial intended to evaluate the ability of SYN-004 (ribaxamase) to prevent CDI, *C. difficile* associated diarrhea (CDAD) and AAD in patients hospitalized for a lower respiratory tract infection and receiving IV ceftriaxone.

On October 6, 2016, we announced the award of a government contract by the CDC's Broad Agency Announcement (BAA) 2016-N-17812. The contract amount is up to \$521,014. The award will support research conducted during our ongoing, randomized, placebo-controlled Phase 2b proof-of-concept clinical study of SYN-004 (ribaxamase) and the CDC's efforts to assess how selective pressure from IV antibiotics may lead to the emergence of antibiotic resistance in the gut microbiome. The funding will also support research to evaluate SYN-004's (ribaxamase's) ability to reduce selective pressure associated with the emergence of antibiotic-resistant organisms in the gut microbiomes of patients enrolled in our Phase 2b clinical trial. We will examine DNA isolated from longitudinal samples obtained during the clinical trial and look for changes to the patient's gut resistome, specifically examining for alterations in the presence and/or abundance of antibiotic resistance genes.

### **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 Corporation, we changed our name to Synthetic Biologics, Inc. on February 15, 2012.

### **Corporate Information**

Our principal executive offices are located at 9605 Medical Center Drive, Suite 270, Rockville, Maryland 20850. Our telephone number is (301) 417-4364, and our website address is [www.syntheticbiologics.com](http://www.syntheticbiologics.com). The information contained on, or that can be accessed through, our website is not part of, and should not be construed as being incorporated by reference into, this prospectus supplement.

For further information regarding us and our financial information, you should refer to our recent filings with the SEC. See “Where You Can Find More Information.”

S-4

**The Offering**

Common stock  
offered by us            shares

Series A warrants to purchase up to            shares of our common stock, which may be exercised beginning on their date of issuance. The Series A warrants are exercisable until the four year anniversary of the issuance date. The Series A warrants have an exercise price of \$1.43 per share of common stock, subject to adjustment.

Warrants  
offered by us

Series B warrants to purchase up to            shares of our common stock, which may be exercised beginning on their date of issuance. The Series B warrants are exercisable until December 31, 2017. The Series B warrants have an exercise price of \$1.72 per share of common stock, subject to adjustment.

Subject to applicable laws, the warrants are separately tradeable immediately after issuance at the option of the holders and may be transferred at the option of the holders.

This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the warrants.

Option to  
purchase  
additional  
shares and  
warrants

We have granted the underwriter the option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to            additional shares of our common stock and warrants to purchase up to            additional shares of our common stock.

Common stock  
to be  
outstanding  
  
after this  
offering

                  shares (assuming none of the warrants issued in this offering are exercised and            shares if the warrants are exercised if full). If the underwriter’s option to purchase additional shares and warrants is exercised in full, the total number of shares of common stock outstanding immediately after this offering would be            shares (assuming none of the warrants are exercised and            shares if the warrants are exercised in full).

Risk Factors

Investing in our securities involves a high degree of risk. See “Risk Factors” section of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus for a discussion of factors that you should consider before investing in our

securities.

Use of proceeds We intend to use the net proceeds from this offering primarily to provide the necessary funding for the continued clinical development of SYN-010, including initiation of our planned Phase 2b/3 clinical trial, and progression of SYN-004 to Phase 2 data readout and initiation of the planned Phase 3 clinical trial for SYN-004. The net proceeds from this offering may also be used 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 and to in-license, acquire or invest in complementary businesses or partnerships and intellectual property. See “Use of Proceeds” on page S-9.

Listing Our common stock is listed on the NYSE MKT under the trading symbol “SYN.” There is no established public trading market for the offered warrants and we do not expect a market to develop. In addition, we do not intend to apply for listing of the warrants on any securities exchange or recognized trading system. The warrants will be issued in book-entry form pursuant to a warrant agreement between us and Corporate Stock Transfer, Inc., as warrant agent.

The number of shares of our common stock to be outstanding immediately after the offering is based on 91,652,351 shares of common stock outstanding as of September 30, 2016 and excludes as of that date:

8,513,552 shares of our common stock subject to options outstanding having a weighted-average exercise price of \$2.15 per share;

6,655,176 shares of our common stock that have been reserved for issuance in connection with future grants under our stock option plans; and

7,858,899 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants having a weighted-average exercise price of \$1.77 per share.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriter of its option to purchase additional shares of our common stock and warrants and excludes shares of our common stock that may be issuable upon exercise of the warrants offered hereby.

