

Synthetic Biologics, Inc.  
Form 424B3  
December 06, 2012

**Filed Pursuant to Rule 424(b)(3)**

**Registration Statement No. 333-180562**

**December 6, 2012**

**PROSPECTUS SUPPLEMENT NO. 12**

**SYNTHETIC BIOLOGICS, INC.**

**112,573 Shares of Common Stock**

This prospectus supplement amends and supplements our prospectus, dated July 26, 2012 relating to the resale, from time to time, of up to 112,573 shares of common stock of Synthetic Biologics, Inc. upon the exercise of warrants issued in July 2011 at an exercise price of \$1.00 per share and warrants sold in our July 2010 offering at an exercise price of \$1.32 per share. We will receive proceeds if the warrants are exercised for cash; to the extent we receive such proceeds, they will be used for working capital purposes.

Our common stock became eligible for trading on the NYSE MKT October 16, 2008. Our common stock is eligible for quotation on the NYSE MKT under the symbol "SYN". The closing price of our stock on December 5, 2012 was \$1.86.

This prospectus supplement is being filed to include the information set forth in the Current Report on Form 8-K filed on December 6, 2012, which is set forth below. This prospectus supplement should be read in conjunction with the prospectus dated July 26, 2012, supplement no. 1 dated August 9, 2012, prospectus supplement no. 2 dated August 15, 2012, prospectus supplement no. 3 dated August 15, 2012, prospectus supplement no. 4 dated September 12, 2012, prospectus supplement no. 5 dated October 9, 2012, prospectus supplement no. 6 dated October 17, 2012, prospectus supplement no. 7 dated November 1, 2012, prospectus supplement no. 8 dated November 14, 2012; prospectus supplement no. 9 dated November 15, 2012; prospectus supplement no. 10 dated November 15, 2012; and prospectus

supplement no. 11 which are to be delivered with this prospectus supplement.

**Investing in our securities involves a high degree of risk. See “Risk Factors” beginning on page 4 of the original prospectus for more information.**

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

The date of this Prospectus Supplement No. 12 is December 6, 2012.



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(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Item 7.01. Regulation FD Disclosure**

Jeffrey Riley, Chief Executive Officer and President of Synthetic Biologics, Inc. (the “Company”), will be presenting at the LD MICRO Conference in Los Angeles, CA, as well as making several investor presentations during the next few weeks, the first of which will be on December 6, 2012. In connection with the presentations, Mr. Riley intends to discuss the slide presentation furnished as Exhibit 99.1 hereto, which is incorporated herein by reference.

The slide presentation attached as Exhibit 99.1 to this Report includes “safe harbor” language pursuant to the Private Securities Litigation Reform Act of 1995, as amended, indicating that certain statements contained in the slide presentation are “forward-looking” rather than historical.

The information included in this Item 7.01 and in Exhibit 99.1 shall not be deemed filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that Section or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing. The Company undertakes no duty or obligation to update or revise information included in this Report or the Exhibit.

**Item 9.01. Financial Statements and Exhibits**

(d) Exhibits

The following exhibit is being filed as part of this Report.

**Exhibit**

**Number Description**

99.1 Presentation materials to be provided at the Synthetic Biologics, Inc.’s investor presentations.

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SYNTHETIC BIOLOGICS, INC.

Date: December 6, 2012 By: /s/ C. Evan Ballantyne  
Name: C. Evan Ballantyne  
Title: Chief Financial Officer

**EXHIBIT INDEX**

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99.1 Presentation materials to be used at Synthetic Biologics, Inc.'s investor presentations.

NYSE MKT: SYN December 2012



**Forward - Looking Statements** This presentation includes forward - looking statements on Synthetic Biologics' current expectations and projections about future events . In some cases forward - looking statements can be identified by terminology such as "may," "should," "potential," "continue," "expects," "anticipates," "intends," "plans," "believes," "estimates," "indicates," and similar expressions . These statements are based upon current beliefs, expectations and assumptions and are subject to a number of risks and uncertainties, many of which are difficult to predict and include statements regarding our clinical trials, our establishment of collaborations and our execution of our growth strategy . The forward - looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those set forth or implied by any forward - looking statements . Important factors that could cause actual results to differ materially from those reflected in Synthetic Biologics' forward - looking statements include, among others, a failure of our product candidates to be demonstrably safe and effective, a failure to initiate clinical trials and if initiated, a failure to achieve the desired results, a failure to obtain regulatory approval for our product candidates or to comply with ongoing regulatory requirements, regulatory limitations relating to our ability to promote or commercialize our product candidates for the specific indications, a lack of acceptance of our product candidates in the marketplace, a failure of us to become or remain profitable, a failure to establish collaborations, our inability to obtain or maintain the capital or grants necessary to fund our research and development activities, a loss of any of our key scientists or management personnel, and other factors described in Synthetic Biologics' report on Form 10 - K/A for the year ended December 31 , 2011 , subsequent Form 10 - Qs and any other filings with the SEC . The information in this presentation is provided only as of the date presented, and Synthetic Biologics undertakes no obligation to update any forward - looking statements contained in this presentation on account of new information, future events, or otherwise, except as required by law . 2

