Synthetic Biologics, Inc.
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Registration No. 333-206266

Prospectus Supplement

(To Prospectus dated August 18, 2015)

Up to $40,000,000 of Shares

Common Stock

We have entered into an At Market Issuance Sales Agreement, or sales agreement, with FBR Capital Markets & Co. ("FBR") dated August 5, 2016, relating to shares of our common stock offered by this prospectus supplement. In accordance with the terms of the sales agreement, under this prospectus supplement we may offer and sell up to $40,000,000 of shares of our common stock, $0.001 par value per share, from time to time through FBR, acting as sales agent.

Our common stock is listed on the NYSE MKT under the symbol "SYN." On August 4, 2016, the closing price of our common stock was $1.68 per share.

Sales of our common stock, if any, under this prospectus supplement will be made by any method permitted that is deemed an "at the market offering" as defined in Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"), including sales made directly on or through the NYSE MKT, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices, and/or any other method permitted by law. FBR is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

FBR will be entitled to compensation at a commission rate equal to up to 3.0% of the gross sales price per share sold. In connection with the sale of the common stock on our behalf, FBR may be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of FBR may be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to FBR with respect to certain liabilities, including liabilities under the Securities Act.

Investing in our common stock involves a high degree of risk. Before making an investment decision, please read the information under the heading "Risk Factors" beginning on page S-6 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

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

FBR

The date of this prospectus supplement is August 5, 2016.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement that we filed with the Securities and Exchange Commission (the "SEC") using a "shelf" registration process and consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. Under the shelf registration process, we may offer shares of our common stock having an aggregate offering price of up to $40,000,000 from time to time under this prospectus supplement at prices and on terms to be determined by market conditions at the time of 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 to this "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 the information incorporated or deemed to be incorporated by reference therein. We have not and FBR has 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 FBR 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 of the information you should consider before investing in our common stock. Therefore, you should read the entire prospectus supplement and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the "Risk Factors" section and other documents or information included or incorporated by reference in this prospectus supplement before making any investment decision. 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 product candidates in Phase 2 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:

C- Cedars-Sinai Medical Center Collaboration
I-Intrexon Collaboration
T- The University of Texas at Austin Collaboration

Summary of Clinical and Preclinical Programs

Therapeutic Area	Product Candidate	Status
Treatment of IBS-C	SYN-010 (oral modified-release lovastatin lactone)	· Reported positive topline data from two Phase 2 clinical trials (4Q 2015 & 1Q 2016) · Received Type C meeting responses from FDA regarding late-stage aspects of clinical pathway (2Q 2016) · Presented detailed data supporting previously reported positive topline data from two Phase 2 clinical trials at DDW 2016 (May 2016) · Held End of Phase 2 meeting with FDA (Summer 2016) · Plan to initiate first Phase 2b/3 pivotal adaptive clinical trial (1Q 2017) · Collaboration with Cedars-Sinai Medical Center
Prevention of CDI and AAD (Degrade IV beta-lactam antibiotics)	SYN-004 (ribaxamase) (oral enzyme)	· Reported positive Phase 1a/1b data (1Q 2015) · Initiated Phase 2b proof-of-concept clinical trial (3Q 2015); to date, enrollment of 374 patients across global sites; anticipate interim analysis of blinded data by independent monitoring committee (2H 2016) · Reported supportive topline data from first Phase 2a clinical trial (4Q 2015) · Reported supportive topline data from second Phase 2a clinical trial (2Q 2016) · Plan to announce topline data from Phase 2b proof-of-concept clinical trial (1Q 2017) · Plan to initiate Phase 3 clinical trial(s) (end of 2017) · Received USAN approval for the generic name “ribaxamase” for SYN-004
Prevention of CDI and AAD	SYN-007 (oral enzyme)	· Preclinical work ongoing to determine ability of SYN-007 to protect the gut microbiome and degrade oral beta-lactam antibiotics

(Degrade oral beta-lactam antibiotics)		
Prevention and Treatment of pertussis	SYN-005 (monoclonal antibody therapies)	· Reported positive 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

Recent Developments

In May 2016, we presented detailed data supporting previously reported positive topline data from two Phase 2 clinical trials of two dose strengths of SYN-010 at DDW2016.

Clinical data from the 57 patients who completed Study 1 and 54 patients who completed Study 2 showed clinically meaningful improvements in measurable endpoints, including:

- Data from Study 1 demonstrating that patients on either the 21 mg or 42 mg dose strength of SYN-010 used 60% less rescue medication than patients in the placebo group.