## **RISK FACTORS**

*Investing in our securities involves a high degree of risk. 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, 2015, 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, 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 and accompanying warrants. If any of these events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could adversely affect the value of an investment in our common stock and accompanying warrants and you may lose all or part of your investment. Moreover, the risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled “Special Note Regarding Forward-Looking Statements.”*

### **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 primarily to provide the necessary funding for the continued clinical development of SYN-010, including initiation of our planned Phase 2b/3 clinical trial and progression of SYN-004 to Phase 2 data readout and initiation of our planned Phase 3 clinical trial for SYN-004. The net proceeds from this offering may also 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 and to in-license, acquire or invest in complementary businesses or products and intellectual property, although 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 securities. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.



***If you purchase securities 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 and accompanying warrants in this offering attributable to our common stock exceeds the net tangible book value per share of our common stock outstanding prior to this offering. Assuming we sell all of the securities in this offering at the public offering price of \$        per share, after deducting the estimated underwriting discounts and commissions 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 September 30, 2016 after giving effect to this offering and the public offering price, without giving effect to the potential exercise of the warrants being offered in this offering. 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. 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 92,172,714 shares of our common stock outstanding as of November 11, 2016. As of that date, stock options and warrants outstanding represented 16,322,868 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.

***You may experience future dilution as a result of future equity offerings.***

In order to raise additional capital, we may in the future issue additional shares of our common stock, including, but not limited to, in an “at the market offering,” or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the offering price paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share attributable to the common stock paid by investors in this offering. You will incur dilution upon any such sale of additional shares if the price at which such shares are sold is higher than the net tangible book value per share of our common stock at the time of such sale.

***There is no public market for the warrants to purchase common stock in this offering.***

There is no established public trading market for the warrants being sold in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the warrants on any securities exchange or recognized trading system. Without an active market, the liquidity of the warrants will be limited.

***The warrants are a risky investment. You may not be able to recover your investment in the warrants, and the warrants may expire worthless.***

Whether the warrants will have any value will depend on the results of certain of our clinical trials as well as market conditions for our common stock generally, which conditions will depend on factors related and unrelated to the success of our clinical development program, and cannot be predicted at this time.

If our common stock price does not increase to an amount sufficiently above the exercise prices of the warrants during the periods the warrants are exercisable, you will be unable to recover any of your investment in the warrants. There can be no assurance that any of the factors that could impact the trading price of our common stock will result in the trading price increasing to an amount that will exceed the exercise price or the price required for you to achieve a positive return on your investment in the warrants.

***Holders of the warrants will have no voting rights as common stockholders until they acquire our common stock.***

Until you acquire shares of our common stock upon exercise of the warrants, you will have no voting rights with respect to our common stock issuable upon exercise of the warrants voting. Upon exercise of your warrants, you will be entitled to exercise all the voting rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

***Because we do not intend to declare cash dividends on our shares of common stock in the foreseeable future, stockholders must rely on appreciation of the value of our common stock for any return on their investment.***

We have never declared or paid cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or

paying any cash dividends in the foreseeable future. In addition, the terms of any existing or future debt agreements may preclude us from paying dividends. As a result, we expect that only appreciation of the price of our common stock, if any, will provide a return to investors in this offering for the foreseeable future.

**Significant holders or beneficial holders of our common stock may not be permitted to exercise warrants that they hold.**

The warrant agreement governing the warrants being offered hereby will prohibit a holder from exercising its warrants if doing so would result in such holder (together with such holder's affiliates and any other persons acting as a group together with such holder or any of such holder's affiliates) beneficially owning more than 9.99% of our common stock outstanding immediately after giving effect to the exercise, provided that, at the election of a holder and notice to us, such beneficial ownership limitation shall be 4.99% of our common stock outstanding immediately after giving effect to the exercise. As a result, you may not be able to exercise your warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such circumstance you could seek to sell your warrants to realize value, but you may be unable to do so.

**We may not have the ability to repurchase the warrants.**

Under certain circumstances, if an extraordinary transaction (as defined in the warrant agreement) occurs, holders of the warrants may require us to repurchase the remaining unexercised portion of such warrants for an amount of cash equal to the value of the warrant as determined in accordance with the Black Scholes option pricing model and the terms of the warrants. Our ability to repurchase the warrants depends on our ability to generate cash flow in the future. To some extent, this is subject to general economic, financial, competitive, legislative and regulatory factors and other factors that are beyond our control. We cannot assure you that we will maintain sufficient cash reserves or that our business will generate cash flow from operations at levels sufficient to permit us to repurchase the warrants.