Emerging Worldwide Crisis 3 Antibiotic - resistant infectious diseases Brad Spellberg , M.D., author of the book, Rising Plague 1 : Infections were the second leading cause of death worldwide in 2002, killing nearly 15 million people – almost 1 in 3 deaths across the globe Antibiotic - resistant microbes infect more than 2 million Americans each year, killing over 100,000 people

Targeting Infectious Diseases 4 Synthetic Biologics is utilizing monoclonal antibodies, proteins, peptides and enzymes to execute a “ sniper” approach to address infectious disease indications vs. a broad spectrum “shotgun” approach. Strategically, this has been successfully validated over the past 15 years in another disease state: oncology. A biologics approach.

Management Team 5 • Jeffrey Riley, CEO Pfizer, Nichols Institute (Quest), SmithKline Beecham, QIC • C. Evan Ballantyne , CFO Clinical Data, Inc., Avedro , ZymeQuest , ACNielsen, IMS • John Monahan, Ph.D., EVP R&D Avigen , Somatix , Triton Biosciences, Hoffman - LaRoche • Carol Reed, M.D., SVP Clinical/Regulatory Clinical Data, Inc., Genaissance Pharmaceuticals, Inc., Bayer Pharmaceuticals, Inc. • Michael Kaleko , M.D., Ph.D ., SVP R&D Genetic Therapy, Inc. (Novartis)

Corporate Overview • Build out pipeline with later clinical - stage opportunities • Targeting multidrug - resistant infectious diseases using biologics approach Clostridium difficile infections Acinetobacter baumannii – gram - negative Additional undisclosed infectious disease - specific programs • Additional programs Synthetic DNA for pulmonary arterial hypertension (PAH) Proprietary oral estriol for multiple sclerosis (MS) • Two strategic collaborations with Intrexon Corporation – Private biotechnology company led by CEO, RJ Kirk 6 NYSE MKT: SYN

Corporate Focus • Infectious disease outbreaks increasing while intervention options decline 2 Widespread multidrug - resistant pathogens Increasing numbers of immuno - compromised patients New pathogens • Utilize targeted biologics approach – similar to cancer drugs 15 years ago • Large and growing markets Significant unmet medical need • Counter - cyclical strategy Big pharma has not invested in this area for many years • GAIN Act: Enhances regulatory pathway for novel infectious disease treatments Includes additional 5 years of market protection, fast track and accelerated NDA reviews • Opportunity to monetize/partner infectious disease programs Revolutionize the treatment of infectious diseases 7

Product Pipeline 8

9 • Prophylactic treatment for prevention of C. diff infection Develop SYN - 004, a proprietary oral  $\beta$ -lactamase enzyme, to be co-administered with  $\beta$ -lactam antibiotics, such as penicillins and cephalosporins ~8.7 million Americans administered IV  $\beta$ -lactam antibiotics during 2011 3 Acts locally in GI tract protecting microflora against harmful effects of  $\beta$ -lactam antibiotics Maintain natural GI microflora balance No systemic exposure Does not affect systemic action of  $\beta$ -lactam antibiotics • Acquired  $\beta$ -lactamase assets for prevention of C. diff infection Phase I and II studies demonstrated safety, tolerability and efficacy Infectious Diseases: Clostridium difficile (C. diff) Acquired clinical - stage program November 2012



