UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT UNDER SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE FISCAL YEAR ENDED: DECEMBER 31, 2017

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

For the transition period from to

Commission File Number: 001-35268

SYNERGY PHARMACEUTICALS INC.

(Exact name of registrant as specified in its charter)

Delaware	**33-0505269**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)

420 Lexington Avenue, Suite 2012, New York, New York 10170

(Address of principal executive offices) (Zip Code)

(212) 297-0020

(Registrant's telephone number)

(Former Name, Former Address and Former Fiscal Year, if changed since last report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.0001 par value	The NASDAQ Global Select Market

Securities registered pursuant to section 12(g) of the Act:

Title of class: **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 registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 (the "Exchange Act") 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 Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T 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 registrant'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. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company." and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☒	Accelerated filer ☐
Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐ Emerging growth company ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was $893,167,759 as of June 30, 2017, based upon the closing price on the NASDAQ Global Select market reported for such date.

The number of the registrant's shares of common stock outstanding was 246,660,367 as of March 1, 2018.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the definitive proxy statement for our 2018 Annual Meeting of Stockholders are incorporated by reference into Part III of this report.

SYNERGY PHARMACEUTICALS INC.

FORM 10-K

TABLE OF CONTENTS

PART I

This Report on Form 10-K for Synergy Pharmaceuticals Inc. may contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Such forward-looking statements are characterized by future or conditional verbs such as "may," "will," "expect," "intend," "anticipate," believe," "estimate" and "continue" or similar words. You should read statements that contain these words carefully because they discuss future expectations and plans, which contain projections of future results of operations or financial condition or state other forward-looking information. Such statements are only predictions and our actual results may differ materially from those anticipated in these forward-looking statements. We believe that it is important to communicate future expectations to investors. However, there may be events in the future that we are not able to accurately predict or control. Factors that may cause such differences include, but are not limited to, those discussed under Item 1A. Risk Factors and elsewhere in this Form 10-K for the year ended December 31, 2017, as filed with the Securities and Exchange Commission, including the uncertainties associated with product development, the risk that products that appeared promising in early clinical trials do not demonstrate safety and efficacy in larger-scale clinical trials, the risk that we will not obtain approval to market our products in development, fluctuations in our operating results and financial condition, the volatility of the market price of our common stock, our ability to successfully commercialize pharmaceutical products in a timely manner, the impact of competition, the effect of any manufacturing or quality control problems, our ability to manage our growth, the reduction or loss of business with any significant customer, substantial revenues derived from sale of one product, the restrictions imposed by our credit facility, our level of indebtedness and liabilities and the potential impact on cash flow available for operations, the availability of additional funds in the future, the uncertainty of patent litigation and other legal proceedings, product development risks and the difficulty of predicting FDA filings and approvals, consumer acceptance and demand for our pharmaceutical products, the impact of market perceptions of us and the safety and quality of our products, changes to FDA approval requirements, our ability to successfully conduct clinical trials, our reliance on third parties to conduct clinical trials and testing, impact of illegal distribution and sale by third parties of counterfeits or stolen products, the availability of raw materials and impact of interruptions in our supply chain, our policies regarding returns, rebates, allowances and chargebacks, the effect of current economic conditions on our industry, business, results of operations and financial condition, our ability to comply with legal and regulatory requirements governing the healthcare industry, the regulatory environment, the effect of certain provisions in our government contracts, our ability to protect our intellectual property, exposure to product liability claims, changes in tax regulations, uncertainties involved in the preparation of our financial statements, our ability to maintain an effective system of internal control over financial reporting, the effect of terrorist attacks on our business, expansion of social media platforms, the risks associated with dependence upon key personnel and the need for additional financing. We do not assume any obligation to update forward-looking statements as circumstances change.

ITEM 1. BUSINESS

Unless the context requires otherwise, the words "Synergy," "the Company," "we," "us," refer to Synergy Pharmaceuticals Inc. and, where appropriate, our subsidiaries. TRULANCE® is a trademark of Synergy Pharmaceuticals Inc. Any other trademarks reference in this Form 10-K are the property of their respective owners. All rights reserved.

Business Overview

Synergy Pharmaceuticals Inc. is a biopharmaceutical company focused on the development and commercialization of novel gastrointestinal (GI) therapies. We have pioneered discovery, research and development efforts around analogs of uroguanylin, a naturally occurring and endogenous human GI peptide, for the treatment of GI diseases and disorders. We discovered and own 100% worldwide rights to our proprietary uroguanylin based GI platform which includes one commercial product and one development stage compound.

Our first and only commercial product, plecanatide, is available and being marketed by us in the United States (U.S.), under the trademark name TRULANCE®, for the treatment of adults with chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C). On February 27, 2018 we entered into a definitive licensing agreement with Cipher Pharmaceuticals under which we granted Cipher the exclusive right to develop, market, distribute and sell TRULANCE in Canada. Under the terms of the licensing agreement, Synergy received an upfront payment of $5.0 million and is eligible for an additional milestone payment, as well as royalties from product sales in Canada. We are continuing to evaluate other potential ex-US business development opportunities for TRULANCE.

Dolcanatide is our development stage compound that has demonstrated proof-of-concept in treating patients with ulcerative colitis. We are currently exploring potential business development opportunities to further advance dolcanatide

development in ulcerative colitis. In addition, we have shown proof-of-concept with dolcanatide in treating patients with opioid-induced constipation (OIC), demonstrating the utility of our uroguanylin based platform in OIC. We are considering OIC as a potential lifecycle growth opportunity for TRULANCE.

TRULANCE (plecanatide)

With the exception of a single amino acid substitution for greater binding affinity, TRULANCE is structurally identical to human uroguanylin and is the only treatment thought to replicate the pH-sensitive activity of uroguanylin. Uroguanylin activates GC-C receptors in a pH-sensitive manner primarily in the small intestine, stimulating fluid secretion and maintaining stool consistency necessary for regular bowel function.

In January 2017, the FDA approved TRULANCE 3 mg tablets for the once-daily treatment of adults with CIC. We began commercializing TRULANCE in the U.S. in March 2017. In January 2018, the FDA approved TRULANCE for the treatment of adults with IBS-C. The efficacy and safety of TRULANCE for the treatment of CIC and IBS-C was established in four 12-week, double-blind, placebo-controlled, randomized, multicenter clinical studies involving over 3,100 patients. TRULANCE demonstrated improvement in the abdominal pain, constipation, stool consistency and straining with bowel movements associated with IBS-C, as well as in the constipation, stool consistency and straining with bowel movements associated with CIC. These patient-reported symptoms returned within one week following discontinuation of TRULANCE. The most common adverse event in both CIC and IBS-C studies was diarrhea (≤5.0% vs. 1.0% placebo). TRULANCE is the only prescription medication for adults with CIC and IBS-C that can be taken once-daily, with or without food, at any time of the day. TRULANCE is packaged in a unique, 30-day calendar blister pack.

Ongoing Post Marketing Commitments

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), clinical studies are underway assessing the efficacy and safety of TRULANCE in pediatric patients with CIC and in late planning stages for assessment of the efficacy and safety of TRULANCE in pediatric patients with IBS-C. In addition, development and validation of an anti-drug antibody assay is underway to assess patient clinical trial samples for the potential presence of anti-plecanatide antibodies. As agreed with the FDA following Trulance approval in the CIC indication, we continue with the execution of a milk-only lactation study and the assessment of GC-C receptor density in infants and children (age 0-6 years).

CIC / IBS-C

CIC and IBS-C are chronic, functional GI disorders that afflict millions of people worldwide. An estimated 33 million adults suffer from CIC and 12 million adults suffer from IBS-C in the U.S. alone.

People with CIC have persistent symptoms of difficult-to-pass and infrequent bowel movements. In addition to physical symptoms including abdominal bloating and discomfort, CIC can adversely affect an individual's quality of life, including increasing stress levels and anxiety. Many patients attempt to manage CIC symptoms with improved diet, fiber, and over-the-counter laxatives; however, these options can be ineffective or may not provide long-term relief. For those patients with persistent symptoms, prescription therapy is recommended. Many patients taking prescription medications fail to respond to therapy, or suffer from treatment-related adverse events, such as nausea and diarrhea.

Irritable bowel syndrome (IBS) is characterized by recurrent abdominal pain associated with 2 or more of the following criteria: related to defecation, associated with a change in the frequency of stool, or associated with a change in the form (appearance) of the stool. IBS can be subtyped by the predominant stool form as measured by the Bristol Stool Form Scale (BSFS): constipation (IBS-C), diarrhea (IBS-D), or mixed (IBS-M). Those within the IBS-C subtype experience Bristol types 1 or 2 (hard or lumpy) stools more than 25 percent of the time they have an abnormal bowel movement, and Bristol types 6 or 7 (loose or watery) stools less than 25 percent of the time they have an abnormal bowel movement. Some of the IBS treatment approaches recognized by the American College of Gastroenterology (ACG), including specialized diets, fiber, and psychological interventions, may not always effectively address abdominal pain and discomfort experienced by these patients. While there are prescription drug options, not all patients find complete relief, and many struggle with adverse events.

Dolcanatide (SP-333)

Dolcanatide is designed to be an analog of uroguanylin with enhanced resistance to standard digestive breakdown by proteases in the intestine. We have demonstrated the potential anti-inflammatory role of uroguanylin and uroguanylin analogs in a number of preclinical colitis models. In these earlier animal studies, oral treatment with dolcanatide was shown to ameliorate DSS- and TNBS-induced acute colitis in murine models and ameliorate spontaneous colitis in T-cell receptor alpha knockout mice.

In January 2016, we announced positive proof-of-concept with dolcanatide in a phase 1b trial evaluating 28 patients with mild-to-moderate ulcerative colitis. We are exploring business development opportunities to further advance dolcanatide development in ulcerative colitis.

Competition

The biopharmaceutical industry is characterized by rapidly evolving technology and intense competition. Our competitors include major pharmaceutical and biotechnology companies focusing on GI such as Ironwood Pharmaceuticals, Inc., Allergan plc, Takeda Pharmaceuticals America, Inc., Sucampo Pharmaceuticals, Inc. (acquired by Mallinckrodt plc), AstraZeneca, Valeant Pharmaceuticals International, Inc. and Shire, Plc. Most of our competitors have financial, technical and marketing resources significantly greater than our resources. Academic institutions, governmental agencies and other public and private research organizations are also conducting research activities and seeking patent protection and may commercialize products on their own or through joint ventures. We are aware of certain development projects for products to prevent or treat certain diseases targeted by us. The existence of these potential products or other products or treatments of which we are not aware, or products or treatments that may be developed in the future, may adversely affect our ability to market the products we develop.

Research and Development Expenses

Research and development costs include expenditures in connection with operating an in-house research and development laboratory, salaries and staff costs, application and filing for regulatory approval of proposed products, purchased in-process research and development, regulatory and scientific consulting fees, as well as contract research, patient costs, drug formulation and tableting, data collection, monitoring, clinical trial insurance. Research and development expenses for the year ended December 31, 2017 were approximately $48.3 million, as compared to approximately $87.1 million and $78.0 million for the years ended December 31, 2016 and 2015, respectively.

In accordance with FASB ASC Topic 730-10-55, Research and Development, we recorded prepaid research and development costs of approximately $0.1 million as of December 31, 2017 and $0.5 million as of December 31, 2016, for nonrefundable pre-payments for production of drug substance, analytical testing services and clinical trial costs for our drug candidates. In accordance with this guidance, we expense deferred research and development costs when drug compound is delivered or services are performed.

Manufacturing and Supply

We currently manage our global supply and distribution of TRULANCE through third party contract manufacturers. It is our objective to produce safe, pure and effective medicine. TRULANCE production consists of three phases-manufacture of (i) the active pharmaceutical ingredient, or API (sometimes referred to as drug substance), (ii) manufacture of drug product and (iii) manufacture of packaged finished goods, as well as distribution agreements. We have entered into arrangements with third party manufacturers for the production of TRULANCE. We continue to pursue additional commercial supply agreements with additional manufacturers for TRULANCE for U.S. and worldwide use. We believe our commercial suppliers will have the capabilities to produce TRULANCE in accordance with current good manufacturing practices, or GMP, on a sufficient scale to meet our commercial needs.

Patents and Proprietary Rights

We are able to protect our technology from unauthorized use by third parties only to the extent that it is covered by valid and enforceable patents or is effectively maintained as a trade secret or is protected by confidentiality agreements. Accordingly, patents or other proprietary rights are an essential element of our business.

As of December 31, 2017 we have 24 issued United States patents related to guanylate cyclase agonists. Two of these patents cover the composition-of-matter of TRULANCE and were issued on May 9, 2006 and September 21, 2010; they will expire in 2023 and 2022, respectively. The patent that issued on May 9, 2006 has claims directed to the species of TRULANCE, whereas the patent that issued on September 21, 2010 has claims directed to a genus of peptides that are identical in length to TRULANCE and is inclusive of TRULANCE. In addition, we have several granted United States patents that cover methods of using TRULANCE. One patent, which issued February 14, 2012, covers certain methods of treating inflammatory bowel disease using TRULANCE and will expire in 2022. Another issued patent was granted January 28, 2014 and covers methods of stimulating water transport in the gastrointestinal tract using TRULANCE and will expire in 2022. Another patent, granted on March 3, 2015, covers methods of use of TRULANCE and expires in 2030. We also have a patent, granted November 8, 2016, that covers compositions containing TRULANCE or dolcanatide and 5-aminosalicyclic acid and will expire in 2034. Furthermore, in 2017 we received three additional granted US patents related to TRULANCE. One of the patents

relates to the methods of manufacture of TRULANCE was issued on February 28, 2017 and will expire in 2032. The two other granted patents relate to the formulations and method of using TRULANCE for treating constipation. One issued on April 4, 2017 and the other issued on April 11, 2017. They are both projected to expire in 2031.

We also have an issued United States patent that covers the composition-of-matter of dolcanatide which issued on February 1, 2011 and expires in 2028. Another patent was granted December 2, 2014 and covers composition-of-matter of dolcanatide and expires in 2028. Another two patents granted on January 19, 2016 and February 23, 2016 cover composition-of-matter of dolcanatide and certain analogs of TRULANCE and dolcanatide and will expire in 2028. In addition we have another patent, granted May 6, 2014, that covers certain methods of treating a variety of gastrointestinal and other disorders using dolcanatide and will expire in 2029. Another patent, granted January 17, 2017, covers method of colonic cleansing using dolcanatide.

We also have several issued United States patents that cover analogs of TRULANCE and dolcanatide. One patent was granted October 11, 2011 and covers the composition-of-matter of certain analogs related to TRULANCE and dolcanatide and will expire in 2029. Another patent, granted on June 26, 2012, covers an additional composition-of-matter related to certain analogs of TRULANCE and dolcanatide and will expire in 2029. A further patent, granted on January 22, 2013, covers another composition-of-matter related to certain analogs of TRULANCE and will expire in 2029. A further patent, granted on July 30, 2013, covers another composition-of-matter related to certain analogs of TRULANCE and will expire in 2029. Another three patents that also cover compositions-of-matter related to certain analogs of TRULANCE were issued on February 5, 2013, October 29, 2013, and March 4, 2014, and will expire in 2029. A further patent, granted July 28, 2015, covers an additional composition-of-matter related to certain analogs of TRULANCE and dolcanatide and will expire in 2028. Another patent, granted November 29, 2016, covers analogs related to TRULANCE and will expire in 2029.

In addition, we have numerous granted foreign patents which cover the composition-of-matter of TRULANCE and expire in 2022. These foreign patents cover Austria, Belgium, Switzerland, Cyprus, Germany, Denmark, Spain, Finland, France, the United Kingdom, Greece, Hong Kong, Ireland, Italy, Liechtenstein, Luxembourg, Monaco, the Netherlands, Portugal, Sweden, Turkey, Armenia, Azerbaijan, Belarus, Kazakhstan, the Kyrgyz Republic, Moldova, the Russian Federation, Tajikistan, Turkmenistan, Canada, China and Japan. We also have numerous granted foreign patents that cover the composition-of-matter related to dolcanatide that expire in 2028. These patents cover Switzerland, Germany, Denmark, Spain, France, the United Kingdom, Ireland, Italy, the Netherlands, Hong Kong, Armenia, Azerbaijan, Belarus, Kazakhstan, the Kyrgyz Republic, Moldova, the Russian Federation, Tajikistan, Turkmenistan, China, Australia, Japan and Mexico. We also have five foreign patents that cover composition-of-matter of certain analogs related to TRULANCE and methods of use to treat Ulcerative Colitis that expire in 2029. These patents cover Australia, Hong Kong, France, Germany, Italy, Spain and the United Kingdom. We also have several foreign patents that cover composition-of-matter of certain analogs related to TRULANCE and methods of use to treat gastrointestinal disorders and expires in 2029. These patents cover Australia, France, Germany, Italy, Spain, United Kingdom and Hong Kong. We also have six foreign patents related to TRULANCE that cover treatment and prevention of Hypercholesterolemia and expire in 2030. These patents cover Australia, China, Japan, Mexico, France, Germany, Italy, Spain and the United Kingdom. We also have three patents related to gastrointestinal specific formulations of TRULANCE and dolcantide. These patents cover Australia, Japan, Germany, France, Italy, Spain and the United Kingdom. We also have one patent family related to manufacture of TRULANCE.

Additionally, as of the date of this report on Form 10-K, we have 19 pending United States utility patent applications; and 98 pending foreign patent applications relating to TRULANCE and dolcanatide, various derivatives and analogs of TRULANCE and dolcanatide, and their uses and manufacture.

On September 14, 2012 we entered into a binding letter of intent with Ironwood Pharmaceuticals, Inc. (“Ironwood”), pursuant to which we and Ironwood agreed to enter into a definitive license agreement giving us an exclusive worldwide license to Ironwood’s method of use patents on TRULANCE. The letter of intent contemplates a low single digit royalty on net sales of TRULANCE and both parties agreed not to challenge each other’s patents covering certain GC-C agonists, except that we retain the right to challenge Ironwood’s method of use patents on TRULANCE.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

While trade secret protection is an essential element of our business and we have taken security measures to protect our proprietary information and trade secrets, we cannot give assurance that our unpatented proprietary technology will afford us significant commercial protection. We seek to protect our trade secrets by entering into confidentiality agreements with third parties, employees and consultants. Our employees and consultants also sign agreements requiring that they assign to us their

interests in intellectual property arising from their work for us. All employees sign an agreement not to engage in any conflicting employment or activity during their employment with us and not to disclose or misuse our confidential information. However, it is possible that these agreements may be breached or invalidated, and if so, there may not be an adequate corrective remedy available. Accordingly, we cannot ensure that employees, consultants or third parties will not breach the confidentiality provisions in our contracts, infringe or misappropriate our trade secrets and other proprietary rights or that measures we are taking to protect our proprietary rights will be adequate.

In the future, third parties may file claims asserting that our technologies or products infringe on their intellectual property. We cannot predict whether third parties will assert such claims against us or against the licensors of technology licensed to us, or whether those claims will harm our business. If we are forced to defend ourselves against such claims, whether they are with or without merit and whether they are resolved in favor of, or against, our licensors or us, we may face costly litigation and the diversion of management's attention and resources. As a result of such disputes, we may have to develop costly non-infringing technology or enter into licensing agreements. These agreements, if necessary, may be unavailable on terms acceptable to us, or at all.

Government Regulation

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food and Drug Administration, and Cosmetic Act and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. The FDA has very broad enforcement authority and failure to abide by applicable regulatory requirements can result in administrative or judicial sanctions being imposed on us, including warning letters, refusals of government contracts, clinical holds, civil penalties, injunctions, restitution, disgorgement of profits, recall or seizure of products, total or partial suspension of production or distribution, withdrawal of approval, refusal to approve pending applications, and criminal prosecution.

FDA Approval Process

Our product candidates are regulated by the FDA as drugs. No manufacturer may market a new drug until it has submitted a New Drug Application, or NDA, to the FDA, and the FDA has approved it. The steps required before the FDA may approve an NDA generally include:

- preclinical laboratory tests and animal tests conducted in compliance with FDA's good laboratory practice requirements;
- development, manufacture and testing of active pharmaceutical product and dosage forms suitable for human use in compliance with current good manufacturing practices, or GMP;
- the submission to the FDA of an investigational new drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product for its specific intended use(s);
- the submission to the FDA of a New Drug Application, or NDA; and
- FDA review and approval of the NDA.

Preclinical tests include laboratory evaluation of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. The conduct of the pre-clinical tests must comply with federal regulations and requirements including good laboratory practices. We must submit the results of the preclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol to the FDA as part of an IND, which must become effective before we may commence human clinical trials. The IND will automatically become effective 30 days after its receipt by the FDA, unless the FDA raises concerns or questions before that time about the conduct of the proposed trials. In such a case, we must work with the FDA to resolve any outstanding concerns before clinical trials can proceed. We cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trials. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board for approval. An institutional review board may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the institutional review board's requirements or may impose other conditions.

Clinical trials involve the administration of the product candidate to humans under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are typically conducted in three sequential phases, though the phases may overlap or be combined. In Phase 1, the initial introduction of the drug into healthy human subjects, the drug is usually tested for safety (adverse effects), dosage tolerance and pharmacologic action, as well as to understand how the drug is taken up by and distributed within the body. Phase 2 usually involves studies in a limited patient population (individuals with the disease under study) to:

- evaluate preliminarily the efficacy of the drug for specific, targeted conditions;
- determine dosage tolerance and appropriate dosage as well as other important information about how to design larger Phase 3 trials; and
- identify possible adverse effects and safety risks.

Phase 3 trials generally further evaluate clinical efficacy and test for safety within an expanded patient population. The conduct of the clinical trials is subject to extensive regulation, including compliance with good clinical practice regulations and guidance.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. We may also suspend clinical trials at any time on various grounds.

The results of the preclinical and clinical studies, together with other detailed information, including the manufacture and composition of the product candidate, are submitted to the FDA in the form of an NDA requesting approval to market the drug. FDA approval of the NDA is required before marketing of the product may begin in the U.S. If the NDA contains all pertinent information and data, the FDA will "file" the application and begin review. The FDA may "refuse to file" the NDA if it does not contain all pertinent information and data. In that case, the applicant may resubmit the NDA when it contains the missing information and data.

Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of new drug applications. Most such applications for non-priority drug products are reviewed within 10 months. The review process, however, may be extended by FDA requests for additional information, preclinical or clinical studies, clarification regarding information already provided in the submission, or submission of a risk evaluation and mitigation strategy. The FDA may refer an application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Before approving an NDA, the FDA will typically inspect the facilities at which the product candidate is manufactured and will not approve the product candidate unless GMP compliance is satisfactory. FDA also typically inspects facilities responsible for performing animal testing, as well as clinical investigators who participate in clinical trials. The FDA may refuse to approve an NDA if applicable regulatory criteria are not satisfied, or may require additional testing or information. The FDA may also limit the indications for use and/or require post-marketing testing and surveillance to monitor the safety or efficacy of a product. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

The testing and approval process requires substantial time, effort and financial resources, and our product candidates may not be approved on a timely basis, if at all. The time and expense required to perform the clinical testing necessary to obtain FDA approval for regulated products can frequently exceed the time and expense of the research and development initially required to create the product. The results of preclinical studies and initial clinical trials of our product candidates are not necessarily predictive of the results from large-scale clinical trials, and clinical trials may be subject to additional costs, delays or modifications due to a number of factors, including difficulty in obtaining enough patients, investigators or product candidate supply. Failure by us to obtain, or any delay in obtaining, regulatory approvals or in complying with requirements could adversely affect the commercialization of product candidates and our ability to receive product or royalty revenues.

Other Regulatory Requirements

After approval, drug products are subject to extensive continuing regulation by the FDA, which include company obligations to manufacture products in accordance with Good Manufacturing Practice, or GMP, maintain and provide to the FDA updated safety and efficacy information, report adverse experiences with the product, keep certain records and submit periodic reports, obtain FDA approval of certain manufacturing or labeling changes, and comply with FDA promotion and advertising requirements and restrictions. Failure to meet these obligations can result in various adverse consequences, both voluntary and FDA-imposed, including product recalls, withdrawal of approval, restrictions on marketing, and the imposition of civil fines and criminal penalties against the NDA holder. In addition, later discovery of previously unknown safety or efficacy issues may result in restrictions on the product, manufacturer or NDA holder.

We and any manufacturers of our products are required to comply with applicable FDA manufacturing requirements contained in the FDA's GMP regulations. GMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation. The manufacturing facilities for our products must meet GMP requirements to the satisfaction of the FDA pursuant to a pre-approval inspection before we can use them to manufacture our products. We and any third-party manufacturers are also subject to periodic inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations.

With respect to post-market product advertising and promotion, the FDA imposes a number of complex regulations on entities that advertise and promote pharmaceuticals, which include, among others, standards for direct-to-consumer advertising, promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), industry- sponsored scientific and educational activities, and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, risk minimization action plans and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product.

Outside the United States, our ability to market a product is contingent upon receiving marketing authorization from the appropriate regulatory authorities. The requirements governing marketing authorization, pricing and reimbursement vary widely from jurisdiction to jurisdiction. At present, foreign marketing authorizations are applied for at a national level, although within the European Union registration procedures are available to companies wishing to market a product in more than one European Union member state.

We are also subject to various environmental, health and safety regulations including those governing laboratory procedures and the handling, use, storage, treatment, and disposal of hazardous materials. From time to time, and in the future, our operations may involve the use of hazardous materials.

Employees

As of March 1, 2018, we had 313 employees. Approximately 16 were in our scientific and drug development organization, 15 were in technical operations and quality assurance, 254 were in our sales and commercial team, and 26 were in general and administrative functions. None of our employees are represented by a labor union, and we consider our employee relations to be good.

Our Website

Our website address is ***www.synergypharma.com.*** Information found on our website is not incorporated by reference into this report. We make available free of charge through our website our Securities and Exchange Commission, or SEC, filings furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

ITEM 1A. RISK FACTORS

The risks described below are not the only ones we face. Additional risks we are not presently aware of or that we currently believe are immaterial may also impair our business operations. Our business could be harmed by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing these risks, you should also refer to the other information contained or incorporated by reference into this Form 10-K, including our financial statements and related notes.

Risks Related to Our Business

We are largely dependent on the commercial success of TRULANCE in the U.S. for the foreseeable future. We cannot guarantee when, or if, we will attain profitability or positive cash flows.