- Data from all patients who participated in both Study 1 and Study 2 and who were administered the 42 mg dose strength of SYN-010 for at least eight weeks demonstrated an inverse correlation (p=0.0259) between breath methane AUC and complete spontaneous bowel movements (CSBM). A similar inverse correlation (p=0.0028) was observed between breath methane AUC and spontaneous bowel movements (SBM).

- Data demonstrating the 42 mg dose strength of SYN-010 had a similar overall drug response rate to comparable FDA approved and clinical stage therapies for the treatment of IBS-C with a significantly lower rate of diarrhea in study participants.

- Data demonstrating clear improvements in abdominal pain, bloating and quality of life measures (IBS-SSS) in participants who were administered SYN-010.

In May 2016, we reported results from a separate completed randomized, open-label clinical study of healthy volunteers which evaluated the pharmacokinetic (PK) profile of the active ingredient of SYN-010. The PK data in healthy volunteers supported the modified-release profile of SYN-010, which is designed to avoid drug release in the stomach and deliver the antimethanogenic drug form, lovastatin lactone, into the lower small intestine and colon while reducing systemic exposure to the cholesterol-lowering lovastatin beta-hydroxyacid metabolite. Data reported from this study demonstrate that the administration of SYN-010 did not result in adverse changes to the lipid profiles of study participants.

In May 2016, we also reported supportive topline results from our second Phase 2a clinical trial of ribaxamase, including data that demonstrated a correlation of the 150 mg dose of ribaxamase, both alone and in the presence of the proton pump inhibiter (PPI), esomeprazole, with the degradation of residual IV ceftriaxone to levels that were near or

below detectable in the intestinal chyme (digestive fluid in the small intestine) of 14 healthy participants with functioning ileostomies. In addition, ceftriaxone plasma concentrations in study participants were very similar in the presence or absence of an oral PPI, suggesting limited drug-drug interactions. The 150 mg dose strength of ribaxamase was well tolerated by all participants in this clinical trial.

Data from an additional study conducted in humanized pigs demonstrated that when administered in accordance with ceftriaxone, ribaxamase prevented ceftriaxone-remediated changes in the pig fecal microflora, protecting the microbiome from antibiotic-mediated damage when compared to pigs who only received ceftriaxone.

Phase 3 Development of SYN-010

On July 20, 2016, we participated in an End of Phase 2 meeting with the U.S. Food and Drug Administration (the "FDA"). Following a review of data from two Phase 2 clinical trials of SYN-010 conducted by us, a collaborative and positive discussion ensued with FDA to determine the optimal pathway to advance SYN-010 into Phase 3 development. In accordance with guidance from the FDA, our plans include the development of a Phase 2b/3 adaptive design study for our first pivotal trial of SYN-010 which will address further dose exploration and sensitivity analysis of breath methane levels for trial participation. We plan to submit a study protocol design and corresponding statistical analysis plan to the FDA during the second half of 2016 and anticipate initiating this clinical trial during the first quarter of 2017.

Phase 2b Clinical Trial Design / Phase 3 Planning

In September 2015, we initiated a randomized placebo-controlled Phase 2b proof-of-concept clinical trial intended to evaluate the ability of ribaxamase to prevent CDI, *C. difficile* associated diarrhea (CDAD) and AAD in patients hospitalized for a lower respiratory tract infection and receiving IV ceftriaxone. An exploratory endpoint will be to evaluate the ability of ribaxamase to limit disruption of the gut microbiome diversity, also known as dysbiosis. Once either 120 patients complete treatment and there are 10 confirmed cases of CDI, or 186 patients complete treatment, an interim futility analysis to evaluate baseline rate of CDI in the placebo group is anticipated. We intend to have an independent monitoring committee perform an interim futility analysis of the blinded data during the second half of 2016. As a result of stronger than expected enrollment of 374 patients to date, we anticipate greater than 400 patients to enroll by the end of the third quarter and anticipate announcing topline results from our Phase 2b clinical trial during the first quarter of 2017. In 2017, we also plan to enter into strategic discussions with the CDC, hold an end of Phase 2 meeting with the FDA, and expect to initiate Phase 3 trial(s) towards the end of 2017.

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 amended our Articles of Incorporation to change 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*. The information contained on 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."