## **SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus supplement, the accompanying prospectus and the documents we file with the SEC that are incorporated by reference herein and therein contain “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”), and Section 21E of the Exchange Act. These forward-looking statements 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 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. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

You should not assume that the information contained in this prospectus supplement is accurate as of any date other than the date on the front of this prospectus supplement, or that any information incorporated by reference into this prospectus is accurate as of any date other than the date of the document so incorporated by reference. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements.

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, the accompanying prospectus and in the documents we file with the SEC that are incorporated by reference herein that could cause actual results to differ.

S-8

## USE OF PROCEEDS

We estimate that the net proceeds from the sale of the \_\_\_\_\_ shares of common stock and accompanying warrants that we are offering, excluding the proceeds, if any, from the exercise of the warrants issued in this offering, will be approximately \$ \_\_\_\_\_ million (\$ \_\_\_\_\_ million if the underwriter's option to purchase additional shares of common stock and warrants is exercised in full) based on the public offering price of \$ \_\_\_\_\_ per share of common stock and accompanying warrants, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering primarily to provide the necessary funding for the continued clinical development of SYN-010, including initiation of our planned Phase 2b/3 clinical trial, and progression of SYN-004 to Phase 2 data readout and initiation of our planned Phase 3 clinical trial for SYN-004. We may also 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 and to in-license, acquire or invest in complementary businesses or products and intellectual property, although we have no current commitments or agreements 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-10

## DILUTION

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

Our net tangible book value on September 30, 2016 was approximately \$(6.0) million, or \$(0.07) 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 our sale of \_\_\_\_\_ shares of common stock and warrants to purchase an additional \_\_\_\_\_ shares of common stock offered by us at the public offering price of \$ \_\_\_\_\_ per share and accompanying warrants (excluding shares of common stock to be issued and any proceeds received upon exercise of the warrants), after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2016 would have been approximately \$ \_\_\_\_\_ million, or \$ \_\_\_\_\_ per share. Assuming the completion of the offering, this represents an immediate increase in net tangible book value of \$ \_\_\_\_\_ per share to existing stockholders and immediate dilution in net tangible book value of \$ \_\_\_\_\_ per share to new investors participating in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share and accompanying warrants	\$
Net tangible book value per share as of September 30, 2016	\$(0.07)
Increase in net tangible book value per share attributable to new investors participating in this offering	
As adjusted net tangible book value per share after giving effect to this offering	
Dilution per share to new investors purchasing participating in this offering	\$

If the underwriter exercises in full its option to purchase up to \_\_\_\_\_ additional shares of common stock and warrants to purchase an additional \_\_\_\_\_ shares of common stock at the public offering price of \$ \_\_\_\_\_ per share and accompanying warrant (excluding shares of common stock to be issued and any proceeds to be received upon exercise of the warrants), 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.

The above discussion and table are based on 91,652,351 shares of our common stock outstanding as of the close of business on September 30, 2016. This number excludes, as of the close of business on September 30, 2016, the shares



of our common stock issuable upon exercise of the warrants offered hereby and also excludes:

8,513,552 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of \$2.15 per share;

6,655,176 shares of common stock which were reserved for future equity awards that may be granted in the future under our equity incentive plans; and

7,858,899 shares of our common stock reserved for issuance upon the exercise of outstanding warrants, each with a weighted-average exercise price of \$1.77 per share.

To the extent that any of these outstanding options or warrants are exercised, there will be further dilution to new investors. In addition, investors that purchase common stock upon the exercise of the warrants offered hereby may experience dilution depending on our net tangible book value at the time of exercise.

## DESCRIPTION OF SECURITIES WE ARE OFFERING

We are offering \_\_\_\_\_ shares of our common stock and warrants to purchase an additional \_\_\_\_\_ shares of our common stock.

The common stock and warrants will be sold together. Each share of common stock will be sold with one Series A warrant and one Series B warrant.

The shares of common stock and warrants are immediately separable and will be issued separately. The shares of common stock issuable from time to time upon exercise of the warrants, if any, are also being offered pursuant to this prospectus.