We began selling TRULANCE in the U.S. in the first quarter of 2017 for CIC and in the first quarter of 2018 for IBS-C. The commercial success of TRULANCE depends on a number of factors, including:

- the effectiveness of TRULANCE as a treatment for adult patients with CIC or IBS-C;
- the size of the treatable patient population;
- the effectiveness of the sales, managed markets and marketing efforts by us;
- the adoption of TRULANCE by physicians, which depends on whether physicians view it as a safe and effective treatment for adult patients with CIC or IBS-C;
- our success in educating and activating adult CIC and IBS-C patients to enable them to more effectively communicate their symptoms and treatment history to their physicians;
- our ability to both secure and maintain adequate reimbursement for, and optimize patient access to, TRULANCE by providing third party payers with a strong value proposition based on the existing burden of illness associated with CIC and IBS-C and the benefits of TRULANCE;
- the effectiveness of our partners' distribution networks;
- the occurrence of any side effects, adverse reactions or misuse, or any unfavorable publicity in these areas, associated with TRULANCE; and
- the development or commercialization of competing products or therapies for the treatment of CIC and IBS-C, or their associated symptoms.

Our revenues from the commercialization of TRULANCE are subject to these factors, and therefore may be unpredictable from quarter-to-quarter. Ultimately, we may never generate sufficient revenues from TRULANCE to reach or maintain profitability for our company or to sustain our anticipated levels of operations.

A substantial portion of our total revenues is derived from sales to a limited number of customers.

We derive a substantial portion of our revenue from sales to a limited number of customers. In 2017, our three major customers, McKesson Corporation, Cardinal Health, AmerisourceBergen, accounted for 37%, 31%, and 29%, respectively, or an aggregate of 97%, of our gross revenue.

A reduction in, or loss of business with, any one of these customers, or any failure of a customer to pay us on a timely basis, would adversely affect our business.

TRULANCE may cause undesirable side effects or have other properties that could limit its commercial potential.

The most commonly reported adverse reaction in the Phase III placebo-controlled trials for TRULANCE in CIC and IBS-C was diarrhea. Severe diarrhea was reported in 2% or less of the TRULANCE-treated patients, and its incidence was similar between the IBS-C and CIC populations in these trials. If we or others identify previously unknown side effects, if known side effects are more frequent or severe than in the past, if we or others detect unexpected safety signals for TRULANCE or any products perceived to be similar to TRULANCE, or if any of the foregoing are perceived to have occurred, then in any of these circumstances:

- sales of TRULANCE may be impaired;
- regulatory approvals for TRULANCE may be denied, restricted or withdrawn;

- we may decide to, or be required to, send product warning letters or field alerts to physicians, pharmacists and hospitals;
- reformulation of the product, additional nonclinical or clinical studies, changes in labeling or changes to or reapprovals of manufacturing facilities may be required;
- we may be precluded from pursuing additional development opportunities to enhance the clinical profile of TRULANCE within its indicated populations, as well as be precluded from studying TRULANCE in additional indications, populations and formulations;
- our reputation in the marketplace may suffer; and
- government investigations or lawsuits, including class action suits, may be brought against us.

Any of the above occurrences would harm or prevent sales of TRULANCE, increase our expenses and impair our ability to successfully commercialize TRULANCE.

Furthermore, as we explore development opportunities to enhance the clinical profile of TRULANCE through additional clinical trials, the number of patients treated with TRULANCE within and outside of its current indications or patient populations may expand, which could result in the identification of previously unknown side effects, increased frequency or severity of known side effects, or detection of unexpected safety signals. As a result, regulatory authorities, healthcare practitioners, third party payers or patients may perceive or conclude that the use of TRULANCE is associated with serious adverse effects, undermining our commercialization efforts.

In addition, the FDA-approved label for TRULANCE contains a boxed warning about its use in pediatric patients. TRULANCE is contraindicated in pediatric patients less than 6 years of age based on nonclinical data from studies in neonatal mice approximately equivalent to human pediatric patients less than 2 years of age. There is also a warning advising physicians to avoid the use of TRULANCE in pediatric patients 6 to less than 18 years of age. This warning is based on data in young juvenile mice and the lack of clinical safety and efficacy data in pediatric patients of any age group.

We may need to raise additional capital to fund our operations, and our failure to obtain funding when needed may force us to delay, reduce or eliminate our development programs or commercialization efforts or even discontinue or curtail our operations.

During the year ended December 31, 2017, our operating activities used net cash of approximately $212.9 million. During the year ended December 31, 2016 and December 31, 2015, our operating activities used net cash of approximately $129.8 million and $101.0 million, respectively. In addition, as of December 31, 2017 and December 31, 2016 our cash and cash equivalents was $137.0 million and $82.4 million, respectively, consisting of checking accounts and short-term money market mutual funds.

Purchasing commercial quantities of pharmaceutical products, developing product candidates, conducting clinical trials, and commercializing products are expensive and uncertain. Circumstances, our strategic imperatives, or opportunities to create or acquire new programs, as well as maturities, redemptions or repurchases of our outstanding Notes, could require us to, or we may choose to, seek to raise additional funds.

The amount and timing of our future funding requirements will depend on many factors, including, but not limited to:

- the level of underlying demand for TRULANCE by prescribers and patients in the U.S.;
- the level of acceptance for TRULANCE among physicians, patients and the medical community;
- the costs associated with commercializing TRULANCE in the U.S.;
- the costs of maintaining and/or expanding sales, marketing and distribution capabilities for TRULANCE;
- the rate of progress, the cost of our clinical trials and the other costs associated with our product development programs;
- the costs and timing of in-licensing additional products or product candidates or acquiring other complementary companies;
- the status, terms and timing of any collaboration, licensing, co-commercialization or other arrangements;
- the timing of any regulatory approvals of our product candidates;
- whether the holders of our outstanding Notes hold the notes to maturity without conversion into our common stock and whether we are required to repurchase our Notes prior to maturity upon a fundamental change, as defined in the indenture governing the Notes; and

- whether we seek to redeem or repurchase all or part of our outstanding Notes through cash purchases and/or exchanges, in open market purchases, privately negotiated transactions, by tender offer or otherwise.

We may need to raise additional capital to fund our future operations and we cannot be certain that funding will be available on acceptable terms on a timely basis, or at all. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience significant dilution. Any debt financing, if available, may involve restrictive covenants that may impact our ability to conduct our business. If we are unable to raise additional capital when required or on acceptable terms, we may have to significantly delay, scale back or discontinue the development and/or commercialization of our product candidates or our commercialization efforts. We also may be required to:

- seek collaborators for our product candidates at an earlier stage than otherwise would be desirable and on terms that are less favorable than might otherwise be available; and/or
- relinquish license or otherwise dispose of rights to technologies, product candidates or products that we would otherwise seek to develop or commercialize ourselves on unfavorable terms.

Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern, which may hinder our ability to obtain future financing.

Our consolidated financial statements as of December 31, 2017 have been prepared under the assumption that we will continue as a going concern for the next twelve months. Our independent registered public accounting firm has issued a report that includes an explanatory paragraph referring to our recurring and continuing losses from operations, covenants associated with our Term Loan, and expressing substantial doubt in our ability to continue as a going concern without additional capital becoming available. Our ability to continue as a going concern is dependent upon our ability to obtain additional equity or debt financing, attain further operating efficiencies, reduce expenditures, and to generate significant revenue. Our consolidated financial statements as of December 31, 2017 did not include any adjustments that might result from the outcome of this uncertainty.

We have incurred significant losses since inception and anticipate that we will incur continued losses for the foreseeable future.

As of December 31, 2017, we had an accumulated deficit of approximately $807 million. We will incur significant and increasing operating losses for the next several years if we expand our research and development, continue our clinical trials of TRULANCE for the treatment of additional GI disorders, acquire or license technologies, advance other product candidates into clinical development, including dolcanatide, complete clinical trials, seek regulatory approval, commercialize TRULANCE and, if we receive FDA approval, commercialize our other product candidates. Because of the numerous risks and uncertainties associated with product development efforts, we are unable to predict the extent of any future losses or when we will become profitable, if at all. If we are unable to achieve and then maintain profitability, the market value of our common stock will likely experience significant decline.

Clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Our product candidates may not prove to be safe and efficacious in clinical trials and may not meet all the applicable regulatory requirements needed to receive regulatory approval. In order to receive regulatory approval for the commercialization of our product candidates, we must conduct, at our own expense, extensive preclinical testing and clinical trials to demonstrate safety and efficacy of these product candidates for the intended indication of use. Clinical testing is expensive, can take many years to complete, if at all, and its outcome is uncertain. Failure can occur at any time during the clinical trial process.

The results of preclinical studies and early clinical trials of new drugs do not necessarily predict the results of later-stage clinical trials. The design of our clinical trials is based on many assumptions about the expected effects of our product candidates, and if those assumptions are incorrect may not produce statistically significant results. Preliminary results may not be confirmed on full analysis of the detailed results of an early clinical trial. Product candidates in later stages of clinical trials may fail to show safety and efficacy sufficient to support intended use claims despite having progressed through initial clinical testing. The data collected from clinical trials of our product candidates may not be sufficient to support the filing of an NDA or to obtain regulatory approval in the United States or elsewhere. Because of the uncertainties associated with drug development and regulatory approval, we cannot determine if or when we will have an approved product for commercialization or achieve sales or profits.

Delays in clinical testing could result in increased costs to us and slow down our product development.

We may experience delays in clinical testing of our product candidates. We do not know whether planned clinical trials will begin on time, will need to be redesigned or will be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays in obtaining regulatory approval to commence a clinical trial, in securing clinical trial agreements with prospective sites with acceptable terms, in obtaining institutional review board approval to conduct a clinical trial at a prospective site, in recruiting patients to participate in a clinical trial or in obtaining sufficient supplies of clinical trial materials. Many factors affect patient enrollment, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial, competing clinical trials and new drugs approved for the conditions we are investigating. Clinical investigators will need to decide whether to offer their patients enrollment in clinical trials of our product candidates versus treating these patients with commercially available drugs that have established safety and efficacy profiles. Any delays in completing our clinical trials will increase our costs and slow down our product development and timeliness and approval process.

We may be required to suspend or discontinue clinical trials due to unexpected side effects or other safety risks that could preclude approval of our product candidates.

Our clinical trials may be suspended at any time for a number of reasons. For example, we may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to the clinical trial patients. In addition, the FDA or other regulatory agencies may order the temporary or permanent discontinuation of our clinical trials at any time if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements or that they present an unacceptable safety risk to the clinical trial patients.

Administering any product candidate to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of our product candidates and could result in the FDA or other regulatory authorities denying further development or approval of our product candidates for any or all targeted indications. Ultimately, some or all of our product candidates may prove to be unsafe for human use. Moreover, we could be subject to significant liability if any volunteer or patient suffers, or appears to suffer, adverse health effects as a result of participating in our clinical trials. Any of these events could prevent us from achieving or maintaining market acceptance of TRULANCE and could substantially increase commercialization costs.

If we fail to comply with healthcare regulations, we could face substantial enforcement actions, including civil and criminal penalties and our business, operations and financial condition could be adversely affected.

As a developer of pharmaceuticals, even though we do not intend to make referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse, false claims and patients' privacy rights are and will be applicable to our business. We could be subject to healthcare fraud and abuse laws and patient privacy laws of both the federal government and the states in which we conduct our business.

The laws include:

- the federal healthcare program anti-kickback law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, and which may apply to entities like us which provide coding and billing information to customers;
- the federal Health Insurance Portability and Accountability Act of 1996, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- the Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug manufacturing and product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the

privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

If TRULANCE is unable to compete effectively with marketed drugs targeting similar indications as TRULANCE, our commercial opportunity will be reduced or eliminated.

We face competition generally from established pharmaceutical and biotechnology companies, as well as from academic institutions, government agencies and private and public research institutions. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Small or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize GI drugs that are safer, more effective, have fewer side effects or are less expensive than TRULANCE.

TRULANCE competes with at least two currently approved prescription therapies for the treatment of CIC and IBS-C, namely, Amitiza and Linzess. In addition, over-the-counter products are also used to treat certain symptoms of CIC and IBS-C. We believe other companies are developing products that will compete with TRULANCE should they be approved by the FDA. To our knowledge, other potential competitors are in earlier stages of development. If potential competitors are successful in completing drug development for their product candidates and obtain approval from the FDA, they could limit the demand for TRULANCE. We expect that our ability to compete effectively will depend upon our ability to:

- maintain a proprietary position for our products and manufacturing processes and other related product technology;
- attract and retain key personnel;
- ensure competitive patient access to our products in the U.S. based on any required discounts and rebates to payors;
- develop relationships with physicians prescribing these products; and
- build and maintain an adequate sales and marketing infrastructure for TRULANCE.

Because we will be competing against significantly larger companies with established track records, we will have to demonstrate that, based on clinical data, side-effect profiles and other factors, our products are competitive with other products. If we are unable to compete effectively in the GI drug market and differentiate our products from other marketed GI drugs, we may never generate meaningful revenue.

If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our products and product candidates.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management and scientific staff. The loss of one or more of our senior management could delay or prevent the successful completion of any planned or ongoing clinical trials, any ongoing regulatory activities with FDA or the commercialization of our products and product candidates.

The competition for qualified personnel in the biotechnology and pharmaceuticals field is intense. We will need to hire additional personnel as we expand our commercial and supply chain activities. We may not be able to attract and retain quality personnel on acceptable terms given the competition for such personnel among biotechnology, pharmaceutical and other companies.

We may need to increase the size of our organization, and we may experience difficulties in managing growth.

We are a small company with 313 employees as of March 1, 2018. To continue our clinical/post-marketing trials and to commercialize our products and product candidates, we may need to expand our employee base for managerial, operational,

financial and other resources. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. Over the next 12 months, we may need to add additional employees to assist us with our commercial programs. Our future financial performance and our ability to commercialize our products and product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to:

- manage development efforts effectively;
- manage our commercialization activities effectively;
- integrate additional management, administrative, manufacturing and sales and marketing personnel;
- maintain sufficient administrative, accounting and management information systems and controls; and
- hire and train additional qualified personnel.

We may not be able to accomplish these tasks, and our failure to accomplish any of them could harm our financial results and impact our ability to achieve commercial and development milestones.

We are in the early stages of operating our commercial organization. If we are unable to maintain a direct sales force in the U.S. to promote our products, the commercial opportunity for our products may be diminished.

We are in the early stages of operating our commercial organization. We will incur significant additional expenses and commit significant additional management resources to maintain our own sales force. We may not be able to maintain such capabilities despite these additional expenditures. We will also have to compete with other pharmaceutical and biotechnology companies to recruit, hire and train sales and marketing personnel. If we elect to rely on third parties to sell our products and product candidates in the United States, we may receive less revenue than if we sold our products directly. In addition, although we would intend to use due diligence in monitoring their activities, we may have little or no control over the sales efforts of those third parties. In the event we are unable to maintain our own sales force or collaborate with a third party to sell our products and product candidates, we may not be able to commercialize our products and product candidates which would negatively impact our ability to generate revenue.

We may need to rely on third parties to market and commercialize TRULANCE and our product candidates in international markets.

Currently, we do not have any commercial infrastructure in international markets. In the future, if appropriate regulatory approvals are obtained, we may commercialize TRULANCE and our product candidates in international markets. On February 27, 2018, we entered into a definitive licensing, development and commercialization agreement with Cipher Pharmaceuticals for the Canadian market. Significant commercialization of TRULANCE in Canada is several years away, if at all. If Cipher Pharmaceuticals is not able to effectively register and commercialize TRULANCE in Canada, we may not be able to generate revenue from the license agreement as a result of sales of TRULANCE in Canada.

We have not decided how to commercialize TRULANCE and our product candidates in other international markets. We may decide to build our own sales force or sell our products through third parties. If we decide to sell TRULANCE and our product candidates in international markets through a third party, we may not be able to enter into any marketing arrangements on favorable terms or at all. In addition, these arrangements could result in lower levels of income to us than if we marketed TRULANCE and our product candidates entirely on our own. If we are unable to enter into a marketing arrangement for TRULANCE and our product candidates in international markets, we may not be able to develop an effective international sales force to successfully commercialize those products in international markets. If we fail to enter into marketing arrangements for our products and are unable to develop an effective international sales force, our ability to generate revenue would be limited.

If the manufacturers upon whom we rely fail to produce TRULANCE and our other product candidates, including dolcanatide, in the volumes that we require on a timely basis, or fail to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the development and commercialization of our products and product candidates.

We do not currently possess internal manufacturing capacity. We currently utilize the services of contract manufacturers to manufacture our clinical supplies and commercial products. With respect to the manufacturing of TRULANCE, we have executed supply agreements with contract manufacturers sufficient to meet our foreseeable clinical trial and commercial requirements. If any of our suppliers were to limit or terminate production or otherwise fail to meet the quality or delivery requirements needed to satisfy the supply, the process of locating and qualifying alternate sources could require up to several months, during which time our production could be delayed. Pursuant to the license agreement with Cipher Pharmaceuticals,

we have agreed to supply Cipher Pharmaceuticals with TRULANCE for development and commercialization in Canada. Any curtailment in the availability of TRULANCE would have a material adverse effect on our business, financial position and results of operations and adversely affect our relationship with Cipher Pharmaceuticals. In addition, because regulatory authorities must generally approve raw material sources for pharmaceutical products, changes in raw material suppliers may result in production delays or higher raw material costs.

Since the commercial manufacturing process for TRULANCE is single sourced for Active Pharmaceutical Ingredient, or API, and Drug Product, we are currently at risk until we establish secondary suppliers. We continue to pursue additional API and drug product supply agreements with other contract manufacturers. We may be required to agree to minimum volume requirements, exclusivity arrangements or other restrictions with the contract manufacturers. We may not be able to enter into long-term agreements on commercially reasonable terms, or at all. If we change or add manufacturers, the FDA and comparable foreign regulators may require approval of the changes. Approval of these changes could require new testing by the manufacturer and compliance inspections to ensure the manufacturer is conforming to all applicable laws and regulations, including good manufacturing practices, or GMP. In addition, the new manufacturers would have to be educated in or independently develop the processes necessary for the production of our products and product candidates. Peptide manufacturing is a highly specialized manufacturing process. While we believe we will have long term arrangements with a sufficient number of contract manufacturers, if we lose a manufacturer, it would take us a substantial amount of time to identify and develop a relationship, and seek regulatory approval, where necessary, for an alternative manufacturer.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products may encounter difficulties in production, particularly in scaling up production. These problems include difficulties with production costs and yields, quality control, including stability of the product and quality assurance testing, shortages of qualified personnel, as well as compliance with federal, state and foreign regulations. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of our clinical trials, increase the costs associated with conducting our clinical trials and, depending upon the period of delay, require us to commence new clinical trials at significant additional expense or to terminate a clinical trial.

We are responsible for ensuring that each of our contract manufacturers comply with the GMP requirements of the FDA and other regulatory authorities from which we seek to obtain product approval. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. The approval process for NDAs includes a review of the manufacturer's compliance with GMP requirements. We are responsible for regularly assessing a contract manufacturer's compliance with GMP requirements through record reviews and periodic audits and for ensuring that the contract manufacturer takes responsibility and corrective action for any identified deviations. Manufacturers of TRULANCE and other product candidates, including dolcanatide, may be unable to comply with these GMP requirements and with other FDA and foreign regulatory requirements, if any. While we will oversee compliance by our contract manufacturers, ultimately we will not have control over our manufacturers' compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of TRULANCE or other product candidates is compromised due to a manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize TRULANCE or other product candidates, and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical trials, regulatory submissions, approvals or commercialization of TRULANCE or other product candidates, entail higher costs or result in us being unable to effectively commercialize TRULANCE or other product candidates. Furthermore, if our manufacturers fail to deliver the required commercial quantities on a timely basis and at commercially reasonable prices, we may be unable to meet demand for any approved products and would lose potential revenues.

Materials necessary to manufacture TRULANCE and our product candidates may not be available on commercially reasonable terms, or at all, which could impair commercialization of TRULANCE and may delay the development of our product candidates.

We rely on third-party manufacturers of TRULANCE and our product candidates to purchase from third-party suppliers the materials necessary to produce the bulk APIs and product candidates for our clinical trials, and we rely on such manufacturers to purchase such materials to produce the APIs and finished products for any commercial distribution of TRULANCE. Suppliers may not sell these materials to our manufacturers at the time they need them in order to meet our required delivery schedule or on commercially reasonable terms, if at all. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. Moreover, we currently do not have any agreements for the production of these materials. If we, or our manufacturers, are unable to purchase these materials, the commercialization of TRULANCE would be

impaired and there could be a shortage in supply of such product, which would harm our ability to generate revenues from such product and achieve or sustain profitability and adversely impact our relationship with Cipher Pharmaceuticals.

TRULANCE may not gain acceptance among physicians, patients and the medical community, thereby limiting our potential to generate revenues.

The degree of market acceptance of any approved product by physicians, healthcare professionals and third-party payors and our profitability and growth will depend on a number of factors, including:

- demonstration of safety and efficacy;
- changes in the practice guidelines and the standard of care for the targeted indication;
- relative convenience and ease of administration;
- the prevalence and severity of any adverse side effects;
- budget impact of adoption of our product on relevant drug formularies
- the availability, cost and potential advantages of alternative treatments, including less expensive generic drugs;
- pricing, reimbursement and cost effectiveness, which may be subject to regulatory control;
- effectiveness of our or any of our partners' sales and marketing strategies;
- the product labeling or product insert required by the FDA or regulatory authority in other countries; and
- the availability of adequate third-party insurance coverage or reimbursement.

If any product candidate that we develop does not provide a treatment regimen that is as beneficial as, or is perceived as being as beneficial as, the current standard of care or otherwise does not provide patient benefit, that product candidate, if approved for commercial sale by the FDA or other regulatory authorities, likely will not achieve market acceptance. Our ability to effectively promote and sell any approved products will also depend on pricing and cost-effectiveness, including our ability to produce a product at a competitive price and our ability to obtain sufficient third-party coverage or reimbursement. If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, patients and third-party payors, our ability to generate revenues from that product would be substantially reduced. In addition, our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources, may be constrained by FDA rules and policies on product promotion, and may never be successful.

Guidelines and recommendations published by various organizations can impact the use of our products and product candidates.

Government agencies promulgate regulations and guidelines directly applicable to us and to our products and product candidates. In addition, professional societies, practice management groups, private health and science foundations and organizations involved in various diseases from time to time may also publish guidelines or recommendations to the health care and patient communities. Recommendations of government agencies or these other groups or organizations may relate to such matters as usage, dosage, route of administration and use of concomitant therapies. Recommendations or guidelines suggesting the reduced use of our products and product candidates or the use of competitive or alternative products that are followed by patients and health care providers could result in decreased use of our products and product candidates.

We face potential product liability exposure, and, if claims brought against us are successful, we could incur substantial liabilities.

The use of our product candidates in clinical trials and the sale of marketed products expose us to product liability claims. Currently, we are not aware of any anticipated product liability claims with respect to our products or product candidates. In the future, an individual may bring a liability claim against us if one of our products or product candidates causes, or merely appears to have caused, an injury. If we cannot successfully defend ourselves against the product liability claim, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our approved products;
- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs of related litigation;
- initiation of investigations by regulators;
- substantial monetary awards to patients or other claimants;

- distraction of management's attention from our primary business;
- product recalls;
- loss of revenue; and
- the inability to commercialize our product candidates.

We currently have product liability insurance coverage for the commercial sale of TRULANCE and for the clinical trials of our product candidates which is subject to industry-standard terms, conditions and exclusions. Our current insurance coverage may prove insufficient to cover any liability claims brought against us. In addition, because of the increasing costs of insurance coverage, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy liabilities that may arise. A successful product liability claim or series of claims could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Our failure to successfully discover, acquire, develop and market additional product candidates or approved products could impair our ability to grow.

As part of our growth strategy, we intend to develop and market additional products and product candidates. We are pursuing various therapeutic opportunities through our pipeline. We may spend several years completing our development of any particular current or future internal product candidate, and failure can occur at any stage. The product candidates to which we allocate our resources may not end up being successful. In addition, because our internal research capabilities are limited, we may be dependent upon pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select, discover and acquire promising pharmaceutical product candidates and products. Failure of this strategy would impair our ability to grow.

The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all. In addition, future acquisitions may entail numerous operational and financial risks, including:

- disruption of our business and diversion of our management's time and attention to develop acquired products or technologies;
- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- higher than expected acquisition and integration costs;
- difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;
- increased amortization expenses;
- assumption of known and unknown liabilities;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to motivate key employees of any acquired businesses.

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities.

Even though TRULANCE is approved by the FDA for the treatment of adults with CIC and IBS-C, it faces post-approval development and regulatory requirements, which will present additional challenges.

In January 2017, the FDA approved TRULANCE as a once-daily treatment for adult men and women suffering from CIC and in January 2018 for IBS-C. TRULANCE will be subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, promotion, recordkeeping and submission of safety and other post-market indications. Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with GMP regulations. If we or a regulatory agency discovers previously unknown problems with a

product, such as adverse events of unanticipated severity or frequency, or problems with a facility where the product is manufactured, a regulatory agency may impose restrictions on that product or the manufacturer, including requiring implementation of a risk evaluation and mitigation strategy program, withdrawal of the product from the market or suspension of manufacturing. If we, our partners or the manufacturing facilities for TRULANCE fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require us to initiate a product recall.

Even though TRULANCE is approved for marketing in the U.S., we or our partners may never receive approval to commercialize TRULANCE or our other product candidates outside of the United States.

In the future, we may seek to commercialize TRULANCE and/or our other product candidates, including dolcanatide, in foreign countries outside of the United States. In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other jurisdictions regarding safety and efficacy. Approvals procedures vary among jurisdictions and can involve product testing and administrative review periods different from, and greater than, those in the United States. The time required to obtain approval in other jurisdictions might differ from that required to obtain FDA approval. Pursuant to our license agreement with Cipher Pharmaceuticals, Cipher is responsible for all regulatory activities in Canada. If Cipher cannot obtain regulatory approval for TRULANCE in Canada, our relationship with Cipher will be adversely affected and we will not be able to generate any revenue from the license agreement with Cipher. In addition, even if we and Cipher obtains marketing approval for TRULANCE in Canada, Health Canada may impose restrictions on TRULANCE's conditions for use, distribution or marketing and in some cases may impose ongoing requirements for post-market surveillance, post-approval studies or clinical trials.

