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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2016

OR

☐ **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 001-37880

Novan, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**20-4427682**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
4105 Hopson Road Morrisville, North Carolina	**27560**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (919) 485-8080

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 per share	The NASDAQ Global Market

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

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

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

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 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 X 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 (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes X No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) 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. X

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	X (Do not check if a small reporting company)	Small reporting company	☐

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

As of June 30, 2016, the last business day of the registrant's most recently completed second fiscal quarter, the registrant was a privately-held company and there was no established public market for the registrant's common stock. The registrant's common stock began trading on the NASDAQ Global Market on September 21, 2016. The aggregate market value of common stock held by non-affiliates of the registrant computed by reference to the closing price of the registrant's common stock on September 21, 2016 of $18.10 was approximately $212.5 million (assuming the closing of the registrant's initial public offering and the conversion of all outstanding shares of the registrant's convertible preferred stock to shares of common stock immediately prior to the closing of the offering).

The number of shares of registrant's common stock outstanding as of March 17, 2017 was 15,969,493.

Portions of the registrant's proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant's 2017 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant's fiscal year ended December 31, 2016.

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SPECIAL NOTE ABOUT FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (this "Annual Report") contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Act of 1934, as amended (the "Exchange Act"), that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "potential," "predict," "project," "estimate," or "continue" and similar expressions or variations.

These statements are based on the beliefs and assumptions of our management based on information currently available to management. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Factors that could cause or contribute to these differences include those set forth in the "Risk Factors" section of this Annual Report.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Such forward-looking statements speak only as of the date of this Annual Report. Except as may be required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date of such statements.

PART I

Item 1. Business.

Overview

We are a late-stage pharmaceutical company focused on redefining the standard of care in dermatology through the development and commercialization of innovative therapies using our nitric oxide platform. Nitric oxide plays a vital role in the natural immune system response against microbial pathogens and is a critical regulator of inflammation. Our ability to harness nitric oxide and its multiple mechanisms of action has enabled us to create a platform with the potential to generate differentiated, first-in-class product candidates. The two key components of our nitric oxide platform are our proprietary Nitricil technology, which drives the creation of new chemical entities, or NCEs, and our topical formulation science, both of which we use to modulate, or "tune," our product candidates for specific indications. We are using our platform to transform a useful, naturally occurring molecule into a therapeutic pipeline for a host of skin diseases.

We are rapidly advancing programs in five dermatological conditions with significant unmet medical need. These are some of the most prevalent diseases in dermatology, and together represent a large market opportunity with an underserved patient population surpassing 150 million Americans and 1.5 billion individuals globally.

Our lead product candidate is SB204, a cosmetically elegant topical gel that targets multiple mechanisms of action for the treatment of acne vulgaris, the most common skin disease in the United States. We recently reported top-line results from two identically designed Phase 3 pivotal clinical trials of SB204 conducted with a total of 2,639 patients with acne vulgaris. SB204 demonstrated statistical significance compared to vehicle on all three co-primary endpoints in one of the trials, but demonstrated statistical significance on only one of three co-primary endpoints in the other trial. We conducted an in-depth examination of the full data sets from these trials, including post hoc analyses, with extensive assistance from third-party expert consultants in biostatistics and regulatory affairs. Based on the results of this analysis, we intend to pursue a pre-submission meeting with the U.S. Food and Drug Administration, or FDA, to discuss the entirety of the SB204 development program in the third quarter of 2017. Our meeting with the FDA could lead to a new drug application, or NDA, submission targeted in the first quarter of 2018, assuming among other things successful completion of our ongoing long-term safety study. Following our meeting with the FDA, we also expect to initiate an additional clinical trial for SB204 to be conducted in parallel with the FDA review to support NDA approval.

Our other product candidates include SB206, SB208 and SB414, which are targeted toward the treatment of either a specific microorganism or inflammatory components of a disease pathology. SB206 is a first-in-class, topical antiviral gel in Phase 2 clinical development for the treatment of viral skin infections such as external genital and perianal warts caused by human papillomavirus, or HPV. We announced top-line results from our Phase 2 clinical trial for SB206 in the fourth quarter of 2016. Based on the data generated in this Phase 2 dose-ranging trial, we expect to discuss the entirety of the SB206 development program with the FDA in the second quarter of 2017 and, assuming a successful end-of-Phase 2 meeting with the FDA, plan to initiate our late-stage program with Phase 3 pivotal clinical trials of SB206 by the end of 2017. SB208 is a topical broad-spectrum antifungal product candidate for the treatment of fungal infections of the skin and nails. We commenced Phase 2 clinical testing of SB208 for the treatment of infections caused by dermatophytes such as *Trichophyton rubrum,* or *T. rubrum*, in July 2016, completed enrollment in December 2016 and expect to announce top-line results in the second quarter of 2017. SB414, a topical cream in preclinical development for the treatment of inflammatory skin diseases such as psoriasis and atopic dermatitis, rounds out the current pipeline. We expect to initiate clinical development of SB414 in the second quarter of 2017 with the filing of an Investigational New Drug application, or IND, followed by a Phase 2 proof-of-concept study in patients with psoriasis.

Nitric oxide is one of the most researched molecules in human physiology and has been extensively studied in many areas of medicine including in microbial diseases and in the modulation of inflammation. However, the scarcity of nitric oxide-based therapeutic products is due to the challenges associated with controlling the release of a gas, the poor stability and low storage capacity of nitric oxide-loaded molecules, the inability to target specific tissues and the toxicity of several small molecules used as backbones to store nitric oxide. We believe the following key components of our nitric oxide platform fuel the creation of differentiated product candidates and address each of these limitations:

(1) **Our Nitricil technology** enables us to engineer tunable NCEs that allow for the stable chemical storage of large amounts of nitric oxide in solid form by loading it on an inert macromolecule, or polymer. The advantages of our proprietary Nitricil technology include tunability, stability, high storage capacity, targeted delivery and what we believe is an attractive safety profile. Our ability to select from several nitric oxide-loaded starting materials has driven our library of over 200 Nitricil compositions, each of which possesses a unique nitric oxide release profile.

(2) **Our formulation science** enables us to further tune the release of nitric oxide when applied to the skin by using proprietary combinations of inactive ingredients. This additional level of control enables us to use one NCE for multiple indications by altering the nitric oxide pharmacology with the composition of the topical formulation. This component of our nitric oxide platform creates an additional barrier to entry, which we believe positions us to prolong the period of market exclusivity for each of our product candidates. Additionally, our formulation science allows us to customize the drug delivery method for the relevant anatomical location of a skin disease while considering physician and patient preferences for aesthetically pleasing and convenient products.

We maintain exclusive, worldwide commercial rights for all product candidates currently in our pipeline, with the exception of the rights we licensed to Sato Pharmaceutical Co., Ltd., or Sato, in January 2017 to develop, use and sell SB204 in certain topical dosage forms in Japan for the treatment of acne vulgaris. Our intent is to build a dermatology-focused sales organization, with approximately 75 representatives in the field, to sell our product candidates that receive regulatory approval in the United States. Our sales force will initially target high-volume prescribing dermatologists and other healthcare providers. Our commercialization strategy will leverage our NCEs with differentiated mechanisms of action to enhance reimbursement potential and facilitate broad patient access. We are also evaluating strategic partnerships to commercialize our dermatology products in select international markets, such as the Sato license agreement. We believe that our management team's significant experience in nitric oxide science, drug development and commercialization of dermatological products positions us to execute on our vision to be a commercially successful leader in the field of dermatology.

Our Dermatology-Focused Nitric Oxide Platform

Why Nitric Oxide?

Nitric oxide, or NO, is a two-atom molecule that is produced naturally by the human body. Since the Nobel Prize-winning discovery in 1998 that nitric oxide is responsible for regulating blood flow, or vasodilation, the effects of nitric oxide have been extensively studied in many areas of physiology, including in microbial diseases and in the modulation of inflammation.

As a fundamental component in host defense against invading organisms, cells of the immune system naturally generate nitric oxide using the enzyme nitric oxide synthase, or NOS, and the amino acid precursor L-arginine. Nitric oxide is released in a targeted manner to kill microbial pathogens, including bacteria, fungi and viruses. Nitric oxide and its metabolites drive cell death within bacteria and fungi by targeting metal centers or amino acids on proteins critical to sustaining microbial viability. In virally infected cells, nitric oxide inhibits viral replication by binding directly to free sulfurs or metals that are a part of key enzymes that can induce apoptosis, or programmed cell death, in cells where tumor suppressors have been degraded or disabled.

We believe that nitric oxide has significant potential as a novel antimicrobial agent due to its multiple mechanisms of action and its ability as a gas to diffuse freely through cell membranes unlike many other pharmaceutical agents. Importantly, the pharmacologic activity of nitric oxide is such that its production is localized at or near the site of infection. Because nitric oxide is a key component of the immune system's natural response to invading organisms,

we believe that it may provide an ideal therapeutic solution for degrading and killing microorganisms without the development of antimicrobial resistance.

Beyond nitric oxide's essential role in pathogen control, a large number of cells produce and respond to nitric oxide for several other immunoregulatory functions. According to an article published in *Nature Immunology* in 2001, nitric oxide exerts its anti-inflammatory and immunosuppressive effects in part through the inhibition of T cell proliferation and leukocyte recruitment. The modulation of signaling cascades, transcription factors like NF-κB, and enzymes that process cytokine precursors are all mechanisms by which nitric oxide exerts its anti-inflammatory effects. Additionally, macrophage production of nitric oxide has been reported to suppress T helper type 1 cell responses and lead to the induction of a new class of nitric oxide-derived regulatory T cells, reported in the *Proceedings of the National Academy of Sciences* in 2007 to inhibit the pro-inflammatory Th17 differentiation and function.

Limitations of Other Nitric Oxide-Based Approaches

Despite its therapeutic potential, there is currently only one FDA-approved use of nitric oxide, which is for the treatment of pulmonary hypertension in neonatal infants with nitric oxide gas. However, the delivery of nitric oxide from a gas tank is inconvenient and limits practical applications. The scarcity of nitric oxide-based products is due to the historical challenges associated with developing safe and effective approaches for the chemical storage and controlled release of a gas for therapeutic applications. Synthetic approaches for creating molecules that store nitric oxide in solid form have significant limitations that have prevented the translation of these laboratory chemistries into commercially viable products. Some of these key limitations include:

- ***Lack of tunability***—Therapeutic delivery of nitric oxide to patients at safe and effective levels requires the ability to control the release rate to selectively modulate a specific disease pathology. Other chemical approaches release or donate nitric oxide either too fast or too slow, rendering them potentially unsafe or therapeutically ineffective.
- ***Unfavorable stability profile***—Most nitric oxide-loaded molecules in development decompose too rapidly, prematurely releasing nitric oxide and impairing shelf life stability. Based on the chemistries involved, slight increases in temperature, exposure to ambient humidity or irradiation with light all significantly diminish nitric oxide potency.
- ***Low storage capacity***—Other small molecule strategies only permit the loading, or storage, of one or two units of nitric oxide per unit of drug, leaving them with an inability to deliver sufficient therapeutic quantities of nitric oxide to the desired site. Conversely, macromolecular scaffolds to date have had limited storage sites to bind nitric oxide as a percentage of total weight.
- ***Lack of targeting***—Other nitric oxide-based approaches are primarily small molecule-based and are limited in their ability to be delivered to or target specific tissues, and the organ destination or systemic half-life is dictated by the molecule to which nitric oxide was attached.
- ***Backbone toxicity***—Several small molecules developed in laboratory settings used to store nitric oxide have never been translated into clinical use due to the carcinogenic potential of nitrosamines or risk of cyanide poisoning from sodium nitroprusside.

Advantages of Our Nitric Oxide Platform

We believe that our platform harnesses the potential of nitric oxide in a manner that leads to the creation of differentiated product candidates that address all these limitations by (1) engineering tunable NCEs using our Nitricil technology and (2) using our formulation science to customize the drug delivery method for the anatomical location of a skin disease.

As a result, we believe that we are able to unlock the therapeutic potential of nitric oxide in numerous dermatological indications. We have chosen to focus on dermatology because nitric oxide's multiple mechanisms of action converge in the largest organ of the body, the skin. All of the major cell types that comprise the three layers of the skin, including keratinocytes, fibroblasts, melanocytes and endothelial cells, are capable of producing nitric oxide at different rates, and these cells play an important part in organizing the skin's unique ability to repair itself

and maintain barrier function. Our ability to tune its release profile allows us to deploy nitric oxide into its wide range of pharmacological effects when host systems fail or are overwhelmed by invading microorganisms.

The two key components of our nitric oxide platform are described below in further detail.

(1) Our Nitricil Technology

Our innovative Nitricil technology allows for the chemical storage of large amounts of nitric oxide in solid form by loading it on a polysiloxane macromolecule. The macromolecule is a polymer comprised of two monomers, one that forms the scaffold and the other that stores nitric oxide by converting amines to diazeniumdiolate nitric oxide donors. The resulting salts of nitric oxide in solid form are stable under ambient conditions, but can liberate nitric oxide in aqueous physiological environments. Upon application to the body, Nitricil compounds release the gaseous nitric oxide with release rates further controlled by local pH. Details on the synthesis and characterization of Nitricil have been published in peer reviewed journals by Novan co-founder, Dr. Mark Schoenfisch.

Our ability to select from eight unique nitric oxide-loaded monomers and two discrete scaffold monomers, to alter the polymerization ratio between the two monomers and to vary the counterion has led to our current library of over 200 different Nitricil compositions, each of which possesses a unique nitric oxide release profile. We use our Nitricil technology to generate new NCEs tailored to address the pharmacological needs of specific skin diseases.

The macromolecular delivery vehicles created by our Nitricil technology are designed to address the limitations associated with the delivery of nitric oxide. The key advantages of our Nitricil technology include:

- ***Tunability***—We employ a synthetic approach that allows us the ability to engineer NCEs, each with unique nitric oxide release properties, through the alteration of the macromolecule size, hydrophobicity, buffer capacity and the targeted local chemical environment.
- ***Favorable stability profile***—The ability to keep nitric oxide covalently bound as a salt on the macromolecule enables drug stability and therefore prolonged storage until administration to the patient.
- ***High storage capacity***—Our proprietary selection of monomeric starting materials allows us to avoid dependence on external polymer chemistry that is not rationally designed to load nitric oxide. This customized approach for the assembly of Nitricil macromolecules enables us to store a large percentage of nitric oxide by weight, and at the storage level we believe is necessary to deliver therapeutic quantities of nitric oxide.
- ***Ability to be targeted***—The macromolecular scaffold overcomes the challenges of site-specific delivery through control over particle size, electrostatic potential and surface functionality, all tailored to bind to a specific tissue target. For example, we have the ability to build our macromolecular scaffold to a desired size, ranging from small nanometer sized particles up to micron sized particles required to localize the delivery to the skin and prevent systemic exposure.
- ***Attractive safety profile***—We use an inert and biocompatible macromolecular scaffold that does not interact adversely with the body following the release of nitric oxide.

(2) Our Formulation Science

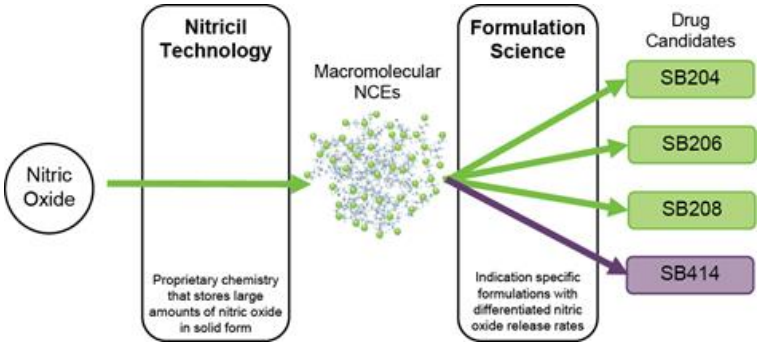
The topical formulations of dermatology products have a significant impact on product performance and synthesizing a stable NCE is only half of the process required to unlock drugable nitric oxide. The nitric oxide must remain stable when compounded into the final product, and classical approaches in formulation science may be incompatible with our Nitricil compounds. Our Nitricil-based NCEs are very sensitive to small changes in formulation. As a result, we select a customized set of ingredients based on their known safety profile, chemical compatibility, lack of irritation potential and the desired cosmetic properties, while allowing for the controlled release of nitric oxide when administered to the patient. This fine tuning of nitric oxide release rate using a proprietary combination of inactive ingredients creates a unique nitric oxide release profile for each indication of interest. In our discussions with the FDA, the agency has indicated its understanding of the importance of release rate on pharmacology and as a critical quality attribute of our potential products.

Historically, the prescribing behavior of dermatologists has been significantly influenced by formulation type. Cosmetically elegant formulations are desired in acne vulgaris care to maintain patient compliance while ointment formulations are known to drive penetration of the active ingredients deeper into the plaques of psoriasis. Hard-to-treat locations of the body, such as the top of the head, are more accessible with sprays and foams. Creams provide both moisturizing and barrier-repair components useful for cracked, drying or irritated skin like that found with atopic dermatitis. Therefore, we plan to utilize dermatologist and patient preferences for certain topical formulations to create differentiated nitric oxide therapies. In addition to tailoring the product formulation, we are able to adjust the dose to target specific diseases and plan to package our product candidates in indication-specific containers.

As shown in Figure 1 below, our Nitricil technology and formulation science are used in combination to effectively transform a useful, naturally occurring molecule into a therapeutic pipeline of product candidates.

Figure 1:

Our Nitric Oxide Platform



Our goal with each product candidate is to balance the need for safe, effective and convenient delivery of nitric oxide with physician and patient preferences for formulation aesthetics. Furthermore, we believe our nitric oxide platform allows us to leverage our knowledge of the analytical methodologies, process development, scale-up manufacturing and tracking of nitric oxide metabolites *in vivo* and a safety profile that translates across multiple Nitricil based NCEs to reduce future development expenses and timelines across our entire product candidate pipeline.

Our Strategy

Our strategy is to develop and commercialize novel nitric oxide-based therapies that redefine the standard of care in dermatology. We are focused on creating topical, dermatological therapies in indications with underserved patient populations and well-defined clinical and regulatory development pathways. In order to pursue our strategy, we plan to:

- ***Complete development of our late-stage product candidate, SB204, and submit for regulatory approval in the United States.*** In the first quarter of 2017, we reported top-line results from two identically designed Phase 3 pivotal clinical trials for our lead product candidate, SB204, in a total of 2,639 patients with acne vulgaris. SB204 demonstrated statistical significance compared to vehicle on all three co-primary endpoints in one of the trials, but demonstrated statistical significance on only one of three co-primary endpoints in the other trial. We conducted an in-depth examination of the full data sets from these trials, including post hoc analyses, with extensive assistance from third-party expert consultants in biostatistics and regulatory affairs. Based on the results of this analysis, we intend to pursue a pre-submission meeting with the FDA to discuss the entirety of the SB204 development program in the third quarter of 2017. Our meeting with the FDA could lead to an NDA submission targeted in the first quarter of 2018, assuming among other things successful completion of our ongoing long-term safety study.

Following our meeting with the FDA, we also expect to initiate an additional clinical trial for SB204 to be conducted in parallel with the FDA review to support NDA approval.

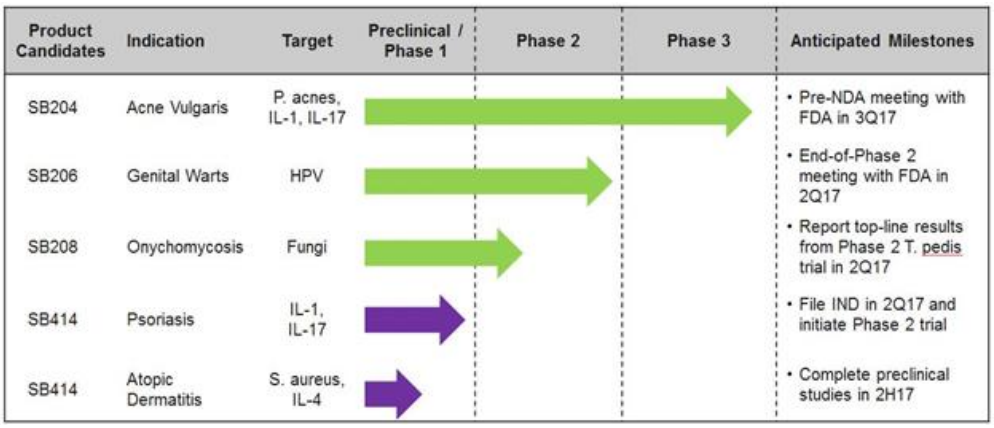
- ***Achieve proof-of-concept for our antimicrobial product candidates and advance them into late-stage development.*** We are expanding our platform through the initiation of Phase 2 proof-of-concept trials to evaluate the therapeutic potential of nitric oxide as an antiviral and antifungal agent. In 2015, we commenced a Phase 2 clinical trial with SB206 to evaluate tolerability, safety and efficacy in patients with external genital and perianal warts, and we announced top-line results of the trial in the fourth quarter of 2016. Based on the results of our Phase 2 trial, we are planning an end-of-Phase 2 meeting with the FDA for the second quarter of 2017 and, assuming a successful end-of-Phase 2 meeting with the FDA, the initiation of our Phase 3 development program for the antiviral gel by the end of 2017. As part of our ongoing efforts targeting microbial skin infections, we initiated our Phase 2 clinical program with SB208 in July 2016 and completed enrollment in December 2016. The Phase 2 program will include the ongoing clinical trial designed to assess tolerability, safety and antifungal activity of SB208 in patients with athlete's foot infected with dermatophytes such as *T. rubrum* and a second dose-ranging clinical trial of SB208 in patients with onychomycosis, a *T. rubrum* infection of the nails. We are targeting to report top-line results for the ongoing SB208 Phase 2 trial in the second quarter of 2017.
- ***Achieve proof-of-concept for our immunomodulatory product candidate and advance it into late-stage development.*** SB414 is our cream-based product candidate currently in preclinical studies for the topical treatment of inflammatory skin diseases such as psoriasis or atopic dermatitis. In preclinical studies to date, we observed that SB414 significantly ($p<0.05$) reduced composite psoriasis scores, which consist of erythema and plaque scores, and pro-inflammatory cytokines, including interleukin-17, or IL-17, in a psoriasis mouse model. Based on the data generated in this preclinical in vivo study, as well as data from toxicology studies currently being conducted, we expect to initiate clinical development in the second quarter of 2017 with the filing of an IND, followed by a Phase 2 proof-of-concept trial of SB414 as a topical treatment for psoriasis, which will include an active head-to-head comparator. The Phase 2 study is also designed to evaluate key biomarkers such as IL-17 in lesions in patients in the treatment arm with the strongest response.
- ***Expand our existing pipeline by efficiently developing topical nitric oxide-based product candidates for new dermatological indications.*** We believe that the breadth of our nitric oxide platform will enable us, independently or with strategic collaborators, to develop and commercialize future nitric oxide-based product candidates for the treatment of several additional anti-microbial and anti-inflammatory dermatological indications. Also, we believe that our technology may be further applied to the field of medical aesthetics. Finally, we believe that our focus on topical dermatological applications for nitric oxide enables efficiently developed product candidates that potentially have lower development costs, reduced risk of side effects and a faster time to market than systemically administered therapies.
- ***Establish our own sales and marketing organization to commercialize our products in the United States.*** Our intent is to build a dermatology-focused sales organization, with approximately 75 representatives in the field to sell our product candidates that receive regulatory approval in the United States. Our sales force will initially target high-volume prescribing dermatologists and other healthcare providers. Our commercialization strategy will also leverage our NCEs with new mechanisms of action to enhance reimbursement potential and facilitate broad patient access. We have begun to execute on this strategy by hiring key executives with a strong track record in commercializing dermatology products. Additionally, we continue to evaluate strategic partnerships to commercialize our dermatology products in select international markets, such as the Sato license agreement.

Our Product Candidates

We have conducted and plan to conduct the clinical development of our product candidates under one or more INDs filed with the FDA. We are the sponsor of a single IND that became effective in September 2012, which covers our NVN1000 NCE and under which we are conducting clinical trials on our product candidates SB204 and SB206 in the United States. NVN1000 rapidly releases the large concentrations of nitric oxide needed to replicate the burst created by immune cells. NVN1000-based product candidates are aimed at deploying the antibacterial, antiviral and antifungal and anti-inflammatory activity of nitric oxide and are currently in development for the treatment of acne

vulgaris (SB204), HPV-associated genital warts (SB206), onychomycosis (SB208) and psoriasis and atopic dermatitis (SB414). Our SB208 product candidate is currently in a clinical study outside of the United States. We intend to submit new INDs prior to initiating our Phase 3 programs for SB206 and SB208. Assuming successful completion of our ongoing toxicology studies for SB414, we expect to submit an IND covering the cream product candidate in the second quarter of 2017 and initiate clinical development of SB414 for the treatment of psoriasis. The status of our development programs is summarized in Table 1.

Table 1:



SB204 for the Treatment of Acne Vulgaris

We are developing SB204 as a once-daily, fast-acting, topical first-line monotherapy for the treatment of acne vulgaris. SB204 contains the NVN1000 active pharmaceutical ingredient. We believe that acne vulgaris, in addition to being the most common skin disease in the United States, continues to be characterized by unmet medical needs, due to the difficulty of balancing efficacy, systemic safety and cutaneous tolerability, as well as the growing concern with antibacterial resistance with existing therapies. In our more than 3,200-patient SB204 clinical development program, topical application of SB204 has been well-tolerated with no significant safety concerns identified. In maximal-use pharmacokinetic trials that we conducted in adult and pediatric patients with acne vulgaris, we observed no detectable systemic exposure from SB204 following its topical application.

We reported top-line results from two identically designed Phase 3 pivotal clinical trials of SB204 for the treatment of acne vulgaris in the first quarter of 2017. SB204 demonstrated statistical significance compared to vehicle on all three co-primary endpoints in one of the trials, but demonstrated statistical significance on only one of three co-primary endpoints in the other trial. We conducted an in-depth examination of the full data sets from these trials, including post hoc analyses, with extensive assistance from third-party expert consultants in biostatistics and regulatory affairs. Based on the results of this analysis, we intend to pursue a pre-submission meeting with the FDA to discuss the entirety of the SB204 development program in the third quarter of 2017. Our meeting with the FDA could lead to an NDA submission targeted in the first quarter of 2018, assuming among other things successful completion of our ongoing long-term safety study. Following our meeting with the FDA, we also expect to initiate an additional clinical trial for SB204 to be conducted in parallel with the FDA review to support NDA approval.

Acne Vulgaris Disease Overview

Acne vulgaris is the most common skin disease in the United States. According to The American Academy of Dermatology, approximately 50 million Americans have acne vulgaris. The disease ranges in severity from mild to severe cystic acne vulgaris and causes both physical and psychological effects, including permanent scarring, anxiety, depression and poor self-esteem. Even in cases of mild acne vulgaris, the social stigma associated with the

disease frequently results in significant emotional distress and other psychological issues. Due to the frequency of recurrence or relapse and necessary treatment over a prolonged number of years, the American Academy of Dermatologists considers acne vulgaris to be a chronic inflammatory disease.

Acne vulgaris is caused by genetic and environmental factors and results from the complex interplay of four major pathogenic factors:

- overproduction of oils, or sebum, by the sebaceous gland;
- abnormal keratinization in the follicle, narrowing the pores;
- colonization by the anaerobic, lipophilic bacterium *Propionibacterium acnes*, or *P. acnes*; and
- release of pro-inflammatory mediators into the skin which in turn perpetuate the chronic inflammatory cycle of microcomedo formation.

There are two types of acne lesions, inflammatory and non-inflammatory. The effective treatment of acne vulgaris often requires resolution of both types of lesions. Acne lesions begin when excess sebum production, a pro-inflammatory cascade, or both, result in abnormal proliferation of the cells of the epidermis to clog a follicle, forming a microscopic lesion known as a microcomedo. Non-inflammatory lesions occur when a microcomedo progresses to an open or closed comedone, commonly referred to as a "blackhead" or "whitehead," respectively.

Inflammatory lesions occur when *P. acnes* proliferates in the anaerobic, lipid-rich environment of the microcomedo. *P. acnes* is central to the disease pathology because its endotoxins stimulate pro-inflammatory mediators like toll-like receptors and other inflammatory pathways. These inflammatory lesions are red and painful, and are manifested as papules, pustules or cysts.

Current Treatment Landscape

For more than 30 years, the prescription treatment landscape for acne vulgaris has been predominately served by topical retinoids for the treatment of the non-inflammatory component of the disease and antibiotics for the treatment of the inflammatory component of the disease.

Topical retinoids, such as tretinoin, adapalene and tazarotene, target the abnormal proliferation of cells to stop the narrowing of the follicle and also inhibit the pro-inflammatory cascade that initiates lesion formation. Retinoids often show efficacy over prolonged treatment durations, but can lead to undesirable dryness, irritation and scaling.

Antibiotics, topical and systemic, have long been the mainstay of dermatologists to manage the inflammatory lesion component of the disease due to the link between *P. acnes* and inflammation. However, the widespread use and extended treatment periods of antibiotics for over 30 years has led to the emergence of the antibiotic resistance of *P. acnes* and, in turn, the virtual discontinuation of some drugs such as erythromycin from clinical use. Recent attention from the U.S. Centers for Disease Control and Prevention, or CDC, and the World Health Organization, or WHO, on the use of antibiotics and microbial resistance highlights the increasing need to curtail the overuse of antibiotics. According to a 2014 article in *Dermatology Times,* dermatologists represent 1% or less of the U.S. physician population but prescribe almost 5% of the antibiotic prescriptions. Despite the onset of antibiotic resistance, the topical antibiotic clindamycin and clindamycin combination products continue to be prescribed to manage the inflammatory component of the disease. According to IMS, approximately seven million units of products containing clindamycin, monotherapies and combination products combined, were dispensed in the United States in 2015.