### Common Stock

The material terms and provisions of our common stock and each other class of our securities which qualifies or limits our common stock are described under the caption “Description of Capital Stock—Common Stock” starting on page 9 of the accompanying prospectus.

### Warrants

*The material terms and provisions of the warrants being issued in this offering are summarized below. The following description is subject to, and qualified in its entirety by, the form of warrant and the warrant agreement between us and the warrant agent, each of which will be filed as an exhibit to a Current Report on Form 8-K to be filed by us with the SEC in connection with this offering and incorporated by reference into the registration statement of which this prospectus forms a part. You should review the form of warrant and the warrant agreement for a complete description of the terms and conditions applicable to the warrants. See “Where You Can Find More Information” on page S-18.*

Each purchaser of shares will receive, for each share of common stock purchased, one Series A warrant and one Series B warrant, each representing the right to purchase one share of common stock. The number of shares of common stock underlying the warrants issued to each purchaser will be equal to the number of shares of common stock purchased by such purchaser in this offering multiplied by two.

*Exercisability.* The Series A and Series B warrants may be exercised at any time on or after their date of issuance. The Series A warrants will have an exercise price of \$1.43 per share and are exercisable until the four year anniversary of the issuance date. The Series B warrants will have an exercise price of \$1.72 per share and are exercisable until December 31, 2017.

The warrants will be exercisable, at the option of each holder, in whole or in part by delivering to the warrant agent a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise.

*Exercise Limitations.* A holder of a warrant will not have the right to exercise any portion of the warrant if the holder (together with its affiliates) would beneficially own in excess of 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the warrants provided that at the election of a holder and notice to us such percentage ownership limitation shall be 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise. However, any holder may increase or decrease such percentage to any other percentage not in excess of 9.99% upon at least 61 days' prior notice from the holder to us.

*Exercise Price.* The initial per share exercise price of the Series A warrants is \$1.43 and the initial per share exercise price of the Series B warrant is \$1.72. The respective exercise prices are subject to adjustment in the event of stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock.

*Transferability.* Subject to applicable laws, the warrants are separately tradeable immediately after issuance at the option of the holders and may be transferred at the option of the holders. The warrants will be issued in book-entry form under a warrant agreement between the warrant agent and us, and shall initially be represented by one or more book-entry certificates deposited with The Depository Trust Company, or DTC, and registered in the name of Cede & Co., a nominee of DTC, or as otherwise directed by DTC.

*No Listing.* There is no established public trading market for the warrants and we do not expect a market to develop. In addition, we do not intend to apply for listing of the warrants on any securities exchange or recognized trading system. Without an active market, the liquidity of the warrants will be limited.

*Extraordinary Transactions.* In the event of an extraordinary transaction, as described in the warrant agreement and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the warrants will be entitled to receive upon exercise of the warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the warrants immediately prior to such fundamental transaction. In the event of an extraordinary transaction, we or any successor entity will pay at the holder's option, exercisable at any time concurrently with or within 30 days after the consummation of the extraordinary transaction, an amount of cash equal to the value of the warrant as determined in accordance with the Black Scholes option pricing model and the terms of the warrants.

#### *Cashless Exercise*

If, at the time a holder exercises its warrant, there is no effective registration statement registering, or the prospectus contained therein is not available for an issuance of the shares underlying the warrant to the holder, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of our common stock determined according to a formula set forth in the warrant. In the event of a cashless exercise, if we fail to timely deliver the shares underlying the warrants, we will be subject to certain buy-in provisions.

*Rights as a Stockholder.* Except as otherwise provided in the warrants or warrant agreement or by virtue of a holder's ownership of shares of our common stock, the holders of the warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until they exercise their warrants.

#### *Variable Rate Transactions*

For the period that our lock-up agreement with Cantor Fitzgerald & Co., as described under "Underwriting- No Sales of Similar Securities," is in effect, we are prohibited from effecting or entering into any issuance of common stock or Common Stock Equivalents (as defined in the warrant agreement) involving a Variable Rate Transaction (as defined in the warrant agreement).

*Amendments.* Amendments and waivers of the terms of the Series A warrants or the Series B warrants require the written consent of the holders of sixty- seven percent (67%) of such series of warrants then outstanding and us.

#### **Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is Corporate Stock Transfer, Inc. Corporate Stock Transfer, Inc. will act as the registrar and transfer agent for the warrants. Its address is 3200 Cherry Creek Drive South, Denver, Colorado 80209.