The approval process varies and the time needed to secure approval in any region such as the European Union or in a country with an independent review procedure may be longer or shorter than that required for FDA approval. We cannot assure you that clinical trials conducted in one country will be accepted by other countries or that an approval in one country or region will result in approval elsewhere. Regulatory approval in one jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory processes in others. Failure to obtain regulatory approvals in other jurisdictions or any delay or setback in obtaining such approvals could have an adverse effect on us. Such effects include the risks that TRULANCE or our other product candidates may not be approved for all indications for use included in proposed labeling or for any indications at all, which could limit the uses of TRULANCE or other product candidates and have an adverse effect on our products' commercial potential or require costly post-marketing studies.

We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to seek or obtain regulatory approval for or commercialize our product candidates.

We have agreements with third-party contract research organizations, or CROs, under which we have delegated to the CROs the responsibility to coordinate and monitor the conduct of our clinical trials and to manage data for our clinical programs. We, our CROs and our clinical sites are required to comply with current Good Clinical Practices, or GCPs, regulations and guidelines issued by the FDA and by similar governmental authorities in other countries where we are conducting clinical trials. We have an ongoing obligation to monitor the activities conducted by our CROs and at our clinical sites to confirm compliance with these requirements. In the future, if we, our CROs or our clinical sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP regulations, and may require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to their failure to adhere to our

clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

Reimbursement may not be available for TRULANCE or our other product candidates, which would impede sales.

Market acceptance and sales of TRULANCE and other potential product candidates may depend on coverage and reimbursement policies and health care reform measures. Decisions about formulary coverage as well as levels at which government authorities and third-party payers, such as private health insurers and health maintenance organizations, reimburse patients for the price they pay for our products as well as levels at which these payors pay directly for our products, where applicable, could affect whether we are able to commercialize these products. We cannot be sure that reimbursement will be available for any of these products. Also, we cannot be sure that coverage or reimbursement amounts will not reduce the demand for, or the price of, our products. If coverage and reimbursement are not available, are available only at limited levels, or are available and then withdrawn, we may not be able to successfully commercialize our products.

In recent years, officials have made numerous proposals to change the health care system in the United States. These proposals include measures that would limit or prohibit payments for certain medical treatments or subject the pricing of drugs to government control. In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. If our products are or become subject to government regulation that limits or prohibits payment for our products, or that subjects the price of our products to governmental control, we may not be able to generate revenue, attain profitability or commercialize our products.

As a result of legislative proposals and the trend towards managed health care in the United States, third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. They may also impose strict prior authorization requirements and/or refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly-approved drugs, which in turn will put pressure on the pricing of drugs.

In addition, there is a degree of unpredictability with regard to the eventual pricing and reimbursement levels of medications in markets outside the United States. If the pricing and reimbursement levels of TRULANCE are lower than we anticipate, then affordability of, and market access to, TRULANCE may be adversely affected and thus market potential in these territories would suffer. Furthermore, with regard to any indications for which we may gain approval in territories outside the United States, the number of actual patients with the condition included in such approved indication may be smaller than we anticipate. If any such approved indication is narrower than we anticipate, the market potential in these countries for our product would suffer.

We will incur significant liability if it is determined that we are promoting any "off-label" use of TRULANCE.

Physicians are permitted to prescribe drug products and medical devices for uses that are not described in the product's labeling and that differ from those approved by the FDA or other applicable regulatory agencies. Such "off-label" uses are common across medical specialties. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict communications on the subject of off-label use. Companies are not permitted to promote drugs or medical devices for off-label uses. Accordingly, we do not permit promotion of TRULANCE in the U.S. for use in any indications other than CIC and IBS-C or in any patient populations other than adult men and women. Similarly, we do not permit promotion of any other approved product we develop, license, co-promote or otherwise partner for any indication, population or use not described in such product's label. The FDA and other regulatory and enforcement authorities actively enforce laws and regulations prohibiting promotion of off-label uses and the promotion of products for which marketing approval has not been obtained. A company that is found to have promoted off-label uses will be subject to significant liability, including civil and administrative remedies as well as criminal sanctions.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific exchange concerning their products. We intend to engage in medical education activities and communicate with healthcare providers in compliance with all applicable laws, regulatory guidance and industry best practices. Although we believe we have put in place a robust compliance program, which is designed to ensure that all such activities are performed in a legal and compliant manner, we cannot be certain that our program will address all areas of potential exposure and the risks in this area cannot be entirely eliminated.

If we fail to comply with healthcare and other regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected.

TRULANCE is marketed in the U.S. and is covered by federal healthcare programs; and, as a result, certain federal and state healthcare laws and regulations pertaining to product promotion and fraud and abuse are applicable to, and may affect, our business. These laws and regulations include:

- federal healthcare program anti-kickback laws, which prohibit, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, information or claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent, and which may apply to us for reasons including providing coding and billing advice to customers;
- the federal Health Insurance Portability and Accountability Act of 1996, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- the Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;
- the so-called "federal sunshine" law, which requires pharmaceutical and medical device companies to monitor and report certain financial interactions with physicians and other healthcare professionals and healthcare organizations to the federal government for re-disclosure to the public; and
- state law equivalents of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, state transparency laws and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts.

Our global activities are subject to the U.S. Foreign Corrupt Practices Act which prohibits corporations and individuals from paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. We are also subject to similar anti-bribery laws in the other countries in which we do business.

If our operations are found to be in violation of any of the laws described above or any other laws, rules or regulations that apply to us, we will be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, rules or regulations, we cannot be certain that our program will address all areas of potential exposure and the risks in this area cannot be entirely eliminated, particularly because the requirements and government interpretations of the requirements in this space are constantly evolving. Any action against us for violation of these laws, rules or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business, as well as damage our business or reputation. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security, fraud and reporting laws may prove costly.

Healthcare reform and other governmental and private payer initiatives could hinder or prevent our products' or product candidates' commercial success.

The U.S. government and other governments have shown significant interest in pursuing continued healthcare reform. Any government-adopted reform measures could adversely impact the pricing of healthcare products and services in the United States or internationally and the amount of reimbursement available from governmental agencies or other third party payors. The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors

of health care services to contain or reduce health care costs may adversely affect our ability to set prices for our products which we believe are fair, and our ability to generate revenues and achieve and maintain profitability.

New laws, regulations and judicial decisions, or new interpretations of existing laws, regulations and decisions, that relate to healthcare availability, methods of delivery or payment for products and services, or sales, marketing or pricing, may limit our potential revenue, and we may need to revise our research and development programs. The pricing and reimbursement environment may change in the future and become more challenging due to several reasons, including policies advanced by the current executive administration in the United States, new healthcare legislation or fiscal challenges faced by government health administration authorities. Specifically, in both the United States and some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the health care system in ways that could affect our ability to sell our products profitably.

For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA has substantially changed the way healthcare is financed by both government health plans and private insurers, and significantly impacts the pharmaceutical industry. The PPACA contains a number of provisions that are expected to impact our business and operations in ways that may negatively affect our potential revenues in the future. For example, the PPACA imposes a non-deductible excise tax on pharmaceutical manufacturers or importers that sell branded prescription drugs to U.S. government programs which we believe will increase the cost of our products. In addition, as part of the PPACA's provisions closing a funding gap that currently exists in the Medicare Part D prescription drug program (commonly known as the "donut hole"), we will be required to provide a discount on branded prescription drugs equal to 50% of the government-negotiated price, for drugs provided to certain beneficiaries who fall within the donut hole. Similarly, PPACA increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1% and requires collection of rebates for drugs paid by Medicaid managed care organizations. The PPACA also includes significant changes to the 340B drug discount program including expansion of the list of eligible covered entities that may purchase drugs under the program. At the same time, the expansion in eligibility for health insurance benefits created under PPACA is expected to increase the number of patients with insurance coverage who may receive our products. While it is too early to predict all the specific effects the PPACA or any future healthcare reform legislation will have on our business, they could have a material adverse effect on our business and financial condition.

Some of the provisions of the PPACA have yet to be implemented, and there have been legal and political challenges to certain aspects of the PPACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed repeal legislation, the Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. Congress may consider other legislation to repeal or replace elements of the PPACA.

Congress periodically adopts legislation like the PPACA and the Medicare Prescription Drug, Improvement and Modernization Act of 2003, that modifies Medicare reimbursement and coverage policies pertaining to prescription drugs. Implementation of these laws is subject to ongoing revision through regulatory and sub regulatory policies. Congress also may consider additional changes to Medicare policies, potentially including Medicare prescription drug policies, as part of ongoing budget negotiations. While the scope of any such legislation is uncertain at this time, there can be no assurances that future legislation or regulations will not decrease the coverage and price that we may receive for our proposed products. Other third-party payors are increasingly challenging the prices charged for medical products and services. It will be time consuming and expensive for us to go through the process of seeking coverage and reimbursement from Medicare and private payors. Our proposed products may not be considered cost-effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our proposed products on a profitable basis. Further federal and state proposals and health care reforms are likely which could limit the prices that can be charged for our products and product candidates that we develop and may further limit our commercial opportunities. Our results of operations could be materially adversely affected by proposed healthcare reforms, by the Medicare prescription drug coverage legislation, by the possible effect of such current or future legislation on amounts that private insurers will pay and by other health care reforms that may be enacted or adopted in the future.

Individual states have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what

pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce ultimate demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

In addition, given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform, the cost of prescription drugs and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may result in decreased reimbursement for drugs, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to generate revenues. Increases in importation or re-importation of pharmaceutical products from foreign countries into the United States could put competitive pressure on our ability to profitably price our products, which, in turn, could adversely affect our business, results of operations, financial condition and prospects. We might elect not to seek approval for or market our products in foreign jurisdictions in order to minimize the risk of re-importation, which could also reduce the revenue we generate from our product sales. It is also possible that other legislative proposals having similar effects will be adopted.

In September 2007, the Food and Drug Administration Amendments Act of 2007 was enacted, giving the FDA enhanced post-marketing authority, including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information, and compliance with risk evaluations and mitigation strategies approved by the FDA. The FDA's exercise of this authority could result in delays or increased costs following the commercial launch of TRULANCE for the treatment of adult men and women suffering from CIC and IBS-C and could result in potential restrictions on the sale and/or distribution of TRULANCE, even in its approved indication and patient populations.

Security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers and business partners, as well as personally identifiable information of clinical trial participants and employees. Similarly, our business partners and third party providers possess certain of our sensitive data. The secure maintenance of this information is critical to our operations and business strategy. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information, including our data being breached at our business partners or third-party providers, could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation which could adversely affect our business.

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our product candidates, and the methods used to manufacture them, as well as successfully defending these patents against third-party challenges. We will only be able to protect our product candidates from unauthorized making, using, selling and offering to sell or importation by third parties to the extent that we have rights under valid and enforceable patents or trade secrets that cover these activities.

For example:

- others may be able to make compounds that are competitive with our products but that are not covered by the claims of our patents;
- we may not have been the first to make the inventions covered by our pending patent applications;
- we may not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents
- it is possible that our issued patents could be narrowed in scope, invalidated, held to be unenforceable, or circumvented;
- we may not develop additional proprietary technologies that are patentable; or
- the patents of others may have an adverse effect on our business.

We also may rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. While we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights and we may be unable to protect our rights to, or use, our technology.

If we choose to go to court to stop someone else from using the inventions claimed in our patents, that individual or company has the right to ask the court to rule that these patents are invalid and/or should not be enforced against that third party. These lawsuits are expensive and would consume time and other resources even if we were successful in stopping the infringement of these patents. In addition, there is a risk that the court will decide that these patents are not valid and that we do not have the right to stop the other party from using the inventions. There is also the risk that, even if the validity of these patents is upheld, the court will refuse to stop the other party on the ground that such other party's activities do not infringe our rights to these patents.

Furthermore, a third party may claim that we are using inventions covered by the third party's patent rights and may go to court to stop us from engaging in our normal operations and activities, including making or selling our product candidates. These lawsuits are costly and could affect our results of operations and divert the attention of managerial and technical personnel. There is a risk that a court would decide that we are infringing the third party's patents and would order us to stop the activities covered by the patents. In addition, there is a risk that a court will order us to pay the other party damages for having violated the other party's patents. The biotechnology industry has produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our products or methods of use either do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid, and we may not be able to do this. Proving invalidity, in particular, is difficult since it requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents.

Because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until eighteen months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our issued patents or our pending applications or that we were the first to invent the technology. Our competitors have filed, and may in the future file, patent applications covering technology similar to ours. Any such patent application may have priority over our patent applications and could further require us to obtain rights to issued patents covering such technologies. If another party has filed a United States patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the PTO, to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful, resulting in a loss of our United States patent position with respect to such inventions.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentaries, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

We have not yet registered trademarks for the company name "Synergy Pharmaceuticals," TRULANCE or other potential drug names for plecanatide in all our potential markets, and failure to secure those registrations could adversely affect our ability to market TRULANCE, other product candidates and our business.

We have applied to register trademarks for our company name and for TRULANCE in the United States and other jurisdictions, but may not have covered all potential markets. Our trademark applications have received registrations in some jurisdictions. Our remaining trademark applications may not be allowed for registration, and our registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the United States and in foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Oppositions or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. In jurisdictions where we have not yet filed trademark applications, we may be conflicted from obtaining registration if/when we do file trademark applications due to third party conflicts. Failure to secure trademark registrations in the United States and in foreign jurisdictions could adversely affect our ability to market TRULANCE, our other product candidates and our business.

We received a demand letter from a large pharmaceutical company, or PharmCo, demanding that we withdraw our applications for TRULANCE in the United States and elsewhere, claiming that the mark is too similar to a mark used in connection with products and services related to diabetes. On November 2, 2016, we entered into a Trademark Consent Agreement pursuant to which PharmCo agreed to our use and registration of the TRULANCE mark in connection with products for the treatment of constipation and irritable bowel syndrome and related conditions in oral tablet form. We agreed not to use such TRULANCE or any mark including the term TRULANCE or commencing with the letters TRUL on or in connection with products and services related to diabetes or any product involving subcutaneous injection and, where possible, to amend our trademark filings to include the limitation "all of the aforesaid excluding pharmaceutical preparations for the treatment of diabetes." PharmCo has reserved its right to object and take legal action in the event we use a mark with the prefix TRU in connection with drugs in the diabetes field.

In addition, an opposition has been filed in the European Union to our application to register SYNERGY PHARMACEUTICALS.

Confidentiality agreements with employees and others may not adequately prevent disclosure of our trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete.

Because we operate in the highly technical field of research and development of small molecule drugs, we rely in part on trade secret protection in order to protect our proprietary trade secrets and unpatented know-how. However, trade secrets are difficult to protect, and we cannot be certain that others will not develop the same or similar technologies on their own. We have taken steps, including entering into confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, manufacturers and other advisors, to protect our trade secrets and unpatented know-how. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. We also typically obtain agreements from these parties that provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Enforcing a claim that a party illegally obtained and is using our trade secrets or know-how is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets or know-how. The failure to obtain or maintain trade secret protection could adversely affect our competitive position.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Risks Related to the Convertible Senior Notes

The indenture for our senior convertible notes, or the Notes, contains covenants limiting our financial and operating flexibility.

The indenture for the Notes contains covenants that will restrict our ability and the ability of certain of our subsidiaries to:

- declare or pay any dividends on our or our subsidiaries' capital stock;
- redeem or repurchase capital stock, or prepay or repurchase subordinated debt.

These restrictive covenants could limit our ability to pursue our growth plans, restrict our flexibility in planning for, or reacting to, changes in our business and industry and increase our vulnerability to general adverse economic and industry conditions. We may enter into additional financing arrangements in the future, which could further restrict our flexibility.

Any defaults of covenants contained in the Notes may lead to an event of default under the Notes and the indenture. We may not be able to pay any amounts due to holders of the Notes in the event of such default, and such default may significantly impair our ability to satisfy our obligations under the Notes.

We will not make any adjustment to the conversion rate for Notes converted in connection with a fundamental change, and noteholders will not be compensated for any lost value of their Notes as a result of such transaction.

We will not increase or make any other adjustment to the conversion rate upon a conversion of Notes in connection with a fundamental change or similar event. Therefore, noteholders will not be compensated for any lost value of their Notes as a result of such transaction.

The Notes are effectively subordinated to any of our future secured debt and any liabilities of our subsidiaries.

The Notes will rank senior in right of payment to our future indebtedness that is expressly subordinated in right of payment to the Notes; equal in right of payment to our trade payables and other future unsecured indebtedness that is not so subordinated; effectively junior to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all future indebtedness (including trade payables) incurred by our subsidiaries. In the event of our bankruptcy, liquidation, reorganization or other winding up, our assets that secure debt ranking senior or equal in right of payment to the Notes will be available to pay obligations on the Notes only after the secured debt has been repaid in full. There may not be sufficient assets remaining to pay amounts due on any or all of the Notes then outstanding.

Servicing our debt will require a significant amount of cash, and we may not have sufficient cash flow from our business to pay our debt.

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, including the Notes, depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service our debt and make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

Recent regulatory actions may adversely affect the trading price and liquidity of the Notes.

We expect that investors in, and potential purchasers of, the Notes may employ, or seek to employ, an arbitrage strategy with respect to the Notes. Investors that employ an arbitrage strategy with respect to the Notes typically implement that strategy by selling short the common stock underlying the Notes and dynamically adjusting their short position while they hold the Notes. Investors may also implement this hedging strategy by entering into swaps on our common stock in lieu of or in addition to short selling the common stock.

The Securities and Exchange Commission, or SEC, and other regulatory and self-regulatory authorities have implemented various rules and may adopt additional rules in the future that may impact those engaging in short selling activity involving equity securities (including our common stock), including Rule 201 of SEC regulation SHO, the Financial Industry Regulatory Authority, Inc.'s "Limit Up-Limit Down" program, market-wide circuit breaker systems that halt trading of stock for certain

periods following specific market declines, and rules stemming from the enactment and implementation of the Dodd-Frank Wall Street Reform and Consumer Protection Act. Past regulatory actions, including emergency actions or regulations, have had a significant impact on the trading prices and liquidity of equity-linked instruments. Any governmental action that similarly restricts the ability of investors in, or potential purchasers of, the Notes to effect short sales of our common stock could similarly adversely affect the trading price and the liquidity of the Notes.

Volatility in the market price and trading volume of our common stock could adversely impact the trading price of the Notes.

The stock market in recent years has experienced significant price and volume fluctuations that have often been unrelated to the operating performance of companies. The market price of our common stock could fluctuate significantly for many reasons, including in response to the risks described in this section and elsewhere in this Form 10-K or for reasons unrelated to our operations, such as reports by industry analysts, investor perceptions or negative announcements by our customers, competitors or suppliers regarding their own performance, as well as industry conditions and general financial, economic and political instability. A decrease in the market price of our common stock would likely adversely impact the trading price of the Notes. The market price of our common stock could also be affected by possible sales of our common stock by investors who view the Notes as a more attractive means of equity participation in us and by hedging or arbitrage trading activity that we expect to develop involving our common stock. This trading activity could, in turn, affect the trading prices of the Notes. This may result in greater volatility in the trading price of the Notes than would be expected for non-convertible debt securities.

Subject to certain limitations, we continue to have the ability to incur debt; if we incur substantial additional debt, these higher levels of debt may affect our ability to pay the principal of and interest on the Notes.

Subject to certain limitations, we and our subsidiaries may be able to incur substantial additional debt in the future, some of which may be secured debt. The indenture governing the Notes does not restrict our ability to incur additional subordinated indebtedness or require us to maintain financial ratios or specified levels of net worth or liquidity. If we incur substantial additional indebtedness in the future, these higher levels of indebtedness may affect our ability to pay the principal of and interest on the Notes, or any fundamental change purchase price, and our creditworthiness generally.

We may not have the ability to raise the funds necessary to purchase the Notes as required upon a fundamental change, and our future debt may contain limitations on our ability to purchase the Notes.

Following a fundamental change as defined, holders of Notes will have the right to require us to purchase their Notes for cash. A fundamental change may also constitute an event of default or prepayment under, and result in the acceleration of the maturity of, our then-existing indebtedness. We cannot assure noteholders that we will have sufficient financial resources, or will be able to arrange financing, to pay the fundamental change purchase price in cash with respect to any Notes surrendered by holders for purchase upon a fundamental change. In addition, restrictions in our then existing credit facilities or other indebtedness, if any, may not allow us to purchase the Notes upon a fundamental change. Our failure to purchase the Notes upon a fundamental change when required would result in an event of default with respect to the Notes which could, in turn, constitute a default under the terms of our other indebtedness, if any. If the repayment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and purchase the Notes.

Some significant restructuring transactions may not constitute a fundamental change, in which case we would not be obligated to offer to purchase the Notes.

Upon the occurrence of a fundamental change as defined, noteholders have the right to require us to purchase their Notes. However, the fundamental change provisions will not afford protection to holders of Notes in the event of certain transactions that could adversely affect the Notes. For example, transactions such as leveraged recapitalizations, refinancings, restructurings or acquisitions initiated by us would not constitute a fundamental change requiring us to repurchase the Notes. In addition, holders will not be entitled to require us to purchase their Notes upon a significant change in the composition of our board. In the event of any such transaction, holders of the Notes would not have the right to require us to purchase their Notes, even though each of these transactions could increase the amount of our indebtedness, or otherwise adversely affect our capital structure or any credit ratings, thereby adversely affecting holders of the Notes.

Future sales of our common stock in the public market could lower the market price for our common stock and adversely impact the trading price of the Notes.

In the future, we may sell additional shares of our common stock to raise capital. In addition, a substantial number of shares of our common stock are reserved for issuance upon the exercise of stock options and warrants and upon conversion of

the Notes. We cannot predict the size of future issuances or the effect, if any, that they may have on the market price for our common stock. The issuance and sale of substantial amounts of common stock, or the perception that such issuances and sales may occur, could adversely affect the trading price of the Notes and the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities.

The Notes may not have an active market, and the price may be volatile, so noteholders may be unable to sell their Notes at the price they desire or at all.

The Notes are a new issue of securities for which there is currently no active trading market. We cannot be certain that a liquid market will develop for the Notes, that noteholders will be able to sell any of the Notes at a particular time (if at all) or that the prices they receive if or when noteholders sell the Notes will be above their initial offering price. In addition, we do not intend to apply to list the Notes on any securities exchange or for inclusion of the Notes on any automated dealer quotation system. The initial purchasers have advised us that they intend to make a market in the Notes, but they are not obligated to do so and may discontinue any market-making in the Notes at any time in their sole discretion and without notice. Future trading prices of the Notes on any market that may develop will depend on many factors, including our operating performance and financial condition, prevailing interest rates, the market for similar securities and general economic conditions.

Moreover, even if noteholders are able to sell their Notes, they may not receive a favorable price for their Notes. Future trading prices of the Notes will depend on many factors, including, among other things, prevailing interest rates, our operating results, the price of our common stock and the market for similar securities. Historically, the market for convertible debt has been subject to disruptions that have caused volatility in prices. It is possible that the market for the Notes will be subject to disruptions that may have a negative effect on the holders of the Notes, regardless of our prospects or financial performance.

Any adverse rating of the Notes may negatively affect the trading price and liquidity of the Notes and the price of our common stock.

We do not intend to seek a rating on the Notes. However, if a rating service were to rate the Notes and if such rating service were to assign the Notes a rating lower than the rating expected by investors or were to lower its rating on the Notes below the rating initially assigned to the Notes or otherwise announce its intention to put the Notes on credit watch, the trading price or liquidity of the Notes and the price of our common stock could decline.

The conversion rate of the Notes may not be adjusted for all dilutive events.

The conversion rate of the Notes is subject to adjustment for certain events, including, but not limited to, the issuance to all or substantially all holders of our common stock of stock dividends, certain rights, options or warrants, capital stock, indebtedness, assets or cash, and subdivisions and combinations of our common stock, and certain issuer tender or exchange offers as defined. However, the conversion rate will not be adjusted for other events, such as a third-party tender or exchange offer or an issuance of common stock for cash, that may adversely affect the trading price of the Notes or the common stock. An event that adversely affects the value of the Notes may occur, and that event may not result in an adjustment to the conversion rate.

The Notes are protected by restrictive covenants only to a limited extent.

The indenture governing the Notes does not contain any financial or operating covenants or restrictions on the incurrence of indebtedness or the issuance or repurchase of securities by us or any of our subsidiaries. The indenture does not contain covenants or other provisions to afford protection to holders of the Notes in the event of a fundamental change except as defined. We could engage in many types of transactions, such as acquisitions, refinancings or recapitalizations that could substantially affect our capital structure and the value of the Notes and shares of our common stock but may not constitute a fundamental change that permits holders to require us to purchase their Notes. For these reasons, noteholders should not consider the covenants in the indenture or the fundamental change purchase feature of the Notes as significant factors in evaluating whether to invest in the Notes.

The issuance of shares of common stock upon conversions of the Notes will dilute the ownership interest of our existing stockholders, including holders who had previously converted their Notes.

The issuance of shares of common stock upon the conversion of some or all of the Notes will dilute the ownership interests of our existing stockholders. Any sales in the public market of such shares of our common stock could adversely affect prevailing market prices of our common stock. In addition, the existence of the Notes may encourage short selling by market participants because the conversion of the Notes could depress the price of our common stock.

Noteholders are not entitled to any rights with respect to our common stock, but are subject to all changes made with respect to our common stock to the extent noteholders convert their Notes and receive shares of our common stock.

Holders who convert their Notes will not be entitled to any rights with respect to our common stock (including, without limitation, voting rights and rights to receive any dividends or other distributions on our common stock) until the conversion date relating to such Notes, but holders of Notes will be subject to all changes affecting our common stock. For example, if an amendment is proposed to our second amended and restated certificate of incorporation, as amended or our amended and restated by-laws requiring stockholder approval and the record date for determining the stockholders of record entitled to vote on the amendment occurs prior to the conversion date with respect to any Notes surrendered for conversion, then the holder surrendering such Notes will not be entitled to vote on the amendment, although such holder will nevertheless be subject to any changes affecting our common stock.

Upon conversion of the Notes, holders may receive less valuable consideration than expected because the value of our common stock may decline after they exercise their conversion right but before we settle our conversion obligation.