As disease severity increases, oral antibiotics are employed to supplement topical antibiotics in the management of inflammatory lesions, but often demonstrate limited efficacy against the non-inflammatory lesion component of the disease, which continues to be managed with topical retinoids. For example, Solodyn, a branded oral minocycline, achieved sales of over $700 million in 2011, according to IMS, notwithstanding its narrowly defined indication for inflammatory lesions of moderate to severe acne vulgaris. In addition, the prescribing information for Solodyn specifically states that it did not demonstrate any effect on non-inflammatory acne vulgaris lesions. Oral antibiotics

are also associated with systemic side effects, including gastrointestinal tract irritation, photosensitivity of skin, headache, dizziness, anemia, bone and joint pain and nausea.

The most effective therapies for acne vulgaris are those that can address more than one of the major causes of acne vulgaris pathogenesis. This has led to the development of fixed-dose combination products that combine antibiotics, retinoids or the over-the-counter agent benzoyl peroxide, or BPO, to create new branded medicines. Approved topical combination products have demonstrated modest improvements in clinical efficacy over monotherapies but also combine the tolerability issues and side effects associated with each active ingredient in the combination drug. These combination products highlight the limited innovation in acne care products over the last 30 years. Product manufacturers have successfully negotiated with managed care providers to ensure patient access to these branded products in a heavily genericized market, despite these products constituting the combination of two generically available agents. For example, Epiduo, the branded topical combination of benzoyl peroxide and adapalene, had U.S. sales volume of over one million units in 2015, amounting to $470 million in sales, according to IMS.

The oral retinoid isotretinoin, also known as Accutane, is the only drug claiming to affect all four pathogenic factors associated with acne vulgaris. However, the strong efficacy profile of isotretinoin is compromised by its severe side effect profile, given that the drug is a known teratogen that can cause birth defects and has also been linked to depression, psychosis and, in extreme circumstances, suicide. Therefore, its use has been reserved for the most severe form of the disease, and in 2009, the manufacturer of Accutane withdrew the branded product from the market.

As a result of the limited ability of single agent antibiotics and retinoids to act significantly on both the non-inflammatory and inflammatory components of acne vulgaris, physicians have adopted a poly-pharmacy approach to treatment by prescribing several treatment modalities for the management of the disease.

Our Nitric Oxide-Based Solution for the Treatment of Acne Vulgaris

We believe that SB204 has the potential to address the limitations of the current treatment landscape by potentially offering an efficacious topical monotherapy for both lesion types with a favorable safety profile. In our preclinical studies, nitric oxide was effective in rapidly killing *P. acnes*. Moreover, after many lifecycles exposed to our drug, the bacteria did not develop resistance to our drug. The antimicrobial activity of nitric oxide is due to the multiple nitrosative species generated upon exposure to nitric oxide that lead to bacterial damage.

Nitric oxide is also an endogenous component of the innate immune response. According to a 2015 report in the *Journal of Investigative Dermatology*, nitric oxide inhibits *P. acnes* -stimulated inflammatory cytokine release in peripheral blood mononuclear cells and cultured human keratinocyte cells through inhibition of caspase-1. Caspase-1 is known to activate pro-inflammatory cytokines, including IL-1ß, a cytokine known to induce keratinocyte proliferation and lead to the narrowing of the follicle at the beginning of an acne vulgaris lesion. As reported in an article published in *Nature Immunology* in 2012, nitric oxide also has the potential to disrupt the propagation of IL-17 locally in the skin through its ability to disrupt the assembly and activity of the NLRP3 inflammasome. Recently, a peer-reviewed article in the *British Journal of Dermatology* implicated IL-17 as a key proinflammatory cytokine linked to the mechanism and severity of a number of inflammatory skin diseases, including acne.

We believe that SB204 is a first-in-class immunomodulatory agent and has the following potential advantages over other topical therapies currently used for the treatment of acne vulgaris:

- activity against both lesion types from a single NCE with dual mechanisms of action;
- a superior safety profile due to the lack of systemic exposure;
- favorable skin tolerability profile;
- elimination of patient, parental and societal concerns arising from antibiotic resistance;
- improved patient compliance due to the non-bleaching, non-staining and non-irritating properties of the formulation;

- first-in-class NCE with no generically equivalent substitutes; and
- a convenient, once-daily dosing schedule with no limitations on sunlight exposure.

SB204 Clinical Development Program

To date, the SB204 clinical development program includes one completed first-in-human trial, seven completed Phase 1 clinical trials, two completed Phase 2 clinical trials, two completed Phase 3 clinical trials and an ongoing long-term safety trial involving patients suffering from acne vulgaris.

In the first quarter of 2017, we reported top-line results from two identically designed Phase 3 pivotal clinical trials for our lead product candidate, SB204, in a total of 2,639 patients with acne vulgaris. SB204 demonstrated statistical significance compared to vehicle on all three co-primary endpoints in one of the trials, but demonstrated statistical significance on only one of three co-primary endpoints in the other trial. We conducted an in-depth examination of the full data sets from these trials, including post hoc analyses, with extensive assistance from third-party expert consultants in biostatistics and regulatory affairs. Based on the results of this analysis, we intend to pursue a pre-submission meeting with the FDA to discuss the entirety of the SB204 development program in the third quarter of 2017. Our meeting with the FDA could lead to an NDA submission targeted in the first quarter of 2018, assuming among other things successful completion of our ongoing long-term safety study. Following our meeting with the FDA, we also expect to initiate an additional clinical trial for SB204 to be conducted in parallel with the FDA review to support NDA approval.

In both of our Phase 2 clinical trials, we observed reduction in lesion counts as early as week four and sustained through 12 weeks of treatment, with separation from vehicle comparable to that observed for currently available combination products. Vehicle control in our clinical trials consists of the same topical gel formulation used in our product candidate without the active ingredient. The combined results of our Phase 2a and Phase 2b clinical trials showed a dose-dependent response against inflammatory lesions. These data were important in selecting SB204 4% once-daily as the minimum effective dose for the Phase 3 trials.

The topical application of SB204 to patients with acne vulgaris has been well-tolerated, with no safety concerns identified. In a completed maximal-use pharmacokinetic study, we observed no detectable systemic exposure to the drug itself and no difference in biomarkers for nitric oxide exposure between patients treated twice-daily with an 8% concentration of SB204, or SB204 8%, or vehicle. In a separate pharmacokinetic study in adolescents treated with SB204 4% once-daily for 21 days there again was no detectable systemic exposure to the parent compound, NVN1000, and no change in endogenous nitrate levels after single or repeat dosing. The analysis of electrocardiograph data on patients treated with the therapeutic dose SB204 4%, or with three times the therapeutic dose of SB204 12%, showed no clinically significant effects on heart rate or any other cardiovascular assessments. The adverse events, or AE, profile has been similar in SB204 and vehicle-treated patients for the entire development program and no treatment-related serious AEs have been reported. Asymptomatic, transient erythema has been observed in some patients treated with SB204, but was resolved within minutes following its application. To date, we have not observed any clinically significant changes in laboratory results, including methemoglobin.

Phase 3 Clinical Program

In two, identically designed Phase 3 multi-center, randomized, double-blinded, vehicle-controlled, parallel group pivotal clinical trials, NI-AC301 and NI-AC302, a total of 2,639 patients, ages 9 and older, with moderate to severe acne were enrolled across a total of 110 sites in the United States, randomized in a 1:1 ratio to two treatment arms, SB204 4% once-daily or vehicle once-daily, and treated over 12 weeks. We previously completed an end-of-Phase 2 meeting with the FDA and submitted the protocols for the Phase 3 program under a special protocol assessment, or SPA, for review by the FDA. We reached agreement with the FDA on the primary endpoints for our Phase 3 clinical trials, but did not pursue a full formal SPA agreement with the FDA.

The co-primary efficacy endpoints in our Phase 3 clinical trials were:

- the absolute change in inflammatory lesion counts from baseline to either week 12 or early termination, or ET;
- the absolute change in non-inflammatory lesion counts from baseline to week 12 or ET; and
- the proportion of success according to the dichotomized IGA. A patient was considered a success if the IGA at week 12 or ET was at least two grades below the baseline score and was either "clear," with a score of 0, or "almost clear," with a score of 1.

The secondary efficacy endpoints were:

- the percent change in inflammatory lesion count from baseline to week 12 or ET;
- the percent change in non-inflammatory lesion count from baseline to week 12 or ET;
- the median time to improvement as assessed by a 35% reduction from baseline in inflammatory lesion counts; and
- the median time to a minimum two-grade improvement in IGA score.

Investigational drug was delivered from a dual chamber pump dispenser consistent with both of our Phase 2 clinical trials. The pump dispensed product from two chambers, containing active gel in one chamber and a buffered hydrogel in the other, or the corresponding vehicle gel in one chamber and a buffered hydrogel in the other, which was mixed together in the palm for approximately five seconds by the patient and applied to the entire face once-daily after washing. We intend to use this dispensing method in our commercial product, if approved. Cutaneous tolerability assessments included evaluation of facial erythema, scaling, dryness, itching and burning or stinging. Other safety assessments include reportable adverse events, physical exams, blood pressure, pulse rate and urine pregnancy tests. Patients returned for post-baseline evaluation after weeks 2, 4, 8 and 12 or prior to an ET.

Of the 2,639 patients enrolled in the two Phase 3 trials, more than 86% of patients in each SB204 and vehicle dose group completed the trials. At baseline across all treatment groups, the mean inflammatory lesion count was approximately 27, and the mean non-inflammatory lesion count was 41. Lesion counts were consistent across treatment groups in both Phase 3 trials, and the mean inflammatory lesion count was consistent with that of the Phase 2b trial. The majority of patients had an IGA score of "moderate," or 3, at baseline.

SB204 demonstrated statistical significance compared to vehicle on all three co-primary endpoints in one of the trials, but demonstrated statistical significance on only one of three co-primary endpoints in the other trial. As shown below in Table 2, the absolute change from baseline in the number of non-inflammatory lesions in NI-AC301 was -15.4, or 39%, for SB204 and -13.4, or 34%, for vehicle (p=0.030), and in NI-AC302 was -14.9, or 42%, for SB204 and -12.3, or 34%, for vehicle (p=0.001). The absolute change from baseline in the number of inflammatory lesions in NI-AC301 was -12.1, or 46%, for SB204 and -11.1, or 43%, for vehicle (p=0.114), and in NI-AC302 was -12.9, or 51%,for SB204 and -10.6, or 41%, for vehicle (p<0.001). The proportion of patients with IGA success in NI-AC301 was 13.4% for SB204 and 13.8% for vehicle (p=0.866), and in NI-AC302 was 18.9% for SB204 and 14.3% for vehicle (p=0.032).

Table 2:

	NI-AC301	NI-AC302
	ITT* (n = 1306)	ITT* (n = 1327)
Non-Inflammatory Lesion Reduction		
SB204	-15.4	-14.9
Vehicle	-13.4	-12.3
p-value	p=0.030**	p=0.001**
Inflammatory Lesion Reduction		
SB204	-12.1	-12.9
Vehicle	-11.1	-10.6
p-value	p=0.114†	p<0.001**
IGA Success		
SB204	13.4%	18.9%
Vehicle	13.8%	14.3%
p-value	p=0.866	p=0.032**

Absolute changes in lesion count reduction are shown as LSMean.
*ITT analysis. Missing data imputed using multiple imputation methodology.
**p<0.05
†In a modified-ITT analysis excluding patients on oral contraceptive prescriptions with an acne indication, the absolute change in inflammatory lesions for NI-AC301 was statistically significant.

The statistical analyses and data shown in Table 2 are on the intent-to-treat, or ITT, population. Randomized clinical trials analyzed by the ITT approach provide unbiased comparisons among the treatment groups. In an ITT population, none of the patients are excluded and the patients are analyzed according to the randomization scheme. In other words, for the purposes of ITT analysis, everyone who is randomized in the trial is considered to be part of the trial regardless of whether he or she is dosed at all or completes the trial per protocol for the recommended duration of treatment. Discontinuations were treated statistically with the multiple imputation methodology for missing data for the SB204 Phase 3 program data sets shown above. P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of less than 0.050 is generally considered to represent statistical significance, meaning that there is a less than five percent likelihood that the observed results occurred by chance.

There are multiple methodologies for handling missing data and other statistical considerations to take into account that the FDA may utilize when analyzing the robustness of any data set during NDA review. As part of our in-depth examination of the full data sets from the Phase 3 trials, we conducted a number of post hoc analyses. The measure of statistical significance on all of the co-primary endpoints for the NI-AC302 trial was consistently strong when analyzed with two other sensitivity analysis methodologies for missing data, last observation carried forward and baseline observation carried forward. We believe this confirms the robustness of the data from the NI-AC302 trial, and these stricter statistical analyses for missing data do not diminish the strength of the data from the NI-AC302 trial. However, these additional analyses do not change the outcomes of the NI-AC301 trial, and the FDA may disagree with our conclusions from the post hoc analyses we conducted.

In a post hoc analysis of the data from the NI-AC301 and NI-AC302 trials in a modified-ITT population that excludes women on oral contraceptive prescriptions with an acne indication such as Yaz or Ortho-Tricyclen, SB204 demonstrated statistically significant reductions over vehicle in both inflammatory and non-inflammatory lesion counts. We believe the inclusion of these 14 patients on birth control, 8 in the SB204 arm of the trial and 6 in the vehicle arm, contributed to the reduced separation from vehicle in the NI-AC301 trial observed for inflammatory lesions in our primary analysis. The FDA had encouraged us, as part of our discussions regarding an SPA, to evaluate treatment effectiveness in women on oral contraceptive prescriptions with an acne indication. Whether or not this subset of patients will be included in future trials is still to be determined.

Both SB204 and vehicle treatments were generally well tolerated in the Phase 3 trials, with less than 2% of patients discontinuing due to treatment-emergent adverse events in aggregate. The most common treatment-emergent adverse events reported in patients treated with SB204, all less than 4% incidence, were application site pain, redness, itching and dryness, with correspondingly low incidences of these same adverse events in those treated with vehicle. Other treatment-emergent adverse events occurring in more than 1% of patients were common cold and headache.

We also assessed cutaneous tolerability by recording the erythema, scaling, dryness, itching and burning or stinging on a four-point scale from 0 to 3, or "none" to "severe," at baseline and at each visit. These measurements are either measured by the physician or reported by the patient. The integrated NI-AC301 and NI-AC302 tolerability data for SB204 is shown in comparison to vehicle-treated patients in Table 3. The table reflects the percentage of patients with any score other than "none" observed at weeks 2 and 12. Acne patients are often experiencing many of these local intolerabilities at baseline, before ever initiating treatment with study drug. In general, more patients treated with SB204 had scores of "mild" or "moderate" than patients treated with vehicle, and scores other than "none" or "mild" were uncommon in either treatment group for any assessment and rarely led to treatment discontinuation or modification. In most cases, maximum severity occurred early, by week 2, during treatment and decreased over time. More than 95% of patients had scores of "mild" or "none" for each of the scoring criteria at week 12.

Table 3:

	SB204									Vehicle								
	Baseline			Week 2			Week 12			Baseline			Week 2			Week 12		
	Mild	Mod	Sev	Mild	Mod	Sev	Mild	Mod	Sev	Mild	Mod	Sev	Mild	Mod	Sev	Mild	Mod	Sev
Erythema[1]	19%	11%	<1%	24%	9%	0%	19%	4%	<1%	19%	9%	0%	19%	6%	0%	15%	3%	<1%
Scaling[1]	12%	1%	0%	14%	1%	0%	9%	1%	0%	11%	1%	0%	8%	<1%	0%	6%	<1%	<1%
Dryness[1]	14%	4%	0%	20%	4%	<1%	17%	2%	<1%	14%	3%	0%	17%	2%	0%	15%	<1%	<1%
Itching[2]	10%	3%	<1%	11%	2%	0%	8%	2%	<1%	9%	2%	0%	9%	<1%	0%	7%	<1%	<1%
Burning / Stinging[2]	8%	2%	0%	20%	3%	<1%	11%	<1%	<1%	7%	2%	0%	16%	2%	0%	9%	<1%	<1%

1 Physician observations
2 Patient reported

NI-AC303, A Phase 3 Multi-Center, Open-Label Study Evaluating the Long-Term Safety of SB204 Once-Daily in the Treatment of Acne Vulgaris, is a long-term safety study currently ongoing in eligible patients who completed 12 weeks of treatment in the NI-AC301 or NI-AC302 trials. We enrolled the last of more than 600 patients for this study in July of 2016, with a maximum planned treatment duration of 40 weeks, and expect to report top-line results in the third quarter of 2017. Additional planned clinical work, which is consistent with other dermatology product development programs, in support of a future NDA submission for SB204 includes Phase 1 clinical trial dermal safety studies required to screen all dermatological drugs in healthy volunteers, which we plan to complete prior to an NDA submission.

NI-AC202: A Phase 2, Multi-Center, Randomized, Evaluator-Blinded, Vehicle-Controlled Clinical Trial Comparing the Efficacy, Tolerability, and Safety of SB204 and Vehicle Once or Twice-Daily in the Treatment of Acne Vulgaris

In a Phase 2 multi-center, double-blinded, clinical trial, 213 patients between the ages of 12 and 40 with moderate to severe acne vulgaris were enrolled and treated over 12 weeks with SB204 2% twice-daily, or BID, SB204 4% twice-daily, SB204 4% once-daily or vehicle once or twice-daily. The patients enrolled in the study were randomized in a

2:2:2:1:1 ratio, yielding approximately 50 patients per SB204 dose group. More than 92% of the patients in each SB204 dose group completed the study, and approximately 79% of the patients in the vehicle group completed the study. The clinical trial was conducted across 20 sites throughout the United States. The primary endpoints were absolute change in the number of each of inflammatory and non-inflammatory lesions and the proportion of success at the end of treatment, according to the IGA score, with success being defined as achieving IGA score of 0 or 1, and an improvement of at least two grades in the IGA score from baseline.

Our three goals for this Phase 2 clinical trial were to 1) evaluate the efficacy of once versus twice-daily dosing regimens to establish the dosing frequency for Phase 3 trials; 2) conduct a time-to-event analysis to strengthen the statistical analysis on the fast-acting nature of the efficacy observed in a previous Phase 2 trial; and 3) obtain an estimate of effect size on IGA score to inform the power calculation for the Phase 3 pivotal trials.

At baseline across all treatment groups, the mean inflammatory lesion count was 27, the mean non-inflammatory lesion count was 38, and the majority of patients had an IGA score of "moderate," or 3.

The absolute change from baseline in the number of non-inflammatory lesions was -14.1, or 37%, for SB204 4% once-daily and -7.6, or 17%, for pooled vehicle, with a p-value of 0.032. The absolute change from baseline in the number of inflammatory lesions was -11.3, or 42%, for SB204 4% once-daily and -5.8, or 19%, for pooled vehicle, with a p-value of 0.004. The SB204 4% once-daily treatment group was the only treatment arm that showed a statistically significant separation from vehicle on both lesion types.

Percent reduction in lesion counts from baseline at week 12 was statistically significantly different compared to vehicle for both non-inflammatory and inflammatory lesions for all SB204 dose groups. Percent change from baseline at week 12 in the number of non-inflammatory lesions was 34% for SB204 2% twice-daily, 37% for SB204 4% once-daily, 33% for SB204 4% twice-daily and 17% for pooled vehicle, with a p-value for each dose group of 0.05 or less. Percent change from baseline at week 12 in the number of inflammatory lesions was 42% for SB204 2% twice-daily, 42% for SB204 4% once-daily, 42% for SB204 4% twice-daily and 19% for pooled vehicle, with a p-value for each dose group of 0.05 or less.

The dichotomized IGA success rate, defined as achieving an IGA score of 0 or 1 and at least a two-grade improvement in the IGA score, was 7.4% for the vehicle once-daily and 6.9% for the vehicle twice-daily resulting in combined 7.1% for the pooled vehicle arm, compared to 15.1% for the SB204 2% twice-daily arm, 11.5% for the SB204 4% once-daily arm and 13.7% for the SB204 4% twice-daily arm. The number of IGA successes varied between six and eight patients for each of the SB204 dose groups.

We believe that our dose selection of SB204 4% once-daily for our Phase 3 clinical trials is further supported by our secondary efficacy analyses which included a Kaplan-Meier analysis for median time to improvement as assessed by the reduction from baseline in inflammatory lesion counts. With an efficacy threshold of a 35% reduction in the number of inflammatory lesions, we observed a time-to-median reduction of 4.1 weeks with the SB204 4% once-daily treatment compared to 11.6 weeks for vehicle, with a p-value of 0.014. The SB204 4% once-daily treatment was the fastest acting of all treatment groups at this efficacy threshold, and consistently demonstrated the highest percentage of successes by week 2 across all efficacy thresholds tested.

We also assessed cutaneous tolerability by recording the erythema, scaling, dryness, itching and burning or stinging on a four-point scale from 0 to 3 at baseline and at each visit. These measurements are either measured by the physician or reported by the patient. Acne patients are often experiencing many of these local intolerabilities at baseline, before ever initiating treatment with study drug. Overall, the active and vehicle treatments were well tolerated. None of the scores at the end of treatment were markedly elevated compared to baseline incidence for the SB204 or vehicle treatment groups, illustrating the favorable tolerability profile of SB204. More than 95% of patients had scores of "mild" or "no" intolerability for each of the scoring criteria at Week 12.

The aggregate scores of 1, for "mild," 2, for "moderate," or 3, for "severe," on dryness, itching or burning/stinging at most time points throughout the conduct of the study were observed as being a few percentage points higher in patients treated with SB204 4% twice-daily than patients treated once-daily with the same dose, further supporting our selection of the 4% once-daily regimen for the Phase 3 program. The maximum incidence of a patient showing any mild, moderate or severe score at any of the assessment time points during treatment with SB204 4% once-daily

for each of the tolerability categories was 39.2% erythema, 19.2% scaling, 21.2% dryness, 11.8% itching and 19.2% burning/stinging. For comparison, topical retinoid products have maximum severities of approximately 40% for erythema, 45-60% for scaling and burning/stinging and 60% for dryness (information for itching not publicly available).

NI-AC104: A Thorough ECG Clinical Trial in Subjects with Acne Vulgaris Treated With SB204

All NCEs submitted to the FDA for approval are required to conduct a cardiovascular safety study to measure the effect of the drug on the QT interval, a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. In further support of our SB204 program, we executed a four-period cross-over trial in the fourth quarter of 2015 to examine the effect of SB204 on the QT interval in 48 adult patients with acne vulgaris. Patients were randomized and each received topical treatment to approximately 17% of their body surface area. The four treatment arms were: SB204 4% once-daily; SB204 12% once-daily; vehicle; and moxifloxacin. Moxifloxacin, which is known to promote the lengthening of the QT interval, was included as an active control arm. Electrocardiograph, or ECG, recordings and blood samples to assess pharmacokinetics were obtained at multiple time points after each treatment. The primary endpoint was to define the ECG effect of SB204 at therapeutic and supratherapeutic dose concentrations as measured by the difference between the time-matched baseline-adjusted QTcF interval for the groups receiving SB204 and vehicle. The secondary endpoint was a categorical analysis of the QTc interval to determine number and percentage of time points and patients by dose group with absolute QT/QTc greater than 450, 480 and 500 ms.

The results showed no systemic absorption of SB204 and no tolerability or safety concerns. The analysis of ECG data on patients treated with either the proposed therapeutic dose or three times the therapeutic dose of SB204 showed no clinically significant effects on heart rate, QT interval or any other cardiovascular assessments. We submitted the results from this trial to the FDA prior to the start of the Phase 3 pivotal clinical trials in the first quarter of 2016.

NI-AC101: A Phase 1, Single-center, Double-Blind, Randomized, Cross-over Pharmacokinetic, Safety and Tolerability Trial of SB204 8%, or Vehicle

We conducted a maximal-use pharmacokinetic trial in 18 patients with acne vulgaris and observed no detectable exposure to the NVN1000 NCE and no difference in plasma levels of nitrate in patients treated with SB204 8% or vehicle. The total daily dose selected for evaluation of pharmocokinetics in this trial was four times higher than SB204 4% once-daily, the dose we have selected for the Phase 3 pivotal clinical trials and commercial use for the treatment of acne vulgaris, if approved. The formulation used in NI-AC101 is the same formulation used in the Phase 3 clinical trials.

In this trial, the 18 patients with moderate to severe acne vulgaris were randomized, and in the first treatment period administered either SB204 8% or vehicle, applied topically, twice-daily to the maximal-use surface area, consisting of 17% of their body surface area, including on the face, chest, back and upper shoulders. Patients received a low nitrate diet during the five-day treatment period. After a nine-day washout period, dosing was re-initiated with the opposite regimen (active or vehicle) for a second treatment period. Serial plasma samples were obtained at day one and day five for each patient for both treatment periods. The primary endpoint was the pharmacokinetic assessment of nitrate and silicon in the plasma of patients treated with SB204. Secondary endpoints included safety assessments based on physical exams, electrocardiogram tests, serum chemistry, hematology, urinalysis and an assessment of cutaneous tolerability. Eighteen patients completed the first treatment period, but one patient did not return for the second treatment period due to family emergency. Seventeen patients entered the second treatment period, but one patient discontinued due to contact dermatitis on the fifth day of treatment with SB204 8%.

Upon topical application of SB204, the NVN1000 NCE releases nitric oxide from the polysiloxane macromolecule. The assessment of systemic exposure was determined by evaluating the primary pharmacokinetic profiles of metabolites from both the NVN1000 NCE and nitric oxide.

NVN1000 exposure was assessed by measuring plasma concentrations of hMAP3, a product from the hydrolysis of NVN1000. The results showed no measurable systemic exposure to NVN1000 and all plasma hMAP3 values were below the lower limit of quantitation. Nitric oxide exposure was assessed separately by measuring plasma nitrate

concentrations. Nitrate forms following the rapid oxidation of nitric oxide under physiological conditions. Our analysis showed no change in systemic nitrate levels. These results showed that background systemic levels of nitrate were not affected by administration of SB204 8%.

Based on these data, we have characterized the pharmacokinetic profile of hMAP3 and nitrate following topical treatment with SB204 8% under maximal use conditions in patients with moderate to severe acne vulgaris, and we did not observe any systemic exposure.

NI-AC103: A Phase 1, Single-Center, Open-label Pharmacokinetic, Safety and Tolerability Study of SB204 in Adolescents with Moderate to Severe Acne Vulgaris

We conducted a pharmacokinetic study in eighteen adolescent patients age 9 to 16 years old with acne on the face, chest, back and shoulders. Patients were treated with SB204 4% once-daily for 21 days. The exposure data from this study was consistent with our previously reported pharmacokinetic data in adults, which also demonstrated no detectable systemic exposure to the parent compound, NVN1000, and no change in nitrate levels after topical treatment with SB204. Based on these data, we have characterized the pharmacokinetic profile of hMAP3 and nitrate following topical treatment with SB204 4% under maximal use conditions in adolescent patients with moderate to severe acne vulgaris, and we did not observe any systemic exposure.

Preclinical Safety

We have completed over 30 preclinical studies with NVN1000 to assess pharmacology, pharmacokinetics, biodistribution and toxicology. In our pharmacokinetic evaluations of NVN1000, we evaluated administration by dermal, intravenous, intra-muscular and oral routes on mice, rats, rabbits and miniature swine. We observed from the resulting toxicokinetic data from miniature swine that systemic absorption of NVN1000 after dermal administration at supra-therapeutic doses was minimal.

We have conducted several preclinical toxicology studies to evaluate the local safety and tolerability of NVN1000, both the active pharmaceutical ingredient by itself and formulated as SB204, following dermal administration. Dermal toxicology studies involving repeat doses of SB204 have included 4-week and 13-week dermal toxicology studies in miniature swine and a 13-week dermal toxicology study in both rats and mice. In the case of both the miniature swine and mice, we did not observe any significant toxicological effects from doses of NVN1000 up to 28-fold higher in concentration compared to our expected clinical doses and applied on more than 3-fold larger surface area. The most relevant and persistent finding has been transient dermal erythema that is concentration-dependent and believed to be a consequence of a vascular dilation "flushing" effect. During the chronic, 39-week repeat dose dermal toxicology study conducted with SB204 in miniature swine we observed no systemic toxicity and minimal to moderate findings as a function of dose at the skin dose-site. Microscopic observations of thickening of epithelium and inflammatory cell infiltration were observed, which are consistent with an irritant contact dermatitis, presumably due to the high pH of the test article at the SB204 8% BID dose. The findings were considered to be non-adverse upon pathological review and led to a NOAEL, or no observable adverse effect level, of SB204 8% BID. No effect on acute dermal irritation or skin sensitization was observed in additional safety studies in rabbits and guinea pigs. As expected, due to its alcohol-based formulation, NVN1000 gel was found to be an ocular irritant.

We observed NVN1000 to be positive for genotoxicity in a standard *in vitro* assay in bacteria, negative in a chromosome aberration test in cultured human peripheral blood lymphocytes and negative in three *in vivo* mutagenicity assays. The in-life phase of a 104-week repeat dose dermal carcinogenicity study in CD-1 mice was initiated in October 2015 with a scheduled end of in-life in September 2017. To date, there has been no test article-related toxicity seen after 72 weeks of dosing. Additionally, in SEG I and II reproductive toxicology studies conducted in rats and rabbits, the oral administration of NVN1000 resulted in supratherapeutic levels of nitrate and hMAP3 showed minimal effects on fertility or fetal development.

SB206, a Topical Antiviral for the Treatment of External Genital and Perianal Warts

We are developing SB206 as a nitric oxide-releasing topical antiviral gel for the treatment of viral skin infections, such as warts caused by HPV. All warts, including genital warts, are caused by HPV, and we believe that SB206 is well-positioned to address several wart indications with the potential to provide substantial improvements over currently approved therapies for warts, including shorter treatment duration, better local tolerability and decreased incidence of wart recurrence. In our preclinical studies, we observed complete inhibition of papilloma virus growth *in vivo* and inhibition of HPV viral replication *in vitro*. We initially evaluated SB206's antiviral activity in a Phase 2 randomized, double blinded, vehicle-controlled clinical trial in 107 patients with genital warts caused by HPV. We announced top-line results from this Phase 2 clinical trial in the fourth quarter of 2016.