#### **NYSE MKT Listing**

Our common stock is listed on the NYSE MKT under the symbol "SYN." There is no established public trading market for the warrants and we do not expect a market to develop. We do not plan on making an application to list the warrants on the NYSE MKT, any securities exchange or any recognized trading system.

## **UNDERWRITING**

Subject to the terms and conditions of the underwriting agreement, dated November 1, 2016, between us and Cantor Fitzgerald & Co., as underwriter, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, the shares of common stock and accompanying warrants offered by this prospectus supplement.

The underwriting agreement provides that the obligations of the underwriter are subject to certain conditions precedent such as the receipt by the underwriter of officers' certificates and legal opinions and approval of certain legal matters by its counsel. The underwriting agreement provides that the underwriter will purchase all of the shares of common stock and accompanying warrants if any of them are purchased. We have agreed to indemnify the underwriter and certain of its controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriter may be required to make in respect of those liabilities.

The underwriter has advised us that, following the completion of this offering, it currently intends to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriter is not obligated to do so, and the underwriter may discontinue any market-making activities at any time without notice in its sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriter is offering the shares of common stock and accompanying warrants, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters by its counsel and other conditions specified in the underwriting agreement. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

### **Commissions and Expenses**

The following table shows the public offering price, the underwriting discounts and commissions and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriter's option to purchase additional shares and warrants.

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$200,000. We also have agreed to reimburse the underwriter for

up to \$ of expenses related to the review of this offering by the Financial Industry Regulatory Authority, Inc. (“FINRA”). In accordance with FINRA Rule 5110, this reimbursed FINRA expense is deemed underwriting compensation for this offering.

	PER SHARE AND ACCOMPANYING WARRANTS		TOTAL	
	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES AND	WITH OPTION TO PURCHASE ADDITIONAL SHARES AND	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES AND	WITH OPTION TO PURCHASE ADDITIONAL SHARES AND
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions paid by us				
Proceeds to us, before expenses	\$	\$	\$	\$

The underwriter proposes to offer the common stock and accompanying warrants offered by us to the public at the public offering price set forth on the cover of this prospectus supplement. If all of the common stock and accompanying warrants offered by us are not sold at the public offering price, the underwriter may change the offering price and other selling terms.

**Other**

One of our directors has indicated an interest in purchasing up to \$300,000 of shares of our common stock and warrants to purchase shares of our common stock in this offering. An indication of interest is not binding and the director may purchase some, none or all of the securities for which he has indicated an interest.

### **Option to Purchase Additional Shares and Warrants**

We have granted the underwriter an option, exercisable for 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of \_\_\_\_\_ additional shares and accompanying warrants to purchase up to an additional \_\_\_\_\_ shares from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions.

### **Discretionary Accounts**

The underwriter has advised us that it does not intend to confirm sales of the securities offered hereby to any account over which it exercises discretionary authority.

### **No Sales of Similar Securities**

We, our officers, directors and certain of our stockholders have agreed, subject to specified exceptions, not to directly or indirectly for a period of 90 days after the date of this prospectus supplement without the prior written consent of Cantor Fitzgerald & Co. :

- 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 publicly announce the intention to
- otherwise dispose of or transfer any shares of common stock or any securities convertible into or exchangeable or exercisable for common stock, or file, or cause to be filed, any registration statement under the Securities Act with respect to any of the foregoing; or
- 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 any shares of common stock or any securities convertible into or exchangeable or exercisable for common stock.

Cantor Fitzgerald & Co. may, in its sole discretion and at any time or from time to time before the termination of the 90-day period release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriter and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.



## **Stabilization**

The underwriter has advised us that, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either “covered” short sales or “naked” short sales.

“Covered” short sales are sales made in an amount not greater than the underwriter’s option to purchase additional shares of our common stock in this offering. The underwriter may close out any covered short position by either exercising its option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriter 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 shares through the option to purchase additional shares.

“Naked” short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriter 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 underwriter is concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriter for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriter to reduce a short position incurred by the underwriter in connection with the offering. Similar to other purchase transactions, the underwriter’s purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriter to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriter is not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

## **Passive Market Making**

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

S-15

## Notice to Investors

**United Kingdom.** In the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the Order) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

**European Economic Area.** In relation to each Member State of the European Economic Area (each, a Relevant Member State), no offer of securities may be made to the public in that Relevant Member State other than:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriter; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require us or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any securities or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a “qualified investor” within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any securities being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the securities acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any securities to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the underwriter has been obtained to each such proposed offer or resale.