10 SYN - 004: Prevention of C. difficile Protects against damaging/harmful effects of  $\beta$ -lactam antibiotics  
N O N N S  
O O O H H N O N N H S O H H O O H Active  $\beta$ -lactam Inactive Ampicilloic acid P3A Orally administered P3A i.v.  
administered  $\beta$ -lactams P3A degrades active  $\beta$ -lactam antibiotics in GI tract to inactive ampicilloic acid Biliary  
secretion of  $\beta$ -lactams  $\beta$ -lactams SYN - 004 Inactive Ampicilloic acid Active  $\beta$ -lactam N O N N S O O O H H N O  
N N H S O H H O O H Active  $\beta$ -lactam Inactive Ampicilloic acid P3A Orally administered P3A i.v. administered  
 $\beta$ -lactams P3A degrades active  $\beta$ -lactam antibiotics in GI tract to inactive ampicilloic acid Biliary secretion of  $\beta$ -  
lactams  $\beta$ -lactams Orally administer SYN - 004 Biliary secretion of  $\beta$ -lactams IV administered  $\beta$ -lactam antibiotic  
SYN - 004 intended to degrade active  $\beta$ -lactam antibiotics in GI tract to inactive ampicilloic acid • SYN - 004 is not  
an antibiotic but a bio-engineered serine  $\beta$ -lactamase enzyme • SYN - 004 intended to degrade active  $\beta$ -lactam  
antibiotics in GI tract to inactive ampicilloic acid

SYN - 004: Acting locally in the GI Tract without Affecting Systemic Action of Antibiotics

PIPERACILLIN-TAZOBACTAM + IPSAT P1A 28 mg (N=12) PIPERACILLIN-TAZOBACTAM + IPSAT P1A 56 mg (N=12) PIPERACILLIN-TAZOBACTAM + Placebo (N=12) FAECAL PIPERACILLIN CONCENTRATIONS ( $\mu\text{g/g}$ ) 0 25 50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 DAY 1DAY 1DAY 1 DAY 2DAY 2DAY 2 DAY 3DAY 3DAY 3 DAY 4DAY 4DAY 4 DAY 5DAY 5DAY 5 DAY 6DAY 6DAY 6 LINEAR SCALE PIPERACILLIN-TAZOBACTAM + IPSAT P1A 28 mg (N=12) PIPERACILLIN-TAZOBACTAM + IPSAT P1A 56 mg (N=12) PIPERACILLIN-TAZOBACTAM + Placebo (N=12) PLASMA CONCENTRATION ( $\mu\text{g/ml}$ ) 0 40 80 120 160 200 240 280 320 360 TIME (h) H0 H0.5 H1 H2 H3 H4 H5 H6 0 40 80 120 160 200 240 280 GI Tract Systemic 11 Oral First Generation Candidate (formerly known as P1A) Degrades Pip/ Tazo in GI Tract WITHOUT Affecting Systemic pK of Pip/ Tazo in Humans Ipsat Therapeutics Phase I Trial: IT - 008 data acquired from Prev AbR LLC; November 2012.

12 • Increasing incidence and often drug resistant • Toxins produced by C. diff bacteria result in diarrhea, and in serious cases lead to pseudomembranous colitis and possibly death • In the U.S. during 2009, infections caused by C. diff resulted in: – More than 337,000 hospitalizations 4 – 30,000 deaths 4 – \$8.2 billion in costs associated with C. diff - related stays in the hospital 5 • Currently the leading cause of hospital acquired infections (HAIs) C. difficile : Market Overview Impact on patients and growing economic burden There are currently no approved products for the prevention of C. diff infections

Acinetobacter Infection : Market Overview  
Deadly gram - negative bacteria • Mortality rates as high as 43% reported  
6 • Multi - billion dollar market opportunity  
7 • Multidrug - resistant due to pathogen's ability to rapidly mutate  
8 • Survives on dry surfaces for up to 36 days  
Survives twice as long as non - biofilm - forming pathogens  
9 • Acinetobacter disease profile  
2.6% of HAIs  
10 1.3% of bloodstream infections  
10 7% of ICU respiratory tract infections in U.S.  
10 Pneumonia , bacteremia, endocarditis, skin and soft tissue infections, urinary tract infections and meningitis  
• Increasing trauma center risk for wounded military personnel and natural disaster victims  
11 13

Acinetobacter : Monoclonal Antibody Approach 14 Intrexon collaboration for mAb development Intrexon's proprietary technologies/processes produce mAbs to detect and destroy viruses, bacteria and toxins • mAbLogix™ – fully human antibody discovery platform • LEAP™ – rapid identification and selection of targeted cells of interest • Protein engineering – improved or novel protein functions mAbLogix™ and LEAP™ are registered trademarks of Intrexon Corporation.