In our Phase 2 clinical trial, specific observations included:

- statistically significant improvement in the incidence of complete clearance of all baseline warts compared to vehicle treatment after 12 weeks in both the ITT and per-protocol, or PP, analyses with the highest dose tested, SB206 12%;
- favorable cutaneous tolerability in the once-daily treatment arms, including the most effective dose, 12% once-daily.

Based on the results of the Phase 2 clinical trial, we plan to seek regulatory input via an end-of-Phase 2 meeting with the FDA in the second quarter of 2017 and proceed to Phase 3 development by the end of 2017. From our preliminary analysis, we believe that the Phase 3 clinical development program for the genital and perianal wart indication will require substantially fewer patients to be enrolled compared to the current acne vulgaris Phase 3 clinical development program because we believe the SB204 program will have generated substantial clinical safety data required for the first FDA approval of the NVN1000 NCE. The FDA has published a guideline entitled "*The extent of population exposure to assess clinical safety: For drugs intended for longterm treatment of non-life-threatening condition*," which was prepared by the International Conference on Harmonisation of the Technical Requirements for Registration of Pharmaceuticals for Human Use. The guideline recommends that 1,500 individuals be exposed to an investigational new drug, including short-term exposure. At the completion of our SB204 development program, we anticipate having more than 1,500 patients dosed with the NVN1000 active ingredient across a range of concentrations and what we believe will be a large safety data set to utilize for a second indication with this active ingredient. We plan to solicit FDA feedback on this approach as part of the SB206 development program and have had no correspondence with the FDA on the SB206 Phase 3 program to date.

Human Papillomavirus Disease Overview

HPV refers to a large family of double-stranded DNA viruses that induce hyperproliferative lesions of either cutaneous or mucosal surfaces. HPV affects nearly 80 million Americans, and an estimated 14 million people become infected with the virus each year, according to the CDC. There are over 100 subtypes of the virus, characterized as low-risk or high-risk based on their oncogenic potential. Several HPV vaccines have successfully been developed that target certain cancer-causing subtypes for the prevention of cervical neoplasias and cervical cancer, but these vaccines do not cover the range of HPV subtypes that cause the multitude of skin lesions. The virus is typically transmitted through direct skin-to-skin contact through disruptions in the normal epithelial barrier of the skin. Examples of skin warts caused by HPV that could potentially be addressable with our nitric oxide platform include:

- genital and perianal warts, collectively typically classified as genital warts;
- common warts on the hands, elbows and knees;
- flat warts found on the face and forehead in children;
- plantar warts found on the soles of the feet; and
- subungual and periungual warts that appear under and around the fingernails or toenails.

Genital and Perianal Warts

Genital warts, which include both genital and perianal warts, are among the world's most common sexually transmitted diseases. Genital warts are usually flesh-colored growths, or lesions, that can be raised, flat or cauliflower-shaped. In males, they can appear on the surface of the penis, scrotum, thigh or groin, or in and around the anus. In females, warts can grow inside the vagina or on the cervix, making them hard to see. Genital warts carry a substantial psychosocial burden due to the shame and embarrassment related to having a sexually transmitted disease, as well as the inconvenience and discomfort of current treatment modalities.

Current Treatment Landscape

Currently, there are no FDA-approved treatments with an antiviral mechanism of action for the treatment of genital warts. The Gardasil HPV vaccine, which is primarily indicated for the prevention of cervical neoplasias and cervical cancer, is also indicated for the prevention of genital warts caused by HPV subtypes 6 and 11. The adoption rates of eligible adolescent males and females in the United States remains approximately 50%, according to the CDC, and this product cannot be used to treat genital warts. Current treatment strategies for HPV-induced skin lesions target removing the hyperproliferative growth instead of eliminating the underlying viral infection. These treatments are currently administered either as topical therapies or locally destructive, or ablative, procedures.

Topical therapies consist of three classes of drugs that are most often prescribed for genital warts—imiquimod, marketed as Aldara and Zyclara, podofilox, marketed as Condylox, and sinecatechins, marketed as Veregen. Developing treatments for warts caused by HPV has historically been problematic due to the inability of drugs to penetrate the heavily keratinized wart. Thus, the available topical therapies are slow-acting, which drives a large number of patients toward painful ablative or surgical removal of the warts. The modest efficacy of topical products along with inconvenient dosing schedules and local application site inflammatory reactions lead to poor compliance and inadequate patient outcomes. As an example, the manufacturer of Zyclara reports only a 27% to 29% incidence of complete clearance of warts present at baseline after 16 weeks. Ablative procedures effect local tissue destruction at the site of the wart and include cryotherapy, lasers, electrodessication and curettage. Patients commonly experience pain during the procedure and may also suffer from persistent hypopigmentation or hyperpigmentation. Rarely, treatment can result in disabling chronic pain syndromes, including vulvodynia and hyperesthesia of the treatment site, or, in the case of perianal warts, painful defecation or fistulas.

According to the CDC's Sexually Transmitted Disease Control Guidelines issued in 2015, there is no definitive evidence that any of the available treatments are superior to any other and no single treatment is ideal for all patients. Both topical and ablative therapies are associated with high recurrence rates because the cells surrounding the damaged tissue still remain infected with HPV DNA and over a period of time take over the host cells to proliferate and grow new warts. Treatments for genital warts remain largely ineffective in achieving long-term wart eradication, with average recurrence rates ranging from 30% to 70% within the first 6 months, according to *Expert Review of Dermatology*.

Our Nitric Oxide-Based Solution for the Treatment of Genital and Perianal Warts

We are developing a topical nitric oxide-releasing gel therapy for the treatment of viral skin infections, the first indication of which will be in genital and perianal warts. Nitric oxide has been reported to inhibit the replication of a variety of viruses, such as DNA viruses, RNA viruses and retroviruses, and therefore we believe it may inhibit HPV viral replication to promote viral clearance and to prevent further spread of the virus. In preclinical studies, we observed that a faster burst of nitric oxide is more effective at inhibiting the growth of warts than slow, sustained release. This led to our selection of the NVN1000 NCE for further development. We believe the release profile of nitric oxide generated from NVN1000 promotes greater skin penetration and may enhance the probability of eliminating HPV-induced genital warts. The nitric oxide gas released from NVN1000 can diffuse through the calloused skin layers and overcomes the historical inability of drugs to penetrate the heavily keratinized wart.

SB206 utilizes the same NCE as SB204, but the nitric oxide release profile has been modulated via the chemical properties of the topical formulation to promote a faster release rate and delivery of elevated doses of nitric oxide to the skin. We believe that SB206 could potentially deliver the following advantages over other topical therapies currently used for genital warts:

- lower rates of genital wart recurrence based on the antiviral mechanism of action;
- a shortened duration of therapy;
- a convenient dosing schedule that helps patients better adhere to therapy; and
- easy application to affected areas.

NI-WA201: A Phase 2, Multi-Center, Double-Blind, Randomized, Vehicle-Controlled, Ascending Dose Study Assessing Tolerability, Safety and Efficacy of Topical NVN1000 in Subjects with External Genital Warts and Perianal Warts

In this randomized, double-blinded, vehicle-controlled clinical trial, we evaluated the safety and efficacy of SB206 in 107 patients with external genital warts and perianal warts. We explored dose and dosing frequency of SB206 in four ascending dose cohorts. Patients were randomized in a 3:1 ratio to either SB206 or vehicle and treated for up to 12 weeks with doses including SB206 4% twice-daily, 4% once-daily, 8% once-daily and the highest dose evaluated, 12% once-daily. Patients eligible for this clinical trial were males or females, 18 to 50 years of age, with 2 to 20 warts on the genital or perianal area. The mean wart count burden per patient at baseline was 7.4 warts. There were 107 patients in the ITT population and 66 patients in the PP population. A total of 108 patients were enrolled, but one patient was randomized in error and therefore not included in the analyses.

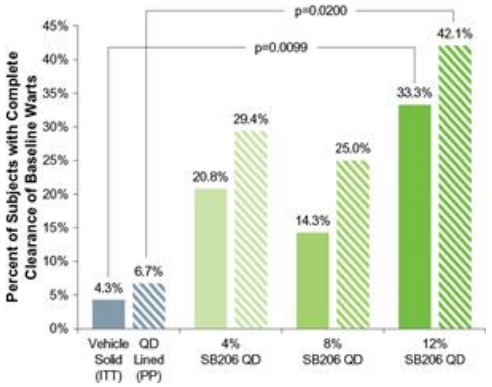
The cutaneous tolerability of SB206 was carefully monitored and recorded using scores on a four-point grading scale for erythema, edema, erosions or ulcers and burning or stinging. The once-daily treatment arms were generally well tolerated, including the most effective dose, 12% once-daily. The most frequently reported treatment-emergent adverse events were application site reactions, the percentage of which was highest in patients treated with SB206 4% twice-daily as shown below in Table 4. Based on the local application site adverse-event profile and our strict, pre-specified stopping criteria, SB206 4% twice-daily was discontinued, and all of the remaining cohorts were dosed once-daily at two-fold and three-fold higher concentrations of NVN1000. As a result, SB206 4% BID was not included in the analysis. By design, the majority of the patients in this trial were preserved for enrollment at the highest doses, where enhanced antiviral activity was observed in preclinical animal models.

Table 4:

	Vehicle gel QD/BID (n = 27)	SB206 4% gel BID (n = 12)	SB206 4% gel QD (n = 23)	SB206 8% gel QD (n = 14)	SB206 12% gel QD (n = 30)
General Disorders and Administration-Site Conditions	1 (4.2%)	6 (50.0%)	6 (26.1%)	1 (7.1%)	5 (16.7%)
Burn	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Erosion	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	2 (6.7%)
Erythema	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	2 (6.7%)
Exfoliation	0 (0.0%)	0 (0.0%)	3 (13.0%)	0 (0.0%)	0 (0.0%)
Pain	0 (0.0%)	3 (25.0%)	1 (4.3%)	0 (0.0%)	2 (6.7%)
Pruritus	0 (0.0%)	1 (8.3%)	5 (21.7%)	0 (0.0%)	0 (0.0%)
Rash	0 (0.0%)	1 (8.3%)	1 (4.3%)	0 (0.0%)	0 (0.0%)
Reaction	1 (4.2%)	2 (16.7%)	1 (4.3%)	0 (0.0%)	0 (0.0%)
Ulcer	0 (0.0%)	1 (8.3%)	0 (0.0%)	1 (7.1%)	0 (0.0%)
Pyrexia	0 (0.0%)	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)

The primary endpoint for this clinical trial was the proportion of patients who were completely clear of warts that were present at baseline at or before week 12. In the ITT analysis, 10 of 30 patients, or 33.3%, achieved complete clearance of all warts by week 12 when treated with SB206 12% once-daily, 2 of 14, or 14.3%, with SB206 8% once-daily, 5 of 24, or 20.8%, with SB206 4% once-daily, compared to only 1 of 23 patients, or 4.3%, achieving complete clearance with vehicle once-daily. In the PP analysis containing patients who completed a full 12 weeks of dosing, 8 of 19 patients, or 42.1%, achieved complete clearance of all warts when treated with SB206 12% once-daily, 1 of 4, or 25%, with SB206 8% once-daily, 5 out of 17%, or 29.4%, with SB206 4% once-daily compared to only 1 of 15 patients, or 6.7%, achieving complete clearance with vehicle once-daily. Figure 2 below shows the percent of patients with complete clearance of baseline warts at week 12 in the ITT and PP populations for all of the once-daily treatment arms. In twice-daily arms of the trial, 2 of 12 patients, or 16.7%, achieved complete clearance of all warts by week 12 when treated with SB206 4% twice-daily in the ITT population and 2 of 7, or 28.6%, in the PP population, compared to 2 of 4 patients, or 50%, achieving complete clearance with vehicle twice-daily in both populations.

Figure 2:



Preclinical Pharmacology Studies

In a cottontail rabbit papilloma virus, or CRPV, model, we evaluated several nitric oxide-releasing drug candidates to determine the effect of release rate on the inhibition of papilloma formation. Two weeks following viral inoculation, topical treatment was initiated with daily treatment occurring five times per week for five weeks. Using this model, we observed that the modulation of nitric oxide dose and release rate both influence antiviral activity. Lower concentrations of drug and formulations with slower nitric oxide release rates showed limited efficacy, leading to our selection of SB206 as the lead candidate. In an *in vivo* CRPV study, we observed a dose responsive inhibition of both wild type and E8 mutant papilloma growth following daily topical treatment of SB206 gel, five doses per week for five weeks compared to imiquimod as a positive control. We observed complete inhibition of the E8 mutant CRPV papillomas with SB206 at the highest dose compared to 26% inhibition for imiquimod. Biopsies from animals treated with SB206 10% lacked any evidence of viral infection. We also observed that histological assessment of inflammation and quantitative cytokine gene expression were similar across all dose groups, suggesting immune activation was not a significant component of the antiviral activity observed with SB206 treatment.

The antiviral activity of the NVN1000 used in SB206 was then measured in organotypic cultures of primary human keratinocytes infected with HPV-18. We observed dose responsive inhibition of viral replication as determined by quantitative polymerase chain reaction analysis following the exposure of HPV-18 infected raft cultures for one hour per day for six days. NVN1000 at 0.75, 1.0 and 1.5 mg/mL inhibited viral copy number by 25%, 62% and 85%, respectively. No significant cytotoxicity was observed at any dose in human keratinocyte cultures. In follow-on preclinical studies in the raft culture model, we observed direct antiviral activity of nitric oxide against high risk HPV, fundamentally decreasing viral protein expression.

SB208, a Topical Antifungal for the Treatment of Onychomycosis

We are developing SB208 as a topical antifungal gel utilizing the NVN1000 NCE for the treatment of fungal infections of the skin and nails. NVN1000 has been observed *in vitro* to release nitric oxide that rapidly diffuses through human nails and directly kills fungal species, as opposed to only inhibiting the growth of the fungus. NVN1000 has demonstrated broad-spectrum activity *in vitro* against *Trichophyton mentagrophytes*, or *T. mentagrophytes*, and *Candida albicans*, or *C. albicans*, in addition to *T. rubrum.* We believe SB208 has the potential to elevate the standard of care in fungal infections such as tinea pedis and onychomycosis by delivering high concentrations of nitric oxide to rapidly penetrate targeted tissues and potentially improve upon current efficacy rates observed with topical therapies while maintaining an attractive safety profile.

We initiated our Phase 2 program in July 2016 with a clinical trial designed to assess tolerability, safety and antifungal activity of three doses of SB208 in patients with tinea pedis (athlete's foot) infected with dermatophytes such as *T. rubrum* to narrow the dose range prior to beginning work in onychomycosis. Approximately 220 patients were randomized 1:1:1:1 to three active and one vehicle treatment arms, applying either SB208 Gel (2%, 4% or 16%) or vehicle once-daily for two weeks, followed by a four-week post-treatment observation. Endpoints will include assessments of mycological cure, clinical cure and therapeutic cure, which includes both clinical cure and mycological cure. We completed enrollment of the six-week Phase 2 trial in December of 2016 and expect to report top-line results in the second quarter of 2017. The results of the ongoing Phase 2 trial will position us to conduct a second 52-week Phase 2 trial in patients with onychomycosis. We believe the safety data generated in our other NVN1000 trials supports our ability to proceed directly to late-stage development with SB208, consistent with our approach and regulatory strategy with SB206.

Onychomycosis Disease Overview

Onychomycosis is a chronic fungal infection of the nails, and we estimate that it affects more than 40 million people in the United States. The prevalence of disease increases with age, and more than 50% of patients are 70 years or older. The dermatophytes *T. rubrum* and *T. mentagrophytes* are causative agents for the majority of infections and often result in a painful thickening, deformation and discoloration of the nail and sometimes splitting, separation of the nail plate from the nail bed and an inability of the nail to perform its natural protective function. Because the fungi that cause onychomycosis are present in many common locations such as floors, the soil, socks and shoes, the nail can become re-infected and additional courses of treatment are frequently required after successful treatment.

Onychomycosis is particularly dangerous in diabetic patients. In a 2015 report in *Podiatry Management*, the risk of diabetic patients contracting onychomycosis was reported to be 2.77 times greater than that of non-diabetic individuals. This enhanced susceptibility is further compounded by the fact that onychomycosis is now considered an important predictor of diabetic foot infection, with a three-fold higher risk of gangrene or foot ulcers in diabetic patients. The combination of morbidity now linked to onychomycosis in diabetic patients, the growing diabetic population, the diminished ability of diabetic patients to fight infection due to elevated blood glucose levels and restrictions on diabetic patients taking oral therapeutic drugs due to concomitant medications create a serious need for topical interventions for the diabetic population.

There are currently five commonly used classes of chemicals for the treatment of onychomycosis: allylamines, azoles, morpholines, dihydropyrimidinones and the newly approved oxaboroles. Despite new therapeutic options approved in recent years, approximately 60% to 70% of patients fail to achieve complete cures, even with oral therapies.

Treatments are segmented into two approaches, either oral therapies, such as terbinafine, or topical products, such as Jublia, an azole, and Kerydin, an oxaborole. Worldwide sales of the branded terbinafine product Lamisil, the most prescribed systemic drug for onychomycosis, were $1.2 billion in 2004 and $978 million in 2006, when it became generically available. A 12 week course of oral therapy was historically the only method of treatment, but the potential for liver failure and interactions between drugs, particularly for an aging patient population with common comorbidities, created the demand for safer and more effective treatment options.

Given the significant safety issues associated with oral therapy, topical therapies are now increasingly used due to their better safety profile. However, topical therapies administered for 48 weeks are associated with significantly more modest efficacy profiles, including complete cure rates of less than 20%. The lack of safe oral therapies has driven physicians to prescribe these topical therapies despite their limited effectiveness. We believe that there is an unmet need in the treatment landscape for onychomycosis for a novel therapeutic solution that improves efficacy without compromising safety. We are aware of certain drugs in development, including reformulations of terbinafine, topical luliconazole and orally administered VT-1161.

Our Nitric Oxide-Based Solution for the Treatment of Onychomycosis

We believe SB208 has the potential to improve upon current efficacy rates observed with topical therapies while maintaining an attractive safety profile. According to reports in the *Journal of Applied Microbiology* and the *Journal of American Academy of Dermatology*, nitric oxide has been effective *in vitro* against the dermatophytes *T. rubrum* and *T. mentagrophytes*, and has shown evidence of clinical efficacy against tinea pedis, which is also routinely caused by *T. rubrum* and *T. mentagrophytes*. We believe that a significant barrier to translating antifungal efficacy into a successful onychomycosis treatment is the difficulty in achieving adequate penetration of the drug through the nail plate to reach the nail bed and treat the fungal infection. For example, in the two clinical trials cited in Jublia's prescribing information, only 17.8% and 15.2% of patients, respectively, treated with Jublia achieved complete cure as defined by clear nail growth, the absence of detectable fungus and negative fungal cultures.

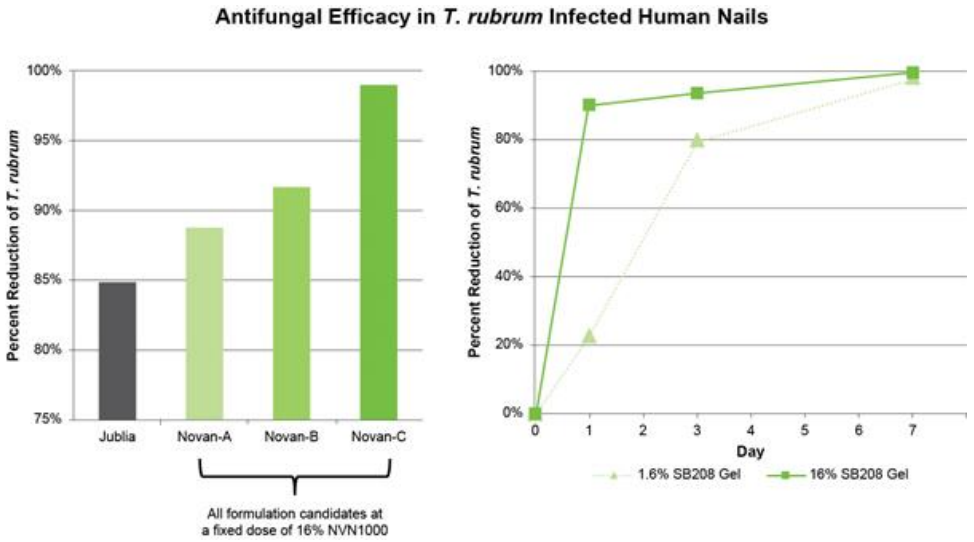
In contrast to azoles or other antifungals, when applied topically, nitric oxide as a gas quickly diffuses across the nail bed reaching the underlying nail bed tissues that harbor the fungal infection. Additionally, the dense keratin fibers of the nail are rich in cysteine residues that can react with nitric oxide to generate nitrosothiols, which serve as secondary reservoirs for nitric oxide within the nail bed to amplify the antifungal activity.

Preclinical Pharmacology Studies

We have observed *in vitro* that nitric oxide exhibits rapid fungicidal activity. NVN1000, the NCE used in SB208, was added to *T. rubrum* cultures and evaluated for fungicidal effects at increasing concentrations. As early as four hours after the addition of NVN1000, we observed a greater than 1.0-log, or 90%, reduction in fungal growth in all concentrations of NVN1000. At 24 hours after exposure, we observed greater than 4-log, or 99.99%, reduction in bacterial counts, with 2, 4 and 8 mg/mL NVN1000.

We further evaluated multiple nitric oxide-releasing formulations, including gel, cream and lacquer-based compositions in a preclinical model designed to measure fungal kill through the human nail plate using ChubTur cells. This model was utilized previously in the drug development of Kerydin, as reported in the *Journal of Drugs in Dermatology* in 2015, and Jublia, as reported in the *Journal of Antimicrobial Agents and Chemotherapy* in 2014. Organism viability on the underside of the nail following topical treatment was measured using an adenosine triphosphate assay. As shown in Figure 3 below, three candidate formulations were screened for antifungal efficacy in *T. rubrum* infected human nails with Jublia as a positive control. Following a single application, all three formulations decreased fungal viability as much or more than Jublia. NVN1000 incorporated into experimental formulations at a concentration of 16% resulted in variable percent reductions up to 99%, compared to untreated infected control nails, illustrating our ability to tune the drug's activity by adjusting the formulation. We optimized the SB208 gel formulation based on our observations in this preclinical study and repeated the infected human nail assay with multiple applications of both a low dose, SB208 1.6%, and a high dose, SB208 16%, of NVN1000. As shown in Figure 3, the onset of antifungal activity was rapid and dose dependent, increasing to approximately 99% killed after once-daily applications for seven days in both treatment groups.

Figure 3:



SB414, a Topical Cream for the Treatment of Inflammatory Skin Diseases

SB414 is our cream-based product candidate currently in preclinical studies for the topical treatment of inflammatory skin diseases such as psoriasis or atopic dermatitis. In preclinical studies to date, we observed that SB414 significantly ($p<0.05$) reduced composite psoriasis scores, which consist of erythema and plaque scores, and reduced pro-inflammatory cytokines, including IL-17, in a psoriasis mouse model. We have commenced toxicology studies for SB414 in support of the submission of an IND to the FDA, and based on the data generated in our preclinical *in vivo* study expect to submit an IND covering the cream product candidate in the second quarter of 2017 followed by a Phase 2 proof-of-concept trial of SB414 as a topical treatment for psoriasis, which will include an active head-to-head comparator. The Phase 2 study is also designed to evaluate key biomarkers such as IL-17 in lesions in patients in the treatment arm with the strongest response. Our intent is to develop SB414 and potentially future product candidates for patients with mild to moderate inflammatory skin diseases who are not eligible for systemic therapy and who have limited topical treatment choices.

Inflammatory Skin Disease Overview

According to a recent peer-reviewed article in the *British Journal of Dermatology*, IL-17 is a key inflammatory cytokine known to be or is likely to be related to the mechanism and severity of a number of inflammatory skin disorders, including psoriasis, acne, atopic dermatitis, vitiligo and alopecia areata. IL-17 activation leads to the propagation of several pro-inflammatory signaling cascades and perpetuates chronic inflammation. IL-1ß is an instrumental cytokine in the initiation and orchestration of both innate and adaptive immune responses and is one of the key signals responsible for triggering the maturation of naïve T cells into Th17 cells. In several inflammatory skin disorders the aberrant activation and dysregulation of this helper T-cell phenotype results in the production and release of IL-17, which serves as a signal to prolong the inflammatory cascade through this positive feedback loop.

Current Treatment Landscape

While the healthcare market has seen an increase in the introduction of systemic therapies, including biologics, to treat severe psoriasis, and there is at least one near-term biologic in development for atopic dermatitis, systemic therapies are only indicated for patients with moderate-to-severe disease. According to a study published in the *International Journal of Pharmacy and Life Science*, these patients with moderate-to-severe disease comprise only 20% of the afflicted population.

Topical corticosteroids are the predominant therapies used for both mild to moderate psoriasis and mild to moderate atopic dermatitis, with the latter also being treated with other topical immunomodulators. However, treatment-related side effects associated with corticosteroid use, such as local application-site reactions, including skin atrophy with prolonged use, and profound effects on hypothalamic-pituitary-adrenal axis function, which can lead to growth retardation in adolescents and an increased risk for diabetes, underscoring the need for novel therapies to treat this disease. Non-steroidal topical therapies used in the treatment of atopic dermatitis also include topical calcineurin inhibitors, but boxed warnings for rare malignancies and other side effects have limited their use. These treatments attempt to reduce inflammation and itchiness associated with atopic dermatitis and maintain the protective integrity of the skin, but no topical treatments indicated for atopic dermatitis specifically address the contribution of *Staphylococcus aureus*, or *S. aureus*, colonization and microbiome imbalance to the disease.

Our Nitric Oxide-Based Solution for Inflammatory Skin Diseases

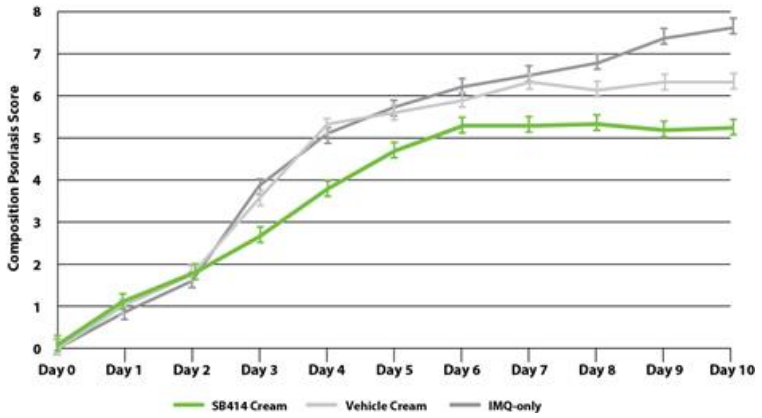
We believe that the use of a topical nitric oxide product has the potential to significantly improve outcomes in patients with inflammatory skin diseases, using new mechanisms of action and will have an improved safety profile over currently approved topical therapies. The cream-based product candidates, consisting of an active phase ointment and an accompanying hydrogel, are mixed together to generate a homogenous pH-controlled cream admixture that is designed to exert its immunomodulatory effects locally in the skin. Our initial efforts in inflammatory skin diseases are focused on psoriasis and atopic dermatitis. We believe nitric oxide potentially suppresses the key inflammatory cytokine IL-17 that is primarily produced by T helper (Th) 17 cells. IL-17 activation leads to propagation of several pro-inflammatory signaling cascades and perpetuates chronic inflammation. Binding of IL-17 to its cognate receptor signals keratinocytes and other cell types to generate and release IL-1ß and IL-6, as well as other pro-inflammatory cytokines resulting in antibody release, neutrophil migration and enhanced inflammasome activation. Additionally, according to a study published in the *American Journal of Pathology*, psoriatic patients have an overexpression of the enzyme arginase that degrades L-arginine and thus eliminates the production of sufficient levels of nitric oxide needed to clear the skin. We believe higher levels of topically applied nitric oxide can restore the normal healing process and break the unending cycle of keratinocyte proliferation that would otherwise lead to thick scaly plaque. Moreover, we believe that our anti-inflammatory product candidate will have a favorable safety profile, due to nitric oxide's natural physiological role and based on the clinical safety data we have gathered across our nitric oxide platform.

Preclinical Evidence for Psoriasis

Experimental data published in *Journal of Immunology* has shown that imiquimod (IMQ)-induced dermatitis in mice closely resembles human psoriatic lesions in regards to both the phenotypic and histological assessments of the lesions as well as in the development of theses lesions, which is dependent upon the IL-23/IL-17 axis. The application of imiquimod cream topically to mouse skin results in the stimulation of keratinocytes to increase

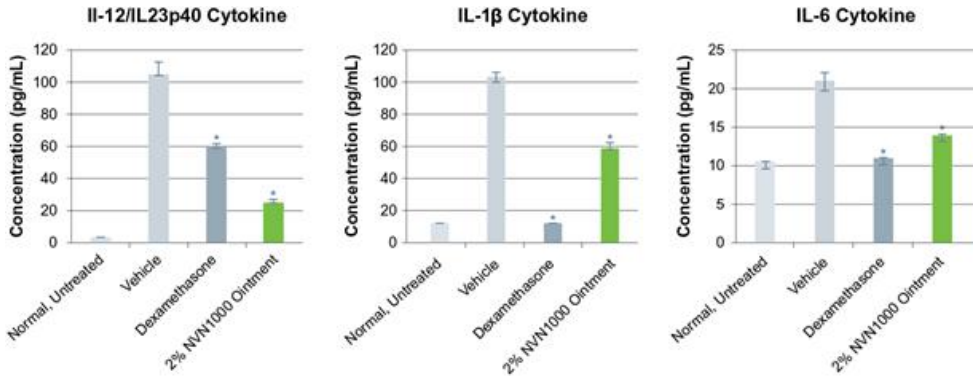
cytokine production and the rapid proliferation of dendritic cells. As shown in the Figure 4 below, application of topical SB414 Cream in the imiquimod-induced psoriasis-like mouse model demonstrated statistically significant reduction of the overall composite psoriasis score, a score compiled from daily scoring of the observed erythema and scaling, when compared to topical vehicle treatment. We believe that the statistically significant reduction in this composite psoriasis score demonstrates nitric oxide's potential to dampen the inflammatory loop associated with chronic psoriasis inflammation and to abrogate the persistent keratinocyte proliferation that characterizes psoriasis.