We, the underwriter and its affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus supplement has been prepared on the basis that any offer of securities in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of securities. Accordingly, any person making or intending to make an offer in that Relevant Member State of securities which are the subject of the offering contemplated in this prospectus supplement may only do so in circumstances in which no obligation arises for us or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither we nor the underwriter have authorized, nor do they authorize, the making of any offer of securities in circumstances in which an obligation arises for us or the underwriter to publish a prospectus for such offer.

For the purpose of the above provisions, the expression “an offer to the public” in relation to any securities 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 securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

**Hong Kong.** The securities may not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the Securities and Futures Ordinance and any rules and regulations made under that Ordinance.

**Japan.** The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, “Japanese Person” shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

**Canada.** The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (“NI 33-105”), the underwriter is not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

**Electronic Distribution.** A prospectus supplement and the accompanying prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by the underwriter or its affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriter may agree with us to allocate a specific number of securities for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriter on the same basis as other allocations. Other than the prospectus supplement and the accompanying prospectus in electronic format, the information on the underwriter’s web site and any information contained in any other web site maintained by the underwriter is not part of this prospectus supplement and the accompanying prospectus, has not been approved and/or endorsed by us or the underwriter and should not be relied upon by investors.

**Other Relationships.** The underwriter and its affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

**Listing on the NYSE MKT.** Our common stock is traded on the NYSE MKT under the symbol “SYN.” The transfer agent for our common stock is Corporate Stock Transfer, Inc. There is no established public trading market for the offered warrants and we do not expect a market to develop. In addition, we do not intend to apply for listing of the warrants on any securities exchange or recognized trading system. The warrants will be issued in book-entry form pursuant to a warrant agreement between us and Corporate Stock Transfer, Inc., as warrant agent.

S-17

## **LEGAL MATTERS**

Gracin & Marlow, LLP, New York, New York is representing us in connection with this offering and will pass upon certain matters relating to the issuance of the warrants. Parsons Behle & Latimer, Reno, Nevada will pass upon certain legal matters relating to the validity of the common stock offered hereby and the common stock issuable upon exercise of the warrants. Latham & Watkins LLP, San Diego, California is counsel for the underwriter in connection with this offering.

## **EXPERTS**

The financial statements of Synthetic Biologics, Inc. as of December 31, 2015 and 2014 and for each of the three years ended in the period ended December 31, 2015 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2015 incorporated by reference in this prospectus supplement and the accompanying 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](http://www.sec.gov). In addition, all of the documents incorporated by reference into this prospectus supplement may be accessed via the Internet at our website: [www.syntheticbiologics.com](http://www.syntheticbiologics.com). We have not incorporated by reference into this prospectus supplement the information on our website, and you should not consider it to be a part of this prospectus

supplement.

## **INCORPORATION OF CERTAIN INFORMATION BY REFERENCE**

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

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2015 filed with the SEC on March 10, 2016 (File No. 001-12584);

Our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2016 filed with the SEC on May 5, 2016, for the quarter ended June 30, 2016 filed with the SEC on August 3, 2016 and for the quarter ended September 30, 2016 filed with the SEC on November 1, 2016 (File No. 001-12584);

Our Current Reports on Form 8-K filed with the SEC on February 2, August 5 and August 26, 2016 (File No. 001-12584);

Our Definitive Proxy Statement on Schedule 14A filed with the SEC on July 6, 2016 (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).

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 that are incorporated by reference into this prospectus supplement and the accompanying prospectus but not delivered with the prospectus supplement, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents to Synthetic Biologics, Inc., Attn: Steve Shallcross, Chief Financial Officer, 9605 Medical Center Drive, Suite 270, Rockville, Maryland 20850, or telephoning us at (301) 417-4364.

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.

S-19

## **PROSPECTUS**

**\$200,000,000**

**Common Stock**

**Warrants**

**Units**

We may offer and sell up to \$200 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 5 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 August 6, 2015, the last reported sale price for the common stock was \$3.10 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 9605 Medical Center Drive, Suite 270, 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 August 18, 2015.