Under the Notes, a converting holder will be exposed to fluctuations in the value of our common stock during the period from the date such holder surrenders Notes for conversion until the date we settle our conversion obligation.

Upon conversion of the Notes, we will be required to deliver the shares of our common stock, together with cash for any fractional share, on the third business day following the relevant conversion date. Accordingly, if the price of our common stock decreases during this period, the value of the shares that noteholders receive will be adversely affected and would be less than the conversion value of the Notes on the conversion date.

The fundamental change purchase feature of the Notes may delay or prevent an otherwise beneficial attempt to take over our company.

The terms of the Notes require us to offer to purchase the Notes for cash in the event of a fundamental change, as defined. A non-stock takeover of our company may trigger the requirement that we purchase the Notes. This feature may have the effect of delaying or preventing a takeover of our company that would otherwise be beneficial to investors.

The market price of our common stock may be volatile and adversely affected by several factors.

The market price of our common stock could fluctuate significantly in response to various factors and events, including:

- the commercial performance of TRULANCE in the U.S.;
- any third-party coverage and reimbursement policies for TRULANCE;
- market conditions in the pharmaceutical and biotechnology sectors;
- our ability to execute our business plan;
- announcements regarding regulatory developments with respect to our product candidates;
- announcements concerning product development results, including clinical trial results, or intellectual property rights of others;
- developments, litigation or public concern about the safety of TRULANCE or our potential products;
- our issuance of additional securities, including debt or equity or a combination thereof, necessary to fund our operating expenses;
- announcements of technological innovations or new products by us or our competitors;
- loss of any strategic relationship;
- industry developments, including, without limitation, changes in healthcare policies or practices or third-party reimbursement policies;
- deviations in our operating results from any guidance we may provide or the estimates of securities analysts;
- economic and other external factors effecting U.S. or global equity markets;
- period-to-period fluctuations in our financial results; and
- discussion of us or our stock price in the financial or scientific press or in online investor communities.

In addition, the securities markets have from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. These market fluctuations may also materially and adversely affect the market price of our common stock.

We have not paid cash dividends in the past and do not expect to pay cash dividends in the foreseeable future. Any return on investment in shares of common stock may be limited to the value of our common stock.

We have never paid cash dividends on our common stock and do not anticipate paying cash dividends on our common stock in the foreseeable future. The payment of dividends on our capital stock will depend on our earnings, financial condition and other business and economic factors affecting us at such time as the board of directors may consider relevant. If we do not pay dividends, our common stock may be less valuable because a return on any investment in shares of our common stock will only occur if the common stock price appreciates.

A sale of a substantial number of shares of the common stock may cause the price of our common stock to decline.

If our stockholders sell, or the market perceives that our stockholders intend to sell for various reasons, substantial amounts of our common stock in the public market it may make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of biotechnology and biopharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of our securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business.

Our quarterly and annual operating results may fluctuate significantly.

We expect our operating results to be subject to frequent fluctuations. Our net profit or loss and other operating results will be affected by numerous factors, including:

- the level of underlying demand for TRULANCE in the U.S. and wholesalers' buying patterns;
- the costs associated with commercializing TRULANCE in the U.S.;
- the cost of manufacturing and distributing TRULANCE;
- variations in the level of expenses related to our development programs;
- any excess or obsolete inventory or asset impairments and associated write-downs;
- initiation or completion of clinical trials;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting our product candidates;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments under these arrangements;
- any material lawsuit in which we may become involved; and
- interest payments on our Term Loan and outstanding Notes.

If our operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our common stock to fluctuate substantially.

Our ability to use our net operating loss carry forwards may be subject to limitation.

Generally, a change of more than 50% in the ownership of a company's stock, by value, over a three-year period constitutes an ownership change for U.S. federal income tax purposes. An ownership change may limit our ability to use our net operating loss carryforwards attributable to the period prior to the change. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may become subject to limitations, which could potentially result in increased future tax liability for us. At December 31, 2017, we had net operating loss carryforwards aggregating approximately $733.6 million. We have determined that an ownership change occurred as of April 30, 2003 pursuant to Section 382 of the Internal Revenue Code of 1986, as amended, or the Code. In addition, the shares of our common stock that we issued from July 14, 2008 through July 8, 2010 have resulted in an additional ownership change. As a result of these events and other prospective dilutive events our ability to utilize our operating loss carry forwards is and may be further limited.

U.S. federal income tax reform could adversely affect us.

On December 22, 2017, President Trump signed into law the "Tax Cuts and Jobs Act" (TCJA) that significantly reforms the Internal Revenue Code of 1986, as amended. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest, allows for the expensing of capital expenditures, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. We do not expect tax reform to have a material impact to our projection of minimal cash taxes or to our net operating losses. Our net deferred tax assets and liabilities will be revalued at the newly enacted U.S. corporate rate, and the impact will be recognized in our tax expense in the year of enactment. We continue to examine the impact this tax reform legislation may have on our business. The impact of this tax reform on holders of our common stock is uncertain and could be adverse. This Annual Report on Form 10-K does not discuss any such tax legislation or the manner in which it might affect purchasers of our common stock. We urge our stockholders to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our common stock.

If we fail to comply with the rules under the Sarbanes-Oxley Act of 2002 related to accounting controls and procedures, or if we discover material weaknesses and deficiencies in our internal control and accounting procedures, our stock price could decline significantly and raising capital could be more difficult.

If we fail to comply with the rules under the Sarbanes-Oxley Act of 2002 related to disclosure controls and procedures, or, if we discover material weaknesses and other deficiencies in our internal control and accounting procedures, our stock price could decline significantly and raising capital could be more difficult. Section 404 of the Sarbanes-Oxley Act requires annual management assessments of the effectiveness of our internal control over financial reporting and a report by our independent auditors addressing these assessments. If material weaknesses or significant deficiencies are discovered or if we otherwise fail to achieve and maintain the adequacy of our internal control, we may not be able to ensure that we can conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act. Moreover, effective internal controls are necessary for us to produce reliable financial reports and are important to helping prevent financial fraud. If we cannot provide reliable financial reports or prevent fraud, our business and operating results could be harmed, investors could lose confidence in our reported financial information, and the trading price of our common stock could drop significantly.

Our certificate of incorporation and bylaws and Delaware law may have anti-takeover effects that could discourage, delay or prevent a change in control, which may cause our stock price, and the value of the Notes, to decline.

Our second amended and restated certificate of incorporation, as amended and our amended and restated bylaws and Delaware law could make it more difficult for a third party to acquire us, even if closing such a transaction would be beneficial to our stockholders or holders of the Notes. We are authorized to issue up to 20,000,000 shares of preferred stock. This preferred stock may be issued in one or more series, the terms of which may be determined at the time of issuance by our board of directors without further action by stockholders. The terms of any series of preferred stock may include voting rights (including the right to vote as a series on particular matters), preferences as to dividend, liquidation, conversion and redemption rights and sinking fund provisions. No preferred stock is currently outstanding. The issuance of any preferred stock could materially adversely affect the rights of the holders of our common stock, and therefore, reduce the value of our common stock and the Notes. In particular, specific rights granted to future holders of preferred stock could be used to restrict our ability to merge with, or sell our assets to, a third party and thereby preserve control by the present management.

Provisions of our second amended and restated certificate of incorporation, as amended and our amended and restated bylaws and Delaware law also could have the effect of discouraging potential acquisition proposals or making a tender offer or delaying or preventing a change in control, including changes a stockholder or holder of the Notes might consider favorable. Such provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. In particular, our second amended and restated certificate of incorporation, as amended and amended and restated bylaws and Delaware law, as applicable, among other things:

- provide the board of directors with the ability to alter the bylaws without stockholder approval;
- place limitations on the removal of directors; and
- provide that vacancies on the board of directors may be filled by a majority of directors in office, although less than a quorum.

We are subject to Section 203 of the Delaware General Corporation Law which, subject to certain exceptions, prohibits "business combinations" between a publicly-held Delaware corporation and an "interested stockholder," which is generally defined as a stockholder who becomes a beneficial owner of 15% or more of a Delaware corporation's voting stock for a three-year period following the date that such stockholder became an interested stockholder. These provisions are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and to encourage persons seeking to acquire control of us to first negotiate with our board. These provisions may delay or prevent someone from acquiring or merging with us, which may cause the market price of our common stock and the value of the Notes to decline.

Risks related to Senior Secured Term Loan ("Term Loan")

Our term loan agreement with CRG Servicing LLC (or CRG) and other lenders party thereto contains restrictions that limit our flexibility in operating our business. We may be required to make a prepayment or repay the outstanding indebtedness earlier than we expect under our Term Loan Agreement if a prepayment event or an event of default occurs, including a material adverse change with respect to us, which could have a materially adverse effect on our business.

In September 2017, we entered into a term loan agreement with CRG. Pursuant to the loan agreement, we borrowed $100 million from the lenders as of the closing date. In February 2018 we amended the Term Loan agreement. The amended Term Loan provides for future borrowings of $25 million, $25 million and $50 million on or before June 30, 2018, September 30, 2018 and December 31, 2018, respectively.

Our agreement with CRG contains various covenants that limit our ability to engage in specified types of transactions. These covenants limit our ability to, among other things:

- incur additional indebtedness;
- enter into a merger, consolidation or certain changing of control events without complying with the terms of the loan agreement;
- change the nature of our business;
- amend, modify or waive any of our material agreements or organizational documents;
- grant certain types of liens on our assets;
- make certain investments;
- pay cash dividends; and
- enter into material transactions with affiliates.

The restrictive covenants of the term loan agreement could cause us to be unable to pursue business opportunities that we or our stockholders may consider beneficial. A breach of any of these covenants could result in an event of default under the term loan agreement. An event of default will also occur if, among other things, a material adverse change in our business, operations or condition occurs, or a material impairment of the prospect of our repayment of any portion of the amounts we owe under the term loan agreement occurs. In the case of a continuing event of default under the agreement, CRG could elect to declare all amounts outstanding to be immediately due and payable and terminate all commitments to extend further credit, proceed against the collateral in which we granted CRG a security interest under the term loan agreement and related agreements, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the term loan agreement are secured by all of our existing and future assets (excluding certain intellectual property).

We may not have enough available cash or be able to raise additional funds on satisfactory terms, if at all, through equity or debt financings to (i) make any required prepayment or (ii) repay such indebtedness at the time any such prepayment event or event of default occurs. In such an event, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant to others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our business, financial condition and results of operations could be materially adversely affected as a result.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None

ITEM 2. PROPERTIES

Our corporate headquarters is located at 420 Lexington Avenue, New York, NY 10170. Our New York office lease expires in March 2022 and has a total monthly rent of approximately $80,000 on a straight line basis, prospectively.

In addition, we lease office space for operations in Chesterbrook, Pennsylvania under a lease through December 2022, at a monthly rate of approximately $31,000.

Rent expense for the years ended December 31, 2017, 2016 and 2015 totaled approximately $1,637,000, $1,365,000, and $909,000, respectively.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we may become involved in various lawsuits, claims, government investigations and other legal proceedings that arise in the ordinary course of business. Litigation is subject to inherent uncertainties, and an adverse result in these or other matters may arise from time to time that may harm our business. These claims or proceedings can involve various types of parties, including governments, competitors, customers, suppliers, service providers, employees, or shareholders, among others. The resolution of these matters often develops over a long period of time and expectations can change as a result of new findings, rulings, appeals or settlement arrangements. Legal proceedings that are material or that we believe could become material are described below.

On November 20, 2017, Cantor Fitzgerald & Co. filed a Complaint against us in the Supreme Court of the State of New York, County of New York for, among other claims, breach of contract for failing to pay Cantor financial advisory and investment banking fees in the amount of $5.25 million it alleges were owed upon the closing of our debt financing in September 2017. On January 5, 2018, we filed an answer to the Complaint denying all the allegations against us, including the allegations that we entered into any agreement with Cantor Fitzgerald & Co. The parties are beginning the discovery process.

On February 8, 2018, a federal securities action, captioned David Lee v. Synergy Pharmaceuticals Inc. et al., was filed in the U.S. District Court for the Eastern District of New York. The complaint names Synergy and certain of its current or former officers and seeks to recover on behalf of a putative class of purchasers of Synergy's common stock between September 5, 2017 and November 14, 2017. On February 14, 2018, another substantially identical lawsuit-captioned Eileen Countryman v. Synergy Pharmaceuticals Inc. et al.-was filed in the same court against the same defendants on behalf of an identical putative class. Both complaints allege that the defendants made false and misleading statements, including in connection with our senior secured loan from CRG Servicing, LLC. Both assert claims under the federal securities laws and seek to recover unspecified damages, as well as interest, costs, and expenses.

ITEM 4. MINE SAFETY DISCLOSURES

Not Applicable.

PART II

ITEM 5. MARKET FOR THE REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS, AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Prices

From August 11, 2008 until February 18, 2011, our common stock was quoted on the Over the Counter Bulletin Board under the symbol "SGYP.OB." From February 22, 2011 until November 30, 2011 our common stock was traded on the OTC QB under the symbol "SGYP." On December 1, 2011 our common stock began trading on The NASDAQ Capital Market under the symbol "SGYP". On February 21, 2013 our common stock began trading on The NASDAQ Global Market under the symbol "SGYP". On January 2, 2014 our common stock began trading on The NASDAQ Global Select Market under the symbol "SGYP".

The following table shows the reported high and low closing prices per share for our common stock as reported on The NASDAQ Global Select Market during the periods indicated.

	High	Low
Year Ended December 31, 2016		
First quarter	$ 5.37	$ 2.59
Second quarter	$ 4.11	$ 2.67
Third quarter	$ 5.83	$ 3.61
Fourth quarter	$ 6.09	$ 4.14
Year Ended December 31, 2017		
First quarter	$ 7.07	$ 4.47
Second quarter	$ 4.74	$ 3.39
Third quarter	$ 4.60	$ 2.57
Fourth quarter	$ 3.46	$ 1.84

Holders of Common Stock

As of March 1, 2018, there were approximately 643 holders of record of our common stock.

Dividends

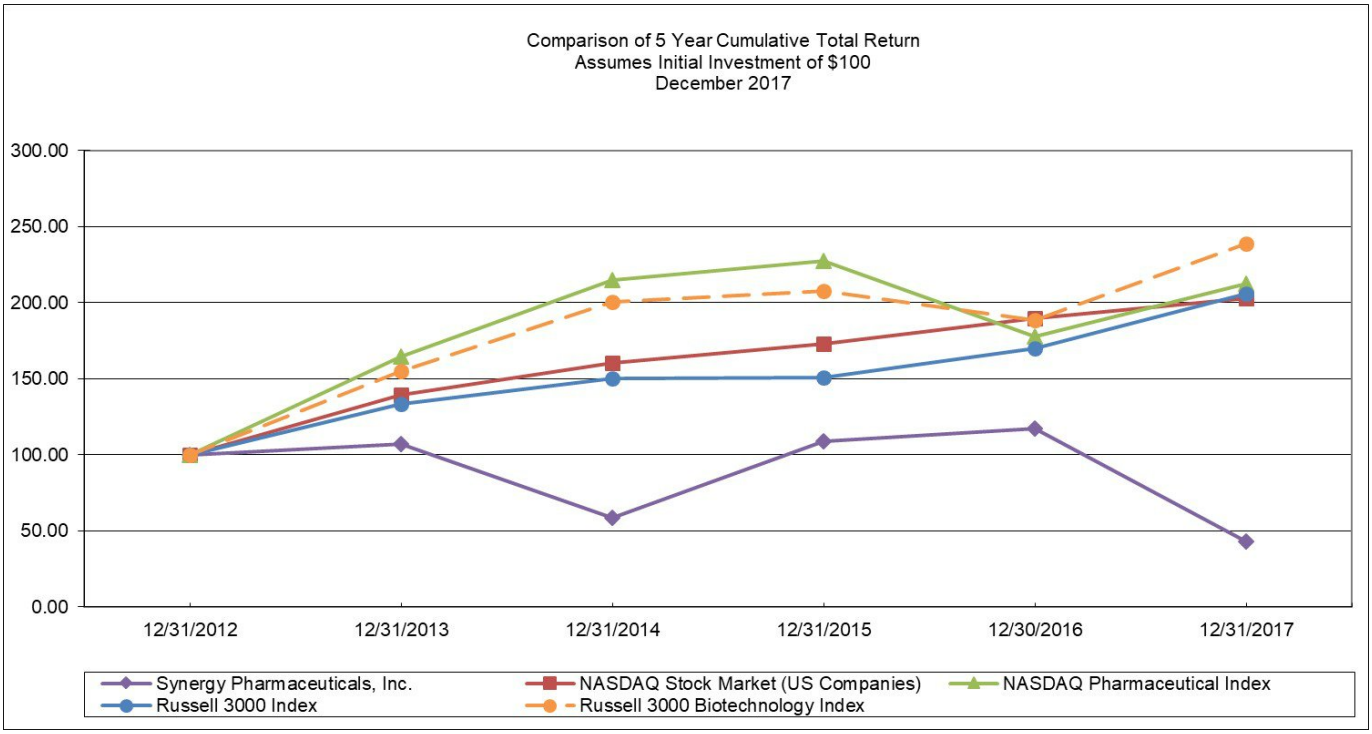
Historically, we have not declared or paid any cash dividends to the holders of our common stock and we do not expect to pay any such dividends in the foreseeable future as we expect to retain our future earnings for use in the operation and expansion of our business.

Stock Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act or the Exchange Act, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the performance of our common stock to the NASDAQ Stock Market (U.S.), the NASDAQ Pharmaceutical Index, the Russell 3000 index and the Russell 3000 Biotechnology Index from December 31, 2012 through December 31, 2017. The comparison assumes $100 was invested after the market closed on December 31, 2012 in our common stock and in each of the foregoing indices, and it assumes reinvestment of dividends, if any.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN
Among the NASDAQ Stock Market (U.S.),
the NASDAQ Pharmaceutical Index, the Russell 3000 Index, Russell 3000 Biotechnology Index,
and Synergy Pharmaceuticals, Inc.



Equity Compensation Information

The following table summarizes information about our equity compensation plans as of December 31, 2017.

Plan Category	(a) Number of Shares of Common Stock to be Issued upon Exercise of Outstanding Options		Weighted-Average Exercise Price of Outstanding Options	Number of Options Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities reflected in column (a))
Equity Compensation Plans Approved by Stockholders	28,113,187	$	4.04	11,886,813
Equity Compensation Plans Not Approved by Stockholders [1]	1,755,104	$	0.50	—
Total	29,868,291	$	3.83	11,886,813

(1) Consists of options issued in conjunction with sales of our common stock as well as for consulting and professional services.

On June 8, 2015, our stockholders approved an increase in the number of our common stock shares reserved for issuance under the 2008 Equity Compensation Incentive Plan (the "2008 Plan") from 15,000,000 to 30,000,000. As of December 31, 2017, there were 27,789,687 stock options outstanding under the 2008 Plan, and 323,500 options outstanding under the 2009 Directors Option Plan, (the "Directors Plan"), with 2,210,313 stock options available for future issuance under the 2008 Plan

and 176,500 stock options available under the Directors Plan. We adopted the 2017 Equity Incentive Plan (the “2017 Plan”) during the quarter ended June 30, 2017. The number of shares of our common stock reserved for issuance under the 2017 Plan is 9,000,000 and no grants have been awarded as of December 31, 2017.

ITEM 6. SELECTED FINANCIAL DATA

The following table sets forth our selected consolidated financial data and has been derived from our audited consolidated financial statements. Consolidated balance sheets as of December 31, 2017 and 2016, as well as consolidated statements of operations for the years ended December 31, 2017, 2016 and 2015, and the report thereon are included elsewhere in this Annual Report on Form 10-K. The information below should be read in conjunction with our audited consolidated financial statements and the notes to such statements, included below in Item 8, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included below in Item 7. Historical results are not necessarily indicative of the results to be expected in the future (in thousands except share and per share data).

	Year Ended December 31,				
	2017	2016	2015	2014	2013
Net sales	$ 16,820	$ —	$ —	$ —	$ —
Cost of goods sold	8,811	—	—	—	—
Gross profit	8,009	—	—	—	—
Costs and Expenses:					
Research and development	48,346	87,056	78,028	83,274	50,630
Selling, general and administrative	181,862	58,230	21,794	11,004	11,681
Loss from Operations	(222,199)	(145,286)	(99,822)	(94,278)	(62,311)
Other Income/(Loss)					
Interest expense, net	(5,270)	(13,390)	(17,284)	(2,875)	38
Debt conversion expense	(1,209)	(40,158)	—	—	—
State R&D tax credits	—	121	—	83	—
Change in fair value of derivative instruments-warrants	4,340	106	(394)	1,362	149
Total other expenses	(2,139)	(53,321)	(17,678)	(1,430)	187
Net loss	$ (224,338)	$ (198,607)	$ (117,500)	$ (95,708)	$ (62,124)
Basic and diluted	225,439,121	164,437,548	105,570,960	94,276,178	85,220,458
Net Loss per Common Share, Basic and Diluted					
Net loss per common share, basic and diluted	$ (1.00)	$ (1.21)	$ (1.11)	$ (1.02)	$ (0.73)

	December 31,				
	2017	2016	2015	2014	2013
Consolidated Balance Sheet Data:					
Cash and cash equivalents and available-for-sale securities	$ 136,986	$ 82,387	$ 111,750	$ 196,367	$ 68,157
Working capital	$ 127,013	$ 59,486	$ 95,476	$ 181,872	$ 56,199
Total assets	$ 166,606	$ 89,852	$ 115,929	$ 201,008	$ 72,558
Long term debt, net	$ 98,660	$ —	$ —	$ —	$ —
Total stockholders' equity/(deficit)	$ (5,518)	$ 37,541	$ (55,213)	$ (5,159)	$ 55,348

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read this discussion together with the Financial Statements, related Notes and other financial information included elsewhere in this Report on Form 10-K. The following discussion contains assumptions, estimates and other forward-looking statements that involve a number of risks and uncertainties, including those discussed under "Risk Factors," and elsewhere in this Form 10-K. To the extent that this Report contains forward-looking statements regarding the financial condition, operating results, business prospects or any other aspect of our company, please be advised that our actual financial condition, operating results and business performance may differ materially from that projected or estimated by us in forward-looking statements and thus you should not unduly rely on these statements.

The following discussion should be read in conjunction with our consolidated financial statements and other financial information appearing elsewhere in this annual report. In addition to historical information, the following discussion and other parts of this quarterly report contain forward-looking statements. You can identify these statements by forward-looking words such as "plan," "may," "will," "expect," "intend," "anticipate," believe," "estimate" and "continue" or similar words. Forward-looking statements include information concerning possible or assumed future business success or financial results. You should read statements that contain these words carefully because they discuss future expectations and plans, which contain projections of future results of operations or financial condition or state other forward-looking information. We believe that it is important to communicate future expectations to investors. However, there may be events in the future that we are not able to accurately predict or control. Accordingly, we do not undertake any obligation to update any forward-looking statements for any reason, even if new information becomes available or other events occur in the future and thus you should not unduly rely on these statements.

The forward-looking statements included herein are based on current expectations that involve a number of risks and uncertainties set forth under "Risk Factors" in our Annual Report on Form 10-K as of and for the year ended December 31, 2017 and other periodic reports filed with the United States Securities and Exchange Commission ("SEC"). Accordingly, to the extent that this Report contains forward-looking statements regarding the financial condition, operating results, business prospects or any other aspect of the Company, please be advised that the Company's actual financial condition, operating results and business performance may differ materially from that projected or estimated by the Company in forward-looking statements and thus you should not unduly rely on these statements.

Business Overview

Synergy Pharmaceuticals Inc. is a biopharmaceutical company focused on the development and commercialization of novel gastrointestinal (GI) therapies. We have pioneered discovery, research and development efforts around analogs of uroguanylin, a naturally occurring and endogenous human GI peptide, for the treatment of GI diseases and disorders. We discovered and own 100% worldwide rights to our proprietary uroguanylin based GI platform which includes one commercial product and one development stage compound.

Our first and only commercial product, plecanatide, is available and being marketed by us in the United States (U.S.), under the trademark name TRULANCE®, for the treatment of adults with chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C). On February 27, 2018 we entered into a definitive licensing agreement with Cipher Pharmaceuticals under which we granted Cipher the exclusive right to develop, market, distribute and sell TRULANCE in Canada. Under the terms of the licensing agreement, Synergy received an upfront payment of $5.0 million and is eligible for an additional milestone payment, as well as royalties from product sales in Canada. We are continuing to evaluate other potential ex-US business development opportunities for TRULANCE.

Dolcanatide is our development stage compound that has demonstrated proof-of-concept in treating patients with ulcerative colitis. We are currently exploring potential business development opportunities to further advance dolcanatide development in ulcerative colitis. In addition, we have shown proof-of-concept with dolcanatide in treating patients with opioid-induced constipation (OIC), demonstrating the utility of our uroguanylin based platform in OIC. We are considering OIC as a potential lifecycle growth opportunity for TRULANCE.

TRULANCE (plecanatide)

With the exception of a single amino acid substitution for greater binding affinity, TRULANCE is structurally identical to human uroguanylin and is the only treatment thought to replicate the pH-sensitive activity of uroguanylin. Uroguanylin activates GC-C receptors in a pH-sensitive manner primarily in the small intestine, stimulating fluid secretion and maintaining stool consistency necessary for regular bowel function.

In January 2017, the FDA approved TRULANCE 3 mg tablets for the once-daily treatment of adults with CIC. We began commercializing TRULANCE in the U.S. in March 2017. In January 2018, the FDA approved TRULANCE for the treatment of adults with IBS-C. The efficacy and safety of TRULANCE for the treatment of CIC and IBS-C was established in four 12-week, double-blind, placebo-controlled, randomized, multicenter clinical studies involving over 3,100 patients. TRULANCE demonstrated improvement in the abdominal pain, constipation, stool consistency and straining with bowel movements associated with IBS-C, as well as in the constipation, stool consistency and straining with bowel movements associated with CIC. These patient-reported symptoms returned within one week following discontinuation of TRULANCE. The most common adverse event in both CIC and IBS-C studies was diarrhea (≤5.0% vs. 1.0% placebo). TRULANCE is the only prescription medication for adults with CIC and IBS-C that can be taken once-daily, with or without food, at any time of the day. TRULANCE is packaged in a unique, 30-day calendar blister pack.