Figure 4:



As shown in Figure 5 below, application of a topical NVN1000 ointment in an IL-23-induced psoriasis mouse model showed statistically significant reductions of pro-inflammatory cytokines when compared to vehicle. Dexamethasone, a corticosteroid, was used as a positive control. IL-23 stimulates Th17 cells to produce the cytokine IL-17 which in turn signals keratinocytes to release IL-1ß and IL-6 among other cytokines. Decreases in the levels of the pro-inflammatory cytokines IL-1ß and IL-6 suggest that topical treatment with nitric oxide may function as an IL-17 inhibitor. Furthermore, IL-17 normally stimulates keratinocytes to produce more IL-23 and continue the inflammatory loop important for prolonging the psoriatic lesion. We believe the statistically significant reduction of IL-23p40 we observed with topical nitric oxide compared to vehicle further illustrates nitric oxide's potential to dampen the inflammatory loop associated with chronic psoriasis inflammation.

Figure 5:



* *p <0.05*

Preclinical Evidence for Atopic Dermatitis

Atopic dermatitis has a complex disease etiology, including impaired skin barrier function and innate immune defects that contribute to a predisposition for colonization or infection with microbes, most significantly *Staphylococcus aureus.* More than 90% of atopic dermatitis patients have skin that is colonized with *S. aureus*, which may play a role in the disease pathogenesis. The density of *S. aureus* colonization has been correlated with both the severity of atopic dermatitis lesions and the degree of cutaneous inflammation. In preclinical studies, NVN1000 has demonstrated broad spectrum anti-microbial activity *in vitro*, including activity against *Staphylococcus* and *Streptococcus species*. In *in vivo* preclinical studies, NVN1000 has demonstrated dose-responsive reductions in the microbial burden of an atopic dermatitis isolate of methicillin-resistant *Staphylococcus aureus* in a disrupted epidermal barrier porcine model, with the highest-tested dose yielding a 99.9% reduction.

Additionally, we have observed statistically significant, dose-responsive topical anti-inflammatory activity in a series of in vivo studies using an oxazolone-induced delayed-type hypersensitivity BALB/c mouse model. This model is frequently utilized as a preliminary model to assess anti-inflammatory activity. The allergic contact dermatitis induced by oxazolone results in an immune response that aims to model the chronic phase of atopic dermatitis. For example, in one study using this model, NVN1000 formulated in a single phase ointment reduced inflammatory swelling by 24% for the 0.3% dose of nitric oxide with a p-value of less than 0.038, by 57% for the 0.6% dose with a p-value of less than 0.001, and by 62 for the 1.2% dose with a p-value of less than 0.001 when compared to the acetone/ethanol vehicle used to administer the positive control. In a recent study utilizing the same model, an optimized NVN1000 pH-controlled cream formulation reduced inflammatory swelling by 48% with the 0.3% dose of nitric oxide with a p-value of less than 0.0002, 67% for the 0.6% dose with a p-value of less than 0.001, and by 76% for the 0.9% nitric oxide dose with a p-value of less than 0.001 when compared to untreated animals. An 80% reduction in inflammation was observed following treatment with the potent topical corticosteroid 0.05% betamethasone cream. In addition, the 0.9% nitric oxide dose exhibited a statistically significant inflammatory reduction of 47% with a p-value of less than 0.05 when compared to the Placebo cream-treated group. We are optimizing the SB414 cream formulation based on the observations in these preclinical studies and are currently conducting preclinical pharmacology and toxicology studies to be completed in the second half of 2017.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We consider our primary potential competition to be existing providers and drug developers of therapeutics to treat acne vulgaris, genital warts, onychomycosis, psoriasis and atopic dermatitis. Any product candidates that we successfully develop and commercialize will compete with these existing therapies as well as new therapies that may become available in the future. Our success will be based in part on our ability to identify, develop and manage a portfolio of product candidates that are safer and more effective than competing products.

Acne Vulgaris

If approved by the FDA for the treatment of acne vulgaris, we anticipate that SB204 would compete with branded and generic oral and topical antimicrobials, oral and topical retinoids, oral contraceptives, other prescription skin cleansers and over-the-counter treatments. We may compete with branded therapeutics, including Epiduo and Epiduo Forte, marketed by Galderma Laboratories, L.P.; Aczone, marketed by Allergan plc; and Onexton, marketed by Valeant Pharmaceuticals International, Inc. There are also product candidates under development that could potentially be used to treat acne vulgaris and compete with SB204. For example, we are aware of olumacostat glasaretil (formerly DRM01), a topical acetyl-CoA carboxylase inhibitor product candidate being developed by Dermira Inc.; FMX01, a minocycline foam product candidate being developed by Foamix Pharmaceuticals Ltd.; Winlevi, a novel-topical antiandrogen candidate, and CB-06-01, an antibiotic candidate, both being developed by Cassiopea SpA; sarecycline, a tetracycline derivative being developed by Allergan for the treatment of acne vulgaris; XEN801, a topical small-molecule inhibitor of stearoyl Co-A desaturase (SCD1) candidate being developed by Xenon Pharmaceuticals Inc.; BPX01, a topical hydrophilic antibiotic (minocycline) candidate being developed by BioPharmX, Inc.; and ANT-1207, a topical botulinum toxin type A candidate being developed by Allergan (Anterios Inc.).

Genital Warts

With respect to SB206 for the treatment of HPV-induced skin lesions, we would primarily face potential competition from Aldara and Zyclara, both marketed by Valeant; Condylox, marketed by Actavis plc; and Veregen, marketed by Fougera Pharmaceuticals, Inc.; as well as their generic equivalents. There are also product candidates under development that could potentially be used to treat HPV-associated genital warts and potentially compete with SB206. CB-06-02, a tellurium-based compound is being developed by Cassiopea. BTA074 is a direct-acting antiviral for the treatment of HPV 6 and 11 infections that is being developed by Biota Pharmaceuticals, Inc. Additional reformulations of generically available imiquimod are also under development.

Onychomycosis

With respect to SB208 for the treatment of onychomycosis, we would face potential competition from Lamisil, an oral therapeutic marketed by Novartis Pharmaceuticals Corporation; Jublia, a topical therapeutic marketed by Valeant; and Kerydin, a topical therapeutic marketed by Pfizer Inc. (Anacor Pharmaceuticals, Inc.); as well as generically available oral antifungals. There are also product candidates under development that could potentially be used to treat onychomycosis and compete with SB208. For example, we are aware of various terbinafine reformulations in clinical development, including HTU-520 being developed by Hisamitsu Pharmaceutical Co., Inc.; P-3058 being developed by Polichem SA; and MOB015 being developed by Moberg Pharma AB; as well as VT-1161, an oral antifungal under development by Viamet Pharmaceuticals, Inc.

Psoriasis and Atopic Dermatitis

With respect to SB414 for the topical treatment of mild to moderate psoriasis, we would face potential competition from companies that market corticosteroids, vitamin D analogues, combinations thereof and calcineurin inhibitors. There are also topical product candidates under development that could potentially be used to treat psoriasis and compete with SB414, including CED 90100, WBI1001, INCB018424, LAS 41004 and PH10. Other product candidates under development that could potentially be used to treat psoriasis and compete with SB414 include Eucrisa, a topical phosphodiesterase 4 (PDE4) inhibitor being developed by Pfizer (Anacor); VTP-43742, a systemic RORγt inhibitor candidate being developed by Allergan (Vitae Pharmaceuticals, Inc.); brodalumab injection, 210 mg, a monoclonal antibody that binds to IL-17, and IDP-119, a topical steroid and retinoid combination, both candidates being developed by Valeant; CT327 and CT103, topical TrkA kinase inhibitor candidates being developed by Sienna Biopharmaceuticals, Inc. (Creabilis SA); multiple foam candidates being developed by Foamix; and multiple topical kinase inhibitors being developed by multiple companies.

With respect to SB414 for the treatment of atopic dermatitis, we would face potential competition from companies that market branded and generic corticosteroids; the topical calcineurin inhibitors, Elidel, which is being marketed by Valeant, and Protopic, which is expected to be marketed by Leo Pharma; and the topical PDE4 inhibitor, Eucrisa, which is expected to be marketed by Pfizer (Anacor). Product candidates under development that could potentially be used to treat atopic dermatitis and compete with SB414 include dupilumab, which is being developed by Regeneron Pharmaceuticals, Inc; VTP-38543, which is being developed by Allergan (Vitae Pharmaceuticals); tralokinumab, which is being developed by Medimmune; GSK2894512, which is being developed by GlaxoSmithKline; ZPL-389, which is being developed by Ziarco; and CT340 and CT101, which are being developed by Sienna (Creabilis).

Intellectual Property

Our success depends in large part upon our ability to obtain and maintain proprietary protection for our products and technologies and to operate without infringing the proprietary rights of others. We seek to avoid the latter by monitoring patents and publications that may affect our business, and to the extent we identify such developments, evaluating and taking appropriate courses of action. With respect to the former, our policy is to protect our proprietary position by, among other methods, filing for patent applications on inventions that are important to the development and conduct of our business with the U.S. Patent and Trademark Office, or USPTO, and its foreign counterparts. We also use other forms of protection, such as trademark, copyright and trade secret protection, to protect our intellectual property, particularly where we do not believe patent protection is appropriate or obtainable.

Patents

As of December 31, 2016, we own or have an exclusive license to 20 patents issued in the United States and more than 35 patents issued in foreign jurisdictions. We also own or have an exclusive license to at least 15 pending patent applications filed in the United States and at least 50 pending non-U.S. patent applications (including applications filed in foreign jurisdictions and international or Patent Cooperation Treaty, or PCT, applications that have not yet entered national phase).

Patent coverage lasts for varying periods according to the date of filing of the patent application or the date of grant or issuance of the patent and the legal term of patents in various countries where patent protection is obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest filing date of a non-provisional patent application. In addition, in certain instances, the term of a patent can be extended to recapture a portion of the USPTO delay in issuing the patent or may be shortened if a patent is terminally disclaimed over another patent that expires earlier. The term of a patent may also be eligible for patent term extension to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the extension term cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest filing date of a non-provisional patent application. However, the actual protection afforded by a patent varies on a product by product basis from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Nitricil

We exclusively license from UNC issued patents and pending applications directed to our library of Nitricil compounds, including patents issued in the United States, Canada, Japan and Australia with claims intended to cover NVN1000, the NCE for our SB204, SB206 and SB208 product candidates, and for our pipeline candidate SB414. Additionally, one such issued patent in the United States has claims specifically directed to the composition of matter of NVN1000. These patents and pending applications, if issued, are projected to expire in 2026 without taking into account any patent term extensions that may be available to us. Additionally, NVN1000 has been classified as an NCE, and patent term extensions may be available to extend the life of a U.S. patent that covers NVN1000 beyond 2026. We also own patents issued in the United States, China, Germany, Spain, France, Great Britain, Ireland, Italy and Switzerland directed to methods of manufacturing Nitricil compounds. These patents are projected to expire in 2032.

SB204, SB206 and SB208

We own patents issued in the United States, Australia, Germany, Spain, France, Great Britain, Italy and Japan and pending applications filed in the United States and in foreign jurisdictions, including Brazil, Canada, China, Europe, South Korea and Mexico directed to methods of reducing sebum production using nitric oxide-releasing macromolecules, including, in certain embodiments, through the use of Nitricil compounds. We also own issued U.S. patents and pending applications filed in the United States, Australia, Brazil, Canada, China, Europe and Japan directed to the alcohol gel component of SB204 and SB206 and/or the SB204 and SB206 two-component formulations. We are pursuing United States, Australia, Brazil, Canada, China, Europe, Japan, South Korea and PCT applications directed to the use of nitric oxide-releasing compounds, including, in certain embodiments, Nitricil compounds, for the treatment of viral skin infections.

Altogether, our issued U.S. and foreign patents and pending U.S. and foreign patent applications, if issued, relating to one or more of our lead product candidates, SB204, SB206 and SB208 are projected to expire between 2026 and 2037, without taking into account any patent term extensions that may be available to us.

Other Patents

In addition to the patents and pending applications we own or have an exclusive license related to Nitricil and our product candidates, we also own or have exclusive licenses to issued patents and pending applications in the United States and in foreign jurisdictions covering other nitric oxide-based therapeutics and methods of use in dermatological indications.

Trade Secrets

We rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by requiring our employees, consultants, contractors and other advisors to execute nondisclosure and assignment of invention agreements, or to include such provisions in their consulting agreement, upon commencement of their respective employment or engagement. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements and provisions, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Trademarks

Novan® is a registered trademark of our company in the United States.

Collaboration and Licensing Agreements

UNC License Agreement

We acquired exclusive rights to our library of Nitricil compounds pursuant to license agreements with UNC entered into in July 2007 and October 2009, which were subsequently amended, restated and consolidated in June 2012. We amended the consolidated license agreement in November 2012 to expand the scope of licensed patents to cover additional nitric oxide technologies in consideration for an upfront cash payment. We plan to obtain similar amendments to the consolidated license agreement to expand the scope of licensed patents to cover future additional nitric oxide technologies in consideration for an upfront cash payment or as improvements on licensed technology. In April 2016, we amended the agreement to clarify the scope of the intellectual property of the consolidated license agreement.

Under the consolidated license agreement with UNC, we are granted an exclusive, worldwide license, with the ability to sublicense, under the licensed UNC patents, including those directed to Nitricil compounds, to develop and commercialize products utilizing the licensed technology. As partial consideration for the consolidated license agreement, we issued 191,052 shares of our common stock to UNC and paid an upfront cash payment of $5,000 to UNC. Additionally, under the consolidated license agreement, we are obligated to pay UNC a running royalty percentage in the low single digits on net sales of licensed products, to pay up to $425,000 to UNC in regulatory and commercial milestones on a licensed product by licensed product basis.

Under the consolidated license agreement, UNC controls prosecution activities with respect to licensed patents owned solely by UNC, we control prosecution activities with respect to licensed patents jointly owned by us and UNC and we are obligated to reimburse UNC for reasonable prosecution and maintenance costs. Pursuant to the consolidated license agreement, we have the first right to defend against third-party claims of patent infringement with respect to the licensed products and to enforce the licensed patents against third-party infringers.

Unless earlier terminated, the consolidated license agreement remains in effect on a country by country and licensed product by licensed product basis until the expiration of the last to expire issued patent covering such licensed product in the applicable country, and upon such expiration, we receive a perpetual, unrestricted, fully-paid and royalty free right to develop and commercialize such licensed products. As of December 31, 2016, the last to expire

issued patent licensed to us under the consolidated license agreement is projected to expire in 2033. UNC may terminate the agreement or render the license granted thereunder non-exclusive for our material breach of the agreement that remains uncured after 90 days of receipt of written notice thereof from UNC, and may also terminate the agreement upon providing written notice for our bankruptcy or insolvency-related events within 30 days of the occurrence of such events. We may terminate the agreement at any time for convenience upon providing written notice of not less than 30 days to UNC.

Separation Transaction and Licensing Arrangements with KNOW Bio

In connection with the December 2015 separation of our non-dermatology assets to KNOW Bio, we granted to KNOW Bio, through two separate agreements, exclusive licenses, with the right to sublicense, to certain U.S. and foreign patents and patent applications controlled by us as of the execution date of the agreement, and, under one of the agreements, patents and patent applications which may become controlled by us during the three years immediately following the execution date of such agreement, directed towards nitric oxide-releasing compositions and methods of manufacturing thereof, including methods of manufacturing Nitricil compounds, and other nitric oxide-based therapeutics. Under the exclusive license, KNOW Bio has the right to develop and commercialize products utilizing the licensed technology (excluding products containing certain particles, including NVN1000 and NVN4000) in all fields of use except generally for the diagnosis, treatment, prevention, and palliation of diseases, conditions, or disorders of the skin, nails, hair or scalp in humans or animals, and all cosmetic uses for the skin, nails, hair or scalp, other than (i) for wound care through formulations of therapeutic product specifically designed to treat chronic wounds, thermal burns, radiation injury, accidental injury, surgical sites or scars, and (ii) therapeutic uses for treating cancer, excluding basal cell carcinoma, squamous cell carcinoma, precancerous conditions of the skin, actinic keratosis, actinic cheilitis, cutaneous horn, Bowen disease, radiation dermatosis, and dysplastic nevi (the "KNOW Bio Field").

Under one of these exclusive license agreements, KNOW Bio granted to us an exclusive license, with the right to sublicense, under any patents and patent applications which may become controlled by KNOW Bio during the three years immediately following the execution date of such agreement and directed towards nitric oxide-releasing compositions and methods of manufacturing thereof, including methods of manufacturing Nitricil compounds, and other nitric oxide-based therapeutics, but not towards medical devices, for use in the diagnosis, treatment, prevention, and palliation of diseases, conditions, or disorders of the skin, nails, hair or scalp in humans or animals, and all cosmetic uses for the skin, nails, hair or scalp, other than (i) for wound care through formulations of therapeutic product specifically designed to treat chronic wounds, thermal burns, radiation injury, accidental injury, surgical sites or scars, and (ii) therapeutic uses for treating cancer, excluding basal cell carcinoma, squamous cell carcinoma, precancerous conditions of the skin, actinic keratosis, actinic cheilitis, cutaneous horn, Bowen disease, radiation dermatosis, and dysplastic nevi, including but not limited to SB204, SB206, SB208, SB414 and our other presently-contemplated pipeline candidates (the "Retained Dermatology Field"). KNOW Bio granted us a right of first negotiation to obtain a license under any patents and patent applications generated by KNOW Bio during the first three years following the execution date of the agreement and directed towards medical devices to develop and commercialize licensed products in the Retained Dermatology Field. Additionally, Novan and KNOW Bio also agreed that neither party will commercialize any products in the other's field of use during the first three years following the execution date of such agreement.

Additionally, we granted to KNOW Bio exclusive sublicenses, with the ability to further sublicense, under certain of the U.S. and foreign patents and patent applications exclusively licensed to us from UNC and another third party directed towards nitric oxide-releasing compositions, including certain Nitricil compounds, to develop and commercialize products utilizing the licensed technology in the KNOW Bio Field. Under the exclusive sublicense to the UNC patents and applications, KNOW Bio is subject to the terms and conditions under the consolidated license agreement with UNC, including milestone and diligence payment obligations.

Under the exclusive license agreements and sublicense agreements, we retain all rights under our owned and exclusively licensed patents and patent applications with respect to development and commercialization of products for use in the Retained Dermatology Field. The exclusive license agreements and sublicense agreements will continue for so long as there is a valid patent claim under the respective agreement, unless earlier terminated, and upon expiration continues as a perpetual non-exclusive license. Under each agreement, Novan and KNOW Bio have

the right to terminate the agreement by subsequent written notice for the other party's material breach which remains uncured within 30 days of receipt of notice thereof. Novan also has the right to terminate each such agreement immediately upon written notice if KNOW Bio, its affiliates or sublicensees challenge the validity of any patent licensed in such agreement. KNOW Bio has the right to terminate each such agreement, with notice, for any reason upon ninety days advance written notice to us.

For additional information about the Separation Transaction, please see the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations—Separation Transaction."

Sato License Agreement

On January 12, 2017, we entered into a license agreement, and related amendment, relating to SB204, our lead drug candidate for the treatment of acne vulgaris in Japan, or the Agreement. Pursuant to the Agreement, we granted to Sato an exclusive, royalty-bearing, non-transferable license under certain of our intellectual property rights, with the right to sublicense with our prior written consent, to develop, use and sell products in Japan that incorporate SB204 in certain topical dosage forms for the treatment of acne vulgaris, and to make the finished form of such products. The rights granted to Sato do not include the right to manufacture the active pharmaceutical ingredient of SB204, for which we will retain the rights to supply to Sato. We will also supply finished product for use in development of SB204 in the licensed territory. During a specified time period, Sato has an exclusive option to negotiate the terms under which its license would be expanded to include certain additional territories within Asia, subject to Sato's payment of a specified option exercise fee. If Sato exercises its option to negotiate for a license in additional territories within Asia, such territories may include: China (including Hong Kong), South Korea, Taiwan, Singapore, Indonesia, Thailand, Philippines, Vietnam, Malaysia, Cambodia, Brunei, Myanmar or Laos. Under the terms of the Agreement, we also have exclusive rights to certain intellectual property that may be developed by Sato in the future, which we may choose to use for our own development and commercialization of SB204 outside of Japan.

The term of the Agreement (and the period during which Sato must pay royalties under the Agreement) expires, on a licensed product-by-licensed product basis, on the tenth anniversary of the first commercial sale of a licensed product in the licensed field in the licensed territory.

For additional information about the Agreement, please see the sections titled "Management's Discussion and Analysis of Financial Condition and Results of Operations—Corporate Updates" and "Note 14—Subsequent Events" of the accompanying financial statements.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's GLP regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human patients under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research patients provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1 clinical trial: The drug is initially introduced into healthy human patients or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- Phase 2 clinical trial: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3 clinical trials: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA, and more frequently if serious adverse events occur. Each of Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Special Protocol Assessment

The SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate, among other things, the proposed design and size of Phase 3 clinical trials that are intended to form the primary basis for determining a drug's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis. The FDA aims to complete SPA reviews within 45 days of receipt of the request.

The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to effectiveness of the indication studied. All agreements and disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Even if the FDA agrees to the design, execution and analyses proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement under the following circumstances:

- public health concerns emerge that were unrecognized at the time of the protocol assessment, or the director of the review division determines that a substantial scientific issue essential to determining safety or efficacy has been identified after testing has begun;
- a sponsor fails to follow a protocol that was agreed upon with the FDA; or
- the relevant data, assumptions or information provided by the sponsor in a request for SPA change are found to be false statements or misstatements, or are found to omit relevant facts.

A documented SPA may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol and if generally such modification is intended to improve the study.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. 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 typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, accelerated approval, priority review and breakthrough therapy designation, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the new PDUFA agreement, these six and ten month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act, or FDASIA, passed in July 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject

to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Coverage and Reimbursement

Sales of our product candidates, if approved, will depend, in part, on the extent to which such products will be covered by third-party payors, such as government healthcare programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly limiting coverage or reducing reimbursements for medical products and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of our products, once approved, and have a material adverse effect on our sales, results of operations and financial condition.

Manufacturing and Supplies

We currently manufacture the NVN1000 active pharmaceutical ingredient, one of our Nitricil NCEs, for all of our product candidates at our facility in Morrisville, North Carolina. We believe that our manufacturing capabilities represent a core competency for our Nitricil technology. We currently contract with a contract manufacturing organization, or CMO, to manufacture SB204, including compounding and primary packaging, and obtain our supplies of finished drug product through individual purchase orders. We expect to qualify other CMOs for the manufacture of drug product for the potential commercialization of SB204, if approved by the FDA, as well as in connection with later-stage trials and commercialization of our other product candidates.

We manufacture our investigational materials in accordance with cGMP required by the FDA, International Committee on Harmonization and other regulatory bodies. Our facilities have been audited for cGMP and Good Laboratory Practice, or GLP, compliance. In addition, our NCE manufacturing processes and operating conditions have been evaluated and tested by qualified vendors to ensure a safe operating environment. These tests include raw materials and product handling, process chemistry, air quality and waste disposal and containment.

We currently rely on third-party suppliers to provide the raw materials that are used by us or third-party manufacturers in the manufacture of our drugs. There are a limited number of suppliers for raw materials, including nitric oxide, that we use to manufacture our drugs.

In the future, we also plan to establish a second facility for active pharmaceutical ingredient production manufacturing to mitigate the risk of relying on a single facility for the production of NCEs from our Nitricil technology. We will also evaluate the potential for transferring our NCE manufacturing process to a CMO for commercial production.

Single Business Segment

We manage our operations and allocate resources as one reporting segment. For additional information, please refer to the notes to our consolidated financial statements included elsewhere in this Annual Report.

Research and Development Expenses

Our research and development expenses were $46.5 million, $16.6 million and $6.8 million for the years ended December 31, 2016, 2015 and 2014, respectively. Our research and development expenses for 2016, 2015 and 2014 consisted primarily of costs associated with the preclinical and clinical development of our product candidates. See Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this Annual Report for more information regarding our research and development expenses.

Employees

As of December 31, 2016, we had 62 employees, including 26 dedicated to the active pharmaceutical ingredient development and manufacturing capability, 8 in clinical and non-clinical development, 6 in regulatory and pharmaceutical development and 22 in general and administrative functions. None of our employees is subject to a collective bargaining agreement or represented by a labor or trade union. We believe that our relations with our employees are good.

Other Information

We were incorporated under the laws of the State of Delaware in 2006. Our principal executive offices are located at 4105 Hopson Road Morrisville, NC 27560, and our telephone number is 919-485-8080.

We maintain an internet website at www.novan.com and make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or

furnish such reports to, the SEC. The information contained on, or that can be accessible through, our website is not incorporated by reference into this Annual Report and should not be considered to be a part of this Annual Report.

Item 1A. Risk Factors.

Our operations and financial results are subject to a high degree of risk. These risks include, but are not limited to, those described below, each of which may have a material and adverse effect on our business, results of operations, cash flows financial conditions, and the trading price of our common stock. You should carefully consider the risks described below, together with all of the other information included in this Annual Report. The realization of any of these risks could have a significant adverse effect on our reputation, business, including our financial condition, results of operations and growth, which we refer to collectively in this section as our business, and ability to accomplish our strategic objectives. In that event, the trading price of our common stock could decline, and you may lose part or all of your investment.

Risks Related to the Development, Regulatory Approval and Commercialization of our Current and Future Product Candidates

Drug development involves a lengthy and expensive process with uncertain outcomes, and results from earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure or delay can occur at any time during the clinical trial process. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials, even after promising results in earlier preclinical studies or clinical trials. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events.

The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the required safety profile or meet the efficacy endpoints despite having progressed through preclinical studies and initial clinical trials. Notwithstanding any potential promising results in earlier testing, we cannot be certain that we will not face similar setbacks. For example, the top-line results of our two identically designed Phase 3 pivotal clinical trials for SB204 revealed that SB204 demonstrated statistical significance on all three co-primary endpoints in one trial, but demonstrated statistical significance on only one of the three co-primary endpoints in the other trial. We currently intend to conduct an additional clinical trial for SB204 in parallel with the FDA review to support FDA approval and in doing so will incur significant additional expenses for the SB204 program. Even if our clinical trials are completed for SB204 or our other product candidates, the results may not be sufficient to obtain regulatory approval for our product candidates.

Delay or termination of planned clinical trials for our product candidates could result in unplanned expenses or significantly adversely impact our commercial prospects with respect to, and ability to generate revenues from, such product candidates.

We have completed two Phase 3 pivotal clinical trials for SB204 and currently intend to conduct an additional clinical trial for SB204 in parallel with the FDA review to support NDA approval. We have completed a Phase 2 dose-ranging clinical trial for SB206 and, assuming a successful end-of-Phase 2 meeting with the FDA in the second quarter of 2017, we plan to initiate our late-stage program with Phase 3 pivotal clinical trials by the end of 2017. We are also currently conducting a Phase 2 clinical trial for SB208 and expect to announce top-line results in the second quarter of 2017. In addition, we are targeting initiation of clinical development of our anti-inflammatory program for SB414 in the second quarter of 2017. We may experience delays in completing and initiating these ongoing and planned trials and we cannot be certain that these trials or any other future clinical trials for our product candidates will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- the FDA disagreeing as to the design or implementation of our clinical trials;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining institutional review board, or IRB, approval at each site;
- the safety profiles of our product candidates;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol;
- addressing patient safety concerns that arise during the course of a trial;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse events, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Even if we complete our trials on schedule, inconsistent trial results may result in a delay in our completion of an overall program for a product candidate. For example, following an in-depth analysis of top-line results from our two identically designed Phase 3 pivotal clinical trials for SB204, we are now planning to conduct an additional clinical trial for SB204 in parallel with the FDA review to support FDA approval.

If we experience delays in the completion, or termination, of any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenues from any of these product candidates will be delayed or not realized at all. Any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

In addition, our ongoing SB414 preclinical studies may not prove successful in demonstrating proof-of concept, or may show adverse toxicological findings, and even if successful may not necessarily predict that subsequent clinical trials will show the requisite safety and efficacy of our product candidates.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends on, among other things, our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- our ability to obtain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials will compete for the recruitment of patients with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors.

Delays in patient enrollment may result in increased costs, which would adversely impact our statement of operations and cash flows, or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates and hurt our competitive position.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of their potential both to gain regulatory approval and to achieve commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or in other indications with greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

Our product candidates may pose safety issues, cause adverse events or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

We, any partner with whom we may collaborate in the future or the FDA may suspend, delay, require modifications to or terminate our clinical trials at any time, for various reasons, including the discovery of serious or unexpected toxicities or other safety issues experienced by trial participants.

In addition, adverse events caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of adverse events or unexpected characteristics. To date, patients treated with our product candidates have experienced drug-related cutaneous tolerability observations, including dryness, scaling, burning, erythema, itching, pain or irritation, and adverse events, including irritation and contact dermatitis.