15 mAbLogix™ Platform for mAb Development Infection disease pathogen (bacteria, viruses & toxins) mAb injection “tags” pathogen Immune system attacks “tagged” pathogen Rapid production of fully human mAbs begins with human tonsil tissue mAbLogix™ is a registered trademark of Intrexon Corporation.

SYN - PAH: Synthetic DNA Therapy Intrexon's proprietary technologies/processes deliver synthetic DNA to the pulmonary arteries generating high levels of prostacyclin to treat PAH • UltraVector® Platform – scalable, rapid development and customization of transgenes • Cellular modeling – cell system informatics for faster design of new gene targets and product pathways • Genome engineering – gene delivery providing optimal expression for desired time at specific location Intrexon collaboration for PAH 16 Synthetic biology is an emerging field being explored/featured by many. In 2012, Fidelity® Investments launched its “Thinking Big” initiative that provides leading - edge insights into topics such as synthetic biology . UltraVector® is registered trademarks of Intrexon Corporation.

PAH: Market Overview 17 • Global PAH market expected to reach \$3.6 billion 12 by 2015 • High morbidity and mortality • Currently three classes of approved therapeutics – Prostacyclin analogs: well - established efficacy but significant systemic side effects that inhibit utility and long - term benefits – Endothelin receptor antagonists: widely - used, but may have dangerous hepatic effects that led to a Black Box Warning for a leading drug – PDE5 inhibitors: moderate efficacy and are often used in combo with the other classes Applying synthetic DNA to PAH



MS: Market Opportunity • According to the National Multiple Sclerosis Society – 400,000 MS patients in U.S. (2.5 million worldwide) – 200 people diagnosed per week in the U.S. – 1.75 million patients worldwide are women • ~60% of patients are women originally diagnosed with relapsing - remitting MS • ~35% of MS patients are women who are affected by cognitive dysfunction • Oral disease - modifying therapies, such as Trimesta TM , are expected to overtake injectables for MS • Global market potential \$8.7 billion 13 • Exploring partnering opportunities Unmet need for oral MS therapies such as SYN's Trimesta TM (oral estriol) 18

MS: Historical Efficacy of Estriol The “Pregnancy Hormone”: Linked to decreased MS relapse rates • Estriol – Hormone produced by placenta during pregnancy – Solid safety profile (approved in Europe/Asia for 40+ years) • Landmark study published in New England Journal of Medicine 14 – Study of 254 women diagnosed with MS prior to pregnancy – Relapse rates were significantly reduced ( $p < 0.001$ ) in the third trimester of pregnancy compared to pre - pregnancy levels – Relapse rates were significantly increased ( $p < 0.001$ ) during the first three months post - partum compared to pre - pregnancy levels – The decrease in relapse rate during pregnancy was more prominent than any other therapeutic effect reported to date 19

MS: Relapsing - Remitting MS Phase II Clinical Trial of Trimesta™ (oral estriol) • Multi - center, randomized, double - blind, placebo - controlled trial – Comparing relapse rates over 2 years between 8 mg of oral Trimesta™ taken daily versus matching placebo – All patients treated with Copaxone® as standard of care – Enrollment complete: 164 patients at 15 U.S. centers – Results expected 2H 2014 • Largest MS Society grant (total grants \$8 million+) – Ongoing Phase II clinical trial in women with relapsing - remitting MS 15 funded to completion • Rhonda Voskuhl, M.D., Professor, UCLA Department of Neurology, Trimesta™ key opinion leader and lead principal investigator 20 Copaxone® is a registered trademark of Teva Pharmaceutical Industries Ltd.

MS: Cognitive Dysfunction • Randomized, double - blind, placebo - controlled clinical trial of female MS patients at UCLA 16 – Enrollment initiated January 2012 – Trimesta TM versus matching placebo over one year with all patients remaining on standard FDA - approved MS treatment – Results expected 2H 2014 • Pilot trial conducted by Dr. Voskuhl demonstrated a 14% improvement in Paced Auditory Serial Addition Test (PASAT) cognitive testing scores (  $p = 0.04$ ) in relapsing - remitting MS patients at 6 months of therapy versus continued cognitive deterioration • Majority of ongoing costs funded by philanthropic foundations, including Skirball Foundation 21 Phase II Clinical Trial of Trimesta TM