Ongoing Post Marketing Commitments

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), clinical studies are underway assessing the efficacy and safety of TRULANCE in pediatric patients with CIC and in late planning stages for assessment of the efficacy and safety of TRULANCE in pediatric patients with IBS-C. In addition, development and validation of an anti-drug antibody assay is underway to assess patient clinical trial samples for the potential presence of anti-plecanatide antibodies. As agreed with the FDA following Trulance approval in the CIC indication, we continue with the execution of a milk-only lactation study and the assessment of GC-C receptor density in infants and children (age 0-6 years).

CIC / IBS-C

CIC and IBS-C are chronic, functional GI disorders that afflict millions of people worldwide. An estimated 33 million adults suffer from CIC and 12 million adults suffer from IBS-C in the U.S. alone.

People with CIC have persistent symptoms of difficult-to-pass and infrequent bowel movements. In addition to physical symptoms including abdominal bloating and discomfort, CIC can adversely affect an individual's quality of life, including increasing stress levels and anxiety. Many patients attempt to manage CIC symptoms with improved diet, fiber, and over-the-counter laxatives; however, these options can be ineffective or may not provide long-term relief. For those patients with persistent symptoms, prescription therapy is recommended. Many patients taking prescription medications fail to respond to therapy, or suffer from treatment-related adverse events, such as nausea and diarrhea.

Irritable bowel syndrome (IBS) is characterized by recurrent abdominal pain associated with 2 or more of the following criteria: related to defecation, associated with a change in the frequency of stool, or associated with a change in the form (appearance) of the stool. IBS can be subtyped by the predominant stool form as measured by the Bristol Stool Form Scale (BSFS): constipation (IBS-C), diarrhea (IBS-D), or mixed (IBS-M). Those within the IBS-C subtype experience Bristol types 1 or 2 (hard or lumpy) stools more than 25 percent of the time they have an abnormal bowel movement, and Bristol types 6 or 7 (loose or watery) stools less than 25 percent of the time they have an abnormal bowel movement. Some of the IBS treatment approaches recognized by the American College of Gastroenterology (ACG), including specialized diets, fiber, and psychological interventions, may not always effectively address abdominal pain and discomfort experienced by these patients. While there are prescription drug options, not all patients find complete relief, and many struggle with adverse events.

Dolcanatide (SP-333)

Dolcanatide is designed to be an analog of uroguanylin with enhanced resistance to standard digestive breakdown by proteases in the intestine. We have demonstrated the potential anti-inflammatory role of uroguanylin and uroguanylin analogs in a number of preclinical colitis models. In these earlier animal studies, oral treatment with dolcanatide was shown to ameliorate DSS- and TNBS-induced acute colitis in murine models and ameliorate spontaneous colitis in T-cell receptor alpha knockout mice.

In January 2016, we announced positive proof-of-concept with dolcanatide in a phase 1b trial evaluating 28 patients with mild-to-moderate ulcerative colitis. We are exploring business development opportunities to further advance dolcanatide development in ulcerative colitis.

Recent Developments

- Total TRULANCE prescription volume in the fourth quarter of 2017 included 42,486 TRULANCE 30-count packs, per IQVIA. For the full year 2017, more than 88,360 TRULANCE 30-count packs were dispensed, increasing 70% on average month-over-month since launch on March 20, 2017, per IQVIA.
- On January 25, 2018, we announced that the U.S. Food and Drug Administration (FDA) approved TRULANCE® (plecanatide) 3 mg tablet for the once-daily treatment of irritable bowel syndrome with constipation (IBS-C) in adults. This is the second indication for TRULANCE, which was first approved for the treatment of adults with chronic idiopathic constipation (CIC) in January 2017.
- Since launch, TRULANCE commercial coverage has more than doubled to over 85% of all lives covered as of the end of February 2018. In addition, TRULANCE coverage on Medicare Part D and Managed Medicaid plans has grown to over 54% of lives covered.
- In February 2018, we completed our field force integration plan by successfully transitioning our former contract sales representatives over to Synergy to coincide with our IBS-C approval and launch.
- On February 27, 2018 we entered into a definitive licensing agreement with Cipher Pharmaceuticals under which we granted Cipher the exclusive right to develop, market, distribute and sell TRULANCE in Canada. Under the terms of the licensing agreement, Synergy received an upfront payment of $5.0 million and is eligible for an additional milestone payment, as well as royalties from product sales in Canada. We are continuing to evaluate other potential ex-US business development opportunities for TRULANCE.
- On December 19, 2017, we announced that Troy Hamilton, Pharm.D., previously Executive Vice President, Chief Commercial Officer, was appointed Chief Executive Officer, effective immediately. Gary S. Jacob, Ph.D., previously President, CEO and Chairman, assumed the position of Executive Chairman of the Board of Directors.
- On November 13, 2017, we announced the pricing of an underwritten offering of 21,705,426 shares of common stock together with accompanying warrants to purchase an aggregate of 21,705,426 shares of common stock at a combined price to the public of $2.58 per share and accompanying warrant. The aggregate offering price, before deducting underwriting discounts and commissions and other offering expenses, was approximately $56 million. Each warrant sold in the offering is cash exercisable for one share of common stock at an exercise price of $2.86 per whole share, and is exercisable from issuance until November 15, 2019. The shares of common stock and warrants sold in the offering were immediately separable and were issued separately.

RESULTS OF OPERATIONS

YEARS ENDED DECEMBER 31, 2017 AND DECEMBER 31, 2016

We had net sales of $16.8 million during the year ended December 31, 2017, and no net sales during the year ended December 31, 2016.

Cost of goods sold (“COGS”) for the year ended December 31, 2017 was $8.8 million, which includes the direct cost of manufacturing and packaging drug product and related technical operations overhead costs which are generally more fixed in nature. Technical Operations is responsible for planning, coordinating, and executing on our inventory production plan and ensuring that product quality satisfies FDA requirements. Costs incurred by our technical operations organization are recorded as expense in the period in which they are incurred.

Research and development expenses for the year ended December 31, 2017 decreased approximately $38.8 million or 44.5%, to approximately $48.3 million from approximately $87.1 million for the year ended December 31, 2016. This decrease in research and development expenses was due primarily to reduced clinical trial spend associated with TRULANCE which was approved in early 2017 and the cost of validation batches and pre-commercial inventory costs which were classified as research and development in 2016.

The following table sets forth our research and development expenses directly related to our product candidates, as well as indirect costs, for the years ended December 31, 2017 and 2016. Direct expenses include external costs associated with chemistry, manufacturing and controls including costs of drug substance and product formulation, as well as preclinical studies and clinical trial costs.

Drug candidates	($ in thousands) Year Ended December 31, 2017	($ in thousands) Year Ended December 31, 2016
TRULANCE (plecanatide)	$ 37,349	$ 73,472
Dolcanatide	815	1,536
Total direct costs	38,164	75,008
Total indirect costs	10,182	12,048
Total Research and Development	$ 48,346	$ 87,056

Indirect research and development costs are comprised of in-house staff compensation, facilities, depreciation, stock-based compensation and research and development support services which are not directly allocated to specific drug candidates. Indirect costs were approximately $10.2 million in the year ended December 31, 2017 as compared to approximately $12.0 million in the year ended December 31, 2016 representing a decrease of approximately $1.8 million which was primarily due to lower consulting services and stock-based compensation expenses.

Selling, general and administrative expenses increased approximately $123.7 million or 212.5%, to $181.9 million for the year ended December 31, 2017 from approximately $58.2 million for the year ended December 31, 2016. These increased expenses primarily reflect the cost of building a commercial organization to launch TRULANCE during the first quarter of 2017. These costs included approximately an $88.1 million increase in marketing and sales expenses related to commercial activities, a $14.0 million increase in compensation and benefit costs, a $10.8 million increase in stock-based compensation expense, and a $3.9 million increase in information technology costs. The increase in stock compensation expense was primarily driven by a $6.6 million charge related to the immediate vesting resulting from the modification of previously granted change of control options, and a $2.7 million charge related to stock option modifications for terminated employees during the year ended December 31, 2017. There are no remaining change of control options outstanding as of December 31, 2017.

As of December 31, 2017 we had 118 full-time employees compared to 92 full-time employees at December 31, 2016.

Net loss for the year ended December 31, 2017 was $224.3 million compared to a net loss of $198.6 million for the year ended December 31, 2016. This increase in our net loss of $25.7 million or 12.9% was primarily the result of the operating items discussed above offset by a decrease in debt conversion expense of approximately $39.0 million and a decrease of approximately $8.2 million in interest expense and amortization of deferred debt costs, both related primarily to the conversion of $25.6 million of our convertible debt in the year ended December 31, 2016.

YEARS ENDED DECEMBER 31, 2016 AND DECEMBER 31, 2015

We had no revenues during the year ended December 31, 2016 and 2015 because we did not have any commercial products for those periods.

Research and development expenses for the year ended December 31, 2016 increased approximately $9.1 million or 11.7%, to approximately $87.1 million from approximately $78.0 million for the year ended December 31, 2015. This increase in research and development expenses was due primarily to greater spending on IBS-C studies, expenses related to filing our CIC NDA in January 2016, additional compensation, consulting services, and TRULANCE API and drug product manufacturing costs for validation batches prepared in anticipation of our commercial launch of TRULANCE for CIC during the first quarter of 2017. The increase in compensation reflects the growth of our Medical Affairs activity and the cost of building a technical operations function fully prepared for the anticipated commercial launch of TRULANCE during first quarter 2017.

The following table sets forth our research and development expenses directly related to our product candidates, as well as indirect costs, for the years ended December 31, 2016 and 2015. Direct expenses include external costs associated with chemistry, manufacturing and controls including costs of drug substance and product formulation, as well as preclinical studies and clinical trial costs.

Drug candidates	($ in thousands) Year Ended December 31, 2016	($ in thousands) Year Ended December 31, 2015
TRULANCE (plecanatide)	$ 73,472	$ 65,170
Dolcanatide	1,536	5,026
Total direct costs	75,008	70,196
Total indirect costs	12,048	7,832
Total Research and Development	$ 87,056	$ 78,028

Indirect research and development costs are comprised of in-house staff compensation, facilities, depreciation, stock-based compensation and research and development support services which are not directly allocated to specific drug candidates. Indirect costs were approximately $12.0 million in the year ended December 31, 2016, as compared to approximately $7.8 million during the year ended December 31, 2015 representing an increase of approximately $4.2 million which was primarily due to an increase in employee compensation of $2.8 million and higher stock-based compensation of $1.0 million. The increase in compensation reflects the cost of building a Technical Operations function for the anticipated commercial launch of TRULANCE during first quarter 2017.

Selling, general and administrative expenses increased approximately $36.4 million or 167.0%, to $58.2 million for the year ended December 31, 2016 from approximately $21.8 million for the year ended December 31, 2015. These increased expenses primarily reflect the cost of building a commercial organization prepared to launch TRULANCE during first quarter 2017. These costs included approximately a $22.5 million increase in marketing and sales expenses related to commercial preparedness and planning, a $1.7 million increase in consulting, a $5.7 million increase in compensation and benefit costs, and a $1.8 million increase in stock-based compensation expense.

As of December 31, 2016 we had 92 full-time employees compared to 41 full-time employees at December 31, 2015.

Net loss for the year ended December 31, 2016 was $198.6 million compared to a net loss of $117.5 million for the year ended December 31, 2015. In addition to the operating items discussed above, this increase in our net loss of $81.1 million or 69% was primarily a result of debt conversion expense of approximately $40.2 million resulting from our March and November 2016 convertible notes exchanges, partially offset by a decrease of approximately $3.9 million in interest expense and amortization of deferred debt costs, both related to our convertible notes.

LIQUIDITY AND CAPITAL RESOURCES

As of December 31, 2017, we had approximately $137.0 million in cash and cash equivalents, compared to approximately $82.4 million as of December 31, 2016. Net cash used in operating activities was $212.9 million for the year ended December 31, 2017 as compared to $129.8 million for the year ended December 31, 2016 and $101.0 million for the year ended December 31, 2015. Net cash provided by financing activities was $267.7 million for the year ended December 31, 2017 as compared to $100.7 million for the year ended December 31, 2016 and $16.4 million for the year ended December 31, 2015. As of December 31, 2017 we had working capital of $127.0 million, as compared to working capital of $59.5 million on December 31, 2016.

From January 1, 2015 through December 31, 2015, we sold 3,435,998 shares of common stock, pursuant to the ATM Agreement with Cantor, yielding gross proceeds of $14.7 million, at an average selling price of $4.27 per share. Selling agent fees related to above financings from January 1, 2015 through December 31, 2015 were $0.4 million.

From January 1, 2015 through December 31, 2015, $41.0 million aggregate principal amount of the Notes was converted into approximately 13.2 million shares of our common stock.

On June 8, 2015, we amended its Articles of Incorporation and increased the number of shares of its common stock authorized for issuance from 200,000,000 to 350,000,000 shares.

On July 2, 2015, we filed a “shelf” registration statement on Form S-3 to offer and sell, from time to time in one or more offerings, any combination of common stock, preferred stock, debt securities, warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units comprised of one or more of the other securities, having an aggregate initial offering price not exceeding $250,000,000. The registration statement was declared effective by the SEC on July 15, 2015. This shelf registration does not currently encompass a Controlled Equity Sales (ATM) program.

From January 1, 2015 through December 31, 2015 warrants to purchase 189,412 shares of common stock were exercised, yielding proceeds to us of $1.0 million. In addition employee stock options to purchase 269,720 shares of common stock were exercised yielding proceeds of $1.1 million.

On March 18, 2016, we announced the closing of separate, privately-negotiated exchanges with eligible holders of approximately 50% of our outstanding 7.50% Convertible Senior Notes (“Notes”) due 2019. At the closing, and in satisfaction of the consideration for $79.8 million in aggregate principal amount of the Notes, we issued 35.3 million shares of our common stock (the “Shares”). We also issued approximately 872,000 Shares in payment of accrued and unpaid interest on Notes accepted in the Exchanges from the applicable last interest payment date to, but not including, March 28, 2016. A total of 25.6 million shares carried a conversion price of $3.11 pursuant to the existing terms of the Notes.

On May 5, 2016 we announced that we had entered into definitive agreements with certain institutional investors to sell 29,948,334 shares of common stock at a price of $3.00 per share. The shares were offered and sold directly to institutional investors by us in a registered direct offering conducted without an underwriter or placement agent. The gross proceeds from the offering were approximately $89.8 million. The offering closed on May 6, 2016.

In November 2016 we exchanged $55.7 million in aggregate principal amount of the Notes, representing approximately 70% of the outstanding aggregate principal amount of Notes, for 20.5 million shares of our common stock, with a total of 17.9 million shares representing the conversion price of $3.11 pursuant to the existing terms of the Notes. The amortization of deferred debt costs was accelerated consistent with the 70% reduction of aggregate principal amount this transaction represented, and resulted in additional interest expense of approximately $2 million. We recognized debt conversion expense of $40.2 million representing 12.2 million shares for the year ended December 31, 2016.

From January 1, 2016 through December 31, 2016 warrants to purchase 2,430,656 shares of common stock were exercised, yielding proceeds to us of $11.3 million.

On January 31, 2017, we entered into an underwriting agreement with Cantor Fitzgerald & Co., as representative of the several underwriters, to issue and sell 20,325,204 shares of our common stock in an underwritten public offering pursuant to a Registration Statement on Form S-3 and a related prospectus and prospectus supplement, in each case filed with the Securities and Exchange Commission (the “Offering”). The public offering price was $6.15 per share of Common Stock. The Offering closed on February 6, 2017, yielding net proceeds of approximately $121.6 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

On February 28, 2017, we received consents from certain holders of our Notes to enter into a Supplemental Indenture which eliminates certain restrictive covenants from the Indenture related to the Notes. The restrictive covenants eliminated from the Indenture are Limitation on Indebtedness, Future Financing Rights for Certain Investors and Licensing Limitations. On February 28, 2017, we entered into the Supplemental Indenture with Wells Fargo, N.A., as trustee. We paid an aggregate of approximately $1.6 million to such holders for the consent.

In March 2017, we exchanged approximately $4.9 million aggregate principal amount of the Notes for approximately 1.8 million shares of its common stock, with approximately 1.6 million shares representing the conversion price of $3.11 pursuant to the existing terms of the Notes. We recognized a debt conversion expense of approximately $1.2 million representing 0.2 million shares during the year ended December 31, 2017. As of December 31, 2017, $18.6 million of the Notes remain outstanding.

On September 1, 2017, we entered into a senior secured term loan of up to $300 million with CRG Servicing LLC, as administrative and collateral agent, and the lenders and guarantors party thereto (the "Term Loan"). The Term Loan is available for working capital and general corporate purposes. We borrowed $100 million at time of closing. In February 2018 we amended the Term Loan agreement. The amended Term Loan provides for future borrowings of $25 million, $25 million and $50 million on or before June 30, 2018, September 30, 2018 and December 31, 2018, respectively. Additionally, the total amount of the commitment was reduced from $300 million to $200 million (excluding PIK loans) and the Minimum Market

Capitalization covenant of $300 million was revised to be 200% of the outstanding principal amount of the Term Loan (excluding PIK loans).

Additionally, the total amount of the commitment was reduced from $300 million to $200 million (excluding PIK loans) and the Minimum Market Capitalization covenant of $300 million was revised to be 200% of the outstanding principal amount of the Term Loan (excluding PIK loans).

The Term Loan has a maturity date of June 30, 2025, unless prepaid earlier. The Term Loan bears interest at a rate equal to 9.5% per annum, with quarterly, interest-only payments until June 30, 2022, subject to extension through the maturity date upon our satisfaction of certain conditions. At our option, until June 30, 2019, a portion of the interest payments may be paid in kind, and thereby added to the principal. Following, the interest-only period, the Term Loans will amortize in equal quarterly installments unless entirely payable at maturity.

On November 13, 2017, we entered into an underwriting agreement with Jefferies LLC, as representative of the several underwriters, to issue and sell 21,705,426 shares of our common stock together with accompanying warrants ("Warrants") to purchase an aggregate of 21,705,426 shares of Common Stock in an underwritten offering pursuant to a Registration Statement on Form S-3ASR (File No. 333-221501) and a related prospectus and prospectus supplement, in each case filed with the Securities and Exchange Commission (the "Offering"). The offering price was $2.58 per share of Common Stock and accompanying Warrant. The net proceeds from the Offering were approximately $52.2 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

Our consolidated financial statements as of December 31, 2017 have been prepared under the assumption that we will continue as a going concern for the next twelve months. The Company has incurred recurring losses from operations and expects to continue to have losses in the future. In addition, the Company's debt agreement is subject to covenants that could restrict the availability of additional loans and accelerate the repayment of that debt if breached. These factors individually and collectively raise substantial doubt about the Company's ability to continue as a going concern. Our independent registered public accounting firm has issued a report that includes an explanatory paragraph referring to such conditions and expressing substantial doubt in our ability to continue as a going concern.

Our ability to continue as a going concern is dependent upon our plans of attaining further operating efficiencies, reducing expenditures, and generating significant revenue and if deemed necessary obtaining additional equity or debt financing, which may not be available on acceptable terms or at all. To the extent that Synergy may need to raise additional funds by issuing equity securities, Synergy's stockholders may experience significant dilution. Any debt financing, if available, may involve restrictive covenants that impact Synergy's ability to conduct business. If Synergy is unable to raise additional capital when required or on acceptable terms, Synergy may have to (i) significantly scale back our commercialization efforts ; (ii) seek commercial partners for our products on terms that are less favorable than might otherwise be available; or (iii) relinquish or otherwise dispose of rights, on unfavorable terms, to technologies, product candidates or products that Synergy would otherwise seek to develop or commercialize itself. Our consolidated financial statements as of December 31, 2017 did not include any adjustments that might result from the outcome of this uncertainty.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

Purchase obligations

In the normal course of business, we issue purchase orders to vendors for services and/or inventory. The purchase orders require performance by the vendors, including the delivery of the services and/or goods prior to a specified cancellation date and compliance with product specifications, quality standards and other requirements. In the event of the supplier's failure to meet the agreed upon terms and conditions, we may cancel the order.

The following table is a summary of contractual obligations for the periods indicated that existed as of December 31, 2017, and is based on information appearing in the notes to Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K.

($ in thousands)	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 years
Long term debt obligations [1]	$ 197,911	$ 11,200	$ 49,181	$ 71,216	$ 66,314
Operating leases	9,845	2,080	5,894	1,871	—
Purchase obligations—principally employment and consulting services[2]	7,212	3,606	3,606	—	—
Purchase obligations—major vendors[3]	21,320	21,320	—	—	—
Total obligations	$ 236,288	$ 38,206	$ 58,681	$ 73,087	$ 66,314

(1) Represents Senior Convertible Notes and Term Loan, including interest. See Note 4 to our Consolidated Financial Statements.

(2) Represents salary, bonus, and benefits for employment and consulting agreements with remaining terms greater than one year.

(3) Represents amounts that will become due upon future delivery of inventory under open purchase orders and the remaining term of our contract sales force agreement. Generally these purchase orders represents commitments to suppliers with cancellation provisions that allow early termination with notice, penalties and payment of certain non-cancelable vendor commitments.

OFF-BALANCE SHEET ARRANGEMENTS

We had no off-balance sheet arrangements as of December 31, 2017.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

Financial Reporting Release No. 60 requires all companies to include a discussion of critical accounting policies or methods used in the preparation of financial statements. Our accounting policies are described in Item 8. Financial Statements —Note 2 *Basis of Presentation and Accounting Policies*. The preparation of financial statements in conformity with accounting principles generally accepted in the United States ("US GAAP") and the rules and regulations of the U.S. Securities & Exchange Commission ("SEC") requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates. We believe that the following discussion represents our critical accounting policies.

Cash and cash equivalents

All highly liquid investments with maturities of three months or less at the date of purchase are classified as cash equivalents. As of December 31, 2017 and December 31, 2016, the amounts of cash and cash equivalents were approximately $137.0 million and $82.4 million, respectively, and consisted of checking accounts and short-term money market funds with U.S. commercial banks. At any point in time, our balance of cash and cash equivalents may exceed federally insured limits.

Accounts Receivable

We make judgments as to our ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed. Our receivables primarily related to amounts due from 3rd party customers for the sale of TRULANCE. In 2017, our three major customers accounted for an aggregate of 97% of our gross revenue. Together, our three major customers, Amerisource Bergen, McKesson Corporation, and Cardinal Health accounted for 39%, 31%, and 25%, respectively, of our accounts receivable as of December 31, 2017.
We believe that credit risks associated with these customers are not significant. To date, we have not had any write-offs of bad debt, and we did not record an allowance for doubtful accounts as of December 31, 2017.

Inventories

Inventories consist of finished goods, work in process and raw materials and are stated at the lower of cost or net realizable value with cost determined under the first-in, first-out basis. Inventory valuation reserves are established based on a number of factors/situations including, but not limited to, raw materials, work in process or finished goods not meeting product specifications, product obsolescence, or application of the lower of cost (first-in, first-out method) or net realizable value concepts.

We capitalize inventories manufactured in preparation for initiating sales of a product candidate when the related product candidate is considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales of the inventories. In determining whether or not to capitalize such inventories, we evaluate, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales. In addition, we evaluate risks associated with manufacturing the product candidate and the remaining shelf life of the inventories.

Costs associated with developmental products prior to satisfying the inventory capitalization criteria are charged to research and development expense as incurred. There is a risk inherent in these judgments and any changes in these judgments may have a material impact on our financial results in future periods.

In July 2015, the FASB issued an accounting standard update (ASU No. 2015-11) intended to simplify the measurement of inventory by requiring inventory to be measured at the lower of cost or net realizable value. Net realizable value is defined as estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal, and transportation, etc. We adopted this standard as of January 1, 2017, which had no impact on the consolidated financial statements.

Revenue recognition

We recognize revenue from sales of TRULANCE when the earnings process is complete, which under Accounting Standards Codification ASC 605, Revenue Recognition is when revenue is realized or realizable and earned, there is persuasive evidence a revenue arrangement exists, delivery of goods or services has occurred, the sales price is fixed or determinable, and collectability is reasonably assured. Product sales are recorded net of all sales related deductions, including but not limited to: customer loyalty programs, trade discounts, fee for service agreements, sales returns and allowances, commercial and government rebates, and chargebacks. We estimate these sales deductions based on contractual terms, historical payment experience, third party data, estimated utilization or redemption rates, government regulations, and customer inventory levels. Accruals for trade discounts, fee for service agreements and chargebacks are reflected as a direct reduction of accounts receivable and accruals for commercial and government rebates and customer loyalty programs are reflected as accrued expenses.

Cost of Goods Sold

Cost of goods sold (“COGS”) includes (i) direct cost of manufacturing and packaging drug product and (ii) technical operations overhead costs which are generally more fixed in nature, including salaries, benefits, consulting, stability testing and other services. Technical operations are responsible for planning, coordinating, and executing our inventory production plan and ensuring that product quality satisfies FDA requirements. Costs incurred by the technical operations organization are recorded as expense in the period in which they are incurred. Certain direct costs associated with pre-commercial inventory, other than packaging, were expensed prior to receiving FDA approval. (See Inventories in Footnote 2 "Basis of Presentation, Accounting Policies and Going Concern").

Derivative Instruments

Our derivative liabilities are related to warrants issued in connection with financing transactions and are therefore not designated as hedging instruments. All derivatives are recorded on our balance sheet at fair value in accordance with current accounting guidelines for such complex financial instruments. Changes in fair value are recorded in our statement of operations.

Fair Value of Financial Instruments

In accordance with Accounting Standards Codification ("ASC") Subtopic 820-10, we measure certain assets and liabilities at fair value on a recurring basis using the three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. The three tiers include:

- Level 1, defined as observable inputs such as quoted prices for identical assets in active markets;
- Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable; and
- Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring management to develop its own assumptions based on best estimates of what market participants would use in pricing an asset or liability at the reporting date.

Financial instruments consist of cash and cash equivalents, marketable securities, accounts receivable, accounts payable and derivative instruments. These financial instruments are stated at their respective historical carrying amounts, which approximate fair value due to their short term nature, except for derivative instruments which are marked to market at the end of each reporting period.

The value of Senior Convertible Notes and Long term debt are stated at their carrying value at December 31, 2017 and 2016. Carrying value approximates fair value because we believe we could obtain similar borrowings at December 31, 2017 at comparable interest rates, therefore, the carrying value approximates fair value.