If safety issues or unacceptable adverse events arise in the development of our product candidates, we, the FDA, the IRBs at the institutions in which our trials are conducted, or the DSMB could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related adverse events could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these adverse events may not be appropriately recognized or managed by the treating medical staff.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and may result in the loss of significant revenues to us, which would materially and adversely affect our results of operations and business.

The regulatory approval processes of the FDA are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we receive regulatory approval of an NDA from the FDA.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA, that such product candidates are safe and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. For example, there are multiple methodologies for handling missing data and other statistical considerations to take into account that the FDA may utilize when analyzing the robustness of any data set during NDA review. As part of our in-depth examination of the full data sets from the Phase 3 trials, we conducted a number of post hoc analyses. The measure of statistical significance on all of the co-primary endpoints for the NI-AC302 trial was consistently strong when analyzed with two other sensitivity analysis methodologies for missing data, last observation carried forward and baseline observation carried forward. We believe this confirms the robustness of the data from the NI-AC302 trial, and these stricter statistical analyses for missing data do not diminish the strength of the data from the NI-AC302 trial. However, these additional analyses do not change the outcomes of the NI-AC301 trial, and the FDA may disagree with our conclusions from the post hoc analyses we conducted. The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program. For example, we intend to pursue a pre-NDA submission meeting in the third quarter of 2017 to discuss the entirety of

the SB204 program, which could lead to an NDA submission targeted in the first quarter of 2018. While we currently intend to conduct an additional trial in parallel with the FDA review to support FDA approval, the FDA could require additional trials or additional information to support our NDA submission or approval.

The FDA can delay, limit or deny approval of our product candidates or require us to conduct additional preclinical or clinical testing or abandon a program for many reasons, including:

- the FDA's disagreement with the design or implementation of our clinical trials;
- negative or ambiguous results from our clinical trials;
- results that may not meet the level of statistical significance required by the FDA for approval;
- serious and unexpected drug-related adverse events experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- our inability to demonstrate to the satisfaction of the FDA that our product candidates are safe and effective for the proposed indication;
- the FDA's disagreement with the interpretation of data from preclinical studies or clinical trials;
- our inability to demonstrate that the clinical and other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's requirement for additional preclinical studies or clinical trials;
- the FDA's disagreement regarding the formulation, labeling or the specifications of our product candidates;
- the FDA's agency's failure to approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or
- the potential for approval policies or regulations of the FDA to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA approval process and become commercialized. The lengthy approval process as well as the unpredictability of outcomes from future clinical trials may result in our failing to obtain regulatory approval to market our product candidates.

Even if we eventually complete clinical testing and receive approval of an NDA or foreign marketing application for our product candidates, the FDA may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, or the implementation of a Risk Evaluation and Mitigation Strategy, or REMS, which may be required to ensure safe use of the drug after approval. The FDA also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate.

Regulatory approval of our product candidates by foreign regulatory authorities may be delayed or denied. We may be subject to pricing controls imposed by foreign governments and regulatory authorities.

We may seek regulatory approval of our product candidates from foreign regulatory authorities in the future. Such regulatory authorities may impose additional regulations and guidelines that differ in form and substance from those imposed by their counterparts in the United States and with which we are more familiar. Accordingly, the regulatory approval of our product candidates in those foreign jurisdictions could be delayed, limited or denied altogether. This could limit the scope of or prevent the commercialization of our products in the future and adversely affect our financial performance.

Further, in some countries, the pricing of pharmaceutical prescriptions is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of

marketing approval for a product candidate. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution or arbitrage between low-priced and high-priced countries can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies, which is time-consuming and costly. If coverage and reimbursement of our product candidates are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

Even if our current product candidates or any future product candidates obtain regulatory approval, they may fail to achieve the broad degree of physician and patient adoption and use necessary for commercial success.

The commercial success of any of our current or future product candidates, if approved, will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. Our product candidates may not be commercially successful. The degree and rate of physician and patient adoption of our current or future product candidates, if approved, will depend on a number of factors, including:

- the clinical indications for which the product is approved and patient demand for approved products that treat those indications;
- the effectiveness of our product as compared to other available therapies;
- the availability of coverage and adequate reimbursement from managed care plans and other healthcare payors for any of our product candidates that may be approved;
- the cost of treatment with our product candidates in relation to alternative treatments and willingness to pay for the product, if approved, on the part of patients;
- acceptance by physicians, major operators of clinics and patients of the product as a safe and effective treatment;
- physician and patient willingness to adopt a new therapy over other available therapies to treat approved indications;
- overcoming any biases physicians or patients may have toward particular therapies for the treatment of approved indications;
- patient satisfaction with the results and administration of our product candidates and overall treatment experience;
- the willingness of patients to pay for certain of our product candidates relative to other discretionary items, especially during economically challenging times;
- the revenue and profitability that our product candidates may offer a physician as compared to alternative therapies;
- the prevalence and severity of adverse events;
- limitations or warnings contained in the FDA-approved labeling for our product candidates;
- any FDA requirement to undertake a REMS;
- the effectiveness of our sales, marketing and distribution efforts;
- adverse publicity about our product candidates or favorable publicity about competitive products; and
- potential product liability claims.

If any of our current or future product candidates are approved for use but fail to achieve the broad degree of physician and patient adoption necessary for commercial success, our operating results and financial condition will be adversely affected, which may delay, prevent or limit our ability to generate revenue and continue our business.

Even if we make a submission under a special protocol assessment, or SPA, from the FDA, there is no guarantee that we will obtain agreement from the FDA on the SPA. Even if we do obtain the FDA's agreement, an SPA would not guarantee approval of any of our product candidates or any other particular outcome from regulatory review.

We currently do not have an SPA in place with respect to any of our product candidates. We have previously made such a submission for an SPA to the FDA in connection with the design of our Phase 3 clinical trials for SB204. We received feedback from the FDA on our Phase 3 trial design that we believed was sufficient to move forward on the Phase 3 development program without further pursuing an SPA. We recognize that the feedback obtained in connection with the SPA discussions does not constitute a formal SPA or a binding declaration from the FDA that it agrees with the Phase 3 clinical trials' design, clinical endpoints or statistical analysis plan. We may, in the future, decide to make a submission for an SPA for any of our current or future product candidates.

The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate, among other things, the proposed design and size of clinical trials that are intended to form the primary basis for determining a drug product's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis. The FDA aims to complete SPA reviews within 45 days of receipt of the request. The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to the effectiveness of the indication studied. All agreements and disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Even if the FDA agrees to the SPA, an SPA agreement does not guarantee approval of a product candidate. Even if the FDA agrees to the design, execution, and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor company fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a request for the SPA change or are found to be false or omit relevant facts. In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol and if generally such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

Moreover, if the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval.

Our product candidates may cause side effects which could delay or prevent their commercialization.

If any of our product candidates receives marketing approval, and we or other companies developing other nitric oxide-based therapies, including KNOW Bio, LLC, which has the right to develop our current nitric oxide-based technology in non-dermatological indications, later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- regulatory authorities may require the addition of labeling statements, such as a ‘‘black box’’ warning or a contraindication;
- we may be required to implement a REMS or create a Medication Guide outlining the risks of such adverse events for distribution to patients;

- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

We expect to educate and train medical personnel so they know how to use our product candidates to understand their potential side effect profiles. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury.

If we are unable to establish sales, marketing and distribution capabilities for our product candidates or any future product candidate that receives regulatory approval, we may not be successful in commercializing those product candidates, if approved.

We do not currently have a sales, marketing or distribution infrastructure in place. To achieve commercial success for any product candidate for which we may obtain marketing approval, we will need to establish a sales, marketing and distribution framework. In the future, we expect to build a focused sales, marketing and distribution infrastructure to market any of our product candidates in the United States. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay market uptake. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and enter into arrangements with third parties to perform these services, this could, in turn, decrease our revenue and our profitability. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We may not have adequate control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Additionally, we have entered into an exclusive license agreement with Sato relating to SB204 for the treatment of acne vulgaris in Japan, and we expect to continue to evaluate strategic partnerships to commercialize our dermatology products in select international markets. We may not be sufficiently familiar or have the requisite resources to penetrate international markets where some of our competitors have already achieved broad recognition and have established commercialization strategies in place. Moreover, we may not succeed in targeting healthcare providers, including physicians, outside the dermatology prescribing base, who may not be familiar with our product candidates.

Our product candidates, if approved, will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration.

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on developing proprietary therapeutics. Numerous companies are engaged in the development, patenting, manufacturing and marketing of healthcare products competitive with those that we are developing. We face

competition from a number of sources, such as pharmaceutical companies, generic drug companies, biotechnology companies and academic and research institutions, many of which have greater financial resources, marketing capabilities, sales forces, manufacturing capabilities, research and development capabilities, clinical trial expertise, intellectual property portfolios, experience in obtaining patents and regulatory approvals for product candidates and other resources than we do. Some of the companies that offer competing products also have a broad range of other product offerings, large direct sales forces and long-term customer relationships with our target physicians, which could inhibit our market penetration efforts. In addition, certain of our product candidates, if approved, may compete with other dermatological products, including over-the-counter treatments, for a share of some patients' discretionary budgets and for physicians' attention within their clinical practices.

Many pharmaceutical companies currently offer products, and continue to develop additional alternative product candidates and technologies, for indications similar to those targeted by our product candidates, including Galderma S.A., Allergan, Inc. and Valeant Pharmaceuticals International, Inc. The markets for dermatological therapies are competitive and are characterized by significant technological development and new product introduction. We anticipate that, if we obtain regulatory approval of our product candidates, we will face significant competition from other approved therapies. If approved, our product candidates may also compete with unregulated, unapproved and off-label treatments. To compete successfully in this market, we will have to demonstrate that the relative cost, safety and efficacy of our approved products, if any, provide an attractive alternative to existing and other new therapies. Such competition could lead to reduced market share for our product candidates and contribute to downward pressure on the pricing of our product candidates.

Due to less stringent regulatory requirements in certain foreign countries, there are many more dermatological products and procedures available for use in those international markets than are approved for use in the United States. In certain international markets, there are also fewer limitations on the claims that our competitors can make about the effectiveness of their products and the manner in which they can market them. As a result, we expect to face more competition in these markets than in the United States.

Even if we obtain marketing approval for any product candidates, the products may become subject to unfavorable third-party coverage or reimbursement policies, which would harm our business.

The success of our product candidates, if approved, depends on the availability of adequate coverage and reimbursement from government authorities and third-party payors, such as private health insurers and health maintenance organizations. Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to product acceptance.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement that will be provided. Coverage decisions may depend on clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Third-party payors may refuse to include a particular branded product in their formularies, or lists of medications for which third-party payors provide coverage and reimbursement, or otherwise restrict patient access through formulary controls or otherwise to a branded product when a less costly generic equivalent or other alternative is available. Coverage may be more limited than the purposes for which a product is approved by the FDA or similar regulatory authorities outside the United States.

Assuming that we obtain coverage for a given product, the resulting reimbursement rates might not be adequate to cover our costs, including research, development, manufacture, sale and distribution, or achieve or sustain profitability, or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Increasingly, third-party payors are requiring that pharmaceutical companies provide them with predetermined discounts from list prices and are challenging the prices charged for products. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for a product can differ significantly from payor to payor. As a result, obtaining and maintaining coverage and reimbursement for a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each payor separately, with no assurance that adequate coverage and reimbursement will be applied consistently or obtained in the first instance.

Governmental and third-party payors in the United States and abroad are developing increasingly sophisticated methods of controlling healthcare costs. Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third-party coverage and reimbursement for our product candidates for which we may receive regulatory approval may not be available, limited, or adequate in either the United States or international markets.

We may face product liability exposure, and if successful claims are brought against us, we may incur substantial liability if our insurance coverage for those claims is inadequate.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. This risk exists even if a product is approved for commercial sale by the FDA and manufactured in facilities licensed and regulated by the FDA or an applicable foreign regulatory authority. Our product candidates are designed to affect important bodily functions and processes. Any adverse events, manufacturing defects, misuse or abuse associated with our product candidates could result in injury to a patient or even death. We cannot offer any assurance that we will not face product liability suits in the future, nor can we assure you that our insurance coverage will be sufficient to cover our liability under any such cases.

In addition, a liability claim may be brought against us even if our product candidates merely appear to have caused an injury. Product liability claims may be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our product candidates, among others. If we cannot successfully defend ourselves against product liability claims we will incur substantial liabilities and reputational harm. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- withdrawal of clinical trial participants;
- decreased enrollment rates of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- the inability to commercialize our product candidates;
- decreased demand for our product candidates;
- impairment of our business reputation;
- product recall or withdrawal from the market or labeling, marketing or promotional restrictions;
- substantial costs of any related litigation or similar disputes;
- distraction of management's attention and other resources from our primary business;
- substantial monetary awards to patients or other claimants against us that may not be covered by insurance; or
- loss of revenue.

We have obtained product liability insurance coverage, with an aggregate limit of $5.0 million, for clinical trials. Large judgments have been awarded in class action or individual lawsuits based on drugs that had unanticipated adverse events. Our insurance coverage may not be sufficient to cover all of our product liability related expenses or losses and may not cover us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost, in sufficient amounts or upon adequate terms to protect us against losses due to product liability. We will need to increase our product liability coverage if any of our product candidates receive regulatory approval, which will be costly, and we may be unable to obtain this increased product liability insurance on commercially reasonable terms,

or at all. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash, negatively impact our statement of operations and could harm our financial condition.

If and when we market our product candidates, our relationships with healthcare providers, customers and third-party payors, as well as our general business operations, may be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, and failure to comply with such regulations could expose us to penalties including criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, customers and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we may obtain marketing approval. Our future arrangements with third-party payors, healthcare providers and customers and our general operations may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any product candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations may include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation.
- the federal false claims and civil monetary penalties laws, including the civil False Claims Act, which impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; in addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to certain payments or other ''transfers of value'' made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members and payments or other ''transfers of value'' to such physician owners; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines

and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or report marketing expenditures and pricing information; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under such laws, it is possible that some of our business activities, including our relationships with physicians and other healthcare providers, some of whom will recommend, purchase or prescribe our products, could be subject to challenge under one or more of such laws.

If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, which would adversely impact our statement of operations and cash flows.

Risks Related to Manufacturing and our Reliance on Third Parties

We may not be successful in continuing to establish development and commercialization collaborations, which could adversely affect, and potentially prohibit, our ability to develop our product candidates.

We may continue to enter into strategic partnerships with third parties to develop and commercialize our product candidates. There can be no assurance that we will be able to establish such collaborations on favorable terms, if at all, or that our current or future collaborative arrangements will be successful. If we are unable to reach successful agreements with suitable collaborators for our product candidates, we would face incremental costs, we may be required to limit the scope and number of our product candidates we can commercially develop or the territories in which we commercialize them and we might fail to commercialize products or programs for which a suitable collaborator cannot be found. Our current and future collaboration partners may not dedicate sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we fail to achieve successful collaborations, our operating results and financial condition will be materially and adversely affected. If we breach or fail to comply with any provision of a collaboration agreement, a collaborator may have the right to terminate, in whole or in part, such agreement or to seek damages. Some of our collaboration agreements are complex and involve sharing of certain data, know-how and intellectual property rights amongst the parties. Our collaborators could interpret certain provisions differently than we do, which could lead to unexpected or inadvertent disputes with our collaborators. Any one of our collaborators could breach covenants or restrictions in our agreements, leading us into disputes and potential breaches of our agreements with other collaborators.

We rely on third parties to conduct some of our preclinical studies and all of our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize any of our product candidates.

We currently do not have the ability to independently conduct preclinical studies that comply with the regulatory requirements known as good laboratory practice, or GLP, requirements. We also do not currently have the ability to independently conduct any clinical trials. The FDA and regulatory authorities in other jurisdictions require us to comply with regulations and standards, commonly referred to as good clinical practice, or GCP, requirements for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and

results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as contract research organizations, or CROs, to conduct GLP-compliant preclinical studies and GCP-compliant clinical trials on our product candidates properly and on time. While we will have agreements governing their activities, we control only certain aspects of their activities and have limited influence over their actual performance. The third parties with whom we contract for execution of our GLP preclinical studies and our GCP clinical trials play a significant role in the conduct of these studies and trials and the subsequent collection and analysis of data. These third parties are not our employees and, except for restrictions imposed by our contracts with such third parties, we have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely on these third parties to conduct our GLP-compliant preclinical studies and GCP-compliant clinical trials, we remain responsible for ensuring that each of our GLP preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. In addition, if any of our CROs terminate their involvement with us for any reason, we may not be able to enter into similar arrangements with alternative CROs within a short period of time, or do so on commercially reasonable terms.

Many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. In addition, since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. If the third parties conducting our GLP preclinical studies or our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or 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 trial protocols or to GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and our preclinical studies or clinical trials may need to be extended, delayed, terminated or repeated. As a result, we may not be able to obtain regulatory approval in a timely fashion, or at all, for the applicable product candidate, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA of any NDA we submit. Any such delay or rejection could prevent us from commercializing our future product candidates.

Unexpected delays in our ability to manufacture our NVN1000 active pharmaceutical ingredient, or any other Nitricil NCEs, in our facility, for support of our development activities could adversely affect our development and commercialization timelines and result in increased costs of our development programs.

We currently manufacture the NVN1000 active pharmaceutical ingredient, one of our Nitricil NCEs, for all of our product candidates at our facility in Morrisville, North Carolina. We have a limited number of personnel that have experience in drug substance manufacturing and who possess the expertise necessary to manufacture NVN1000. If our facility were to sustain significant damage, or if we had significant attrition in our manufacturing personnel, our manufacturing operations could be delayed for an extended period of time. If our existing inventories of active drug substance are depleted, we may be unable to supply necessary materials for preclinical studies and clinical trials, causing longer timelines, increased costs and delays in the commercialization of drug products, if approved by the FDA or other regulatory authorities.

Further, the FDA requires drug product to be manufactured in accordance with current good manufacturing practices, or cGMP. Our facilities have been audited for cGMP and Good Laboratory Practice compliance. In addition, our NCE manufacturing processes and operating conditions have been evaluated and tested by qualified vendors to ensure a safe operating environment. These tests include raw materials and product handling, process

chemistry, air quality and waste disposal and containment. However, if our facilities are found to be noncompliant with applicable regulatory requirements, we may be required to take remedial actions, causing further delays and increased costs.

We rely on third parties to manufacture clinical drug supplies for us and parties with which we contract, and we intend to rely on third parties to produce commercial supplies of any approved product candidate. Failure of those third parties to obtain approval of the FDA or comparable regulatory authorities, to provide us with sufficient quantities of drug product or to provide sufficient quantities of drug product at acceptable quality levels or prices could adversely impact our commercialization of any of our product candidates or result in our breaching our obligations to others.

We do not currently have nor do we plan to acquire the infrastructure or capability internally to completely manufacture clinical drug supplies, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. While we currently manufacture the active drug substance in our own facilities, we rely on third parties to manufacture the finished drug product for our own use and intend to rely on them for finished drug products that we may provide to others. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements, known as current good manufacturing practice, or cGMP, requirements for manufacture of drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

We rely on third-party manufacturers to purchase from third-party suppliers the materials necessary to produce the drug products we require. There are a limited number of suppliers for raw materials, including nitric oxide, that are used in the manufacture of our product candidates, drugs (once approved by the FDA or comparable regulatory authority) or the drug products we supply to others, and there may be a need to assess alternate suppliers to prevent a possible disruption of the manufacture of the materials, importantly nitric oxide, necessary to produce our product candidates for our clinical trials, and if approved, ultimately for commercial sale, or to satisfy our obligations to others. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials, including nitric oxide. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical trial, any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these raw materials, including nitric oxide, after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

We currently contract with a single CMO to manufacture SB204 and our other drug products, including compounding, formulation and primary packaging for our clinical trials. We also currently contract with a single packaging materials supplier for SB204 and our other drug products. If our CMO or packaging materials supplier were unable to manufacture and provide the necessary drug product supplies to conduct our clinical trials, we may not be able to contract with another CMO in a timely manner to meet our specifications and supply needs. As a result, we could experience delays in the development and commercialization timelines of our product candidates, as well as increased costs.

We expect to continue to depend on third-party contract manufacturers for the foreseeable future. We have not entered into long-term agreements with our current contract manufacturers or with any alternate suppliers, and though we intend to do so prior to commercial launch in order to ensure that we maintain adequate supplies of

finished drug product, we may be unable to enter into such an agreement or do so on commercially reasonable terms. We currently obtain our supplies of finished drug product through individual purchase orders.

Our employees, independent contractors, principal investigators, CROs, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could expose us to liability and hurt our reputation.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants, commercial partners and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless or negligent conduct or disclosure of unauthorized activities to us that violates: (i) FDA laws and regulations, including those laws that require the reporting of true, complete and accurate information to the FDA, (ii) manufacturing standards, (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws, or (iv) laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Risks Related to Our Operations

Our business involves the use of hazardous materials and we and our third-party suppliers and manufacturers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

The manufacturing activities of our third-party suppliers and manufacturers involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product candidates such as nitric oxide and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our suppliers' or manufacturers' facilities pending use and disposal. We and our suppliers and manufacturers cannot completely eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, injury to our service providers and others and environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party suppliers and manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our financial resources.

We specialize solely in developing nitric oxide-based dermatology therapeutics, and if we do not successfully achieve regulatory approval for any of our product candidates or successfully commercialize them, we may not be able to continue as a business.

All of our clinical development efforts to date have focused on the development of nitric oxide-based topical therapies. There can be no assurance that the intended or anticipated results from the use of nitric oxide-based therapies will be reaped, and that we will successfully bring our product candidates to market. Because all of our current product candidates are based on nitric oxide and our Nitricil technology, the failure of our Nitricil technology to be safe or efficacious generally will have adverse implications for our entire product candidate

pipeline. If, for any reason, our intended use of nitric oxide does not materialize, we may not be able to redeploy our resources to alternative components or raw materials, efficiently or at all.

We expect to experience significant growth which may adversely disrupt our operations.

As of December 31, 2016, we had 61 full-time employees and one part-time employee. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the area of product development and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our business and operations would suffer in the event of computer system failures, cyber-attacks or deficiencies in our cyber-security.

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material legal claims and liability, and damage to our reputation, and the further development of our product candidates could be delayed.

Risks Related to Government Regulation

Even if we receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties, if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or the conditions of approval, or contain requirements for potentially costly post-market testing and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCP requirements for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation remains unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may fail to obtain any marketing approvals, lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. Notably, on January 23, 2017, President Trump ordered a hiring freeze for all executive departments and agencies, including the FDA, which prohibits the FDA from filling employee vacancies or creating new positions. Under the terms of the order, the freeze will remain in effect until implementation of a plan to be recommended by the Director for the Office of Management and Budget, or OMB, in consultation with the Director of the Office of Personnel Management, to reduce the size of the federal workforce through attrition. An under-staffed FDA could result in delays in FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance or implement or enforce regulatory requirements in a timely fashion or at all. Moreover, on January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality

provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations, however it is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

For example, in the United States, in 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Among the provisions of the ACA of importance to our potential product candidates are the following:

- an annual, nondeductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries under their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

There have been judicial and Congressional challenges to certain aspects of the ACA. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the ACA Since its

enactment. We expect that the new Presidential Administration and U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. In March 2017, the U.S. House of Representatives introduced legislation known as the American Health Care Act, or the AHCA, which, if enacted, would amend or repeal significant portions of the ACA. Among other changes, the AHCA, would repeal the annual fee on certain brand prescription drugs and biologics imposed on manufacturers and importers, eliminate penalties on individuals and employers that fail to maintain or provide minimum essential coverage and create refundable tax credits to assist individuals in buying health insurance. The AHCA would also make significant changes to Medicaid by, among other things, making Medicaid expansion optional for states, repealing the requirement that state Medicaid plans provide the same essential health benefits that are required by plans available on the exchanges, modifying federal funding, including implementing a per capita cap on federal payments to states, and changing certain eligibility requirements. While it is uncertain when or if the provisions in the AHCA will become law, or the extent to which any such changes may impact our business, it is clear that concrete steps are being taken to repeal and replace certain aspects of the ACA.

In addition, other legislative changes have been proposed and adopted in the U.S. since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and, due to the Bipartisan Budget Act of 2015, will remain in effect through 2025 unless additional action is taken by Congress. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates, if approved.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We are subject to governmental economic sanctions and export and import controls that could impair our ability to compete in international markets or subject us to liability if we are not in compliance with applicable laws.

As a U.S. company, we are subject to U.S. import and export controls and economic sanctions laws and regulations, and we are required to import and export our product candidates, technology and services in compliance with those laws and regulations, including the U.S. Export Administration Regulations, the International Traffic in Arms Regulations, and economic embargo and trade sanction programs administered by the Treasury Department's Office of Foreign Assets Control.

U.S. economic sanctions and export control laws and regulations prohibit the shipment of certain products and services to countries, governments and persons targeted by U.S. sanctions. While we are currently taking precautions to prevent doing any business, directly or indirectly, with countries, governments and persons targeted by U.S. sanctions and to ensure that our product candidates, if approved, are not exported or used by countries, governments and persons targeted by U.S. sanctions, such measures may be circumvented.

Furthermore, if we export our product candidates, if approved, the exports may require authorizations, including a license, a license exception or other appropriate government authorization. Complying with export control and sanctions regulations for a particular sale may be time-consuming and may result in the delay or loss of sales opportunities. Failure to comply with export control and sanctions regulations for a particular sale may expose us to government investigations and penalties.

If we are found to be in violation of U.S. sanctions or import or export control laws, it could result in civil and criminal, monetary and non-monetary penalties, including possible incarceration for those individuals responsible for the violations, the loss of export or import privileges and reputational harm.

We are subject to anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act and possibly other anti-bribery and anti-money laundering laws in countries in which we may conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees and third-party intermediaries from authorizing, offering or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. As we commercialize our product candidates and eventually commence international sales and business, we may engage with collaborators and third-party intermediaries to sell our products abroad and to obtain necessary permits, licenses and other regulatory approvals. We or our third-party intermediaries may have direct or indirect interactions with officials and employees of government agencies or state-owned or affiliated entities. We may be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners and agents, even if we do not explicitly authorize such activities.

Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage and other collateral consequences. Responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense costs and other professional fees.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and product candidates may be impaired.

We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our product candidates. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates.

The patent prosecution process is expensive and time-consuming, however, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our technology platform or product candidates before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to or from third parties. In particular, certain patents and patent applications covering our core technology platform are exclusively licensed from the University of North Carolina, or UNC, and under our license agreement with UNC, we rely on UNC to prosecute and maintain such patents and applications. Therefore, these patents and applications, and any other patents and applications that we may license from or to third parties, may not be prosecuted and enforced in a manner consistent with the best interests of our business.

If the patent applications we hold or have in-licensed with respect to our product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our current or any future product candidates, it could have a materially adverse effect on our business. Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned and licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned and licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our owned and licensed patents or narrow the scope of our patent protection while patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The United States Patent Office recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have an adverse effect on our business and financial condition. For example, the first to file system under the Leahy-Smith Act may incentivize companies like us in the biopharmaceutical industry to file patent applications as soon as possible, and filing applications as soon as possible runs the risk that the application will not have the supporting data to claim the broadest protection possible in the United States.

Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our owned and licensed patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Finally, certain of our activities and our licensors' activities have been funded, and may in the future be funded, by the U.S. federal government. When new technologies are developed with U.S. federal government funding, the government obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise "march-in" rights to use or allow third parties to use our patented technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government, U.S. government funding must be disclosed in any resulting patent applications, and our rights in such inventions may be subject to certain requirements to manufacture products in the United States.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, 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.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and other foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign national or international patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of patent rights include, but are not limited to, failure to timely file national and regional stage patent applications based on our international patent application, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our technology platform or product candidates, our competitors might be able to enter the market, which would have an adverse effect on our business.

Changes in U.S. patent laws could diminish the value of patents in general, thereby impairing our ability to protect our products.

The United States has recently enacted and implemented wide-ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future.

We may be involved in lawsuits to protect or enforce our owned and licensed patents, which could be expensive, time-consuming and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

If we were to initiate legal proceedings against a third-party to enforce a patent directed to our product candidates, or one of our future product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would harm our business.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our owned and licensed patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, or at all.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Most of our competitors are larger than we are and have substantially greater resources than we do. They are, therefore, likely to be able to sustain the costs of complex patent or other intellectual property rights litigation longer than we could. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. Litigation could result in substantial costs and diversion of management resources, which could harm our business. In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, or in-license needed technology or other product candidates. There could also be public announcements of the results of the hearing, motions, or other interim proceedings or developments. If securities analysts or investors perceive those results to be negative, it could cause the price of shares of our common stock to decline.

We may not be able to protect our intellectual property rights throughout the world, which could impair our business.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our invention in such countries. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the United States. These products may compete with our product candidates and our owned and licensed patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of some countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our owned and licensed patents generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being

invalidated or interpreted narrowly and our owned and licensed patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

Many countries, including European Union countries, India, Japan and China, have compulsory licensing laws under which a patent owner may be compelled under specified circumstances to grant licenses to third parties. In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We may not be able to obtain licenses to third-party intellectual property. Third parties may initiate legal proceedings alleging infringement of their intellectual property rights.

A third party may hold intellectual property, including patent rights that are important or necessary to the development or commercialization of our product candidates. However, we may not be able to obtain such licenses on commercially reasonable terms, or at all. In addition, our existing licenses may be terminated or may not be renewed, which could hurt our business.

In addition, our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the USPTO. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates or other business activities may be subject to claims of infringement of the patent and other proprietary rights of third parties. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. We have conducted searches for information in support of patent protection and otherwise evaluating the patent landscape for nitric oxide releasing materials and products, and, based on these searches and evaluations to date, we do not believe that there are valid patents which contain granted claims that could be asserted with respect to our nitric oxide-based product candidates.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates or force us to cease some of our business operations. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. If we are found to infringe a third party's intellectual property rights, we could be required to redesign our infringing products or obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. Moreover, we could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at other biotechnology or pharmaceutical companies or universities. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

If we fail to comply with our obligations under any license, collaboration or other agreements, it could have a material adverse effect on our commercialization efforts for our product candidates.