## TABLE OF CONTENTS

	Page
<u>About this Prospectus</u>	1
<u>Prospectus Summary</u>	2
<u>Risk Factors</u>	7
<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>	11
<u>Plan of Distribution</u>	13
<u>Legal Matters</u>	14
<u>Experts</u>	14
<u>Where You Can Find More Information</u>	15
<u>Incorporation of Certain Documents by Reference</u>	15
<u>Disclosure of the Securities and Exchange Commission Position on Indemnification for Securities Act Liabilities</u>	15

**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 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 in collaboration with Intrexon Corporation (NYSE:XON), a preclinical stage monoclonal antibody combination for the treatment of Pertussis, and novel discovery stage biotherapeutics for the treatment of phenylketonuria (PKU).

### *Product Pipeline:*

*Summary of Microbiome Programs:*

**C. difficile infections (CDI):** We are in clinical development of a novel second-generation oral enzyme, 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. An interim analysis of blinded data from the Phase 2b clinical trial is 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 lovastatin 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<sup>®</sup> (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 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 SYN-010 Phase 2 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

*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 July 2015, through our wholly owned subsidiary, we entered into amended license and clinical trial agreements with The Regents of UCLA. We were also 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.

**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 two posters at ECCMID 2015 (European Congress of Clinical Microbiology and Infectious Diseases). We are seeking 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.

**Phenylketonuria (PKU):** In August 2015, we entered into a third worldwide exclusive channel collaboration with Intrexon Corporation through which we intend to develop and commercialize novel biotherapeutics for the treatment of patients with PKU. We will utilize Intrexon Corporation's ActoBiotics™ platform providing a proprietary method of delivering therapeutic protein and peptides to the gastrointestinal tract through food-grade microbes. This program is in the discovery stage.

**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.

All of our programs are supported by growing patent estates that we either own or exclusively license. In total, each potential product has issued patents that provide protection, and we have approximately 100 U.S. and foreign patents and over 55 U.S. and foreign patents pending.

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 \$127.0 million through June 30, 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.

***Recent Developments***

On August 10, 2015, we expanded our relationship with Intrexon Corporation and entered into an Exclusive Channel Collaboration Agreement (the “Channel Agreement”) with Intrexon Corporation that governs a “channel collaboration” arrangement in which we will use Intrexon Corporation’s technology relating to the development and commercialization of novel biotherapeutics (a “Collaboration Product”) for the treatment of patients with PKU. We have agreed to pay Intrexon Corporation a technology access fee by the issuance of 937,500 shares of common stock, having a value equal to \$3 million as of August 7, 2015, within ten days of approval of the issuance by the NYSE MKT. In addition, upon the achievement of certain milestones, we agreed to pay Intrexon Corporation milestone payments of up to \$27 million for each product developed. We will pay Intrexon Corporation royalties on annual net sales of Collaboration Products, calculated on a product-by-product basis equal to a percent of net sales (ranging from mid-single digits on the first \$100 million of net sales to mid-teen digits on net sales in excess of \$750 million).

On July 21, 2015, we completed a public offering of 15.3 million shares of common stock, including the fully exercised over-allotment option by the underwriters covering 2.0 million shares, at an offering price of \$3.00 per share. The total gross proceeds of the offering, including the exercise in full of the over-allotment option, were approximately \$46.0 million. Net proceeds, after deducting the underwriters' discount and other estimated expenses, were approximately \$42.6 million.

On July 8, 2015, Putney Drug Corp., our subsidiary, and The Regents of UCLA, entered into an amendment to the License Agreement, dated July 11, 2005 (as amended previously), and an amendment to the Clinical Trial Agreement, dated as of April 29, 2010.

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 \$127.0 million through June 30, 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 9605 Medical Center Drive, Suite 270, 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](http://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.

6

## **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 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 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**

Unless otherwise set forth in the applicable prospectus supplement, 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, 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 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 250 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 August 6, 2015, 88,596,568 and 88,515,086 of common stock were issued and outstanding, and no shares of preferred stock were issued and 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 August 6, 2015, we had issued and outstanding a total of 7,908,899 warrants to purchase our common stock outstanding at a weighted-average price of \$1.79.

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 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 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 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 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 quarterly report on Form 10-Q for the quarter ended March 31, 2015 filed with the SEC on May 11, 2015 and our quarterly report on Form 10-Q for the quarter ended June 30, 2015 filed with the SEC on August 10, 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, July 9, 2015, July 17, 2015 and August 10, 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).

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: Synthetic Biologics, Inc., 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 of Common Stock**

**Warrants to Purchase                      Shares of Common Stock**

**PROSPECTUS SUPPLEMENT**

**Cantor Fitzgerald & Co.**

**November     , 2016**