Property, equipment and depreciation

Expenditures for additions, renewals and improvements are capitalized at cost. Depreciation is computed on a straight-line method based on the estimated useful lives of the related assets. The estimated useful lives of the major classes of depreciable assets are 2 to 5 years for equipment and furniture and fixtures. Leasehold improvements are depreciated over the shorter of the remaining useful life or remaining lease term of the lease. Expenditures for repairs and maintenance are charged to operations as incurred. We periodically evaluates whether current events or circumstances indicate that the carrying value of our depreciable assets may not be recoverable.

Income Taxes

Income taxes have been determined using the asset and liability approach of accounting for income taxes. Under this approach, deferred taxes represent the future tax consequences expected to occur when the reported amounts of assets and liabilities are recovered or paid. Deferred taxes result from differences between the financial statement and tax bases of our assets and liabilities and are adjusted for changes in tax rates and tax laws when changes are enacted. Valuation allowances are recorded to reduce deferred tax assets when it is more likely than not that a tax benefit will not be realized. The assessment of whether or not a valuation allowance is required often requires significant judgment.

Contingencies

In the normal course of business, we are subject to loss contingencies, such as legal proceedings and claims arising out of its business, that cover a wide range of matters, including, among others, government investigations, shareholder lawsuits, product and environmental liability, and tax matters. In accordance with FASB ASC Topic 450, *Accounting for Contingencies* ("ASC Topic 450"), we record accruals for such loss contingencies when it is probable that a liability will be incurred and the amount of loss can be reasonably estimated. We, in accordance with this guidance, do not recognize gain contingencies until realized. For a discussion of contingencies, see Note 7, *Commitments and Contingencies* below.

Research and Development

Research and development costs include expenditures in connection with an in-house research and development laboratory, salaries and staff costs, application and filing for regulatory approval of proposed products, regulatory and scientific consulting fees, as well as contract research, patient costs, manufacturing process development costs, drug formulation and tableting, data collection, monitoring, and clinical trial insurance.

We recorded inventory, manufactured for sale of a product candidate, when the product candidate was considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales. In determining whether or not to record such inventories, we evaluated, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales. Prior to October 1, 2016, all costs associated with batches of inventory, manufactured for sale, were charged to research and development as incurred. Beginning in the fourth quarter of 2016, we began capitalizing inventory costs for TRULANCE in preparation for its planned launch in the U.S. We will record inventory, manufactured for sale of a product candidate, when the product candidate is considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales. In determining whether or not to record such inventories, we evaluate, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales.

In accordance with FASB ASC Topic 730-10-55, *Research and Development*, we recorded prepaid research and development costs of approximately $72,000 and $33,000 as of December 31, 2017 and December 31, 2016, respectively, of pre-payments for production of drug substance, analytical testing services and clinical trial monitoring for our drug candidates. In accordance with this guidance, we expense these costs when drug substance is delivered and/or services are performed.

Share-Based Compensation

We rely heavily on incentive compensation in the form of stock options to recruit, retain and motivate directors, executive officers, employees and consultants. Incentive compensation in the form of stock options and restricted stock units is designed to provide long-term incentives, develop and maintain an ownership stake and conserve cash during our development stage.

ASC Topic 718 *"Compensation—Stock Compensation"* requires companies to measure the cost of employee services received in exchange for the award of equity instruments based on the estimated fair value of the award at the date of grant. The expense is to be recognized over the period during which an employee is required to provide services in exchange for the award.

Share-based compensation is recognized as an expense in the financial statements based on the grant date fair value. Upon adoption of ASC Topic 718 *"Compensation—Stock Compensation"*, we selected the Black-Scholes option pricing model as the most appropriate model for determining the estimated fair value for stock-based awards. Use of a valuation model requires management to make certain assumptions with respect to selected model inputs. Expected volatility is based on the historical volatility of our stock. The risk-free interest rate is based on observed interest rate appropriate for the expected term of our employee stock options. Forfeiture rates and option term are estimated based on our historical experience plus management's judgment, at the time of grant.

Warrants

We have issued common stock warrants in connection with the execution of certain equity financings. The fair value of certain warrants, deemed to be derivative instruments, is recorded as a derivative liability under the provisions of FASB ASC 815 *Derivatives and Hedging ("ASC 815")* upon issuance. Subsequently the liability is adjusted to fair value as of each reporting period and the changes in fair value of derivative liabilities are recorded in the consolidated statement of operations under the caption "Change in fair value of derivative liabilities."

The fair value of warrants deemed to be derivative instruments is determined using the Black-Scholes or Monte Carlo simulation models using varying assumptions regarding volatility of our common share price, remaining life of the warrant, and risk-free interest rates at each period end. We thus use model-derived valuations where significant value drivers are unobservable to third parties to determine the fair value and accordingly classify such warrants in Level 3 per ASC 820. At December 31, 2017 and 2016 the fair value of such warrants was approximately $17,582,000 and $216,000, respectively, which we classified as a long term derivative liability on our balance sheets.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

Our cash and cash equivalents primarily consist of securities issued by the U.S. Treasury, deposits, and money market mutual funds. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and fiduciary control of cash and investments. We also seek to maximize income from our investments without assuming significant risk.

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of interest rates, particularly because our investments are in short-term money marketable funds and US treasury and U.S. government sponsored entity securities. Due to the short-term maturities of our investment portfolio and the relatively low risk profile of our investments, we do not believe a sudden change in interest rates would have a material effect on the fair market value of our portfolio, nor our operating results or cash flows.

Credit Risk

Our exposure to market risk on the fair values of certain assets is related to credit risk associated with bank checking accounts, securities held in money market mutual funds and accounts receivable. As of December 31, 2017, we held $137.0 million in checking and U.S. Treasury based mutual funds. Our cash and cash equivalents balances are in excess of the Federally insured limit. We believe our cash and cash equivalents do not contain excessive risk, however we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. We limit our credit risk with respect to accounts receivable by performing credit evaluations when deemed necessary. We do not require collateral to secure amounts owed to us by our customers.

In September 2017, we entered into a senior secured term loan of up to $300.0 million. The Term Loan has a fixed annual interest rate of 9.50% and we, therefore, do not have economic interest rate exposure on the Term Loan. However, the Term Loan requires the Company to comply with a minimum market capitalization covenant, and our shares are subject to market risk.

Foreign Currency Risk

We have no operations outside the U.S. and do not hold any foreign currency denominated financial instruments.

Effects of Inflation

We do not believe that inflation and changing prices during the years ended December 31, 2017, 2016 and 2015 had a significant impact on our results of operations.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The full text of our audited consolidated financial statements as of December 31, 2017 and 2016, and for the years ended December 31, 2017, 2016 and 2015 begins on page F-1 of this Annual Report on Form 10-K.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

N/A

ITEM 9A. CONTROLS AND PROCEDURES

a) Disclosure Controls and Procedures

Our chief executive officer and principal financial officer evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Securities Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Securities Exchange Act is accumulated and communicated to the company's management, including our principal executive and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Based on that evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures are effective, at the reasonable assurance level, in ensuring that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

b) Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for our company. Internal control over financial reporting is defined in Rule 13a-15(f) and 15d-15(f) promulgated under the Exchange Act, as a process designed by, or under the supervision of, a company's principal executive and principal financial officer and effected by the our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

(1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company;

(2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made in accordance with authorizations of management and directors of the company; and

(3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible enhancements to controls and procedures.

We conducted an evaluation of the effectiveness of internal control over financial reporting based on the framework in Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this evaluation, our principal executive officer and principal financial officer conclude that, at December 31, 2017, our internal control over financial reporting was effective.

The effectiveness of our internal control over financial reporting at December 31, 2017 has been audited by BDO USA, LLP, an independent registered public accounting firm, as stated in their report which appears herein.

CHANGES IN INTERNAL CONTROL OVER FINANCIAL REPORTING

As required by Rule 13a-15(d) of the Exchange Act, our management, including our principal executive officer and our principal financial officer conducted an evaluation of the internal control over financial reporting to determine whether any changes occurred during the quarter ended December 31, 2017 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting. Based on that evaluation, our principal executive officer and principal financial officer concluded there were no such changes, except for the changes to controls to remediate material weaknesses previously identified for (1) the calculation of stock compensation expense for 'marked to market' consultant options and (2) account reconciliation controls related to accruals. (Also see Part I, Item 4 of our 2017 Form 10-Q filed on August 9, 2017), during the quarter ended December 31, 2017.

Remediation Plan Completed

We implemented a software system to house all issued stock options and to calculate stock based compensation expense, including 'marked to market' consultant options, during quarter ending September 30, 2017. This system has been operating effectively from the quarter ended September 30, 2017 through year end.

In addition, during the quarter ended June 30, 2017, we implemented an automated reconciliation tool to ensure the completeness of account reconciliations. This tool has been operating effectively from the quarter ended June 30, 2017 through year end.

Report of Independent Registered Public Accounting Firm

Stockholders and Board of Directors
Synergy Pharmaceuticals Inc.
New York, New York

Opinion on Internal Control over Financial Reporting

We have audited Synergy Pharmaceuticals Inc.'s (the "Company's") internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "COSO criteria"). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of the Company as of December 31, 2017 and 2016, the related consolidated statements of operations, changes in stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2017, and the related notes and our report dated March 1, 2018 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying "Item 9A, Management's Report on Internal Control over Financial Reporting". Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of internal control over financial reporting in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ BDO USA, LLP

New York, New York

March 1, 2018

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

We have adopted a formal Code of Business Conduct and Ethics applicable to all Board members, executive officers and employees. A copy of that code is available on our corporate website at http://www.synergypharma.com. A copy of our Code of Business Conduct and Ethics will also be provided free of charge upon request to: Secretary, Synergy Pharmaceuticals Inc. 420 Lexington Avenue, Suite 2012, New York, NY 10170. The content on our website is not incorporated by reference into this Annual Report on Form 10-K.

Information required by this item is incorporated by reference from our proxy statement for our 2018 Annual Meeting of Stockholders.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated by reference from our proxy statement for our 2018 Annual Meeting of Stockholders.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item is incorporated by reference from our proxy statement for our 2018 Annual Meeting of Stockholders.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is incorporated by reference from our proxy statement for our 2018 Annual Meeting of Stockholders.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated by reference from our proxy statement for our 2018 Annual Meeting of Stockholders.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) List of Documents Filed as a Part of This Report:

(b) Index to Financial Statement Schedules:

All schedules have been omitted because the required information is included in the consolidated financial statements or the notes thereto, or is not applicable or required.

(c) Index to Exhibits

The Exhibits listed below are identified by numbers corresponding to the Exhibit Table of Item 601 of Regulation S-K. The Exhibits designated by an asterisk (*) are management contracts or compensatory plans or arrangements required to be filed pursuant to Item 15.

Exhibit No.	Description
3.1	Second Amended and Restated Certificate of Incorporation of Synergy Pharmaceuticals Inc. (incorporated by reference to Exhibit 3.1 to Form 8-K filed June 19, 2015).
3.2	Amendment to the Second Amended and Restated Certificate of Incorporation of Synergy Pharmaceuticals Inc. (incorporated by reference to Exhibit 3.1 to Form 8-K filed January 17, 2013).
3.3	Second Amendment to the Second Amended and Restated Certificate of Incorporation of Synergy Pharmaceuticals Inc. (incorporated by reference to Exhibit 3.1 to Form 10-K filed March 15, 2012).
3.4	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.4 to Form 10-K filed March 1, 2017).
4.1	2008 Equity Compensation Incentive Plan (incorporated by reference to Exhibit 4.1 to Form 8-K filed July 18, 2008). *
4.2	2009 Directors Stock Option Plan (incorporated by reference to Exhibit 4.2 to Form 10-K filed March 15, 2010). *
4.3	Form of Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.6 to Form S-3 filed November 24, 2009).
4.6	Form of Warrant in connection with March 4, 2011 financing (incorporated by reference to Exhibit 4.1 to Form 8-K filed March 10, 2011).
4.7	Form of Warrant in connection with October 4, 2011 financing (incorporated by reference to Exhibit 4.1 to Form 8-K filed October 6, 2011).
4.8	Form of Warrant in connection with October 14, 2011 financing (incorporated by reference to Exhibit 4.1 to Form 8-K filed October 14, 2011).
4.9	Form of Warrant in connection with November 17, 2011 financing (incorporated by reference to Exhibit 4.1 to Form 8-K filed November 15, 2011).
4.10	Indenture related to the 7.50% Convertible Senior Notes due 2019, dated as of November 3, 2014, by and between Synergy Pharmaceuticals Inc. and Wells Fargo Bank, National Association, as trustee (incorporated by reference to Exhibit 4.1 to Form 8-K filed November 3, 2014).

4.11	Form of 7.50% Convertible Senior Note due 2019 (incorporated by reference to Exhibit 4.2 to Form 8-K filed November 3, 2014).
4.12	First Supplemental Indenture dated as of February 28, 2017 between Synergy Pharmaceuticals Inc. and Wells Fargo, National Association, as Trustee (incorporated by reference to Exhibit 4.12 to Form 10-K filed March 1, 2017).
4.13	2017 Equity Incentive Plan (incorporated by reference to Annex B to Definitive Proxy Statement on Schedule 14A filed on April 28, 2017). *
10.1	Form of Executive Non-statutory Stock Option Agreement (incorporated by reference to Exhibit 10.4 to Form 8-K filed July 18, 2008). *
10.2	Form of Non-Executive Non-statutory Stock Option Agreement (incorporated by reference to Exhibit 10.5 to Form 8-K filed July 18, 2008). *
10.3	Master Services Agreement dated July 20, 2010 (incorporated by reference to Exhibit 10.1 to Form 10-Q filed November 9, 2010). **
10.4	Master Services Agreement dated August 5, 2010 (incorporated by reference to Exhibit 10.2 to Form 10-Q filed November 9, 2010). **
10.5	Asset Purchase Agreement dated August 17, 2012 between Synergy Pharmaceuticals Inc. and Bristol-Myers Squibb Company (incorporated by reference to Exhibit 10.7 to Form 10-K filed March 18, 2013). **
10.6	Amended and Restated Executive Employment Agreement dated as of July 12, 2013 between Synergy Pharmaceuticals Inc. and Patrick H. Griffin, M.D., FACP (incorporated by reference to Exhibit 10.9 to Form 10-K filed March 16, 2015). *
10.7	Executive Employment Agreement dated as of December 22, 2017 between Synergy Pharmaceuticals Inc. and Troy Hamilton. *
10.8	Amendment to the Amended and Restated Executive Employment Agreement dated as of January 18, 2016 by and between Synergy Pharmaceuticals Inc. and Patrick H. Griffin, M.D., FACP (incorporated by reference to Exhibit 10.12 to Form 10-K filed February 25, 2016). *
10.9	Form of Exchange Agreement Related to 7.50% Convertible Senior Notes (incorporated by reference to Exhibit 99.1 to Form 8-K filed March 18, 2016).
10.10	Form of Securities Purchase Agreement dated May 4, 2016 (incorporated by reference to Exhibit 10.1 to Form 8-K filed May 5, 2016).
10.11	Sixth Amended and Restated Executive Employment Agreement dated the 7th day of November 2017 by and between Synergy Pharmaceuticals Inc. and Gary S. Jacob, Ph.D. (incorporated by reference to Exhibit 10.1 to Form 10-Q filed November 9, 2017). *
10.12	Term Loan Agreement, dated as of September 1, 2017 between Synergy Pharmaceuticals Inc., and CRG Servicing LLC. (incorporated by reference to Exhibit 10.2 to Form 10-Q filed November 9, 2017).
10.13	Seventh Amended Executive Employment Agreement dated the 18th day of December 2017 by and between Synergy Pharmaceuticals Inc. and Gary S. Jacob, Ph.D. *
10.14	Amendment No. 1 dated as of February 26, 2018 to Term Loan Agreement dated as of September 1, 2017 between Synergy Pharmaceuticals Inc. and CRG Servicing LLC.
14	Code of Business Conduct and Ethics (incorporated by reference to Exhibit 14 to Form 10-K filed on March 1, 2017).
21	List of Subsidiaries
23	Consent of BDO USA, LLP, Independent Registered Public Accounting firm
31.1	Certification of Chief Executive Officer required under Rule 13a-14(a)/15d-14(a) under the Exchange Act
31.2	Certification of Principal Financial Officer required under Rule 13a-14(a)/15d-14(a) under the Exchange Act
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

101	Financial statements from the annual report on Form 10-K of Synergy for the year ended December 31, 2017, filed on March 1, 2018, formatted in Extensible Business Reporting Language (XBRL): (i) the Consolidated Balance Sheets, (ii) the Consolidated Statements of Operations, (iii) the Consolidated Statement of Stockholders Equity (Deficit) (iv) the Consolidated Statements of Cash Flows and (v) the Notes to Consolidated Financial Statements tagged as blocks of text.

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* Indicates a management contract or compensatory plan or arrangement.

** Portions of this exhibit were omitted and filed separately with the U.S. Securities and Exchange Commission pursuant to a request for confidential treatment.

ITEM 16. FORM 10K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

SYNERGY PHARMACEUTICALS INC.
(Registrant)

Date: March 1, 2018

By: /s/ TROY HAMILTON
Troy Hamilton

Chief Executive Officer and Director

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ TROY HAMILTON Troy Hamilton	Chief Executive Officer and Director (Principal Executive Officer)	March 1, 2018
/s/ GARY G. GEMIGNANI Gary G. Gemignani	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 1, 2018
/s/ GARY S. JACOB Gary S. Jacob	Director and Executive Chairman of the Board	March 1, 2018
/s/ MELVIN K. SPIGELMAN Melvin K. Spigelman	Director	March 1, 2018
/s/ ALAN JOSLYN Alan Joslyn	Director	March 1, 2018
/s/ THOMAS H. ADAMS Thomas H. Adams	Director	March 1, 2018
/s/ JOHN BRANCACCIO John Brancaccio	Director	March 1, 2018
/s/ TIMOTHY CALLAHAN Timothy Callahan	Director	March 1, 2018
/s/ RICHARD DALY Richard Daly	Director	March 1, 2018

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

SYNERGY PHARMACEUTICALS, INC.

INDEX TO THE CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

Stockholders and Board of Directors
Synergy Pharmaceuticals Inc.
New York, New York

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Synergy Pharmaceuticals Inc. (the "Company") as of December 31, 2017 and 2016, the related consolidated statements of operations, changes in stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2017, and the related notes collectively referred to as the "consolidated financial statements". In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2017**,** in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") and our report dated March 1, 2018 expressed an unqualified opinion thereon.

Going Concern Uncertainty

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 2 to the consolidated financial statements, the Company has incurred recurring losses from operations and expects to continue to have large losses in the future. Additionally, as more fully described in Note 2 to the consolidated financial statements, the Company's debt agreement is subject to covenants that could restrict the availability of additional loans and accelerate the repayment of that debt if breached. These factors individually and collectively raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 2. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ BDO USA, LLP

We have served as the Company's auditor since 2008.

New York, New York

March 1, 2018

SYNERGY PHARMACEUTICALS INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share amounts)

	December 31, 2017	December 31, 2016
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 136,986	$ 82,387
Accounts receivable	6,491	—
Inventories	17,214	5,640
Prepaid expenses and other current assets	4,469	889
Total Current Assets	165,160	88,916
Property and equipment, net	1,134	593
Security deposits	312	343
Total Assets	$ 166,606	$ 89,852
LIABILITIES AND STOCKHOLDERS' (DEFICIT)/EQUITY		
Current Liabilities:		
Accounts payable	$ 23,256	$ 15,584
Accrued expenses	14,658	13,552
Interest payable on senior convertible notes	233	294
Total Current Liabilities	38,147	29,430
Senior convertible notes, net	17,302	22,665
Long term debt, net	98,660	—
Derivative financial instruments, at estimated fair value-warrants	17,582	216
Other long term liabilities	433	—
Total Liabilities	172,124	52,311
Commitments and contingencies		
Stockholders' (Deficit)/Equity:		
Preferred stock, Authorized 20,000,000 shares and none outstanding, at December 31, 2017 and December 31, 2016	—	—
Common stock, par value of $.0001, 400,000,000 shares authorized at December 31, 2017 and 350,00,000 shares authorized at December 31, 2016. Issued and outstanding 246,660,367 shares at December 31, 2017 and 202,737,860 shares at December 31, 2016, respectively.	25	20
Additional paid-in capital	801,787	620,513
Accumulated deficit	(807,330)	(582,992)
Total Stockholders' (Deficit)/Equity	(5,518)	37,541
Total Liabilities and Stockholders' (Deficit)/Equity	$ 166,606	$ 89,852

The accompanying notes are an integral part of these consolidated financial statements.

SYNERGY PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2017	**2016**	**2015**
Net sales	$ 16,820	$ —	$ —
Cost of goods sold	8,811	—	—
Gross profit	8,009	—	—
Costs and Expenses:			
Research and development	48,346	87,056	78,028
Selling, general and administrative	181,862	58,230	21,794
Loss from Operations	(222,199)	(145,286)	(99,822)
Other Income/(Loss)			
Interest expense, net	(5,270)	(13,390)	(17,284)
Debt conversion expense	(1,209)	(40,158)	—
State R&D tax credits	—	121	—
Change in fair value of derivative instruments-warrants	4,340	106	(394)
Total other expenses	(2,139)	(53,321)	(17,678)
Net loss	$ (224,338)	$ (198,607)	$ (117,500)
Weighted Average Common Shares Outstanding			
Basic and Diluted	225,439,121	164,437,548	105,570,960
Net Loss per Common Share, Basic and Diluted	$ (1.00)	$ (1.21)	$ (1.11)

The accompanying notes are an integral part of these consolidated financial statements.

SYNERGY PHARMACEUTICALS INC.
CONSOLIDATED STATEMENT OF CHANGES IN STOCKHOLDERS' EQUITY/(DEFICIT)
(In thousands, except share amounts)

	Common Shares	Common Stock, Par Value	Additional Paid in Capital	Deficit Accumulated	Total Stockholders' (Deficit)/ Equity
Balance, December 31, 2014	96,609,764	$ 11	$ 261,715	$ (266,885)	$ (5,159)
Common stock issued pursuant to a controlled equity "at-the-market" sales agreement, net of issuance costs	3,435,998	—	14,268	—	14,268
Common stock issued in connection with exercise of stock options	269,720	—	1,142	—	1,142
Common stock issued in connection with exercise of warrants	189,412	—	1,012	—	1,012
Shares issued in connection with conversion of Senior Convertible Notes	13,179,712	—	40,989	—	40,989
Change in fair value of warrants due to expiration of certain warrants	—	—	244	—	244
Stock based compensation expense	—	—	9,724	—	9,724
Stock issued in exchange for certain intellectual property	10,000	—	67	—	67
Net loss for the period	—	—	—	(117,500)	(117,500)
Balance, December 31, 2015	113,694,606	$ 11	$ 329,161	$ (384,385)	$ (55,213)
Shares issued in connection with conversion of Senior Convertible Notes	44,432,408	4	137,937	—	137,941
Debt conversion expense	12,161,671	1	40,157	—	40,158
Transaction fees on Note conversions	—	—	(711)	—	(711)
Common stock issued in connection with exercise of stock options	70,185	—	222	—	222
Common stock issued in connection with exercise of warrants	2,430,656	1	11,330	—	11,331
Common stock issued in registered direct offering, net of issuance costs	29,948,334	3	89,842	—	89,845
Stock based compensation expense	—	—	12,575	—	12,575
Net loss for the period	—	—	—	(198,607)	(198,607)
Balance, December 31, 2016	202,737,860	$ 20	$ 620,513	$ (582,992)	$ 37,541
Notes conversions	1,579,099	1	4,911	—	4,912
Debt conversion expense	212,800	—	1,209	—	1,209
Common stock issued in connection with exercise of stock options	99,978	—	347	—	347
Common stock issued in registered direct offering, net of issuance costs	42,030,630	4	173,798	—	173,802
Warrants classified as derivative liability	—	—	(21,706)	—	(21,706)
Stock based compensation expense	—	—	22,715	—	22,715
Net loss for the period	—	—	—	(224,338)	(224,338)
Balance, December 31, 2017	246,660,367	$ 25	$ 801,787	$ (807,330)	$ (5,518)

The accompanying notes are an integral part of these consolidated financial statements.

SYNERGY PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2017	2016	2015
Cash Flows From Operating Activities:			
Net loss	$ (224,338)	$ (198,607)	$ (117,500)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	165	233	163
Amortization of deferred debt costs and debt discount	1,342	6,921	4,566
Accretion of back-end facility fee	106	—	—
Loss on disposal of property and equipment	46	—	—
Stock-based compensation expense	22,715	12,575	9,724
Interest expense — Payment-in-kind (PIK)	3,212	—	—
Value of common stock issued for patent license	—	—	67
Accretion of discount/premium on available for sale securities	—	—	(109)
Change in fair value of derivative instruments—warrants	(4,340)	(106)	394
Common stock issued for interest on Notes		2,445	—
Debt conversion expense	1,209	40,158	—
Changes in operating assets and liabilities:			
Accounts receivable	(6,491)	—	—
Inventories	(11,574)	(5,640)	—
Security deposits	31	—	(180)
Accounts payable and accrued expenses	8,669	11,546	1,867
Prepaid expenses and other current assets	(3,580)	2,416	531
Accrued interest expense on senior convertible notes	(61)	(1,694)	(512)
Total Adjustments	11,449	68,854	16,511
Net Cash used in Operating Activities	(212,889)	(129,753)	(100,989)
Cash Flows From Investing Activities:			
Net sales (purchases) of available-for-sale securities	—	50,097	(200)
Additions to property and equipment	(210)	(297)	(50)
Net Cash (used in) provided by Investing Activities	(210)	49,800	(250)
Cash Flows From Financing Activities:			
Proceeds of sale of common stock, net of issuance costs	173,802	89,845	14,268
Proceeds from borrowings, net of issuance costs	95,140	—	—
Fees and expenses — note conversions	—	(711)	—
Payment for deferred financing costs	(1,591)	—	—
Proceeds from exercise of warrants	—	11,331	1,012
Proceeds from exercise of stock options	347	222	1,142
Net Cash provided by Financing Activities	267,698	100,687	16,422
Net increase (decrease) in cash and cash equivalents	54,599	20,734	(84,817)
Cash and cash equivalents at beginning of period	82,387	61,653	146,470
Cash and cash equivalents at end of period	$ 136,986	$ 82,387	$ 61,653
Supplementary disclosure of cash flow information:			
Cash paid for interest on senior convertible notes	$ 1,396	$ 5,939	$ 13,379
Cash paid for taxes	$ 20	$ 45	$ 258

Supplementary disclosure of non-cash investing and financing activities:			
Conversion of senior convertible notes to Synergy Common Stock	$ 4,912	$ 137,941	$ 40,989
Amount added to principal of term loan for Payment-in-kind (PIK) interest	$ 3,212	$ —	$ —
Non-cash tenant improvement allowance	$ 587	$ —	$ —
Fair value of warrants classified to derivative liability	$ 21,706	$ —	$ —

The accompanying notes are an integral part of these consolidated financial statements.