Our current license with UNC imposes, and any future licenses we enter into may impose, various development, commercialization, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position.

We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees (including through specific provisions in employment contracts), corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be materially impaired.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we expect to rely on third parties to manufacture SB204 and any future product candidates, we must, at times, share trade secrets with them. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may adversely impact our business.

Any trademarks we have obtained or may obtain may be infringed or successfully challenged, materially harming to our business.

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. Once we select new trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Further, our competitors may infringe our trademarks, including with respect to our Nitricil technology and we may not have adequate resources to enforce our trademarks.

Outside of the United States we cannot be certain that any country's patent or trademark office will not implement new rules that could seriously affect how we draft, file, prosecute and maintain patents, trademarks and patent and trademark applications.

We cannot be certain that the patent or trademark offices of countries outside the United States will not implement new rules that increase costs for drafting, filing, prosecuting and maintaining patents, trademarks and patent and trademark applications or that any such new rules will not restrict our ability to file for patent protection. For example, we may elect not to seek patent protection in some jurisdictions or for some product candidates in order to save costs. We may be forced to abandon or return the rights to specific patents due to a lack of financial resources.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage, for reasons including but not limited to the following:

- others may be able to make formulations or compositions that are the same as or similar to certain of our product candidates but that are not covered by the claims of the patents that we own or license;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our trade secret or similar rights;
- issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; and
- we may not develop additional proprietary technologies that are patentable.

Risks Related to our Financial Results

We have incurred significant losses since our inception. We expect to incur losses for at least the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $11.4 million for the year ended December 31, 2014, $28.1 million for the year ended December 31, 2015 and $59.7 million for the year ended December 31, 2016. As of December 31, 2016, we had an accumulated deficit of $123.0 million. As a result of our historical operating losses and expected future negative cash flows from operations, we have concluded that there is substantial doubt about our ability to continue as a going concern. Similarly, the report of our independent registered public accounting firm on our December 31, 2016 financial statements includes an explanatory paragraph indicating that there is substantial doubt about our ability to continue as a going concern. To date, we have financed our operations primarily through the sale of common stock in our initial public offering, or IPO, private placements of our preferred stock, convertible notes and proceeds from government research contracts and grants. We also recently received an upfront payment following the execution of a license agreement for the exclusive right to develop, use

and sell SB204 in certain topical dosage forms in Japan for the treatment of acne vulgaris. We have devoted substantially all of our efforts to research and development, including clinical trials. We have not completed development of any product candidates. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that we will continue to incur substantial expenses if and as we:

- continue to conduct clinical trials for SB204, SB206 and SB208;
- initiate clinical trials of SB414 or for other future product candidates;
- seek regulatory approvals for our product candidates that complete clinical trials;
- qualify contract manufacturing organizations for the manufacture of drug product for the commercial launch of our product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- continue our research and development efforts;
- hire additional clinical, quality control, scientific and management personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This development and commercialization will require us to be successful in a range of challenging activities, including successfully completing clinical trials of our product candidates, obtaining regulatory approval for these product candidates, and marketing and selling those products for which we may obtain regulatory approval. We are only in the preliminary stages of some of these activities. We may never succeed in these activities and may never generate revenues that are significant or large enough to achieve profitability.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, expand our business, maintain our research and development efforts or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Our ability to utilize our net operating loss, or NOL, carryforwards may be limited.

As of December 31, 2016, we had NOL carryforwards available to reduce future taxable income, if any, for federal and state income tax purposes of $105.1 million and $106.7 million, respectively. If not utilized, the federal and state NOL carryforwards will begin expiring in 2028 and 2023 for federal and state tax purposes, respectively. Our ability to utilize NOL carryforward amounts to reduce taxable income in future years may be limited for various reasons, including if future taxable income is insufficient to recognize the full benefit of such NOL carryforward amounts prior to their expiration. Additionally, our ability to fully utilize these U.S. tax assets can also be adversely affected by "ownership changes" within the meaning of Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, in a three-year period. Any ownership change is generally defined as a greater than 50% increase in equity ownership by "5% stockholders," as that term is defined for purposes of Section 382 of the Code in any three year period. We may have experienced an ownership change in connection with our IPO or otherwise in the future as a result of shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce, terminate or eliminate our product development programs, or our commercialization efforts.

We expect to continue to incur substantial expenses in connection with our ongoing activities, including conducting clinical trials of SB204, SB206, SB208, and SB414, and seeking regulatory approval for our product candidates. In addition, if we obtain regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. Furthermore, we expect to continue to incur substantial costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Adequate funding may not be available to us on acceptable terms, or at all. The top-line results from our parallel pivotal SB204 Phase 3 trials, coupled with the recent decline in the market value of our common stock, may negatively impact our available funding options and the acceptability of funding terms. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, terminate or eliminate our product development programs, or our commercialization efforts.

As of December 31, 2016, we had cash and cash equivalents of $34.6 million and working capital of $22.2 million. We believe that our existing cash and cash equivalents, together with the nonrefundable upfront payment received from Sato in January 2017, will be sufficient to meet our anticipated cash requirements at least through December 31, 2017, and will allow us to advance each of our development programs through their nearest-term milestone. We anticipate that we will need substantial additional funding to continue our operating activities and make further advancements in each of our drug development programs beyond their nearest-term milestone and prior to commercialization of SB204 or any other product candidate. Specifically, we anticipate that additional funding will be required to support SB204 through the FDA review process, including an additional SB204 clinical trial, and to conduct the two SB206 Phase 3 pivotal clinical trials.

Our future capital requirements will depend on many factors, including:

- the initiation, progress, timing and costs of our clinical trials and our analysis of the results of such trials for SB204, SB206, SB208 and, beginning in 2017, SB414;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- costs, timing and outcome of regulatory review of our product candidates;
- costs of commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive regulatory approval;
- costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or invest in other businesses, products and technologies;
- our ability to obtain government or other third-party funding for the development of our product candidates;
- the occurrence and timing of potential development and regulatory milestones achieved by Sato, our licensee for SB204 in certain topical dosage forms in Japan;
- our ability to establish additional collaborations on favorable terms, if at all, particularly arrangements to develop, market and distribute our product candidates outside North America; and
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates be approved by the FDA or a similar regulatory authority outside the United States.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially

available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, government contracts, government and other third-party grants or other third-party funding from research, development and manufacturing service contracts, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. We will require substantial funding to fund our operating expenses and other activities. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our existing stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our existing stockholders' rights. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

We have collaborated and intend to collaborate further with third parties for the development and commercialization of our product candidates. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. For example, we have entered into an exclusive license agreement with Sato relating to SB204 for the treatment of acne vulgaris in Japan.

The report of our independent registered public accounting firm on our 2016 consolidated financial statements contains an explanatory paragraph regarding going concern, and we will need additional financing to execute our business plan, to fund our operations and to continue as a going concern.

Since inception, we have experienced recurring operating losses and negative cash flows and we expect to continue to generate operating losses and consume significant cash resources in the foreseeable future. These conditions raise substantial doubt about our ability to continue as a going concern without additional financing. As a result, our independent registered public accounting firm included an explanatory paragraph in its report on our 2016 consolidated financial statements with respect to this uncertainty. Substantial doubt about our ability to continue as a going concern may materially and adversely affect the price per share of our common stock and we may have a more difficult time obtaining financing.

We have prepared our consolidated financial statements on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. Our 2016 consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

We have a limited operating history and no history of commercializing drugs, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced operations in 2006, and our operations to date have been largely focused on developing our Nitricil technology and platform of product candidates. We have not yet demonstrated our ability to obtain regulatory approvals, manufacture a drug on a commercial scale, or arrange for a third-party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing drugs.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to transition at some point from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We may be adversely affected by natural disasters and other catastrophic events, and by man-made problems such as terrorism, that could disrupt our business operations and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters are located in Morrisville, North Carolina, near major hurricane and tornado zones. If a disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as enterprise financial systems, manufacturing resource planning or enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. Our manufacturers' and suppliers' facilities are located in multiple locations, where other natural disasters or similar events, such as blizzards, tornadoes, fires, explosions or large-scale accidents or power outages, could severely disrupt their operations. In addition, acts of terrorism and other geo-political unrest could cause disruptions in our business or the businesses of our collaborators, manufacturers or the economy as a whole. All of the aforementioned risks may be further increased if we do not implement a disaster recovery plan or our collaborators' or manufacturers' disaster recovery plans prove to be inadequate. Any of the above could result in delays in the regulatory approval, manufacture, distribution or commercialization of our product candidates.

Risks Related to Our Common Stock

The price of our common stock may be volatile and fluctuate significantly, which could result in substantial losses for our existing stockholders.

Our stock price has in the past been, and is likely to be in the future, volatile. The stock market in general has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. During the period from September 21, 2016 to March 17, 2017, the closing sales price of our common stock ranged from a high of $29.06 per share to a low of $4.06 per share. Our stock price has experienced significant volatility since we announced the top-line results of our Phase 3 clinical trials of SB204 in late January 2017. As a result of this volatility, our existing stockholders may not be able to sell their stock at a favorable price. The market price for our common stock may be influenced by many factors, including:

- actual or anticipated fluctuations in our financial condition and operating results;
- actual or anticipated changes in our growth rate relative to our competitors;
- potential competition from existing products or new products that may emerge;
- development of new technologies that may address our markets and may make our technology less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less attractive;
- announcements by us, our partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- developments or disputes concerning proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- the recruitment or departure of key personnel;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes to reimbursement levels by commercial third-party payors and government payors, including Medicare, and negative announcements relating to reimbursement levels;

- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In addition, the stock market in general and emerging growth companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. A certain degree of stock price volatility can be attributed to being a newly public company. These broad market and industry fluctuations may negatively impact the price or liquidity of our common stock, regardless of our operating performance. Any actual or perceived negative operational developments or market or industry fluctuations may compound each other's negative impacts on the price of liquidity of our common stock.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources.

Our executive officers, directors and principal stockholders, if they choose to act together, will continue to have the ability to control all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock and their respective affiliates, in the aggregate, hold shares representing approximately 41% of our outstanding voting common stock as of December 31, 2016. As a result, if these stockholders were to choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

The significant concentration of stock ownership may negatively impact the price of our common stock due to investors' perception that conflicts of interest may exist or arise.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;

- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chief executive officer, the chairman, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors;
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us; and
- the requirement that the Court of Chancery of the State of Delaware be the sole and exclusive forum for derivative actions and other corporate claims unless we consent to an alternative forum in writing, which may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers or other employees and discourage lawsuits with respect to such claims.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

We have broad discretion in the use of our financial resources, including our cash and cash equivalents, and may not use them effectively.

Our management has broad discretion in the application of our financial resources, including our cash and cash equivalents, and could spend our cash in ways that do not improve our results of operations or enhance the value of our common stock. Our future use of our financial resources may differ substantially from our current plans. The failure by our management to apply our financial resources effectively could result in financial losses that could have a material adverse effect on our business and cause the price of our common stock to decline. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

Future sales of shares by existing stockholders could cause our stock price to decline.

Approximately 11.2 million shares of our common stock are currently subject to a contractual lock-up that expires on March 20, 2017, and other legal restrictions on resale as discussed in our registration statement declared effective by the Securities and Exchange Commission, or the SEC, on September 20, 2016. If these stockholders sell, or indicate an intent to sell, substantial amounts of our common stock in the public market after the contractual lock-up and other legal restrictions on resale lapse, the trading price of our common stock could decline significantly.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and may remain an emerging growth company until the earliest of (i) the end of the fiscal year in which the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the end of the second fiscal quarter, (ii) the end of the fiscal year in which we have total annual gross revenue of $1.0 billion or more during such fiscal year, (iii) the date on which we issue more than $1.0 billion in non-convertible debt in a three-year period or (iv) December 31, 2021, the end of the fiscal year following the fifth anniversary of the completion of our IPO. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting requirements in this annual report. In particular, we do not intend to provide all of the executive compensation related information that would be required if we were not an emerging growth company. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards and the accompanying demands on time and resources as other public companies that are not emerging growth companies face.

We have and expect to continue to incur substantial costs as a result of operating as a public company, and our management has and will continue to be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we have and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have and will continue to require substantial legal and financial compliance costs and make some activities more time-consuming and costly. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We continue to evaluate these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Our management team has limited experience managing a public company.

Most members of our management team have limited experience managing a publicly traded company, interacting with public company investors and complying with the increasingly complex laws pertaining to public companies. Our management team may not successfully or efficiently manage our transition to being a public company subject to significant regulatory oversight and reporting obligations under the federal securities laws and the continuous scrutiny of securities analysts and investors. These new obligations and constituents require significant attention from our senior management and could divert their attention away from the day-to-day management of our business.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our regulatory clearance timelines, clinical trial results or operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. Any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired which could adversely impact the market price of our stock.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Commencing with our fiscal year ending December 31, 2017, we must perform system and process evaluations and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts.

We have never been required to test our internal control within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may identify weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We currently operate out of two facilities. Our corporate headquarters is in Morrisville, North Carolina, where we lease an existing 51,350 square foot facility under a lease with an initial term expiring in 2026. We have an option to extend the lease agreement by five years upon completion of the initial lease term. We recently completed substantially all build out construction at this facility in December 2016, which is now being utilized for all intended purposes, including our corporate headquarters, primary research, development, and drug compound manufacturing activities to support our nitric oxide technology and drug development programs. This facility replaces our previous facility in Durham, North Carolina.

In addition, we have a 12,147 square foot leased facility in Durham, North Carolina that will support a portion of our research and development activities until the lease terminates in April 2017. We have the option to extend the lease beyond April 2017 on a month-to-month basis.

In the future, we also plan to establish a second facility for active pharmaceutical ingredient production manufacturing and to evaluate the potential for transferring our NCE manufacturing process to a CMO for commercial production.

Item 3. Legal Proceedings.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock has traded on the NASDAQ Global Market under the symbol "NOVN" since September 21, 2016. Prior to that time, there was no public market for our common stock. As a result, we have only set forth quarterly information with respect to the high and low sales prices of our common stock for the two most recent fiscal quarters. The following table states the high and low sales prices of our common stock for each of the last two calendar quarters during the year ended December 31, 2016.

	Low	High
Third Quarter 2016 (beginning September 21, 2016)	$ 13.77	$ 23.79
Fourth Quarter 2016	$ 17.50	$ 30.90

The last price of our common stock as reported on the NASDAQ Global Market on March 17, 2017 was $6.55 per share.

Holders

As of March 17, 2017, there were approximately 326 stockholders of record of our common stock. Holders of record are defined as those stockholders whose shares are registered in their names in our stock records and do not include beneficial owners of common stock whose shares are held in the names of brokers, dealers or clearing agencies.

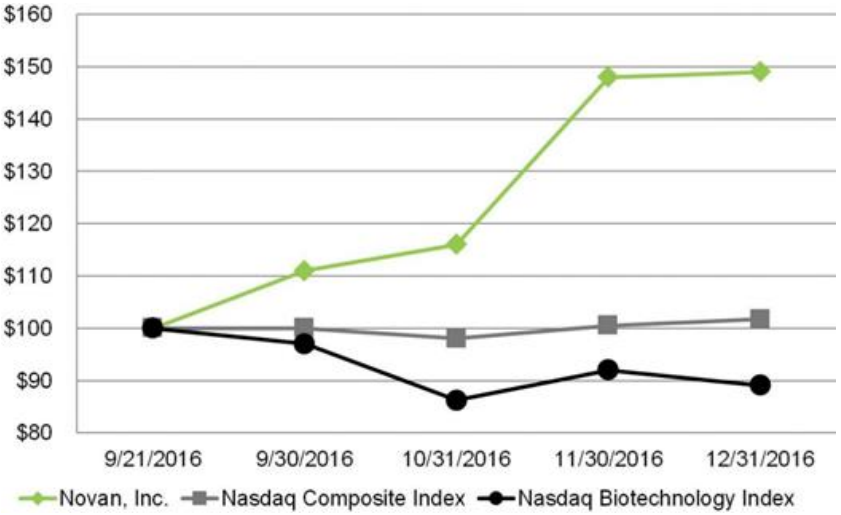
Dividends

We have never paid cash dividends and do not anticipate paying cash dividends in the foreseeable future.

Stock Performance Graph

This performance graph is not "soliciting material," is not deemed filed with the SEC and is not to be incorporated by reference in any filing by us under the Securities Act or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing. The stock price performance shown on the graph is not necessarily indicative of future price performance.

Comparison of Cumulative Total Return
Among Novan, Inc., the NASDAQ Composite Index and the NASDAQ Biotechnology Index



The above graph measures the change in a $100 investment in our common stock from September 21, 2016 (the date our common stock commenced trading on the Nasdaq Global Market) through December 31, 2016. Our relative performance is then compared with the Nasdaq Composite Index (COMPX) and the Nasdaq Biotechnology Index (NBI).

Recent Sales of Unregistered Securities

None.

Use of Proceeds from IPO

On September 20, 2016, the SEC declared our Registration Statement on Form S-1 (File No. 333-213276) effective for our IPO, which closed on September 26, 2016, pursuant to which we sold an aggregate of 4,715,000 shares of our common stock, including the underwriters option to purchase 615,000 additional shares, at a price to the public of $11.00 per share for aggregate gross proceeds of $51.9 million. As a result, we received net proceeds of $44.6 million (after underwriters' discounts, commissions, and reimbursements totaling $4.1 million and additional offering related costs of $3.2 million). The managing underwriter of the offering was Piper Jaffray & Co.

The net proceeds of the IPO have been invested in accordance with our investment policy. There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus dated September 20, 2016 and filed with the SEC on September 22, 2016.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not purchase any of our equity securities during the fourth quarter of 2016.

Item 6. Selected Financial Data.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with the information under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our audited financial statements and the accompanying notes included in this Annual Report on Form 10-K. The consolidated statement of operations data for the years ended December 31, 2016, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016 and 2015 are derived from the audited financial statements included elsewhere in this Annual Report. The selected consolidated balance sheet data as of December 31, 2014, is derived from audited financial statements that are not included in this Annual Report.

	Year Ended December 31,		
	2016	2015	2014
	(in thousands except share and per share data)		
Statement of operations data:			
Government research contracts and grants revenue	$ —	$ —	$ 112
Operating expenses:			
Research and development	46,489	16,569	6,770
General and administrative	13,337	9,265	5,170
Total operating expenses	59,826	25,834	11,940
Operating loss	(59,826)	(25,834)	(11,828)
Other income (expense):			
Interest income	81	48	58
Interest expense	(2)	(1)	(701)
Change in fair value of warrant liability	—	—	(641)
Other income, net	48	1	9
Total other income (expense)	127	48	(1,275)
Loss from continuing operations	(59,699)	(25,786)	(13,103)
Income (loss) from discontinued operations	—	(2,274)	1,715
Net loss and comprehensive loss	$ (59,699)	$ (28,060)	$ (11,388)
Income (loss) per share, basic and diluted:			
Continuing operations	$ (9.97)	$ (11.36)	$ (5.95)
Discontinued operations	—	(1.01)	0.78
Net loss per share, basic and diluted (1)	$ (9.97)	$ (12.37)	$ (5.17)
Weighted-average common shares used in computing net loss per share, basic and diluted (1)	5,985,985	2,269,124	2,203,278

(1) See "Note 1—Organization and Significant Accounting Policies" to our consolidated financial statements included elsewhere in this Annual Report for an explanation of the method used to calculate the historical basic and diluted net loss per share.

	As of December 31,		
	2016	2015	2014
	(in thousands)		
Balance sheet data:			
Cash and cash equivalents	$ 34,611	$ 45,688	$ 7,419
Total current assets	35,569	46,933	7,994
Total assets	52,473	49,816	9,927
Total current liabilities	13,377	5,095	1,767
Total liabilities	21,407	5,099	1,777
Convertible preferred stock	—	104,798	37,699
Accumulated deficit	(123,033)	(63,334)	(29,949)
Total stockholders' equity (deficit)	31,066	(60,081)	(29,549)

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

This Management's Discussion and Analysis of Financial Condition and Results of Operations should be read with our consolidated financial statements and notes thereto included elsewhere in this Annual Report. In addition to historical information, the following discussion contains forward-looking statements that involve risks, uncertainties and assumptions. Where possible, we have tried to identify these forward-looking statements by using words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "potential," "predict," "project," "estimate," or "continue" and similar expressions or variations. Our actual results could differ materially from those anticipated by the forward-looking statements due to important factors and risks including, but not limited to, those set forth in the "Risk Factors" in Part I, Item 1A of this report.

Overview

We are a late-stage pharmaceutical company focused on redefining the standard of care in dermatology through the development and commercialization of innovative therapies using our nitric oxide platform. Nitric oxide plays a vital role in the natural immune system response against microbial pathogens and is a critical regulator of inflammation. Our ability to harness nitric oxide and its multiple mechanisms of action has enabled us to create a platform with the potential to generate differentiated first-in-class product candidates. The two key components of our nitric oxide platform are our proprietary Nitricil technology, which drives the creation of new chemical entities, or NCEs, and our topical formulation science, both of which we use to tune our product candidates for specific indications. We believe that our ability to conveniently deploy nitric oxide on demand in topical formulations allows us the potential to significantly improve patient outcomes in a variety of skin diseases and positions us to be a commercially successful leader in dermatology.

We are rapidly advancing programs in five dermatological conditions with significant unmet medical need. These are some of the most prevalent diseases in dermatology and together represent a large market opportunity with a patient population surpassing 150 million Americans and 1.5 billion individuals globally.

Our lead product candidate is SB204, a cosmetically elegant topical gel that targets multiple mechanisms of action for the treatment of acne vulgaris, the most common skin disease in the United States. We recently reported top-line results from two identically designed Phase 3 pivotal clinical trials of SB204 conducted with a total of 2,639 patients with acne vulgaris. SB204 demonstrated statistical significance compared to vehicle on all three co-primary endpoints in one of the trials, but demonstrated statistical significance on only one of three co-primary endpoints in the other trial. We conducted an in-depth examination of the full data sets from these trials, including post hoc analyses, with extensive assistance from third-party expert consultants in biostatistics and regulatory affairs. Based on the results of this analysis, we intend to pursue a pre-submission meeting with the FDA to discuss the entirety of the SB204 development program in the third quarter of 2017. Our meeting with the FDA could lead to an NDA submission targeted in the first quarter of 2018, assuming among other things successful completion of our ongoing long-term safety study. Following our meeting with the FDA, we also expect to initiate an additional clinical trial for SB204 to be conducted in parallel with the FDA review to support NDA approval.

Our other product candidates include SB206, SB208 and SB414, which are targeted toward the treatment of either a specific microorganism or inflammatory components of a disease pathology. SB206 is a first-in-class, topical antiviral gel in Phase 2 clinical development for the treatment of viral skin infections such as external genital and perianal warts caused by HPV. We announced top-line results from our Phase 2 clinical trial for SB206 in the fourth quarter of 2016. Based on the data generated in this Phase 2 dose-ranging trial, we expect to discuss the entirety of the SB206 development program with the FDA in the second quarter of 2017 and, assuming a successful end-of-Phase 2 meeting with the FDA, plan to initiate our late-stage program with Phase 3 pivotal clinical trials of SB206 in by the end of 2017. SB208 is a topical broad-spectrum antifungal product candidate for the treatment of fungal infections of the skin and nails. We commenced Phase 2 clinical testing of SB208 for the treatment of infections caused by dermatophytes such as *T. rubrum* in July 2016, completed enrollment in December 2016 and expect to announce top-line results in the second quarter of 2017. SB414, a topical cream in preclinical development for the treatment of inflammatory skin diseases such as psoriasis and atopic dermatitis, rounds out our current pipeline. We expect to initiate clinical development of SB414 in the second quarter of 2017 with the filing of an IND followed by a Phase 2 proof-of-concept study in patients with psoriasis.

Since our inception in 2006, we have devoted substantially all of our efforts to developing our nitric oxide platform technology and resulting product candidates, including conducting preclinical and clinical trials and providing general and administrative support for these operations. We conduct these activities in a single operating segment. We have not generated any revenue from product sales and, to date, have funded our operations primarily through the sale of common stock in our IPO, private placements of our convertible preferred stock, the issuance of convertible notes and proceeds from government research contracts and grants. From inception through December 31, 2016, we have raised total equity and debt proceeds of $148.5 million to fund our operations, comprised of $44.6 million from net proceeds from the sale of common stock in our IPO, $99.7 million from the sale of preferred stock, $3.5 million from the issuance of convertible debt and $0.7 from other issuances of common stock. In addition, we have received $11.8 million from government research contracts and grants during that period, the majority of which was associated with our discontinued operations (see "Separation Transaction" below). We recently received an upfront payment of approximately $10.8 million in January 2017 following the execution of a license agreement with Sato for the exclusive right to develop, use and sell SB204 in certain topical dosage forms in Japan for the treatment of acne vulgaris (see the "Corporate Updates" section below).

We have never generated revenue from product sales and have incurred net losses in each year since inception. As of December 31, 2016, we had an accumulated deficit $123.0 million. We incurred net losses of $59.7 million, $28.1 million and $11.4 in the years ended December 31, 2016, 2015 and 2014, respectively. We expect to continue to incur substantial losses in the future as we conduct our planned operating activities. We do not expect to generate revenue from product sales unless and until we obtain regulatory approval from the FDA for our clinical-stage product candidates. If we obtain regulatory approval for SB204 or any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. In addition, we expect that we will continue to incur substantial expenses as we continue clinical trials and preclinical studies for, and research and development of, our product candidates and maintain, expand and protect our intellectual property portfolio. As a result, we will need substantial additional funding to support our operating activities. Adequate funding may not be available to us on acceptable terms, or at all. The top-line results from our parallel pivotal SB204 Phase 3 trials, coupled with the recent decline in the market value of our common stock, may negatively impact our available funding options and the acceptability of funding terms. We are currently reviewing various potential financing options to fund our operations, including traditional private and public equity financings and non-dilutive partnership opportunities across our pipeline of product candidates. Our failure to obtain sufficient funds on acceptable terms as and when needed could cause us to alter or reduce our planned operating activities, including but not limited to delaying planned product candidate development activities, to conserve our cash and cash equivalents. Such actions could delay development timelines and have a material adverse effect on our business, results of operations and financial condition. As further discussed in our audited financial statements and related footnotes included in this Annual Report, these matters raise substantial doubt about our ability to continue as a going concern.

Corporate Updates

Initial Public Offering

On September 26, 2016, we completed the IPO of our common stock. We sold an aggregate of 4,715,000 shares of common stock under the registration statement on Form S-1 declared effective by the SEC on September 20, 2016, at a public offering price of $11.00 per share for aggregate gross proceeds of $51.9 million. Our net proceeds from the IPO were $44.6 million, after deducting underwriting discounts and commissions totaling $4.1 million and offering expenses of $3.2 million. Upon the completion of the IPO, all outstanding shares of our non-voting common stock and convertible preferred stock were automatically converted into 8,967,321 shares of common stock.

Licensing Arrangement

On January 12, 2017, we entered into a license agreement, and a related amendment, with Sato relating to SB204, our lead drug candidate for the treatment of acne vulgaris in Japan, or the Agreement. Pursuant to the Agreement, we granted to Sato an exclusive, royalty-bearing, non-transferable license under certain of our intellectual property rights, with the right to sublicense with our prior written consent, to develop, use and sell products in Japan that incorporate SB204 in certain topical dosage forms for the treatment of acne vulgaris, and to make the finished form of such products. The rights granted to Sato do not include the right to manufacture the active pharmaceutical ingredient of SB204, which we will retain the rights to supply to Sato. We will also supply finished product for use in development of SB204 in the licensed territory. During a specified time period, Sato has an exclusive option to negotiate the terms under which its license would be expanded to include certain additional territories within Asia, subject to Sato's payment of a specified option exercise fee. Under the terms of the Agreement, we also have exclusive rights to certain intellectual property that may be developed by Sato in the future, which we may choose to use for our own development and commercialization of SB204 outside of Japan.

In exchange for the licenses granted to Sato under the Agreement, Sato agreed to pay us an upfront payment, as well as additional milestone payments upon achievement of various future development, regulatory and commercial milestones. Pursuant to the terms of the Agreement, as amended, Sato is required to pay us an upfront payment of 1.25 billion Japanese Yen, or JPY ($10.8 million based on the exchange rate as of January 19, 2017), and up to an aggregate of 2.75 billion JPY ($23.8 million based on the exchange rate as of January 19, 2017) upon the achievement of various development and regulatory milestones. Under the Agreement, Sato also agreed to pay us up to an aggregate of 0.9 billion JPY ($7.8 million based on the exchange rate as of January 19, 2017) in milestone payments upon the achievement of various commercial milestones. Sato must also pay us a royalty equal to a mid-single digit percentage of net sales of licensed products in the licensed territory, subject to a reduction in the royalty payments under specified circumstances.

The term of the Agreement and the period during which Sato must pay royalties under the license agreement expires, on a licensed product-by-licensed product basis, on the tenth anniversary of the first commercial sale of a licensed product in the licensed field in the licensed territory. The term of the Agreement may be renewed by mutual written agreement of the parties for additional two-year periods following expiration of the initial term.

The Agreement obligates us to supply Sato with all quantities of licensed products required by Sato for their development activities in Japan. As part of the Agreement, we and Sato also agreed to negotiate a commercial supply agreement pursuant to which we would be the exclusive supplier to Sato of the active pharmaceutical ingredient of licensed products for the manufacture of licensed products in the licensed territory.