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Corporate Snapshot • Current Price : \$2.00 (as of 11/30/12) • 52 Week Range: \$1.04 - \$ 2.95 • Average Volume (3 months): 48,087 • Shares Outstanding: ~43.7 million (as of 10/31/12 ) • Warrants Outstanding: ~2.0 million \* • Vested Options Outstanding: ~2.6 million \*\* • Market Capitalization: ~\$87 million • Cap Structure: Common, no debt, no preferred • Cash: ~\$14.2 million ( pro forma 10/31/12) • Offices in Rockville, Maryland 22 \* As of October 31, 2012; weighted average exercise price is \$2.72 \*\* As of October 31, 2012; weighted average exercise price is \$1.76; total options outstanding: ~4.3 million NYSE MKT: SYN

23 Upcoming Milestones • Initiate development of recently acquired *C. difficile* clinical program (4Q 2012) • Fully human mAbs for *Acinetobacter* – Design, engineer and optimize lead candidates to confirm in vivo activity (1Q 2013) – Generate panel of recombinant fully human antibodies (1Q 2013) – Develop and manufacture cell lines • Initiate development plans for two other infectious diseases indications (Discussions under way) • Synthetic DNA - based therapy for PAH – Vector optimization underway – Planned animal toxicology studies – Targeting human trials (2014 timeframe) • In - license additional programs from universities and other third parties • Complete Phase II MS clinical trials – Complete patient enrollment in cognitive dysfunction trial (2H 2013) – Results from cognitive dysfunction trial (2H 2014) – Results from relapsing - remitting trial (2H 2014)

NYSE MKT: SYN December 2012 Dec 2012 – v6 – FINAL

References Slide 3 : 1 Spellberg , B. Rising Plague: The Global Threat from Deadly Bacteria and Our Dwindling Arsenal to Fight Them. Copyright 2009. Slide 7 : 2 Saylor, C, Dadachova , E, Casadevall , A, Monoclonal antibody - based therapies for microbial diseases. Vaccine. 2009 December 30; 27 ( Suppl 6): G38 - G46. Slide 9 : 3 GlobalData . Beta - lactam Antibiotics Sales - United States of America, 2011. Prepared for Synthetic Biologics, Inc. November 2012. Slide 11 : 4 U.S. Department of Health & Human Services. Agency for Healthcare Research and Quality. January 25, 2012. Available at <http://www.ahrq.gov/news/nn/nn012512.htm> . Accessed November 5, 2012 . 5 Agency for Healthcare Research and Quality. Healthcare and Cost Utilization Project. Statistical Brief #124. Clostridium difficile Infections (CDI) in Hospital Stays, 2009. January 2012. Available at <http://www.hcup-us.ahrq.gov/reports/statbriefs/sb124.pdf> . Slide 9 : 6 Falagas , ME, Bliziotis , LA, and Siempos , II. Attributable mortality of Acinetobacter baumannii infections in critically ill patients: a systematic review of matched cohort and case - control studies. Critical Care 2006, 10:R48. 7 Barrett, L. Former VP of US Marketing and Global Business Manager Infectious Diseases at Wyeth. Guest Blog, Antibiotic Markets and SPLU. <http://antibiotics-theperfectstorm.blogspot.com/2012/03/antibiotic-markets-and-splu-guest.html> . March 20, 2012 . 8 The Center for Disease Dynamics, Economics & Policy. <http://cddep.org/ResistanceMap/overview> . Trends by U.S. Census Divisions for Multidrug - resistant Acinetobacter baumannii (2010). 9 Espinal P, Martí S, Vila J. Effect of biofilm formation on the survival of Acinetobacter baumannii on dry surfaces. J Hosp Infect. 2012 Jan; 80(1):56 - 60. Epub 2011 Oct 4 . 10 Jones, M, et al. Emerging resistance among bacterial pathogens in the intensive care unit – a European and North American Surveillance study (2000 - 2002). Ann Clin Microbiol Antimicrob ; 3(14).; Wisplinghoff , H, et al. Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study. Clin Infect Dis 2004; 39(3): 309 - 17.; Wachter , K. Step Aside, MRSA, Here Comes Acinetobacter . OB. GYN. News , January 15, 2006 . 11 Camp , C and Tatum, OL. A Review of Acinetobacter baumannii as a Highly Successful Pathogen in Times of War. LABMEDICINE. November 2010, Vol. 41, Number 11. 25



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