SYNERGY PHARMACEUTICALS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Business Overview

Synergy Pharmaceuticals Inc. ("the Company" or "Synergy") is a biopharmaceutical company focused on the development and commercialization of novel gastrointestinal (GI) therapies. The Company has pioneered discovery, research and development efforts around analogs of uroguanylin, a naturally occurring and endogenous human GI peptide, for the treatment of GI diseases and disorders. We control 100% worldwide rights to our proprietary uroguanylin based GI platform which includes one commercial product, TRULANCE®, and one development stage compound, dolcanatide.

Recent Developments

On January 31, 2017, Synergy entered into an underwriting agreement with Cantor Fitzgerald & Co., as representative of the several underwriters, to issue and sell 20,325,204 shares of common stock of the Company in an underwritten public offering pursuant to a Registration Statement on Form S-3 and a related prospectus supplement filed with the Securities and Exchange Commission (the “Offering”). The public offering price was $6.15 per share of Common Stock. The Offering closed on February 6, 2017, yielding net proceeds of approximately $121.6 million, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

On February 28, 2017, Synergy received consents from certain holders of its Notes to enter into a Supplemental Indenture which eliminated certain restrictive covenants from the Indenture related to the Notes. The restrictive covenants eliminated from the Indenture were Limitation on Indebtedness, Future Financing Rights for Certain Investors and Licensing Limitations. On February 28, 2017, Synergy entered into the Supplemental Indenture with Wells Fargo, N.A., as trustee and paid an aggregate of approximately $1.6 million to such holders for the consent. These fees associated with the debt modification were accounted for under Accounting Standards Codification ("ASC") 470-50 and are amortized using the effective interest method over the remaining term of the debt.

In March 2017, Synergy exchanged approximately $4.9 million aggregate principal amount of the Notes for approximately 1.8 million shares of its common stock, with approximately 1.6 million shares representing the conversion price of $3.11 pursuant to the existing terms of the Notes. As of December 31, 2017, approximately $18.6 million of the Notes remain outstanding. The Company recognized a debt conversion expense of $1.2 million representing 0.2 million shares during the year ended December 31, 2017.

On September 1, 2017, Synergy entered into a senior secured term loan of up to $300 million with CRG Servicing LLC, as administrative and collateral agent, and the lenders and guarantors party thereto (the "Term Loan"). The Term Loan is available for working capital and general corporate purposes. The Company borrowed $100 million at time of closing. In February 2018 we further amended the Term Loan agreement. The amended Term Loan provides for future borrowings of $25 million, $25 million and $50 million on or before June 30, 2018, September 30, 2018 and December 31, 2018, respectively. Additionally, the total amount of the commitment was reduced from $300 million to $200 million (excluding PIK loans) and the Minimum Market Capitalization covenant of $300 million was revised to be 200% of the outstanding principal amount of the Term Loan (excluding PIK loans).

The Term Loan has a maturity date of June 30, 2025, unless prepaid earlier. The Term Loan bears interest at a rate equal to 9.5% per annum, with quarterly, interest-only payments until June 30, 2022, subject to extension through the maturity date upon the Company’s satisfaction of certain conditions. At the Company’s option, until June 30, 2019, a portion of the interest payments may be paid in kind, and thereby added to the principal. Following, the interest-only period, the Term Loans will amortize in equal quarterly installments unless entirely payable at maturity.

On November 13, 2017, Synergy entered into an underwriting agreement with Jefferies LLC, as representative of the several underwriters, to issue and sell 21,705,426 shares of common stock of the Company together with accompanying warrants (“Warrants”) to purchase an aggregate of 21,705,426 shares of Common Stock in an underwritten offering pursuant to a Registration Statement on Form S-3ASR and a related prospectus and prospectus supplement, in each case filed with the Securities and Exchange Commission (the “Offering”). The offering price was $2.58 per share of Common Stock and accompanying Warrant. The net proceeds from the Offering were approximately $52.2 million, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

2. Basis of Presentation, Accounting Policies and Going Concern

These consolidated financial statements include Synergy Pharmaceuticals Inc., a Delaware corporation, and its wholly owned subsidiary Synergy Advanced Pharmaceuticals, Inc. All intercompany balances and transactions have been eliminated.

Our consolidated financial statements as of December 31, 2017 have been prepared under the assumption that we will continue as a going concern for the next twelve months. The Company has incurred recurring losses from operations and expects to continue to have losses in the future. In addition, the Company's debt agreement is subject to covenants that could restrict the availability of additional loans and accelerate the repayment of that debt if breached. These factors individually and collectively raise substantial doubt about the Company's ability to continue as a going concern. Our independent registered public accounting firm has issued a report that includes an explanatory paragraph referring to such conditions and expressing substantial doubt in our ability to continue as a going concern.

Our ability to continue as a going concern is dependent upon our plans of attaining further operating efficiencies, reducing expenditures, and generating significant revenue and if deemed necessary obtaining additional equity or debt financing, which may not be available on acceptable terms or at all. To the extent that Synergy may need to raise additional funds by issuing equity securities, Synergy's stockholders may experience significant dilution. Any debt financing, if available, may involve restrictive covenants that impact Synergy's ability to conduct business. If Synergy is unable to raise additional capital when required or on acceptable terms, Synergy may have to (i) significantly scale back our commercialization efforts ; (ii) seek commercial partners for our products on terms that are less favorable than might otherwise be available; or (iii) relinquish or otherwise dispose of rights, on unfavorable terms, to technologies, product candidates or products that Synergy would otherwise seek to develop or commercialize itself. Our consolidated financial statements as of December 31, 2017 did not include any adjustments that might result from the outcome of this uncertainty.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP and the rules and regulations of the SEC requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. The most significant judgments are employed in estimates used in determining fair value of share-based compensation related to equity incentive awards issued to employees and directors, fair value of warrants, legal contingencies and estimates used in applying our revenue recognition policy including those related to sales related deductions. Changes in estimates and assumptions are reflected in reported results in the period in which they become known. Actual results could differ from those estimates.

Reclassifications

Certain prior period amounts were reclassified to conform to the current period presentation and additional information is disclosed in the notes if material.

Cash and cash equivalents

All highly liquid investments with maturities of three months or less at the date of purchase are classified as cash equivalents. As of December 31, 2017 and December 31, 2016, the amounts of cash and cash equivalents were approximately $137.0 million and $82.4 million, respectively, and consisted of checking accounts and short-term money market funds with U.S. commercial banks. At any point in time, the Company's balance of cash and cash equivalents may exceed federally insured limits.

Accounts Receivable

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed. The Company's receivables primarily related to amounts due from 3rd party customers for the sale of TRULANCE. In 2017, our three major customers accounted for an aggregate of 97% of our gross revenue. Together, our three major customers, AmerisourceBergen, McKesson Corporation, and Cardinal Health accounted for 39%, 31%, and 25%, respectively, of our accounts receivable as of December 31, 2017. The Company believes that credit risks associated with these customers are not significant.
To date, the Company has not had any write-offs of bad debt, and the Company did not record an allowance for doubtful accounts as of December 31, 2017.

Inventories

Inventories consist of finished goods, work in process and raw materials and are stated at the lower of cost or net realizable value with cost determined under the first-in, first-out basis. Inventory valuation reserves are established based on a number of factors/situations including, but not limited to, raw materials, work in process or finished goods not meeting product specifications, product obsolescence, or application of the lower of cost (first-in, first-out method) or net realizable value concepts.

Synergy capitalizes inventories manufactured in preparation for initiating sales of a product candidate when the related product candidate is considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales of the inventories. In determining whether or not to capitalize such inventories, Synergy evaluates, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales. In addition, Synergy evaluates risks associated with manufacturing the product candidate and the remaining shelf life of the inventories.

Costs associated with developmental products prior to satisfying the inventory capitalization criteria are charged to research and development expense as incurred. There is a risk inherent in these judgments and any changes in these judgments may have a material impact on our financial results in future periods.

In July 2015, the FASB issued an accounting standard update (ASU No. 2015-11) intended to simplify the measurement of inventory by requiring inventory to be measured at the lower of cost or net realizable value. Net realizable value is defined as estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal, and transportation, etc. The Company adopted this standard as of January 1, 2017, which had no impact on the consolidated financial statements.

Revenue recognition

Synergy recognizes revenue from sales of TRULANCE when the earnings process is complete, which under Accounting Standards Codification ASC 605, Revenue Recognition is when revenue is realized or realizable and earned, there is persuasive evidence a revenue arrangement exists, delivery of goods or services has occurred, the sales price is fixed or determinable, and collectability is reasonably assured. Product sales are recorded net of all sales related deductions, including but not limited to: customer loyalty programs, trade discounts, fee for service agreements, sales returns and allowances, commercial and government rebates, and chargebacks. The Company estimates these sales deductions based on contractual terms, historical payment experience, third party data, estimated utilization or redemption rates, government regulations, and customer inventory levels. Accruals for trade discounts, fee for service agreements and chargebacks are reflected as a direct reduction of accounts receivable and accruals for commercial and government rebates and customer loyalty programs are reflected as accrued expenses.

Cost of Goods Sold

Cost of goods sold ("COGS") includes (i) direct cost of manufacturing and packaging drug product and (ii) technical operations overhead costs which are generally more fixed in nature, including salaries, benefits, consulting, stability testing and other services. Technical operations are responsible for planning, coordinating, and executing the Company's inventory production plan and ensuring that product quality satisfies FDA requirements. Costs incurred by the technical operations organization are recorded as expense in the period in which they are incurred. Certain direct costs associated with pre-commercial inventory, other than packaging, were expensed as research and development ("R&D") prior to receiving FDA approval. (See Inventories in Footnote 2 "Basis of Presentation, Accounting Policies and Going Concern").

Derivative Instruments

The Company's derivative liabilities are related to warrants issued in connection with financing transactions and are therefore not designated as hedging instruments. All derivatives are recorded on the Company's balance sheet at fair value in accordance with current accounting guidelines for such complex financial instruments. Changes in fair value are recorded in the Company's statement of operations.

Fair Value of Financial Instruments

In accordance with Accounting Standards Codification ("ASC") Subtopic 820-10, the Company measures certain assets and liabilities at fair value on a recurring basis using the three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. The three tiers include:

- Level 1, defined as observable inputs such as quoted prices for identical assets in active markets;
- Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable; and
- Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring management to develop its own assumptions based on best estimates of what market participants would use in pricing an asset or liability at the reporting date.

Financial instruments consist of cash and cash equivalents, accounts receivable, accounts payable and derivative instruments. These financial instruments are stated at their respective historical carrying amounts, which approximate fair value due to their short term nature, except for derivative instruments which are marked to market at the end of each reporting period.

The value of Senior Convertible Notes and Long term debt are stated at their carrying value at December 31, 2017 and 2016. Carrying value approximates fair value because the Company believes it could obtain similar borrowings at December 31, 2017 at comparable interest rates, therefore, the carrying value approximates fair value.

Property, equipment and depreciation

Expenditures for additions, renewals and improvements are capitalized at cost. Depreciation is computed on a straight-line method based on the estimated useful lives of the related assets. The estimated useful lives of the major classes of depreciable assets are 2 to 5 years for equipment and furniture and fixtures. Leasehold improvements are depreciated over the shorter of the remaining useful life or remaining lease term of the lease. Expenditures for repairs and maintenance are charged to operations as incurred. Synergy periodically evaluates whether current events or circumstances indicate that the carrying value of its depreciable assets may not be recoverable.

Income Taxes

Income taxes have been determined using the asset and liability approach of accounting for income taxes. Under this approach, deferred taxes represent the future tax consequences expected to occur when the reported amounts of assets and liabilities are recovered or paid. Deferred taxes result from differences between the financial statement and tax bases of Synergy's assets and liabilities and are adjusted for changes in tax rates and tax laws when changes are enacted. Valuation allowances are recorded to reduce deferred tax assets when it is more likely than not that a tax benefit will not be realized. The assessment of whether or not a valuation allowance is required often requires significant judgment.

Contingencies

In the normal course of business, Synergy is subject to loss contingencies, such as legal proceedings and claims arising out of its business, that cover a wide range of matters, including, among others, government investigations, shareholder lawsuits, product and environmental liability, and tax matters. In accordance with FASB ASC Topic 450, *Accounting for Contingencies* ("ASC Topic 450"), Synergy records accruals for such loss contingencies when it is probable that a liability will be incurred and the amount of loss can be reasonably estimated. Synergy, in accordance with this guidance, does not recognize gain contingencies until realized. For a discussion of contingencies, see Note 7, *Commitments and Contingencies* below.

Research and Development

Research and development costs include expenditures in connection with an in-house research and development laboratory, salaries and staff costs, application and filing for regulatory approval of proposed products, regulatory and scientific consulting fees, as well as contract research, patient costs, manufacturing process development costs, drug formulation and tableting, data collection, monitoring, and clinical trial insurance.

The Company recorded inventory, manufactured for sale of a product candidate, when the product candidate was considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales. In determining whether or not to record such inventories, the Company evaluated, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales. Prior to October 1, 2016, all costs associated with batches of inventory, manufactured for sale, were charged to research and development as incurred. Beginning in the fourth quarter of 2016, Synergy began capitalizing inventory costs for TRULANCE in preparation for its planned launch in the U.S. The Company will record inventory, manufactured for sale of a product candidate, when the product candidate is considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales. In determining whether or not to record such inventories, the Company evaluates, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales.

In accordance with FASB ASC Topic 730-10-55, *Research and Development*, Synergy recorded prepaid research and development costs of approximately $72,000 and $33,000 as of December 31, 2017 and December 31, 2016, respectively, of pre-payments for production of drug substance, analytical testing services and clinical trial monitoring for its drug candidates. In accordance with this guidance, Synergy expenses these costs when drug substance is delivered and/or services are performed.

Loss Per Share

Basic and diluted net loss per share is presented in conformity with ASC Topic 260, *Earnings per Share*, (“ASC Topic 260”) for all periods presented. In accordance with this guidance, basic and diluted net loss per common share was determined by dividing net loss applicable to common stockholders by the weighted-average common shares outstanding during the period. Diluted weighted-average shares are the same as basic weighted-average shares because shares issuable pursuant to the exercise of stock options and warrants would have been antidilutive.

The Senior Convertible Notes (the"Notes") face value of $18.6 million is convertible into 5,981,672 shares of common stock at December 31, 2017, the effect of which was excluded from the calculation of diluted loss per share because it was antidilutive. As of December 31, 2016, the face value of these Notes was $23.5 million and was convertible into 7,560,772 shares of common stock, the effect of which was excluded from the calculation of diluted loss per share because it was antidilutive. As of December 31, 2015, the carrying value of the Notes was $159 million and was convertible into 51,128,939 shares of common stock the effect of which was excluded from the calculation of diluted loss per share because it was antidilutive.

The following table sets forth potential common shares issuable upon the exercise of outstanding options, the exercise of warrants, and the conversion of the Senior Convertible Notes, all of which have been excluded from the computation of diluted weighted average shares outstanding as they would be anti-dilutive, including the impact on dilutive net loss per share of in-the-money warrants as per ASC 260-10-45-35 through ASC 260-10-45-37:

	Year Ended December 31, 2017	Year Ended December 31, 2016	Year Ended December 31, 2015
Stock Options	29,868,291	27,867,171	20,953,375
Warrants	22,575,114	919,690	4,726,823
Senior Convertible Notes	5,981,672	7,560,772	51,128,939
Total shares issuable upon exercise or conversion	58,425,077	36,347,633	76,809,137

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued a comprehensive new revenue recognition standard ASC 606 Revenue From Contracts With Customers. The new standard outlines a single comprehensive model for

entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. The core principle of the revenue model is that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. In addition, the standard requires disclosure of the nature, amount, timing and uncertainty of revenue and cash flows arising from contracts with customers. The standard is designed to create greater comparability for financial statement users across industries, jurisdictions and capital markets and also requires enhanced disclosures. The new standard will be effective for the Company beginning January 1, 2018. The guidance permits two methods of adoption: retrospectively to each prior reporting period presented (full retrospective method), or retrospectively with the cumulative effect of initially applying the guidance recognized at the date of initial application (the modified retrospective method). The Company will adopt this standard using the modified retrospective method.

The Company has substantially completed its impact assessment, and expects that the adoption of the new standard will not have a material impact on its consolidated financial statements. In connection with adopting the new standard, the Company does not anticipate implementing significant changes to its internal controls or systems. The Company continues to evaluate the impact of the new guidance on its financial statement disclosures.

In March 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-09, “Compensation - Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting” (“ASU 2016-09”). The standard is intended to simplify several areas of accounting for share-based compensation arrangements, including the income tax impact, classification on the statement of cash flows and forfeitures. ASU 2016-09 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016, and early adoption is permitted. This standard became effective for us on January 1, 2017. The adoption of this standard did not have a material impact on our financial statements.

In February 2016, the FASB issued ASU No. 2016-02 “Leases (Topic 842)” (“ASU 2016-02”). The FASB issued ASU 2016-02 to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheet and disclosing key information about leasing arrangements. Under ASU 2016-02, a lessee will recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-to-use asset representing its right to use the underlying asset for the lease term. The amendments of this ASU are effective for reporting periods beginning after December 15, 2018, with early adoption permitted. An entity will be required to recognize and measure leases at the beginning of the earliest period presented using a modified retrospective approach. The adoption of ASU 2016-02 is not expected to have a material impact on our financial statements and disclosures except at the time of adoption. At time of adoption the Company will recognize right of use assets and lease liabilities on the balance sheet.

In May 2017, the FASB issued ASU No. 2017-09, “Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting,” (“ASU 2017-09”) which clarifies when a change to terms or conditions of a share-based payment award must be accounted for as a modification. The new guidance requires modification accounting if the vesting condition, fair value or the award classification is not the same both before and after a change to the terms and conditions of the award. The new guidance is effective on a prospective basis beginning on January 1, 2018 and early adoption is permitted. The Company is evaluating the potential impact that ASU 2017-09 will have on its consolidated financial statements.

In July 2017, the FASB issued ASU No. 2017-11, Earnings Per Share (Topic 260); Distinguishing Liabilities from Equity (Topic 480); Derivatives and Hedging (Topic 815): (Part I) Accounting for Certain Financial Instruments with Down Round Features, (Part II) Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception (“ASU 2017-11”). ASU 2017-11 was issued to address the complexity associated with applying generally accepted accounting principles (GAAP) for certain financial instruments with characteristics of liabilities and equity. The ASU, among other things, eliminates the need to consider the effects of down round features when analyzing convertible debt, warrants and other financing instruments. As a result, a freestanding equity-linked financial instrument (or embedded conversion option) no longer would be accounted for as a derivative liability at fair value as a result of the existence of a down round feature. The amendments are effective for fiscal years beginning after December 15, 2018, and should be applied retrospectively. Early adoption is permitted, including adoption in an interim period. The Company does not expect the adoption of this standard to have an impact on its consolidated financial statements.

3. Inventory

Inventory as of December 31, 2017 and December 31, 2016 consisted of the following:

	December 31, 2017	December 31, 2016
Raw Materials	$ 5,754	$ 5,347
Work-in-process	7,732	293
Finished goods	3,728	—
Inventories	$ 17,214	$ 5,640

4. Debt

Senior Convertible Notes

On November 3, 2014, Synergy closed a private offering of $200 million aggregate principal amount of 7.50% Convertible Senior Notes due 2019, (the "Notes"), including the full exercise of the over-allotment option granted to the initial purchasers to purchase an additional $25 million aggregate principal amount of the Notes, interest payable semiannually in arrears on May 1 and November 1 of each year, beginning on May 1, 2015. The net proceeds from the offering were $187.3 million after deducting the initial purchasers' discounts and offering expenses.

The Notes are unsecured. Interest expense, not including amortization of deferred debt costs, for the years ended December 31, 2017, 2016 and 2015 was $1.3 million, $6.7 million and $12.9 million, respectively. Accrued interest payable was $0.2 million and $0.3 million as of December 31, 2017 and December 31, 2016, respectively.

The Notes will mature on November 1, 2019, unless earlier purchased or converted. The Notes are convertible, at any time, into shares of Synergy's common stock at an initial conversion rate of 321.5434 shares per $1,000 principal amount of notes, which is equivalent to the original conversion price of $3.11 per share. Subsequent to the exchanges described below, the principal balance of the Notes at December 31, 2017 was $18.6 million as compared to $23.5 million at December 31, 2016.

Initial purchaser's discounts and offering expenses associated with the sale of the Notes of $12.7 million have been deferred and are being recognized as expense over the expected term of the Notes, calculated using the effective interest rate method. Amortization expense, including accelerated amortization attributable to reduction of the principal due to the conversion of the debentures on a prorated basis for year ended December 31, 2017 and December 31, 2016 was $1.1 million and $6.9 million, respectively. The remaining deferred debt costs have been presented as a reduction of the Notes in accordance with the newly adopted Accounting Standards Update ("ASU") No. 2015-3 "*Simplifying the Presentation of Debt Issuance Costs"*.

On March 18, 2016 Synergy entered into an agreement (the "Exchange") for the exchange of $79.8 million in aggregate principal amount of the Notes, representing approximately 50% of the outstanding aggregate principal amount of Notes, for 35.3 million shares of Synergy's common stock, with a total of 25.6 million shares representing the conversion price of $3.11 pursuant to the existing terms of the Notes. Synergy also issued approximately 872,000 shares at the five day average share price of $2.81 in payment of accrued and unpaid interest of $2.4 million on Notes accepted in the Exchanges, from the applicable last interest payment date to, but not including, March 28, 2016. The amortization of deferred debt costs was accelerated consistent with the 50% reduction of aggregate principal amount this transaction represented, and resulted in additional interest expense of approximately $3.6 million. GAAP requires that such conversions be treated as induced conversions with an expense recognized equal to the fair value of the 9.6 million shares transferred in the transaction in excess of the fair value of the securities issuable pursuant to the original conversion terms, with such fair value being measured as of the date the inducement offer is accepted by the convertible debt holder. Accordingly, the Company recognized a debt conversion expense of $25.6 million for the quarter ended March 31, 2016.

In November 2016 Synergy exchanged $55.7 million in aggregate principal amount of the Notes, representing approximately 70% of the outstanding aggregate principal amount of Notes, for 20.5 million shares of Synergy's common stock, with a total of 17.9 million shares representing the conversion price of $3.11 pursuant to the existing terms of the Notes. The amortization of deferred debt costs was accelerated consistent with the 70% reduction of aggregate principal amount this transaction represented, and resulted in additional interest expense of approximately $2 million. The Company recognized a debt conversion expense of $14.5 million representing 2.6 million shares for the quarter ended December 31,2016.

On February 28, 2017, Synergy received consents from certain holders of its Notes to enter into a Supplemental Indenture which eliminates certain restrictive covenants from the Indenture related to the Notes. The restrictive covenants eliminated from the Indenture are Limitation on Indebtedness, Future Financing Rights for Certain Investors and Licensing Limitations. On February 28, 2017, Synergy entered into the Supplemental Indenture with Wells Fargo, N.A., as trustee and paid an aggregate of approximately $1.6 million to such holders for the consent. These fees associated with the debt modification were accounted for under Accounting Standards Codification ("ASC") 470-50 and amortized using the effective interest method over the remaining term of the debt.

In March 2017, Synergy exchanged approximately $4.9 million aggregate principal amount of the Notes for approximately 1.8 million shares of its common stock, with approximately 1.6 million shares representing the conversion price of $3.11 pursuant to the existing terms of the Notes. The Company recognized a debt conversion expense of approximately $1.2 million representing 0.2 million shares for the year ended December 31, 2017. As of December 31, 2017, approximately $18.6 million of the Notes remain outstanding.

A summary of activity and balances associated with the Notes and related deferred debt costs is presented below ($ in thousands):

	Notes Balance	Deferred Debt Costs	Notes, net of Deferred Debt Costs
Balance December 31, 2015	$ 159,011	$ 7,770	$ 151,241
Less: amortization for the year ended December 31, 2016 [1]		(6,921)	6,921
Conversions	(135,497)	—	(135,497)
Balance, December 31, 2016	23,514	849	22,665
Deferred financing cost related to debt modification on February 28, 2017		1,591	(1,591)
Less: amortization for the year ended December 31, 2017 [1]		(1,139)	1,139
Conversions	(4,911)	—	(4,911)
Balance, December 31, 2017	$ 18,603	$ 1,301	$ 17,302

(1) Includes accelerated amortization of deferred debt costs attributable to conversions and exchanges

Long term debt, net

On September 1, 2017, Synergy Pharmaceuticals Inc. entered into a senior secured term loan of up to $300 million with CRG Servicing LLC, as administrative and collateral agent, and the lenders and guarantors party thereto (the "Term Loan"). The Term Loan is available for working capital and general corporate purposes. The Company borrowed $100 million at time of closing. In February 2018 we further amended the Term Loan agreement. The amended Term Loan provides for future borrowings of $25 million, $25 million and $50 million on or before June 30, 2018, September 30, 2018 and December 31, 2018, respectively. Additionally, the total amount of the commitment was reduced from $300 million to $200 million (excluding PIK loans) and the Minimum Market Capitalization covenant of $300 million was revised to be 200% of the outstanding principal amount of the Term Loan (excluding PIK loans).

The Term Loan has a maturity date of June 30, 2025, unless earlier prepaid. The Term Loan bears interest at a rate equal to 9.50% per annum, with quarterly, interest-only payments until June 30, 2022, subject to extension through the maturity date upon the Company's satisfaction of certain conditions. At the Company's option, until June 30, 2019, a portion of the interest payments may be paid in kind, and thereby added to the principal. Following, the interest-only period, the Term Loan will amortize in equal quarterly installments unless entirely payable at maturity.