Sato is responsible for funding the development and commercial costs for the program that are specific to Japan. We have agreed to perform certain oversight, review and supporting activities for Sato, including: (i) using commercially reasonable efforts to obtain marketing approval of SB204 in the U.S, (ii) sharing all future scientific information we may obtain during the term of the Agreement pertaining to SB204, (iii) performing certain additional pre-clinical studies if such studies are deemed necessary by the Japanese regulatory authority, up to and not to exceed a total cost of $1.0 million, and (iv) participating in a joint committee that oversees, reviews, and approves Sato's development and commercialization activities under the Agreement. Additionally, we have granted Sato the option to use our trademarks in connection with the commercialization of licensed products in the licensed territory for no additional consideration, subject to our approval of such use.

The Agreement may be terminated (i) by Sato without cause upon 120 days' advance written notice to us; (ii) by either party in the event of the other party's uncured material breach upon 60 days' advance written notice; (iii) by force majeure; (iv) by either party in the event of the other party's dissolution, liquidation, bankruptcy or insolvency; and (v) by us immediately upon written notice if Sato challenges the validity, patentability, or enforceability of any of our patents or patent applications licensed to Sato under the Agreement.

On January 19, 2017, we received the upfront payment, which was equivalent to $10.8 million when converted to U.S. Dollars. We expect the upfront payment from Sato to increase the period over which our cash and cash equivalents can fund our operating expenses. We are currently assessing the terms of the Sato licensing agreement to determine the appropriate accounting treatment, including the appropriate revenue recognition method, in

accordance with U.S. GAAP. The obligation to supply Sato with necessary quantities of the licensed product during their development process and, if approved, the active pharmaceutical ingredient of SB204 during commercialization is not expected to have a significant effect on our future operating losses. Our other obligations to Sato under the Agreement are expected to result in an increase in our future operating costs.

The intellectual property rights granted to Sato under the Agreement include certain intellectual property rights which we have licensed from UNC. Under our license agreement with UNC, we are obligated to pay UNC a running royalty percentage in the low single digits on net sales of licensed products, including net sales that may be generated by Sato. Additionally, we made a payment to UNC in February 2017 representing the portion of the Sato upfront payment that was estimated to be directly attributable to the UNC intellectual property rights included in the license to Sato.

We also entered into an agreement with a third party to assist us in exploring the SB204 licensing opportunity that led to the execution of the Agreement with Sato. We paid a fee of $0.2 million to the third party upon execution of the Agreement and are obligated to pay the third party a low-single-digit percentage of any future milestone payments we may receive from Sato under the Agreement.

Separation Transaction

On December 16, 2015, our board of directors approved the formation of KNOW Bio, LLC, a wholly owned subsidiary, or KNOW Bio, formed for the purpose of giving effect to the legal separation of certain non-core assets from our company. These non-core assets are non-dermatological assets consisting mainly of intellectual property rights, which were valued at $1.8 million as of December 30, 2015. On December 30, 2015, we made a cash contribution of $5.2 million to KNOW Bio in order to provide it with working capital, and we distributed all of the outstanding member interests of KNOW Bio *pro rata* to our stockholders. These stockholders were not required to pay any cash or other consideration for the equity interests of KNOW Bio and were not required to surrender or exchange shares of our stock in order to receive the member interests. We refer to the foregoing transactions collectively as the Separation Transaction.

Immediately following the distribution of its member interests on December 30, 2015, KNOW Bio became an independent, privately held company. We have no obligation or intention to provide further funding to KNOW Bio. The cash included in the Separation Transaction was recorded as a dividend distribution. The historical financial position and results of operations for the activities attributed to KNOW Bio have been reflected in our consolidated statements of operations, retrospectively, as discontinued operations. Additionally, the liabilities associated with KNOW Bio, but not assumed by KNOW Bio as part of the distribution, as of December 31, 2015 are classified as discontinued operations. See "Note 2—Discontinued Operations" to our consolidated financial statements included elsewhere in this Annual Report.

Components of our Results of Operations

Government Contracts and Grants Revenue and Licensing Revenue

To date, we have not generated revenue from the sale of any products. All of our historical revenue has been derived from government research contracts and grants, which relate to the research and development of our nitric oxide platform. We have recognized $0.1 million in continuing operations revenue from January 1, 2014 through December 31, 2016 from these sources. Revenue from government research contracts and grants is recognized when all of the following criteria are met: (i) persuasive evidence that an arrangement exists; (ii) delivery of the products or services has occurred; (iii) the selling price is fixed or determinable; and (iv) collectability is reasonably assured.

We currently do not expect to derive substantial additional revenue from government contracts and grants and we do not expect to generate any revenue from any product candidates that we develop unless and until we obtain regulatory approval and commercialize our products or enter into other potentially revenue-generating collaborative agreements with third parties.

We expect to recognize licensing revenue beginning in 2017 from the license agreement we entered into with Sato in January 2017. We are currently assessing the terms of the Sato licensing agreement to determine the appropriate revenue recognition method in accordance with U.S. GAAP.

Research and Development Expenses

Since our inception, we have focused our resources on our research and development activities, including conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings for our product candidates. Research and development expenses, including those paid to third parties for which there is no alternative use, are expensed as they are incurred. Research and development expenses include:

- external research and development expenses incurred under agreements with contract research organizations, or CROs, investigative sites and consultants to conduct our clinical trials and preclinical and non-clinical studies;
- costs to acquire, develop and manufacture supplies for clinical trials and preclinical studies, including fees paid to contract manufacturing organizations, or CMOs;
- legal and other professional fees related to compliance with FDA requirements;
- licensing fees and milestone payments incurred under license agreements;
- salaries and related costs, including stock-based compensation and travel expenses, for personnel in our research and development functions; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities, utilities, equipment and other supplies.

From inception through December 31, 2016, we have incurred approximately $88.7 million in research and development expenses to develop, expand or otherwise improve our nitric oxide platform and resulting product candidates. The table below sets forth our external research and development expenses incurred for current product candidates and unallocated internal research and development expenses for the years ended December 31, 2016, 2015 and 2014. All research and development salaries and related personnel costs are included in unallocated internal research and development expenses.

	Year Ended December 31,		
	2016	2015	2014
	(in thousands)		
External:			
SB204	$ 33,158	$ 8,569	$ 4,208
SB206	2,362	2,141	162
SB208	1,431	—	—
Other programs	1,006	975	113
Government contracts and grants	—	—	81
Unallocated internal research and development expenses	8,532	4,884	2,206
Total research and development expenses	$ 46,489	$ 16,569	$ 6,770

We expect that for the foreseeable future, the substantial majority of our research and development efforts will be focused on our clinical programs, SB204, SB206 and SB208, as well as initiating clinical development of SB414, and on our future pipeline development. For SB204, we commenced Phase 3 clinical trials in the first quarter of 2016, continued to conduct these studies through the fourth quarter of 2016, and recently completed the trials and reported top-line results in the first quarter of 2017. For SB206, we completed a Phase 2 clinical trial and announced top-line results in the fourth quarter of 2016. For SB208, we initiated a Phase 2 clinical development program in July 2016 and expect to announce top-line results in the second quarter of 2017. For SB414, we are currently conducting preclinical development activities in support of the submission of an IND to the FDA. We are targeting initiation of clinical development of SB414 in the second quarter of 2017 with the filing of an IND followed by a

Phase 2 proof-of-concept study in patients with psoriasis. Historical costs associated with our SB414 program and other preclinical activities are included in "Other Programs" in the table above.

We expect to continue to incur substantial research and development expenses in the future as we develop our clinical product candidates. In particular, we expect to incur substantial research and development expenses in 2017 associated with the completion of our SB204 Phase 3 clinical trials and long term safety study, the initiation of an additional SB204 clinical study to support NDA approval, the initiation of our SB206 Phase 3 clinical trials, the continued conduct our ongoing SB208 Phase 2 clinical development program, and the initiation of SB414 clinical development activities associated with a Phase 2 proof-of-concept study in patients with psoriasis. Although we expect expenses associated with the previously described 2017 clinical development activities to be substantial, we expect such expenses to be lower in 2017 than research and development expenses incurred in 2016.

The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs required to complete the remaining development of SB204, SB206, SB208, SB414 or any future product candidates. This is due to the numerous risks and uncertainties associated with the development of product candidates. See "Risk Factors" for a discussion of the risks and uncertainties associated with our research and development projects.

General and Administrative Expenses

Our general and administrative expenses consist primarily of salaries and related costs, including stock-based compensation and travel expenses for personnel in our executive, finance, commercial, corporate development and other administrative functions. Other general and administrative expenses include depreciation and facility-related costs, legal costs of pursuing patent protection of our intellectual property, and professional services fees for auditing, tax and general legal services.

We expect to continue to incur substantial general and administrative expenses in 2017 as we conduct our product development operating activities and support our operations in a public company environment, including significant expenses related to legal, accounting, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, directors' and officers' liability insurance premiums and investor relations activities. We do not expect our market research and related commercialization costs to increase in 2017.

Other Income (Expense)

Other income and expense in 2016 and 2015 consists primarily of interest earned on cash and cash equivalents. In 2014, other income and expense also includes income deemed to be earned upon the expiration of preferred stock warrants, interest incurred on our convertible note and re-measurement gain or loss associated with the change in the fair value of our preferred stock warrant liability.

In 2014, we estimated the fair value of our warrant liability using the Black-Scholes option pricing model. We based the estimates in the Black-Scholes option pricing model, in part, on subjective assumptions, including stock price volatility, risk-free interest rate, dividend yield and the fair value of the preferred stock underlying the warrants. The re-measurement gain or loss associated with the changes in the fair value of our preferred stock warrant liability in 2014 was recognized as a component of other income (expense).

Results of Operations

Comparison of Year Ended December 31, 2016 and 2015

The following table sets forth our results of operations for the periods indicated:

	Year Ended December 31,			
	2016	2015	$ Change	% Change
	(in thousands, except percentages)			
Operating expenses:				
Research and development	$ 46,489	$ 16,569	$ 29,920	181%
General and administrative	13,337	9,265	4,072	44%
Total operating expenses	59,826	25,834	33,992	132%
Operating loss	(59,826)	(25,834)	(33,992)	132%
Other income, net	127	48	79	*
Loss from continuing operations	(59,699)	(25,786)	(33,913)	132%
Loss from discontinued operations	—	(2,274)	2,274	*
Net loss	$ (59,699)	$ (28,060)	$ (31,639)	113%

** Not Meaningful*

Research and development expenses

Research and development expenses were $46.5 million for the year ended December 31, 2016, compared to $16.6 million for the year ended December 31, 2015. The increase of $29.9 million was primarily due to increases in our active development programs, including $24.6 million in the SB204 program, $0.2 million in the SB206 program, $1.4 million in the SB208 program, $0.1 million in the SB414 program preclinical development activities. We also had an increase of $3.6 million in unallocated internal research and development expenses. The increases during the year ended December 31, 2016 were primarily associated with the commencement and conduct of our Phase 3 clinical trials for SB204, the continued conduct and completion of our Phase 2 clinical trial for SB206, the commencement and conduct of our Phase 2 clinical program for SB208 and continued preclinical research and development for SB414. The increase in our other unallocated internal research and development expenses was primarily the result of increased personnel and related costs that support and administer our active development programs.

General and administrative expenses

General and administrative expenses were $13.3 million for the year ended December 31, 2016, compared to $9.3 million during the year ended December 31, 2015. The increase of approximately $4.1 million was primarily due to a $1.0 million increase in personnel and related costs to support the growth of our research and development activities and to perform various other administrative functions, a $2.1 million increase in market research and related costs and a $1.0 million increase in professional services, insurance, board compensation and other administrative costs necessary to support our operations as a public company.

Comparison of Year Ended December 31, 2015 and 2014

The following table sets forth our results of operations for the periods indicated:

	Year Ended December 31,			
	2015	2014	$ Change	% Change
	(in thousands, except percentages)			
Government research contracts and grants revenue	$ —	$ 112	$ (112)	(100)%
Operating expenses:				
Research and development	16,569	6,770	9,799	145%
General and administrative	9,265	5,170	4,095	79%
Total operating expenses	25,834	11,940	13,894	116%
Operating loss	(25,834)	(11,828)	(14,006)	(118)%
Other income, net	48	(1,275)	1,323	*
Loss from continuing operations	(25,786)	(13,103)	(12,683)	97%
Loss from discontinued operations	(2,274)	1,715	(3,989)	*
Net loss	$ (28,060)	$ (11,388)	$ (16,672)	146%

** Not Meaningful*

Government research contracts and grants revenue

Government research contracts and grants revenue was $0 for the year ended December 31, 2015, compared to $0.1 million for the year ended December 31, 2014. The decrease was a result of completing a contract with a government agency in the first half of 2014.

Research and development expenses

Research and development expenses were $16.6 million during the year ended December 31, 2015, compared to $6.8 million during the year ended December 31, 2014. The increase of $9.8 million in research and development expenses was primarily due to increases of $4.4 million in the SB204 program, $1.9 million in the SB206 program, $0.9 million in other external programs and $2.7 million in other unallocated internal research and development expenses. These increases were partially offset by a decrease in research and development expense for government research contracts and grants of $0.1 million. During the year ended December 31, 2015, we were conducting and completed the Phase 2 clinical trial for SB204, commenced the Phase 2 clinical trial for SB206 and expanded preclinical research and development for our other programs. The increase in our other unallocated internal research and development expenses was the result of increased personnel and related costs, including stock-based compensation, attributable to increased personnel for clinical programs, formulation process development and analytical support.

General and administrative expenses

General and administrative expenses were $9.3 million during the year ended December 31, 2015, compared to $5.2 million during the year ended December 31, 2014. The increase of $4.1 million in general and administrative expenses was primarily due to the increase of personnel and related costs, including stock-based compensation, to support the growth of our research and development activities and to perform various other administrative functions as well as increased market research, consulting, legal and accounting costs.

Other Income (expense)

Other income (expense) increased to income of $48,000 for the year ended December 31, 2015, compared to expense of $(1.3) million for the year ended December 31, 2014, due primarily to the following factors. Interest expense was ($1,000) during the year ended December 31, 2015, compared to ($0.7) million during the year ended December 31, 2014, due to the conversion of our convertible notes to shares of Mezzanine A preferred stock during the year ended

December 31, 2014. Other expense resulting from the change in fair value of our warrant liability was $0 during the year ended December 31, 2015 compared to $(0.6) million during the year ended December 31, 2014.

Liquidity and Capital Resources

Since our inception through December 31, 2016, we have financed our operations primarily with $148.5 million in net proceeds from the issuance and sale of equity securities and convertible debt securities, including $44.6 million in net proceeds from the sale of common stock in the IPO we completed in September 2016. In addition, we have generated revenues of $11.8 million from government research contracts and other grants, the majority of which was associated with our discontinued operations (see "Separation Transaction" above).

As of December 31, 2016, we had $34.6 million of cash and cash equivalents. Our cash and cash equivalents are held in a variety of interest-bearing instruments, including money market accounts. Cash in excess of immediate requirements is invested with a view toward liquidity and capital preservation, and we seek to minimize the potential effects of concentration and degrees of risk.

In January 2017, we received a nonrefundable upfront payment of approximately $10.8 million following the execution of the Agreement with Sato for the exclusive right to develop, use and sell SB204 in certain topical dosage forms in Japan for the treatment of acne vulgaris (see the "Corporate Updates" section above for more information about this agreement).

Facility lease financing

Throughout 2016, we conducted a construction project to build out a leased facility in Morrisville, North Carolina. The leased facility began to serve as our corporate headquarters and primary research, development and drug compound manufacturing facility during the fourth quarter of 2016. We are leasing the 51,000 square foot facility under a lease agreement entered into in August of 2015. We began to occupy and utilize the facility for administrative purposes in October 2016. Build out construction activities continued during the fourth quarter of 2016. We believe the construction of the tenant improvements to the facility was substantially complete in December 2016, as we began to utilize the facility for all intended purposes.

Under the terms of the lease agreement, the landlord provided for a tenant improvement allowance of $5.5 million; all of which had been utilized as of December 31, 2016. In addition to costs funded by the tenant improvement allowance, we paid $2.2 million towards the build out of the facility as of December 31, 2016.

We have accounted for this lease as a capitalized asset and a corresponding facility financing obligation on our balance sheets. See "Note 1—Organization and Significant Accounting Policies" and "Note 6—Commitments and Contingencies" to the accompanying audited financial statements in Item 8 of this Annual Report for further discussion of the accounting for this lease.

Cash Flows

The following table sets forth our cash flows for the periods indicated:

	Year Ended December 31,		
	2016	2015	2014
	(in thousands)		
Net cash provided by (used in):			
Continuing operating activities	$ (48,911)	$ (20,765)	$ (10,401)
Continuing investing activities	(6,218)	(1,751)	(772)
Continuing financing activities	44,309	62,351	16,063
Net increase (decrease) in cash and cash equivalents – discontinued operations	(257)	(1,566)	1,792
Net increase (decrease) in cash and cash equivalents	$ (11,077)	$ 38,269	$ 6,682

Net Cash Used in Continuing Operating Activities

During the year ended December 31, 2016, net cash used in operating activities was $48.9 million and consisted primarily of a net loss of $59.7 million, with adjustments for non-cash amounts related primarily to depreciation expense of $0.8 million, stock-based compensation expense of $1.6 million, and a $8.5 million favorable change in assets and liabilities. The favorable net change in assets and liabilities was primarily due to increases in accounts payable and accrued expense balances associated with our outside research and development activities during the period, including a $1.4 million increase in accounts payable and a $4.6 million increase in accrued outside research and development services. The increase in accounts payable and accruals for these services was primarily related to (i) our increased development program activities in 2016, including the commencement and conduct of our SB204 Phase 3 clinical trials, SB206 Phase 2 clinical trial, and SB208 Phase 2 clinical program; and (ii) the timing of the invoicing and payment for such services. We expect our accounts payable and accrued outside research and development services balances as of December 31, 2016 to be settled through cash payments during the first half of 2017.

During the year ended December 31, 2015, net cash used in operating activities was $20.8 million and consisted primarily of a net loss of $28.1 million, which was the result of cash used in our research and development activities, with adjustments for loss from discontinued operations of $2.3 million, non-cash amounts related primarily to depreciation expense of $0.6 million, stock-based compensation expense of $2.0 million, a $0.6 million increase in prepaid expenses related to CRO pre-funding payments and a $3.0 million increase in accrued liabilities, primarily related to higher research and development accruals.

During the year ended December 31, 2014, net cash used in operating activities was $10.4 million and consisted primarily of a net loss of $11.4 million, which was the result of cash used in our research and development activities with adjustments for income from discontinued operations of $1.7 million, non-cash amounts related primarily to depreciation expense of $0.4 million, interest expense of $0.7 million, the change in fair value of warrant liability of $0.6 million, stock-based compensation expense of $0.2 million and $0.8 million in changes in assets and liabilities.

Net Cash Used in Continuing Investing Activities

During the year ended December 31, 2016, net cash used in investing activities was $6.2 million, which related to purchases of property and equipment of $6.1 million and the purchase of intangible assets of $0.1 million. The purchases of property and equipment in 2016 were primarily associated with laboratory equipment and our portion of the facility build out costs at our new headquarters and manufacturing facility in Morrisville, North Carolina.

During the years ended December 31, 2015 and 2014, net cash used in investing activities was $1.8 million and $0.8 million, respectively. Net cash used in investing activities during the year ended December 31, 2015 represented purchases of property and equipment of $1.3 million and $0.5 million restricted to secure a letter of credit. Net cash used in investing activities during the year ended December 31, 2014 represented purchases of property and equipment.

Net Cash Provided by Continuing Financing Activities

During the year ended December 31, 2016, net cash provided by financing activities was $44.3 million, consisting primarily of $44.6 million in net proceeds from our IPO, offset by a repurchase of common stock, which is now held as treasury stock, of approximately $0.2 million and payments on facility lease obligations of approximately $0.2 million.

During the year ended December 31, 2015, net cash provided by financing activities was $62.4 million, consisting of $67.1 million from proceeds from the issuance of preferred stock and $0.5 million from the issuance of common stock in connection with the exercise of stock options, offset in part by the $5.2 million of cash distributed as part of the Separation Transaction.

During the year ended December 31, 2014, net cash provided by financing activities was $16.1 million, consisting of proceeds from the issuance of preferred stock of $12.0 million, proceeds from the issuance of convertible notes of $3.5 million and proceeds from the exercise of preferred stock warrants of $0.6 million.

Capital Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate revenue from product sales unless and until we obtain regulatory approval of and commercialize one of our current or future product candidates. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates and begin to commercialize any approved products. We are subject to all of the risks incident in the development of new pharmaceutical products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business, like the inconsistency between the top-line results from our two identically designed Phase 3 pivotal clinical trials of SB204.

Our primary use of our cash is to fund our operating expenses, which consist principally of research and development expenditures necessary to advance our clinical-stage product candidates. We believe that our existing cash and cash equivalents, together with the nonrefundable upfront payment received from Sato in January 2017, will be sufficient to meet our anticipated cash requirements at least through December 31, 2017 and will allow us to advance each of our development programs through their nearest-term milestone. We anticipate that we will need substantial additional funding to continue our operating activities and make further advancements in each of our drug development programs beyond their nearest-term milestone. Specifically, we anticipate that additional funding will be required to support SB204 through the FDA review process, including an additional SB204 clinical trial, and to conduct the two SB206 Phase 3 pivotal clinical trials. We are currently reviewing various potential financing options to fund our operations, including traditional private and public equity financings and non-dilutive partnership opportunities across our pipeline of product candidates. As of December 31, 2016, we had an accumulated deficit of $123.0 million and there is substantial doubt about our ability to continue as a going concern if we do not secure additional financing.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs, results, and evaluation of results of trials for our clinical-stage product candidates, including SB204, SB206, SB208 and, beginning in 2017, SB414;
- the progress, timing, costs and results of preclinical studies relating to other potential applications of our nitric oxide platform, including SB414;
- the number and characteristics of product candidates that we pursue;
- our success in scaling our manufacturing process;
- the outcome, timing and costs of seeking regulatory approvals;
- the occurrence and timing of potential development and regulatory milestones achieved by Sato, our licensee for SB204 in Japan;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights;
- defending against intellectual property related claims;

- the extent to which we in-license or acquire other products and technologies; and
- subject to receipt of marketing approval, revenue received from commercial sales of our product candidates.

We also expect to incur capital expenditures as we continue to invest in information technology systems, equipment and leasehold improvement costs at our recently completed corporate headquarters and manufacturing facility in Morrisville, North Carolina.

Contractual Obligations and Contingent Liabilities

The following summarizes our significant contractual obligations as of December 31, 2016:

	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
			(in thousands)		
Operating leases (1)	$ 69	$ 69	$ —	$ —	$ —
Facility financing obligations (2)	11,916	1,103	2,305	2,446	6,062
Research and development contract obligations (3)	—	—	—	—	—
Total Obligations	$ 11,985	$ 1,172	$ 2,305	$ 2,446	$ 6,062

(1) Represents a non-cancelable operating lease agreement for facilities which is scheduled to expire in April 2017. We have the option to extend the lease beyond April 2017 on a month-to-month basis.

(2) The facility financing obligation relates to our obligations for our corporate headquarters facility leased in Morrisville, North Carolina that is accounted for as an asset financing transaction.

(3) Represents minimum annual license fees payable under our license agreements. We are a party to various license agreements with universities and other third parties, as well as patent assignment agreements, under which we have obtained rights to patents, patent applications and know-how. Under these agreements, in addition to minimum annual license fees, we have agreed to pay the other parties milestone payments upon the achievement of specified clinical, regulatory and commercialization events and royalties based on future sales of products. We have not included these payments in the table as we cannot estimate if, when or in what amounts such payments will become due under these agreements. Please see discussion below for contractual obligations under the Agreement with Sato, which was executed in January 2017.

Facility financing lease

We entered into a lease agreement in August 2015 for a facility totaling approximately 51,350 square feet in Morrisville, North Carolina and began to occupy and utilize the facility in October 2016. The term of the lease commenced April 1, 2016 and terminates June 2026. The total estimated lease payments for this facility over the term of the lease are approximately $12.5 million. In addition, we are obligated to pay the landlord for facility leasehold improvements to the extent their cost exceeds the amount the landlord has agreed to contribute to the project. Construction commenced in April 2016 and we paid the landlord $1.2 million for estimated excess facility leasehold improvement costs. During the fourth quarter of 2016, we exceeded the amount the landlord agreed to contribute and made an additional payment of approximately $1.0 million for excess build out costs necessary to substantially complete the facility's construction.

We have accounted for this lease as a capitalized asset and a corresponding facility financing obligation on our balance sheets. See "Note 1—Organization and Significant Accounting Policies" and "Note 6—Commitments and Contingencies" to the accompanying audited financial statements in Item 8 of this Annual Report for further discussion of the accounting for this lease.

Sato license agreement

Pursuant to the Agreement entered into with Sato in January 2017, we are obligated to supply Sato with all quantities of licensed products required by Sato for their development activities in Japan. As part of the Agreement,

we and Sato also agreed to negotiate a commercial supply agreement pursuant to which we would be the exclusive supplier to Sato of the active pharmaceutical ingredient of licensed products for the manufacture of licensed products in the licensed territory. Additionally, we have agreed to perform certain oversight, review and supporting activities for Sato, including: (i) using commercially reasonable efforts to obtain marketing approval of SB204 in the U.S, (ii) sharing all future scientific information we may obtain during the term of the Agreement pertaining to SB204, (iii) performing certain additional pre-clinical studies if such studies are deemed necessary by the Japanese regulatory authority, up to and not to exceed a total cost of $1.0 million, and (iv) participating in a joint committee that oversees, reviews, and approves Sato's development and commercialization activities under the Agreement. Additionally, we have granted Sato the option to use our trademarks in connection with the commercialization of licensed products in the licensed territory for no additional consideration, subject to our approval of such use. We have not included any payments or costs associated with these obligations in the table above as we cannot estimate if, when or in what amounts such payments will become due under the Agreements.

The intellectual property rights granted to Sato under the Agreement include certain intellectual property rights which we have licensed from UNC. Under our license agreement with UNC, we are obligated to pay UNC a running royalty percentage in the low single digits on net sales of licensed products, including net sales that may be generated by Sato. Additionally, we made a payment to UNC in February 2017 representing the portion of the Sato upfront payment that was estimated to be directly attributable to the UNC intellectual property rights included in the license to Sato.

We also entered into an agreement with a third party to assist us in exploring the SB204 licensing opportunity that led to the execution of the Agreement with Sato. We paid a fee of $0.2 million to the third party upon execution of the Agreement and are obligated to pay the third party a low-single-digit percentage of any future milestone payments we may receive from Sato under the Agreement.

Other

We enter into contracts in the normal course of business with clinical research organizations for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Net Operating Loss and Research and Development Tax Credit Carryforwards

As of December 31, 2016, we had federal and state net operating loss carryforwards of approximately of $105.1 million and $106.7 million, respectively. The net operating loss carryforwards begin to expire in 2028 and 2023 for federal and state tax purposes, respectively. We have research and development tax credits of approximately $3.9 million to offset future federal taxes. These credits begin to expire in 2028.

We record a valuation allowance to offset any net deferred tax assets if, based upon the available evidence, it is more likely than not that we will not recognize some or all of the deferred tax assets. We have had a history of net losses since inception, and, as a result, we have established a 100% valuation allowance of $43.8 million for our net deferred tax assets as of December 31, 2016. If circumstances change and we determine that we will be able to realize some or all of these net deferred tax assets in the future, we will record an adjustment to the valuation allowance.

The Tax Reform Act of 1986 contains provisions which limit the ability to utilize the net operating loss carryforwards in the case of certain events including significant changes in ownership interests. If our net operating loss carryforwards are limited, and we have taxable income which exceeds the permissible yearly net operating loss

carryforwards, we would incur a federal income tax liability even though net operating loss carryforwards would be available in future years.

Jumpstart Our Business Startups Act of 2012 (JOBS Act)

In April 2012, the JOBS Act was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an "emerging growth company." As an "emerging growth company," we are electing not to take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards, and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth public companies. Section 107 of the JOBS Act provides that our decision not to take advantage of the extended transition period is irrevocable. We have chosen to rely on the other exemptions and reduced reporting requirements provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, as an "emerging growth company" we are not required to, among other things, (i) provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act, (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Act, (iii) comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis) and (iv) disclose certain executive compensation-related items, such as the correlation between executive compensation and performance and comparisons of the chief executive officer's compensation to median employee compensation. We may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of the completion of our IPO. However, if certain events occur prior to the end of such five-year period, including if we become a "large accelerated filer," our annual gross revenue equals or exceeds $1.0 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period.

Recent Accounting Pronouncements

Recently issued accounting pronouncements that we have adopted or are currently evaluating are described in detail within "Note 1—Organization and Significant Accounting Policies" to the accompanying audited financial statements included in Item 8 of this Annual Report.

Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

There were no changes in or disagreements with accountants on accounting and financial disclosures.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue and expenses during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in the notes to our financial statements included elsewhere in this annual report, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our financial statements and understanding and evaluating our reported financial results.

Revenue Recognition

Our revenue has historically consisted of revenue under research contracts and grants with Federal government agencies. Beginning in 2017, revenue will also consist of licensing revenue related to non-refundable upfront fees, milestone payments and royalties earned under license agreements. Revenue is recognized when all of the following criteria are met: (i) persuasive evidence that an arrangement exists; (ii) delivery of the products or services has occurred; (iii) the selling price is fixed or determinable; and (iv) collectability is reasonably assured.

Government Contract and Grant Revenues

Under the terms of the contracts and grants awarded, we are entitled to receive reimbursement of our allowable direct expenses, allocated overhead, general and administrative expenses and payment of other specified amounts. Revenues from development and support activities under federal research grants are recorded in the period in which the related costs are incurred for cost reimbursement grants. Revenue is recognized when earned and expenses are recognized when incurred.

Any of the funding sources may request reimbursement for expenses or return of funds, or both, as a result of noncompliance by us with the terms of the grants. No reimbursement of expenses or return of funds for noncompliance has been requested or made since inception of the contract and grants.

