# REPLY EXHIBIT 6

Reply Exhibit 6 – Synthetic Biologics, Inc. Form 10-K filed February 22, 2018 (excerpts)

*Nejmeh v. Theriva Biologics, Inc.*, No. 3:26-cv-00705-ART-CSD (D. Nev.)

Source: SEC EDGAR, Accession No. 0001144204-18-010286.

**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**Washington, DC 20549**

**FORM 10-K**

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended December 31, 2017**

**OR**

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES ACT OF 1934**

**For the transition period from to**

**Commission File Number: 1-12584**

# SYNTHETIC BIOLOGICS, INC.

*(Exact Name of Registrant as Specified in Its Charter)*

| **Nevada** | **13-3808303** |
|---|---|
| *(State or Other Jurisdiction of Incorporation or Organization)* | *(I.R.S. Employer Identification Number)* |
| **9605 Medical Center Drive, Ste. 270 Rockville, MD** | **20850** |
| *(Address of Principal Executive Offices)* | *(Zip Code)* |

**Registrant's telephone number, including area code:**
**(301) 417-4364**

| **Securities registered pursuant to Section 12(b) of the Act:** | **Name of each exchange on which registered:** |
|---|---|
| **Common Stock, $0.001 par value per share** | **NYSE AMERICAN, LLC** |

**Securities registered pursuant to Section 12(g) of the Act:**
***None***

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.
Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.
Yes ☐ No ☒

Indicate by check mark whether the issuer: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.
Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (section 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).
Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of issuer's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

## PART I

### Special Note Regarding Forward-Looking Statements

*This Annual Report on Form 10-K (this "Annual Report") contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 1. "Business," Part I, Item 1A. "Risk Factors," and Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations," but are also contained elsewhere in this Annual Report. In some cases you can identify forward-looking statements by terminology such as "may," "should," "potential," "continue," "expects," "anticipates," "intends," "plans," "believes," "estimates," and similar expressions. These statements are based on our current beliefs, expectations, and assumptions and are subject to a number of risks and uncertainties, many of which are difficult to predict and generally beyond our control, that could cause actual results to differ materially from those expressed, projected or implied in or by the forward-looking statements.*

*You should refer to Item 1A. "Risk Factors" section of this Annual Report for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We do not undertake any obligation to update any forward-looking statements.*

*Unless the context requires otherwise, references to "we," "us," "our," and "Synthetic Biologics," refer to Synthetic Biologics, Inc. and its subsidiaries.*

### Item 1. *Business*

### Overview

We are a late-stage clinical company focused on developing therapeutics designed to preserve the microbiome to protect and restore the health of patients. Our lead candidates poised for Phase 3 development are: (1) 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), overgrowth of pathogenic organisms and the emergence of antimicrobial resistance (AMR), and (2) 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). Our preclinical pursuits include an oral formulation of the enzyme intestinal alkaline phosphatase (IAP) to treat both local GI disorders and systemic diseases as well as monoclonal antibody therapies for the prevention and treatment of pertussis, and novel discovery stage biotherapeutics for the treatment of phenylketonuria (PKU).

Preliminary analysis of the data also demonstrated a significant reduction in new colonization by vancomycin-resistant enterococci (VRE) for patients receiving SYN-004 (ribaxamase) compared to placebo (p-value=0.0002). With agreement from the FDA, the study included a secondary endpoint to assess SYN-004's (ribaxamase) capacity to decrease the incidence of antibiotic-associated diarrhea from all causes. Preliminary analysis of the data suggested a trend towards such a reduction (p-value=0.13), which was due, for the most part, to the reduction of CDI.