THE OFFERING

Common stock offered by us pursuant to this prospectus supplement	Shares of our common stock having an aggregate offering price of up to $40,000,000.
Common stock to be outstanding after this offering	Up to 115,079,109 shares (as more fully described in the notes following this table), assuming sales of 23,809,523 shares of our common stock in this offering at an offering price of $1.68 per share, which was the last reported sale price of our common stock on the NYSE MKT on August 4, 2016. The actual number of shares issued will vary depending on the sales price under this offering.
Manner of offering	"At the market offering" that may be made from time to time on the NYSE MKT or other market for our common stock in the United States through our agent, FBR Capital Markets & Co. See the section entitled "Plan of Distribution" on page S-11 of this prospectus supplement.
Use of proceeds	We intend to use the net proceeds, if any, from this offering for general corporate purposes, which may include, among other things, for clinical trials for our product candidates, paying general and administrative expenses and accounts payable, increasing our working capital, funding research and development and funding capital expenditures. We may also 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, although we have no commitments or agreements with respect to any such licenses, acquisitions or investments as of the date of this prospectus supplement. See "Use of Proceeds" on page S-9.
Risk factors	You should read the "Risk Factors" section of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement for a discussion of factors to consider before deciding to purchase shares of our common stock.
NYSE MKT symbol	SYN

Except as otherwise indicated, all information in this prospectus supplement is based on 91,269,586 shares outstanding as of June 30, 2016 and excludes:

- 8,613,413 shares of our common stock subject to options outstanding as of June 30, 2016 having a weighted-average exercise price of $2.15 per share;

- 557,815 shares of our common stock that have been reserved for issuance in connection with future grants under our stock option plans as of June 30, 2016; and

- 7,858,899 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of June 30, 2016 having a weighted-average exercise price of $1.77 per share.

Unless otherwise stated, all information contained in this prospectus supplement reflects an assumed public offering price of $1.68 per share, which was the last reported sale price of our common stock on the NYSE MKT on August 4, 2016.

RISK FACTORS

Investing 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 Annual Report on Form 10-K for the year ended December 31, 2015, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2016, any subsequent Annual Reports on Form 10-K, any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus supplement and the accompanying prospectus before deciding whether to purchase any of the common stock being offered under this prospectus supplement. Each of the risks described below could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock, and the occurrence of any of these risks might cause you to 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."

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 for general corporate purposes, which may include, among other things, for clinical trials for our product candidates, paying general and administrative expenses and accounts payable, increasing our working capital, funding research and development and funding capital expenditures. We may also 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, although we have no commitments or agreements with respect to any such licenses, acquisitions or investments as of the date of this prospectus supplement. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our common stock. The failure of our management to use these funds effectively could have a material adverse effect on our business, cause the market price of our common stock to decline and impair the commercialization of our products and/or delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing instruments and U.S. government securities. These investments may not yield a favorable return to our stockholders.

If you purchase shares of our common stock sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional equity or convertible debt securities in the future, which may result in additional dilution to investors.

The price per share of our common stock being offered may be higher than the net tangible book value per share of our outstanding common stock prior to this offering. Assuming that an aggregate of 23,809,523 shares of our common stock are sold at a price of $1.68 per share, the last reported sale price of our common stock on the NYSE MKT on August 4, 2016, for aggregate gross proceeds of approximately $40,000,000 million, and after deducting commissions and estimated offering expenses payable by us, new investors in this offering will incur immediate dilution of $1.34 per share. For a more detailed discussion of the foregoing, see the section entitled “Dilution” below. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors.

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

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by 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 paid by investors in this offering.

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.

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

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

The shares of common stock offered under this prospectus supplement and the accompanying prospectus may be sold in "at the market" offerings, and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares under this prospectus supplement and the accompanying prospectus at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum

or maximum sales price. Investors may experience declines in the value of their shares as a result of share sales made at prices lower than the prices they paid.

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, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), these 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 a future or forward-looking nature identify forward-looking statements for purposes of the federal securities laws or otherwise.

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

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USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate gross proceeds of up to $40,000,000 from time to time under the sales agreement. Because there is no minimum offering amount required as a condition to close this offering, the actual total offering amount, commissions and proceeds to us, if any, are not determinable at this time. The amount of proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement with FBR as a source of financing. We intend to use the net proceeds, if any, from this offering for general corporate purposes, which may include, among other things, for clinical trials for our product candidates, paying general and administrative expenses and accounts payable, increasing our working capital, funding research and development and funding capital expenditures. We may also 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, although we have no commitments or agreements with respect to any such licenses, acquisitions or investments as of the date of this prospectus supplement.

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

DIVIDEND POLICY

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

DILUTION

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

Our net tangible book value on June 30, 2016 was approximately $0.9 million, or $0.01 per share. “Net tangible book value” is total assets minus the sum of liabilities and intangible assets. “Net tangible book value per share” is net tangible book value divided by the total number of shares outstanding.