The obligations under the Term Loan are secured, subject to customary permitted liens and other agreed upon exceptions, by a perfected security interest in (i) all tangible and intangible assets of the Company and the Subsidiary Guarantors, except for certain customary excluded property, and (ii) all of the capital stock owned by the Company and Subsidiary Guarantors (limited, in the case of the stock of certain non-U.S. subsidiaries of the Company and certain U.S. subsidiaries substantially all of whose assets consist of equity interests in non-U.S. subsidiaries, to 65% of the capital stock of such subsidiaries, subject to certain exception). The obligations under the Term Loan are guaranteed by Synergy Advanced Pharmaceuticals, Inc. and each of the Company's future direct and indirect subsidiaries (other than certain subsidiaries whose guarantee would result in material adverse tax consequences, subject to certain exceptions).

The Term Loan contains customary affirmative covenants, including covenants regarding the payment of taxes and other obligations, maintenance of insurance, reporting requirements and compliance with applicable laws and regulations. Further, the Term Loan contains customary negative covenants limiting the ability of the Company and its subsidiaries, among other things, to incur future debt, grant liens, make investments, make acquisitions, make certain restricted payments and sell assets, subject to certain exceptions. In addition, the Term Loan requires the Company to comply with a minimum market capitalization covenant, maintain its status as a national exchange listed company, a daily minimum liquidity covenant and an annual revenue requirement based on the sales of TRULANCE.

The Term Loan may be prepaid by the Company at any time, subject to a prepayment premium of up to 40% of the principal amount, depending on the date of prepayment. Upon the occurrence of certain events relating to asset sales above a specified threshold or in the event of a change of control transaction, the Company may also be required to prepay all or a part of the outstanding principal and interest under the Term Loan in addition to the prepayment premium described above on the principal amount prepaid. Upon payment of the Term Loan at maturity or prepayment on any earlier date, a back-end facility fee will apply to the amounts paid or prepaid.

As of the date hereof, the Company is not in default under the terms of the Term Loan. The report and opinion of the Company's independent registered public accounting firm, BDO USA, LLP, contains an explanatory paragraph regarding the Company's ability to continue as a going concern, which is a violation of an affirmative covenant under the Term Loan. The Company entered into a waiver agreement under which the lenders agreed to waive this affirmative covenant as it pertains to the Company's fiscal 2017 audited financial statements.

As of December 31, 2017, the Company was in compliance with all applicable covenants.

As of December 31, 2017, principal and PIK payments under the Term Loan were as follows:

Period Ending December 31,	Principal and PIK Loan Repayments
2018	$ —
2019	—
2020	—
2021	—
2022 and thereafter	100,000
	100,000
Add: Accretion of back-end facility fee	106
Add: PIK interest	3,212
	103,318
Less: Debt financing costs, net of amortization	(4,658)
Balance at December 31, 2017	$ 98,660

5. Accounting for Share-based Payments

Stock Options

ASC Topic 718 *"Compensation—Stock Compensation"* requires companies to measure the cost of employee services received in exchange for the award of equity instruments based on the estimated fair value of the award at the date of grant. The expense is to be recognized over the period during which an employee is required to provide services in exchange for the award. Synergy accounts for shares of common stock, stock options and warrants issued to employees based on the fair value of the stock, stock option or warrant, if that value is more reliably measurable than the fair value of the consideration or services received.

The Company accounts for stock options issued and vesting to non-employees in accordance with ASC Topic 505-50 "*Equity -Based Payment to Non-Employees"* and accordingly the value of the stock compensation to non-employees is based upon the measurement date as determined at either a) the date at which a performance commitment is reached, or b) at the date

at which the necessary performance to earn the equity instruments is complete. Accordingly the fair value of these options is being "marked to market" quarterly until the measurement date is determined.

Synergy adopted the 2008 Equity Compensation Incentive Plan (the "Plan") during the quarter ended September 30, 2008. Stock options granted under the Plan typically vest after three years of continuous service from the grant date and have a contractual term of ten years. On June 8, 2015, Synergy amended its 2008 Equity Compensation Incentive Plan and increased the number of shares of its common stock reserved for issuance under the Plan from 15,000,000 to 30,000,000.

Synergy adopted the 2017 Equity Incentive Plan (the "2017 Plan") during the quarter ended June 30, 2017. The number of shares of its common stock reserved for issuance under the 2017 Plan is 9,000,000 and no grants have been awarded as of December 31, 2017.

In June 2017, the Company modified 2,159,500 stock options, which were previously granted as change of control options, to become immediately vested. The Company recorded a charge of $6.8 million during the three months ended June 30, 2017. There are no outstanding change of control options as of December 31, 2017.

Stock-based compensation has been recognized in operating results as follows:

	Year Ended December 31,		
($ in thousands)	**2017**	**2016**	**2015**
Included in research and development	$ 2,786	$ 3,451	$ 2,452
Included in general and administrative	19,929	9,124	7,272
Total stock-based compensation expense	$ 22,715	$ 12,575	$ 9,724

The unrecognized compensation cost related to non-vested stock options outstanding at December 31, 2017, net of expected forfeitures, was approximately $14.7 million to be recognized over a weighted-average remaining vesting period of approximately 1.49 years.

The estimated fair value of stock option awards was determined on the date of grant using the Black-Scholes option valuation model with the following assumptions during the periods indicated.

	Year Ended December 31,		
	2017	**2016**	**2015**
Risk-free interest rate	1.85%-2.40%	1.13%-2.19%	1.46%-2.02%
Dividend yield	—	—	—
Expected volatility	62%-73%	50%-60%	50%-80%
Expected term (in years)	6 years	6 years	6 years

Risk-free interest rate —Based on the daily yield curve rates for U.S. Treasury obligations with maturities which correspond to the expected term of the Company's stock options.

Dividend yield —Synergy has not paid any dividends on common stock since its inception and does not anticipate paying dividends on its common stock in the foreseeable future.

Expected volatility —Based on the historical volatility of Synergy stock.

Expected term —Synergy has had minimal stock options exercised since inception. The expected option term represents the period that stock-based awards are expected to be outstanding based on the simplified method provided in Staff Accounting Bulletin ("SAB") No. 107, *Share-Based Payment* , ("SAB No. 107"), which averages an award's weighted-average vesting period and expected term for "plain vanilla" share options. Under SAB No. 107, options are considered to be "plain vanilla" if they have the following basic characteristics: (i) granted "at-the-money"; (ii) exercisability is conditioned upon service through the vesting date; (iii) termination of service prior to vesting results in forfeiture; (iv) limited exercise period following termination of service; and (v) options are non-transferable and non-hedgeable.

The Company will continue to use the simplified method for the expected term until it has the historical data necessary to provide a reasonable estimate of expected life in accordance with SAB No. 107, as amended by SAB No. 110. For the expected

term, the Company has "plain-vanilla" stock options, and therefore used a simple average of the vesting period and the contractual term for options granted subsequent to January 1, 2006 as permitted by SAB No. 107.

Forfeitures —ASC Topic 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Synergy estimated future unvested option forfeitures based on its historical experience.

The weighted-average fair value per share of all options granted for the years ended December 31, 2017, 2016 and 2015 estimated as of the grant date using the Black-Scholes option valuation model was $2.47, $1.93 and $3.79 per share, respectively.

A summary of stock option activity and of changes in stock options outstanding under the Plan is presented below:

	Number of Options	Exercise Price Per Share	Weighted Average Exercise Price Per Share	Intrinsic Value (in thousands)	Weighted Average Remaining Contractual Term
Balance outstanding, December 31, 2014	16,567,020	$0.44-17.79	$ 3.20	$ 8,949	7.29 years
Granted	4,961,112	$2.94-9.33	$ 6.51	$ —	
Exercised	(269,720)	$2.98-6.28	$ 4.24	$ 904	
Forfeited	(305,037)	$2.98-9.45	$ 6.22	$ —	
Balance outstanding, December 31, 2015	20,953,375	$0.44-9.12	$ 3.86	$ 42,438	7.15 years
Granted	7,537,000	$2.93-5.63	$ 3.99	$ —	
Exercised	(70,185)	$2.94-4.61	$ 3.17	$ 143	
Forfeited	(553,019)	$2.98-9.12	$ 5.98	$ —	
Balance outstanding, December 31, 2016 [(1)]	27,867,171	$0.44-9.12	$ 3.78	$ 65,618	7.05 years
Granted	3,198,000	$1.89-6.77	$ 3.95	$ —	
Exercised	(99,978)	$0.50-5.34	$ 5.48	$ 201	
Forfeited	(1,096,902)	$0.50-7.91	$ 4.65	$ —	
Balance outstanding, December 31, 2017 [(1)]	29,868,291	$0.44-9.12	$ 3.83	$ 5,346	6.09 years
Exercisable, at December 31, 2017 [(1)]	21,576,652	$0.44-9.12	$ 4.52	$ 5,107	5.05 years

(1) Number of options represented above includes 2,159,500 options that were modified to immediately vest during June 2017.

6. Income Taxes

At December 31, 2017, Synergy has net operating loss carry forwards ("NOLs") aggregating approximately $733.6 million, which, if not used, expire beginning in 2018 through 2037. The utilization of these NOLs is subject to limitations based on past and future changes in ownership of Synergy pursuant to Internal Revenue Code Section 382. The Company has determined that ownership changes have occurred for Internal Revenue Code Section 382 purposes and therefore, the ability of the Company to utilize its NOLs is limited. The Company has no other material deferred tax items. Based upon our analysis, we believe it is more likely than not that the net deferred tax assets will not be realized in the future. Accordingly, a full valuation allowance on the net deferred tax assets has been recorded. Synergy records a valuation allowance against deferred tax assets to the extent that it is more likely than not that some portion, or all of, the deferred tax assets will not be realized. As a result of this valuation allowance there are no income tax benefits reflected in the accompanying consolidated statements of operations to offset pre-tax losses.

The provisions of FASB ASC Topic 740-10-30-7, *Accounting for Income Taxes* were adopted by Synergy on January 1, 2007 and had no effect on Synergy's financial position, cash flows or results of operations upon adoption, as Synergy did not have any unrecognized tax benefits. Synergy's practice is to recognize interest and/or penalties related to income tax matters in income tax expense, and none have been incurred to date. Synergy has no uncertain tax positions subject to examination by the relevant tax authorities as of December 31, 2017 and December 31, 2016. Synergy files U.S. and state income tax returns in jurisdictions with varying statutes of limitations. The 2012 through 2016 tax years generally remain subject to examination by federal and most state tax authorities. The Internal Revenue Service is currently auditing the 2013 and 2015 tax years. So far, there are no changes to the returns. There are no on-going state tax audits but the 2012 through 2016 tax years remain subject to examination by most state authorities.

Synergy periodically files for and receives certain state and local research and development tax credits. As of December 31, 2017 the Company had no outstanding refundable tax credits due. During the year ended December 31, 2016 Synergy reported $121,000 income from R&D tax credits in the Company's statement of operations and none during the year ended December 31, 2015.

7. Commitments and Contingencies

Lease agreements

We lease office space and fleet vehicles under non-cancelable terms. In addition to rent, the leases may require us to pay additional amounts for taxes, insurance, maintenance and other operating expenses.

Synergy's fleet vehicles are leased through December 2020. The total lease cost is approximately $65,000 per month.

Synergy's corporate offices in New York are leased through March 2022. The total monthly rent on this space is approximately $80,000 on straight line basis, prospectively.

In addition, we lease office space for commercial and technical operations in Chesterbrook, Pennsylvania under a lease through December 31, 2022, at a monthly rate of approximately $31,000.

Rent expense was $1,637,000, $1,365,000 and $909,000 for the years ended December 31, 2017, 2016, and 2015, respectively.

Change in Control and Severance Agreements

The Company has agreements with employees which provide for payouts in the event that the Company consummates a change in control. At December 31, 2017, the amount of compensation for which the Company would be liable as a result of this event is approximately $10,300,000, as set forth in the agreements. These employees are also entitled to full vesting of their outstanding equity awards. As of December 31, 2017 and 2016, no amounts have been accrued.

Purchase obligations

Synergy had non-cancelable purchase obligations at December 31, 2017 of approximately $21,300,000, primarily for inventory purchases and the remaining term of the contract sales force.

In the normal course of business, we issue purchase orders to vendors for services and/or inventory. The purchase orders require performance by the vendors, including the delivery of the services and/or goods prior to a specified cancellation date and compliance with product specifications, quality standards and other requirements. In the event of the supplier's failure to meet the agreed upon terms and conditions, we may cancel the order.

Litigation

On November 20, 2017, Cantor Fitzgerald & Co. filed a Complaint against Synergy in the Supreme Court of the State of New York, County of New York for, among other claims, breach of contract for failing to pay Cantor financial advisory and investment banking fees in the amount of $5.25 million it alleges were owed upon the closing of our debt financing in September 2017. On January 5, 2018, Synergy filed an answer to the Complaint denying all the allegations against us, including the allegations that we entered into any agreement with Cantor Fitzgerald & Co. The parties are beginning the discovery process.

On February 8, 2018, a federal securities action, captioned David Lee v. Synergy Pharmaceuticals Inc. et al., was filed in the U.S. District Court for the Eastern District of New York. The complaint names Synergy and certain of its current or former officers and seeks to recover on behalf of a putative class of purchasers of Synergy's common stock between September 5, 2017 and November 14, 2017. On February 14, 2018, another substantially identical lawsuit-captioned Eileen Countryman v. Synergy Pharmaceuticals Inc. et al.-was filed in the same court against the same defendants on behalf of an identical putative class. Both complaints allege that the defendants made false and misleading statements, including in connection with our senior secured loan from CRG Servicing, LLC. Both assert claims under the federal securities laws and seek to recover unspecified damages, as well as interest, costs, and expenses.

In the Company's opinion, a loss in connection with the matters described above is neither probable nor estimable.

8. Stockholders' (Deficit)/Equity

From January 1, 2015 through December 31, 2015, Synergy sold 3,435,998 shares of common stock, pursuant to the ATM Agreement with Cantor, yielding gross proceeds of $14.7 million, at an average selling price of $4.27 per share. Selling agent fees related to above financings from January 1, 2015 through December 31, 2015 were $0.4 million.

On June 8, 2015, Synergy amended its Articles of Incorporation and increased the number of shares of its common stock authorized for issuance from 200,000,000 to 350,000,000 shares.

On July 2, 2015, Synergy filed a "shelf" registration statement on Form S-3 to offer and sell, from time to time in one or more offerings, any combination of common stock, preferred stock, debt securities, warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units comprised of one or more of the other securities, having an aggregate initial offering price not exceeding $250,000,000.

From January 1, 2015 through December 31, 2015 warrants to purchase 189,412 shares of common stock were exercised, yielding proceeds to the Company of $1.0 million. In addition employee stock options to purchase 269,720 shares of common stock were exercised yielding proceeds of $1.1 million.

On March 18, 2016, Synergy entered into an exchange agreement for the exchange of $79.8 million in aggregate principal amount of the Notes, representing approximately 50% of the outstanding aggregate principal amount of Notes, for 35.3 million shares of Synergy's common stock, with a total of 25.6 million shares representing the conversion price of $3.11 pursuant to the existing terms of the Notes. Synergy also issued approximately 872,000 shares at the five day average share price of $2.81 in payment of accrued and unpaid interest of $2.4 million on Notes accepted in the Exchanges, with such shares included in the Shares issued in connection with conversion of Senior Convertible Debentures in the Consolidated Statement of Changes in Stockholders' Equity/(Deficit). In addition, Synergy issued 9.6 million shares of common stock as an inducement for Note holders to convert their Notes into Synergy common stock and recognized debt conversion expense of $25.6 million in the exchange.

In November 2016 Synergy exchanged $55.7 million in aggregate principal amount of the Notes, representing approximately 70% of the outstanding aggregate principal amount of Notes, for 20.5 million shares of Synergy's common stock, with a total of 17.9 million shares representing the conversion price of $3.11 pursuant to the existing terms of the Notes. The amortization of deferred debt costs was accelerated consistent with the 70% reduction of aggregate principal amount this transaction represented, and resulted in additional interest expense of approximately $2 million. The Company recognized debt conversion expense of $14.5 million representing 2.6 million shares in the exchange.

From January 1, 2016 through December 31, 2016, $135.5 million aggregate principal amount of the Notes was converted into approximately 56.6 million shares of Synergy common stock.

On May 5, 2016, Synergy announced that it had entered into definitive agreements with certain institutional investors to sell 29,948,334 shares of common stock at a price of $3.00 per share. The shares were offered and sold directly to institutional investors by the Company in a registered direct offering conducted without an underwriter or placement agent. The gross proceeds from the offering were approximately $89.8 million. The offering closed on May 6, 2016.

From January 1, 2016 through December 31, 2016 warrants to purchase 2,430,656 shares of common stock were exercised, yielding proceeds to us of $11.3 million.

On January 31, 2017, Synergy entered into an underwriting agreement with Cantor Fitzgerald & Co., as representative of several underwriters, to issue and sell 20,325,204 shares of common stock of the Company in an underwritten public offering pursuant to a Registration Statement on Form S-3 and a related prospectus and prospectus supplement, in each case filed with the Securities and Exchange Commission (the "Offering"). The public offering price was $6.15 per share of Common Stock. The Offering closed on February 6, 2017, yielding net proceeds of approximately $121.6 million, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

On June 27, 2017, Synergy increased the number of shares of common stock authorized for issuance from 350,000,000 to 400,000,000.

On November 13, 2017, Synergy entered into an underwriting agreement with Jefferies LLC, as representative of the several underwriters, to issue and sell 21,705,426 shares of common stock of the Company together with accompanying warrants ("Warrants") to purchase an aggregate of 21,705,426 shares of Common Stock in an underwritten offering pursuant to a Registration Statement on Form S-3ASR and a related prospectus and prospectus supplement, in each case filed with the Securities and Exchange Commission (the "Offering"). The offering price was $2.58 per share of Common Stock and accompanying Warrant. Net proceeds from the Offering were approximately $52.2 million, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

9. Derivative Financial Instruments

Synergy Derivative Financial Instruments

Effective January 1, 2009, the Company adopted provisions of ASC Topic 815-40, "Derivatives and Hedging: Contracts in Entity's Own Equity" ("ASC Topic 815-40"). ASC Topic 815-40 clarifies the determination of whether an instrument issued by an entity (or an embedded feature in the instrument) is indexed to an entity's own stock, which would qualify as a scope exception under ASC Topic 815-10.

Synergy's warrants issued on November 13, 2017 (See Footnote 8 "Stockholders' (Deficit)/Equity") were recorded as derivative liabilities and the fair value determined using the Monte Carlo simulation. The assumptions to determine fair value at issuance were $2.44 fair value of stock, 2 year warrant term, 1.62% risk free rate, 66% volatility, and 0% dividend yield.

Based upon the Company's analysis of the criteria contained in ASC Topic 815-40, Synergy has determined that certain warrants issued in connection with sale of its common stock must be classified as derivative instruments. In accordance with ASC Topic 815-40, these warrants are re-measured at each balance sheet date based on estimated fair value, and any resultant changes in fair value are recorded in the Company's statement of operations. The Company estimates the fair value of certain warrants using the *Black-Scholes* option pricing model or a Monte Carlo simulation in order to determine the associated derivative instrument liability and change in fair value described above. The range of assumptions used to determine the fair value of the warrants at each period end was:

	Year Ended December 31, 2017	Year Ended December 31, 2016	Year Ended December 31, 2015
Fair value of Synergy common stock	$ 2.23	$ 6.09	$ 5.67
Expected warrant term	0.2 - 1.9 years	1.2 years	2.2 years
Risk-free interest rate	1.34% - 1.78%	1.03%	1.18%
Expected volatility	50%-67%	50%	50%-80%
Dividend yield	—	—	—

Fair value of stock is the closing market price of the Company's common stock at the end of each reporting period when the derivative instruments are marked to market. Expected volatility is a management estimate of future volatility, over the expected warrant term, based on historical volatility of Synergy's common stock. The warrants have a transferability provision and based on guidance provided in SAB 107 for instruments issued with such a provision, Synergy used the full contractual term as the expected term of the warrants. The risk free rate is based on the U.S. Treasury security rates for maturities consistent with the expected remaining term of the warrants at the date quarterly revaluation.

The following table sets forth the components of changes in the Synergy's outstanding warrants which were deemed derivative financial instruments and the associated liability balance for the periods indicated:

Date	Description	Warrants	Derivative Instrument Liability (in thousands)
12/31/2015	Balance of derivative financial instruments liability	210,000	$ 322
12/31/2016	Change in fair value of warrants during the year ended December 31, 2016	—	(106)
12/31/2016	Balance of derivative financial instruments liability	210,000	216
12/31/2017	Fair value of new warrants issued during the year	21,705,426	21,706
12/31/2017	Change in fair value of warrants during the year ended December 31, 2017	—	(4,340)
12/31/2017	Balance of derivative financial instruments liability	21,915,426	$ 17,582

10. Fair Value Measurements

The following table presents the Company's liabilities that are measured and recognized at fair value on a recurring basis classified under the appropriate level of the fair value hierarchy as of December 31, 2016 and December 31, 2017:

($ in thousands)

Description	Quoted Prices in Active Markets for Identical Assets and Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Balance as of December 31, 2016	Quoted Prices in Active Markets for Identical Assets and Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Balance as of December 31, 2017
Derivative liabilities related to Warrants	$ —	$ —	$ 216	$ 216	$ —	$ —	$ 17,582	$ 17,582

The following table sets forth a summary of changes in the fair value of the Company's Level 3 liabilities for the year ended December 31, 2017 and December 31, 2016:

($ in thousands)

Description	Balance as of December 31, 2015	(Gain) or loss recognized in earning from Change in Fair Value	Balance as of December 31, 2016	Fair Value of warrants upon issuance	(Gain) or loss recognized in earning from Change in Fair Value	Balance as of December 31, 2017
Derivative liabilities related to Warrants	$ 322	$ (106)	$ 216	$ 21,706	$ (4,340)	$ 17,582

The unrealized gains or losses on the derivative liabilities are recorded as a change in fair value of derivative liabilities in the Company's statement of operations. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. At each reporting period, Synergy reviews the assets and liabilities that are subject to ASC Topic 815-40. At each reporting period, all assets and liabilities for which the fair value measurement is based on significant unobservable inputs or instruments which trade infrequently and therefore have little or no price transparency are classified as Level 3.

11. Property and Equipment

Property and equipment, net of accumulated depreciation, consisted of the following:

($ in thousands)	December 31, 2017	December 31, 2016
Furniture and equipment	$ 403	$ 357
Leasehold improvement	1,356	665
Less accumulated depreciation and amortization	(625)	(429)
Property and equipment, net	$ 1,134	$ 593

Depreciation and amortization expense for the years ended December 31, 2017, 2016 and 2015 were approximately $165,000, $233,000 and $163,000, respectively.

12. Quarterly Consolidated Financial Data (Unaudited)

	Quarter Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017 [(b)]
	(dollars in thousands, except share and per share data)			
Net sales	$ 98	$ 2,314	$ 5,008	$ 9,400
Cost of goods sold	1,626	1,643	1,722	3,820
Gross profit	(1,528)	671	3,286	5,580
Costs and Expenses:				
Research and development	18,411	22,069	5,876	1,990
Selling, general and administrative	42,788	52,185	45,110	41,779
Loss from Operations	(62,727)	(73,583)	(47,700)	(38,189)
Other Loss:				
Interest expense, net	(790)	(345)	(1,226)	(2,909)
Debt conversion expense	(1,209)	—	—	—
Change in fair value of derivative instruments—warrants	122	39	55	4,124
Total Other Loss	(1,877)	(306)	(1,171)	1,215
Net loss	$ (64,604)	$ (73,889)	$ (48,871)	$ (36,974)
Weighted Average Common Shares Outstanding—basic and diluted (a)	215,484,670	224,948,622	224,954,941	235,924,350
Net Loss per Common Share—basic and diluted (a)	$ (0.30)	$ (0.33)	$ (0.22)	$ (0.16)

(a) Basic and diluted EPS are computed independently for each of the periods presented. Accordingly, the sum of the quarterly EPS amounts may not agree to the total for the year.

(b) Net sales for the quarter ended December 31, 2017 includes $2.2 million of revenue recognized as a result of our ability to make a reasonable estimate for the right of return.

	Quarter Ended			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
	(dollars in thousands, except share and per share data)			
Net sales	$ —	$ —	$ —	$ —
Costs and Expenses:				
Research and development	20,679	25,906	24,065	16,406
Selling, general and administrative	6,871	10,954	14,417	25,992
Loss from Operations	(27,550)	(36,860)	(38,482)	(42,398)
Other Loss:				
Interest expense, net	(7,036)	(1,673)	(1,674)	(3,007)
Debt conversion expense	(25,615)	—	—	(14,543)
Tax credits	—	—	—	126
Change in fair value of derivative instruments—warrants	260	(23)	(87)	(45)
Total Other Loss	(32,391)	(1,696)	(1,761)	(17,469)
Net Loss	$ (59,941)	$ (38,556)	$ (40,243)	$ (59,867)
Weighted Average Common Shares Outstanding—basic and diluted (a)	117,626,669	168,127,144	179,786,580	190,093,786
Net Loss per Common Share—basic and diluted (a)	$ (0.51)	$ (0.23)	$ (0.22)	$ (0.31)

(a) Basic and diluted EPS are computed independently for each of the periods presented. Accordingly, the sum of the quarterly EPS amounts may not agree to the total for the year.

13. Subsequent Events

On February 28, 2018, Synergy announced a licensing, development and commercialization agreement with Cipher Pharmaceuticals Inc (Cipher). Under the terms of the agreement, Synergy will receive an upfront payment of $5.0 million and is eligible for an additional milestone payment, as well as royalties from product sales in Canada. The agreement provides that Synergy will be responsible for manufacturing and supplying finished product to Cipher.

On February 26, 2018, Synergy and CRG amended the Term Loan Agreement dated September 1, 2017. Under the terms of the amendment, the 2nd tranche borrowing of $100 million prior to February 28, 2018, was replaced with three separate tranches to borrow $25 million, $25 million and $50 million on or before June 30, 2018, September 30, 2018 and December 31, 2018, respectively. Additionally, the total amount of the commitment was reduced from $300 million to $200 million (excluding PIK loans) and the Minimum Market Capitalization covenant of $300 million was revised to be 200% of the outstanding principal amount of loan (excluding PIK loans).