On October 6, 2016 we were awarded a government contract in the amount of $521,014 by the Centers for Disease Control and Prevention's (CDC) Broad Agency Announcement (BAA) 2016-N-17812. Under the CDC BAA, we examined the gut resistome (the anti-microbial resistance genes of the gut microbiome) from the patients in our Phase 2b clinical study with SYN-004 (ribaxamase). During our Phase 2b study, DNA extracted from 350 longitudinal fecal samples were collected and analyzed utilizing whole genome shotgun sequencing. The DNA sequences were then interrogated against the Comprehensive Antimicrobial Resistant Database (CARD) to determine the AMR genes present in the samples. A statistical analysis was then performed to compare the change in relative abundance of AMR genes of interest in the ribaxamase group vs. the placebo group. This analysis identified AMR genes that significantly changed from the screening sample to the post antibiotic samples. These changes included AMR genes that significantly increased and decreased following ceftriaxone treatment. There were approximately four-fold more genes that changed significantly in the placebo group as compared with the ribaxamase group. Among the genes that significantly increased in the placebo group are a family of five beta-lactamase genes which is consistent with the selective pressure from the ceftriaxone administered during the study. There were also several vancomycin resistance genes that increased in the placebo group which is consistent with the significant increase in colonization by vancomycin resistant enterococci seen in the placebo patients. The genes that decreased were mostly tetracycline and erythromycin resistance genes that are associated with normal gut flora. These data are consistent with ribaxamase degrading the ceftriaxone in the upper GI tract and thus relieving the selective pressure of the antibiotics on the gut microbiome. We plan to continue collaborative efforts with the CDC to gain public health support for SYN-004 (ribaxamase).

On April 7, 2017, we met with the CDC to share additional supportive results from several exploratory endpoints from our Phase 2b proof-of-concept clinical trial demonstrating SYN-004 (ribaxamase) successfully protected and preserved the naturally occurring composition of gut microbes in patients receiving SYN-004 (ribaxamase) from the dysbiotic effects of antibiotic-mediated intravenous ceftriaxone compared to placebo. Results indicate that patients who were administered SYN-004 (ribaxamase) in conjunction with IV ceftriaxone demonstrated significantly better maintenance of and recovery of the composition and diversity of the gut microbiome, compared to patients who were administered placebo. Patients receiving SYN-004 (ribaxamase) also demonstrated lower incidences of new colonization by opportunistic and potentially pathogenic microorganisms, such as VRE, compared to patients who received placebo. During a clinical conference which took place during the fourth quarter of 2017, we presented additional supportive results from several exploratory endpoints from our Phase 2b clinical trial which further evaluated SYN-004's (ribaxamase) ability to protect the gut microbiome from opportunistic bacterial infections and prevent the emergence of antimicrobial resistance in the gut microbiome of SYN-004 (ribaxamase) treated patients, versus placebo.

On May 11, 2017, we announced that the FDA granted Breakthrough Therapy Designation (BTD) to SYN-004 (ribaxamase) for the prevention of *Clostridium difficile* infection (CDI). FDA BTD is intended to expedite development and review timelines when preliminary clinical evidence indicates that a drug may demonstrate substantial improvement on one or more clinically significant endpoints over available therapies for serious or life-threatening diseases. Following BTD, we engaged in a Type-B Multidisciplinary meeting with the FDA, focused upon a high-level drug development plan and pathway to marketing approval for SYN-004 (ribaxamase). We plan to continue collaborative discussions with the FDA to solidify the details and components of the Phase 3 drug development plan and regulatory pathway towards marketing approval for SYN-004 (ribaxamase), including our consideration of the FDA's request for the inclusion of additional beta-lactam antibiotics which may potentially expand our originally proposed study design protocol and take additional time to amend our plan per the FDA's request, anticipate holding an End of Phase 2 meeting with the FDA during the second half of 2018, and anticipate initiating a Phase 3 trial(s) in 2019 or later, subject to our successful pursuit of opportunities that will allow us to establish the clinical infrastructure and financial resources necessary to successfully initiate and complete this plan. If approved by the FDA, SYN-004 (ribaxamase) would be the first available drug designed to prevent primary *Clostridium difficile* infection by protecting the gut microbiome from antibiotic-mediated dysbiosis.

***SYN-010 — Treatment of Irritable Bowel Syndrome with Constipation (IBS-C)***

SYN-010 is our proprietary, modified-release formulation of lovastatin lactone that is intended to reduce methane production by certain microorganisms (*M. smithii*) in the gut while minimizing disruption to the microbiome. Methane produced by *M. smithii* is an underlying cause of pain, bloating and constipation associated with IBS-C, and published reports have associated higher intestinal methane production with increased constipation severity in IBS-C patients. SYN-010 is intended to act primarily in the intestinal lumen while avoiding systemic absorption, thereby targeting the major cause of IBS-C, not just the patient's symptoms.