After giving effect to the sale of shares of common stock in this offering in the aggregate amount of $40,000,000 at an assumed offering price of $1.68 per share, which is the last reported sale price of our common stock on the NYSE MKT on August 4, 2016 and after deducting estimated offering commissions and estimated aggregate offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2016 would have been approximately $39.6 million, or $0.34 per share of common stock. This represents an immediate increase in net tangible book value of $0.33 per share to our existing stockholders and an immediate dilution in net tangible book value of $1.34 per share to investors participating in this offering. The following table illustrates this dilution per share to investors participating in this offering:

Assumed Public offering price per share		$1.68
Net tangible book value per share as of June 30, 2016	$0.01	
Increase in net tangible book value per share attributable to new investors purchasing our common stock in this offering	$0.33	
As adjusted net tangible book value per share after giving effect to this offering		$0.34
Dilution per share to investors purchasing our common stock in this offering		$1.34

The above discussion and table are based on 91,269,586 shares of our common stock outstanding as of June 30, 2016, which does not include the following, all as of June 30, 2016:

- 8,613,413 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of $2.15 per share;
- 557,815 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.

The above illustration of dilution per share to investors participating in this offering assumes no exercise of outstanding options to purchase our common stock or outstanding warrants to purchase shares of our common stock. To the extent that any of these outstanding options or warrants are exercised or we issue additional shares under our equity incentive plans, there will be further dilution to new investors. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

PLAN OF DISTRIBUTION

We have entered into the sales agreement with FBR under which we may issue and sell our common stock having an aggregate gross sales price of up to $40,000,000 from time to time through FBR acting as sales agent, subject to certain limitations, including the number of shares registered under the registration statement to which the offering relates. The sales, if any, of shares made under the sales agreement will be made by any method that is deemed an "at the market offering" as defined in Rule 415 promulgated under the Securities Act, including sales made directly on or through the NYSE MKT, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices, and/or any other method permitted by law. We may instruct FBR not to sell common stock if the sales cannot be effected at or above the price designated by us from time to time. We or FBR may suspend the offering of common stock upon notice and subject to other conditions.

FBR will offer our common stock subject to the terms and conditions of the sales agreement as agreed upon by us and FBR. Each time we wish to issue and sell common stock under the sales agreement, we will notify FBR of the number of shares to be issued, the time period during which such sales are requested to be made, any limitation on the number of shares that may be sold in one day, any minimum price below which sales may not be made and other sales parameters as we deem appropriate. Once we have so instructed FBR, unless FBR declines to accept the terms of the notice, FBR has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of FBR under the sales agreement to sell our common stock are subject to a number of conditions that we must meet.

We will pay FBR commissions for its services in acting as agent in the sale of common stock. FBR will be paid a commission in an amount equal to up to 3.0% of the gross sales price per share sold. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse FBR for certain specified expenses, including the fees and disbursements of its legal counsel in an amount not to exceed $30,000. We estimate that the total expenses for the offering, excluding commissions and reimbursements payable to FBR under the terms of the sales agreement, will be approximately $150,000.

Settlement for sales of common stock will generally occur on the third business day following the date on which any sales are made, or on some other date that is agreed upon by us and FBR in connection with a particular transaction, in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of the common stock on our behalf, FBR may, and will with respect to sales effected in an "at the market offering," be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation

of FBR may be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to FBR against certain civil liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to the sales agreement will terminate upon the earlier of (i) the sale of all of our common stock subject to the sales agreement, or (ii) termination of the sales agreement as provided therein. We may terminate the sales agreement at any time upon five days' prior notice to FBR and FBR may terminate the sales agreement at any time upon ten days' prior notice to us.

FBR and its affiliates may in the future provide various investment banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, FBR will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

This summary of the material provisions of the Sales Agreement does not purport to be a complete statement of its terms and conditions. A copy of the Sales Agreement has been filed with the SEC as an exhibit to a Current Report on Form 8-K.

This prospectus in electronic format may be made available on a website maintained by FBR and FBR may distribute this prospectus electronically.

LEGAL MATTERS

Gracin & Marlow, LLP, New York, New York is representing us in connection with this offering. The validity of the securities offered hereby will be passed upon for us by Parsons Behle & Latimer, Reno, Nevada. Duane Morris LLP, Newark, New Jersey is acting as counsel for FBR 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 an effective 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 supplement and the accompanying 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*. 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. 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 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 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 the 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 Report on Form 10-Q for the quarter ended March 31, 2016 filed with the SEC on May 5, 2016 (File No. 001-12584);

- Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2016 filed with the SEC on August 3, 2016 (File No. 001-12584);

- Our Current Reports on Form 8-K filed with the SEC on February 2, 2016 and August 5, 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.

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.

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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® (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*. 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.

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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 o 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 Form10-Q, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus supplement and the accompanying prospectus. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

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

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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.

Up to $40,000,000 of Shares

Common Stock

PROSPECTUS SUPPLEMENT

FBR

August 5, 2016