Licensing Arrangements

We have recently entered into the licensing arrangement with Sato, and may enter into additional licensing arrangements in the future, in exchange for non-refundable upfront payments and potential future milestone and royalty payments. Such arrangements include multiple elements, including the sale of licenses and the provision of services. For arrangements that involve the delivery of more than one element, each product, service and/or right to use assets is evaluated to determine whether it qualifies as a separate unit of accounting. This determination is based on whether the deliverable has "stand-alone value" to the customer. The consideration that is fixed or determinable is then allocated to each separate unit of accounting based on the relative selling prices of each deliverable. The consideration allocated to each unit of accounting is recognized as the related goods and services are delivered, limited to the consideration that is not contingent upon future deliverables. When an arrangement is accounted for as a single unit of accounting, we determine the period over which the performance obligations will be performed and revenue recognized. Management exercises significant judgment in the determination of whether a deliverable has stand-alone value, is considered to be a separate unit of accounting, and in estimating the relative fair value of each deliverable in the arrangement.

We will recognize a milestone payment when earned if it is substantive and we have no ongoing performance obligations related to the milestone. A milestone payment is considered substantive if it: (i) is commensurate with either our performance to achieve the milestone or the enhanced value of the delivered item as a result of a specific outcome from the performance to achieve the milestone; (ii) relates solely to past performance; and (iii) is reasonable relative to all of the deliverables and payment terms, including other potential milestone consideration, within the arrangement.

Accrued Research and Development Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with applicable vendor personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued expenses include fees incurred by CROs in connection with clinical trials, fees paid to investigative sites in connection with clinical trials, professional service fees and unpaid salaries, wages and benefits.

We accrue our expenses related to clinical trials based on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we will adjust the accrual accordingly. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. We do not anticipate the future settlement of existing accruals to differ materially from our estimates.

Common Stock Valuation and Stock-Based Compensation

We record the fair value of stock options, restricted stock awards and other stock-based compensation issued to employees and non-employees as of the grant date as stock-based compensation expense. We typically recognize compensation expense over the requisite service period, which is typically the vesting period. We recorded non-cash stock-based compensation expense from continuing operations for employee and nonemployee stock option grants of, $1.6 million, $2.0 million and $0.2 million for the years ended December 31, 2016, 2015 and 2014, respectively.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of assumptions, some of which are highly subjective, including (i) the fair value of our common stock on the date of grant (described in the following section titled "Determination of the Fair Value of Common Stock"), (ii) the expected volatility of our stock, (iii) the expected term of the award, (iv) the risk-free interest rate and (v) expected dividends. In applying these assumptions, we considered the following factors:

- Due to the lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. In connection with the Separation Transaction, we considered if our peer companies required adjustment to more closely align with our dermatological focus and determined that no adjustment was necessary. Our peer companies utilized have similar clinical-stage research and development activities coupled with recent clinical successes in the dermatological space. We also considered characteristics such as industry, stage of life cycle, financial leverage, enterprise value, risk profiles and position within the industry, along with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.
- We have estimated the expected term of our employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option.
- The risk free interest rate is based on the yields of U.S. Treasury securities with maturities similar to the expected term of granted stock-based awards.
- We have never declared or paid any cash dividends to common stockholders and do not presently plan to pay cash dividends in the foreseeable future. Consequently, we use an expected dividend yield of zero.

See "Note 9—Stock Option Plan" to the accompanying audited financial statements included in Item 8 of this Annual Report for the weighted average assumptions used in the Black-Scholes option-pricing model for awards granted in the years ended December 31, 2016, 2015 and 2014.

We are also required to estimate forfeitures at the time of grant, and to revise those estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual

forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

Determination of the Fair Value of Common Stock—Pre-IPO Stock Option Grants

Prior to our IPO in September 2016, we were a private company with no active public market for our common stock. There were significant assumptions and estimates required in determining the fair value of our common stock for purposes of valuing stock-based compensation grants occurring prior to our IPO. Due to the absence of an active market for our common stock prior to our IPO, the fair value of our common stock was determined in good faith by our board of directors, with the assistance and upon the recommendation of management, based on a number of objective and subjective factors consistent with the methodologies outlined in the American Institute of Certified Public Accountants Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation, referred to as the AICPA Practice Aid, including:

- contemporaneous valuations of our shares of common stock;
- the prices of each of our series of convertible preferred stock sold by us to outside investors in arm's length transactions, and the rights, preferences and privileges of each of these series of preferred stock relative to our common stock;
- our consolidated results of operations, financial position and the status of our research and development efforts;
- the composition of our management team and board of directors;
- the material risks related to our business;
- the market performance of publicly traded companies in the life sciences and biotechnology sectors;
- the likelihood of achieving a liquidity event for the holders of our shares of common stock, such as a sale of the company or an initial public offering, given prevailing market conditions;
- the lack of marketability of our common stock; and
- external market conditions affecting the life sciences and biotechnology industry sectors.

We utilized a combination of the "Last Money In" approach and "Market-Based," or "Comps," approach to estimate our enterprise value prior to our IPO in September 2016. The "Last Money In" approach considered our prior financing rounds, which can provide meaningful indications to determine our enterprise value. The Comps approach considered our enterprise value through an analysis of recent sales and offerings of comparable companies. We then used the option pricing method, or OPM, to estimate the fair value of common stock associated with each pre-IPO stock option grant. Key assumptions reflected in the OPM calculations included the anticipated timing of a potential liquidity event, the estimated volatility of our common stock, and the discount for lack of marketability of our common stock.

Pursuant to the non-employee director compensation policy, each non-employee director who served on the Board as of the pricing date of our IPO was automatically granted an option on September 20, 2016 to purchase the number of shares of common stock that had an aggregate fair value of $100,000 on the pricing date at an exercise price of $11.00 per share.

Determination of the Fair Value of Common Stock—Post-IPO Stock Option Grants

For all grants of stock options made following the completion of our IPO, we have determined, and will determine in the future, fair value based on the closing price of our common stock on the Nasdaq Global Market on the date of determination. As a result, the fair value of our common stock no longer requires a highly complex and subjective estimation process.

Warrant Liability

As of December 31, 2014, all of the warrants to purchase shares of our Series 3 preferred stock had been exercised or expired. Because our Series 3 preferred stock was subject to redemption under circumstances outside of our control, the outstanding shares of this series of preferred stock were presented as temporary equity. Consequently, the warrants to purchase shares of Series 3 convertible preferred stock were accounted for as liabilities and adjusted to fair value at the end of each reporting period. The fair value of the warrants classified as liabilities was estimated using the Black-Scholes option pricing model. The estimates in Black-Scholes option pricing model were based, in part, on subjective assumptions, including stock price volatility, term of the warrants, risk-free interest rate, dividend yield and fair value of the Series 3 convertible preferred stock underlying the warrants. The gain or loss associated with the change in the fair value of the preferred stock warrant liability from the prior period was recognized as a component of other income (expense).

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risks in the ordinary course of our business. Our primary exposure to market risk is currently limited to our cash and cash equivalents, all of which have maturities of less than three months. The primary objectives of our investment activities are the preservation of principal, maintenance of liquidity for the purpose of funding operations and maximizing total return. The related interest income sensitivity is affected by changes in the general level of short-term U.S. interest rates. We place our cash and cash equivalents with high-credit quality financial institutions. Our investment policy prohibits us from holding corporate bonds, auction rate securities, asset-backed securities, municipal obligations, structured investment vehicles, extendable commercial paper or collateralized debt/loan obligations.

As of December 31, 2016, we had cash and cash equivalents of $34.6 million. We believe that an immediate one percentage point increase in interest rates would not materially affect the fair value of these instruments. We do not believe that our cash and cash equivalents have significant risk of default or illiquidity and do not expect our operating results or cash flows to be affected significantly by a sudden change in market interest rates. While we believe our cash and cash equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in fair value. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

Following the execution of the Sato license agreement in January 2017, we have become exposed to some degree of foreign exchange risk as a result of entering into transactions denominated in a currency other than U.S. dollars, particularly in Japanese yen. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made, and all monetary balances are translated to U.S. dollars using period-end exchange rate. A hypothetical 10% change in the exchange rate between the Japanese yen and the U.S. dollar during any of the periods presented would not have had a significant impact on our financial statements.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Novan, Inc.:

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations and comprehensive loss, of convertible preferred stock and stockholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Novan, Inc. as of December 31, 2016 and December 31, 2015, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2016 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

The accompanying consolidated financial statements have been prepared assuming the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations, negative cash flow from operating activities, and has an accumulated deficit that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/PricewaterhouseCoopers LLP
Raleigh, North Carolina
March 20, 2017

NOVAN, INC.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2016	**2015**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 34,611	$ 45,688
Deferred offering costs	—	309
Prepaid expenses and other current assets	958	936
Total current assets	35,569	46,933
Restricted cash	539	539
Intangible assets	75	—
Property and equipment, net	16,290	2,344
Total assets	$ 52,473	$ 49,816
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 3,130	$ 1,626
Accrued compensation	2,305	1,047
Accrued outside research and development services	5,737	1,088
Accrued legal and professional fees	382	512
Other accrued expenses	1,813	534
Deferred rent	—	25
Capital lease obligation, current portion	10	6
Current liabilities of discontinued operations	—	257
Total current liabilities	13,377	5,095
Capital lease obligation, net of current portion	32	4
Facility financing obligation	7,998	—
Total liabilities	21,407	5,099
Commitments and contingencies (Notes 3, 4 and 6)		
Mezzanine B convertible preferred stock, $0.0001 par value, 0 shares designated, issued and outstanding as of December 31, 2016; 5,000,000 shares designated; 1,242,069 shares issued and outstanding as of December 31, 2015; liquidation preference of $32,840 as of December 31, 2015	—	32,840
Mezzanine A convertible preferred stock, $0.0001 par value, 0 shares designated, issued and outstanding as of December 31, 2016; 3,677,622 shares designated, issued and outstanding as of December 31, 2015; liquidation preference of $50,420 as of December 31, 2015	—	50,420
Series 4 convertible preferred stock, $0.0001 par value; 0 shares designated, issued and outstanding as of December 31, 2016; 1,833,333 shares designated, issued and outstanding as of December 31, 2015; liquidation preference of $11,000 as of December 31, 2015	—	11,000

	Year Ended December 31,	
	2016	2015
Series 3 convertible preferred stock, $0.0001 par value; 0 shares designated, issued and outstanding as of December 31, 2016; 1,349,382 shares designated; 1,322,570 shares issued and outstanding as of December 31, 2015; liquidation preference of $7,538 as of December 31, 2015	—	7,538
Series 2 convertible preferred stock, $0.0001 par value; 0 shares designated, issued and outstanding as of December 31, 2016; 1,226,242 shares designated, issued and outstanding as of December 31, 2015; liquidation preference of $2,000 as of December 31, 2015	—	2,000
Series 1 convertible preferred stock, $0.0001 par value; 0 shares designated, issued and outstanding as of December 31, 2016; 1,229,862 shares designated, issued and outstanding as of December 31,2015; liquidation preference of $1,000 as of December 31, 2015	—	1,000
Stockholders' equity (deficit):		
Preferred stock $0.0001 par value; 10,000,000 shares designated as of December 31, 2016; 0 shares designated as of December 31, 2015; 0 shares issued and outstanding as of December 31, 2016 and December 31, 2015	—	—
Common stock $0.0001 par value; 200,000,000 shares authorized as of December 31, 2016; 22,000,000 shares authorized as of December 31, 2015; 15,949,492 and 2,235,838 shares issued as of December 31, 2016 and December 31, 2015; 15,939,992 and 2,235,838 shares outstanding as of December 31, 2016 and December 31, 2015	2	—
Non-voting common stock $0.0001 par value; 0 shares authorized, issued and outstanding as of December 31, 2016; 229,263 shares authorized; 191,052 shares issued and outstanding as of December 31, 2015	—	—
Additional paid-in-capital	154,252	3,253
Treasury stock at cost, 9,500 shares as of December 31, 2016 and 0 shares as of December 31, 2015	(155)	—
Accumulated deficit	(123,033)	(63,334)
Total stockholders' equity (deficit)	31,066	(60,081)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 52,473	$ 49,816

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

NOVAN, INC.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2016	2015	2014
Government research contracts and grants revenue	$ —	$ —	$ 112
Operating expenses:			
Research and development	46,489	16,569	6,770
General and administrative	13,337	9,265	5,170
Total operating expenses	59,826	25,834	11,940
Operating loss	(59,826)	(25,834)	(11,828)
Other income (expense):			
Interest income	81	48	58
Interest expense	(2)	(1)	(701)
Change in the fair value of the warrant liability	—	—	(641)
Other income, net	48	1	9
Total other income (expense)	127	48	(1,275)
Loss from continuing operations	(59,699)	(25,786)	(13,103)
Income (loss) from discontinued operations	—	(2,274)	1,715
Net loss and comprehensive loss	$ (59,699)	$ (28,060)	$ (11,388)
Income (loss) per share, basic and diluted:			
Continuing operations	$ (9.97)	$ (11.36)	$ (5.95)
Discontinued operations	—	(1.01)	0.78
Net loss per share, basic and diluted	$ (9.97)	$ (12.37)	$ (5.17)
Weighted-average common shares outstanding, basic and diluted	5,985,985	2,269,124	2,203,278

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

NOVAN, INC.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share amounts)

	Convertible Preferred Stock												Common Stock				Additional			
	Mezzanine B		Mezzanine A		Series 4		Series 3		Series 2		Series 1		Voting		Non-voting		Paid in	Treasury	Accumulated	
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Stock	Deficit	Total
Balance as of December 31, 2013	—	$ —	—	$ —	1,833,333	$ 11,000	1,226,935	$ 6,135	1,226,242	$ 2,000	1,229,862	$ 1,000	1,977,384	$ —	191,052	$ —	$ 176	—	$ (18,561)	$ (18,385)
Share-based compensation	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	177	—	—	177
Exercise of stock options	—	—	—	—	—	—	—	—	—	—	—	—	67,431	—	—	—	47	—	—	47
Exercise of Series 3 preferred stock warrants	—	—	—	—	—	—	95,635	1,403	—	—	—	—	—	—	—	—	—	—	—	—
Beneficial conversion of notes payable	—	—	—	420	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Conversion of notes payable	—	—	306,484	3,782	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Issuance of Mezzanine A preferred stock	—	—	872,318	11,959	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(11,388)	(11,388)
Balance as of December 31, 2014	—	—	1,178,802	16,161	1,833,333	11,000	1,322,570	7,538	1,226,242	2,000	1,229,862	1,000	2,044,815	—	191,052	—	400	—	(29,949)	(29,549)
Share-based compensation	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2,385	—	—	2,385
Exercise of stock options	—	—	—	—	—	—	—	—	—	—	—	—	191,023	—	—	—	468	—	—	468
Issuance of Mezzanine A preferred stock	—	—	2,498,820	34,259	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Issuance of Mezzanine B preferred stock	1,242,069	32,840	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Distribution of KNOW Bio, LLC	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(5,325)	(5,325)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(28,060)	(28,060)
Balance as of December 31, 2015	1,242,069	32,840	3,677,622	50,420	1,833,333	11,000	1,322,570	7,538	1,226,242	2,000	1,229,862	1,000	2,235,838	—	191,052	—	3,253	—	(63,334)	(60,081)
Share-based compensation	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1,573	—	—	1,573
Exercise of stock options	—	—	—	—	—	—	—	—	—	—	—	—	31,333	—	—	—	35	—	—	35
Repurchase of treasury stock	—	—	—	—	—	—	—	—	—	—	—	—	(9,500)	—	—	—	—	(155)	—	(155)
Automatic conversion to common stock	(1,242,069)	(32,840)	(3,677,622)	(50,420)	(1,833,333)	(11,000)	(1,322,570)	(7,538)	(1,226,242)	(2,000)	(1,229,862)	(1,000)	8,967,321	1	(191,052)	—	104,797	—	—	104,798
Common stock issued through initial public offering, net of underwriting discounts, commissions and offering costs (Note 1)	—	—	—	—	—	—	—	—	—	—	—	—	4,715,000	1	—	—	44,594	—	—	44,595
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(59,699)	(59,699)
Balance as of December 31, 2016	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	15,939,992	$ 2	—	$ —	$ 154,252	$ (155)	$ (123,033)	$ 31,066

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

NOVAN, INC.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2016	2015	2014
Cash flow from operating activities:			
Net loss	$ (59,699)	$ (28,060)	$ (11,388)
Income (loss) from discontinued operations	—	2,274	(1,715)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	757	631	462
Share-based compensation	1,573	1,974	177
Non-cash interest income	—	—	(58)
Non-cash interest expense	—	—	700
Increase in fair value of warrant liability	—	—	641
Loss (gain) on disposal of property and equipment	(36)	8	—
Changes in operating assets and liabilities:			
Contracts and grants receivable	—	—	519
Prepaid expenses and other current assets	(22)	(604)	(278)
Accounts payable	1,372	825	338
Accrued compensation	1,258	769	61
Accrued outside research and development services	4,649	837	251
Accrued legal and professional fees	179	200	3
Accrued expenses	1,083	411	(92)
Other	(25)	(30)	(22)
Net cash used in continuing operating activities	(48,911)	(20,765)	(10,401)
Net cash provided by (used in) discontinued operating activities	(257)	(1,427)	1,798
Net cash used in operating activities	(49,168)	(22,192)	(8,603)
Cash flow from investing activities:			
Purchases of property and equipment	(6,143)	(1,212)	(772)
Purchase of intangible asset	(75)	—	—
Cash restricted to secure letter of credit	—	(539)	—
Net cash used in continuing investing activities	(6,218)	(1,751)	(772)
Net cash used in discontinued investing activities	—	(139)	(6)
Net cash used in investing activities	(6,218)	(1,890)	(778)
Cash flow from financing activities:			
Proceeds from issuance of preferred stock	—	67,099	11,959
Proceeds from issuance of convertible notes	—	—	3,502
Proceeds from initial public offering, net of underwriting fees and commissions	47,785	—	—
Payments related to public offering costs	(3,190)	—	—
Proceeds from exercise of stock options	35	458	57
Proceeds from the exercise of preferred stock warrants	—	—	550
Purchase of treasury stock	(155)	—	—
Dividend Distribution	—	(5,200)	
Payments on capital lease obligation	(7)	(6)	(5)
Payments on facility financing obligation	(159)	—	—
Net cash provided by financing activities	44,309	62,351	16,063
Net increase (decrease) in cash and cash equivalents	(11,077)	38,269	6,682
Cash and cash equivalents as of beginning of period	45,688	7,419	737
Cash and cash equivalents as of end of period	$ 34,611	$ 45,688	$ 7,419
Supplemental disclosure of cash flow information:			
Cash paid for interest, including capitalized interest	$ 410	$ 1	$ 2
Supplemental disclosure of non-cash investing and financing activities:			
Purchases of equipment with accounts payable and accrued expenses	$ 420	$ 92	$ 240
Conversion of notes payable and unpaid interest into preferred stock	$ —	$ —	$ 3,782
Exercise of preferred stock warrants	$ —	$ —	$ 853
Distribution of KNOW Bio, LLC equipment	$ —	$ 125	$ —
Equipment acquired through capital lease	$ 39	$ —	$ —
Non-cash addition to construction in progress related to build-to-suit lease and facility financing obligation	$ 8,157	$ —	$ —
Non-cash addition to deferred offering costs	$ —	$ 309	$ —
Conversion of convertible preferred stock and non-voting common stock to voting common stock	$ 104,798	$ —	$ —
Deferred offering costs reclassified to additional paid-in capital	$ 3,190	$ —	$ —

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

NOVAN, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(dollar values in thousands, except per share data)

Note 1: Organization and Significant Accounting Policies

Business Description and Basis of Presentation

Novan, Inc. ("Novan" and together with its subsidiaries, the "Company"), is a North Carolina-based clinical-stage drug development company focused on the development and commercialization of nitric oxide-based therapies in dermatology. Novan was incorporated in January 2006 under the state laws of Delaware and its subsidiaries were organized in May 2015 under the state laws of North Carolina. In December 2015, KNOW Bio, LLC ("KNOW Bio") was organized under the state laws of North Carolina.

On December 30, 2015, the Company completed the distribution of 100% of the outstanding member interests of KNOW Bio to Novan's stockholders (the "Distribution"), pursuant to which KNOW Bio became an independent privately held company. Beginning in the fourth quarter of 2015, KNOW Bio's financial results for periods prior to the Distribution have been reflected in the Company's consolidated statements of operations, retrospectively, as discontinued operations. Additionally, the related assets and liabilities associated with the discontinued operations in the December 31, 2015 consolidated balance sheet and liabilities outstanding as of December 31, 2015 not assumed by KNOW Bio as part of the distribution are classified as discontinued operations. See Note 2—Discontinued Operations for additional information.

The accompanying consolidated financial statements of the Company have been prepared in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP").

Liquidity and Ability to Continue as a Going Concern

The Company's consolidated financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the settlement of liabilities and commitments in the normal course of business. The accompanying consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from uncertainty related to the Company's ability to continue as a going concern.

The Company has evaluated principal conditions and events that may raise substantial doubt about its ability to continue as a going concern within one year from the date that these financial statements are issued. The Company identified the following conditions:

- The Company has reported a net loss in all fiscal periods since inception and, as of December 31, 2016, the Company had an accumulated deficit of $123,033.
- The Company's primary use of cash is to fund its operating expenses, which consist principally of research and development expenditures necessary to advance its product candidates. The Company has evaluated its expected, probable future cash flow needs and has determined that it expects to incur substantial losses in the future as it conducts planned operating activities. The Company expects that the cash required to fund its planned operating activities within one year from the date that these financial statements are issued will exceed the amount of cash and cash equivalents on hand as of December 31, 2016, together with the nonrefundable upfront payment received from Sato in January 2017 (see Note 14—Subsequent Events).

The Company has concluded that these conditions raise substantial doubt about the Company's ability to continue as a going concern within one year from the date that these financial statements are issued. To mitigate these conditions, the Company needs and intends to raise additional funds through equity or debt financings or generate revenues from collaborative partners prior to the commercialization of the Company's product candidates. There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could cause the Company to alter or reduce its

planned operating activities, including but not limited to delaying planned product candidate development activities, to conserve its cash and cash equivalents. Such actions could delay development timelines and have a material adverse effect on the Company's results of operations and financial condition. Additionally, there is no assurance that the Company can achieve its development milestones or that its intellectual property rights will not be challenged.

Reverse stock-split and amendments to certificate of incorporation

On September 7, 2016, following approval by the Company's Board of Directors and the Company's stockholders, the Company amended its certificate of incorporation effecting a 1-for-1.2 reverse stock split of its voting and non-voting common stock and a proportional adjustment to the existing conversion ratio of each series of its convertible preferred stock. As a result of the reverse stock split, the Company also adjusted the share amounts under its employee incentive plan. All disclosure of common shares and per common share data in the accompanying financial statements and related notes have been adjusted to reflect the reverse stock split and adjustment of preferred stock conversion ratios for all periods presented.

The reverse stock split did not cause an adjustment to the par value or the authorized shares of the voting and non-voting common stock or the convertible preferred stock. However, subsequent to the reverse stock split and in conjunction with the closing of the Company's initial public offering, ("IPO"), the certificate was further amended to provide for an adjustment to the number of authorized shares to 210,000,000 shares of capital stock, of which 200,000,000 shares have been designated as $0.0001 par value common stock, and 10,000,000 shares have been designated as $0.0001 par value preferred stock.

Initial public offering

On September 26, 2016, the Company completed the IPO of its common stock. The Company sold an aggregate of 4,715,000 shares of common stock under the registration statement on Form S-1 declared effective by the Securities and Exchange Commission ("SEC") on September 20, 2016, at a public offering price of $11.00 per share for aggregate gross proceeds of $51,865. Net proceeds were $44,595, after deducting underwriting discounts and commissions of $4,080 and offering expenses of $3,190. Upon the completion of the IPO, all outstanding shares of the Company's non-voting common stock and convertible preferred stock were automatically converted into 8,967,321 shares of common stock. The shares issued as part of the IPO in September 2016 increased the number of shares outstanding, which impacts the comparability of the Company's reported net loss per share calculations between the 2016, 2015 and 2014 periods.

Basis of Consolidation

The accompanying consolidated financial statements reflect the operations of the Company and its wholly owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

Reclassifications

Certain prior period amounts have been reclassified to conform to current period presentation. These changes had no effect on previously reported net loss, financial position or cash flows.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amount of revenues and expenses during the reporting period. Actual results could differ from these estimates.

Cash and Cash Equivalents

The Company considers all highly liquid instruments purchased with a maturity of three months or less to be cash equivalents. Cash and cash equivalents include deposits and money market accounts.

Restricted Cash

The Company included in noncurrent assets restricted cash of $539 as of December 31, 2016 and 2015, which consisted of funds maintained in a separate deposit account to secure a letter of credit for the benefit of the lessor of facility space leased by the Company.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist principally of cash and cash equivalents. The Company places its cash and cash equivalents with financial institutions and these deposits may at times be in excess of insured limits.

Intangible Assets

Intangible assets represent the cost to obtain and register the Company's internet domain. Indefinite-lived intangible assets are not amortized and are assessed for impairment at least annually.

Property and Equipment

Property and equipment are recorded at cost and depreciated using the straight line method over their estimated useful lives as follows:

Computer equipment	3 years
Office equipment	3 years
Furniture and fixtures	5 years
Laboratory equipment	7 years
Building asset under facility lease	25 years

Leasehold improvements are amortized over the shorter of the life of the lease or the useful life of the improvements. Expenditures for maintenance and repairs are expensed as incurred. Improvements and betterments that add new functionality or extend the useful life of an asset are capitalized.

Intellectual Property

The Company's policy is to file patent applications to protect technology, inventions and improvements that are considered important to its business. Patent positions, including those of the Company, are uncertain and involve complex legal and factual questions for which important legal principles are largely unresolved. Due to the uncertainty of future value to be realized from the expenses incurred in developing the Company's intellectual property, the cost of filing, prosecuting and maintaining internally developed patents are expensed as general and administrative costs as incurred.

Leases

The Company leases office space and certain equipment under non-cancelable lease agreements. The leases are reviewed for classification as operating or capital leases. For operating leases, rent is recognized on a straight-line basis over the lease period. For capital leases, the Company records the leased asset with a corresponding liability and amortizes the asset over the lease term. Payments are recorded as reductions to the liability with an appropriate interest charge recorded based on the then-outstanding remaining liability.

The Company considers the nature of the renovations and the Company's involvement during the construction period of newly leased office space to determine if it is considered to be the owner of the construction project during the construction period. If the Company determines that it is the owner of the construction project, it is required to capitalize the fair value of the building as well as the construction costs incurred, including capitalized interest, on its consolidated balance sheet along with a corresponding financing liability ("build-to-suit accounting"). Upon completion of the construction of the facility under a build-to-suit lease, the Company assesses whether the circumstances qualify for sales recognition under the sale-leaseback accounting guidance. If the lease meets the sale-leaseback criteria, the Company will remove the asset and related financial obligation from the balance sheet and evaluate the lease for treatment as a capital or operating lease. If upon completion of construction, the project does not meet the sale-leaseback criteria, the leased property will be treated as an asset financing for financial reporting purposes. The portion of the facility financing obligation representing the principal that will be repaid in the next twelve months will be classified as a current liability in the consolidated balance sheets, with the remaining portion of the obligation classified as a noncurrent liability. Please see Note 6—Commitments and Contingencies for further discussion of the Company's application of this guidance related to the Company's primary facility lease.

Impairment of Long-Lived Assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized for an amount by which the carrying amount of the asset exceeds the fair valued of the asset. There were no impairments of long-lived assets during the years ended December 31, 2016, 2015 and 2014.

Deferred Offering Costs

Deferred offering costs, consisting of legal, accounting, filing and other fees directly related to the offering, are offset against proceeds from each offering. Offering costs incurred prior to the completion of an offering are initially capitalized as assets, evaluated each period for likelihood of completion and subsequently reclassified to additional paid-in capital upon completion of the offering.

Revenue Recognition

The Company's revenue consists of research revenue earned under contracts and grants with Federal government agencies, which relate to the research and development of its nitric oxide platform. Revenue is recognized when all of the following criteria are met: (i) persuasive evidence that an arrangement exists; (ii) delivery of the products or services has occurred; (iii) the selling price is fixed or determinable; and (iv) collectability is reasonably assured. As a result of the Distribution, the majority of the Company's revenues are classified as discontinued operations. See Note 2—Discontinued Operations for additional information.

Government research contracts and grants revenue. Under the terms of the contracts and grants awarded, the Company is entitled to receive reimbursement of its allowable direct expenses, allocated overhead, general and administrative expenses and payment of other specified amounts. Revenues from development and support activities under government research contracts and grants are recorded in the period in which the related costs are incurred for cost reimbursement grants. Revenue is recognized when earned and expenses are recognized when incurred as research and development expense.

Any of the funding sources may request reimbursement for expenses or return of funds, or both, as a result of noncompliance by the Company with the terms of the grants. No reimbursement of expenses or return of funds for noncompliance has been requested or made since inception of the contracts and grants.

During 2013, the Company received a contract from Biomedical Advanced Research and Development Authority ("BARDA") with a total value of $7,869 over a contract performance period from August 2013 through August 2015. Total contract value includes direct, indirect, and allocable overhead costs plus a fixed percentage fee. Revenue recognized under this contract was $0 during the year ended December 31, 2016 and $229 and $2,989

during the years ended December 31, 2015 and 2014, respectively. Total revenue recognized and cash received during the contract performance period was $4,302. As a result of the Distribution, revenue recognized under this contract is classified as discontinued operations. See Note 2—Discontinued Operations for additional information.

Research and Development Expenses

Research and development expenses include all direct and indirect development costs incurred for the development of the Company's drug candidates. These expenses include salaries and related costs, including stock-based compensation and travel costs, for research and development personnel, consulting fees, product development, preclinical studies, clinical trial costs, licensing fees and milestone payments under license agreements and other fees and costs related to the development of the drug candidates. The cost of tangible and intangible assets that are acquired for use on a particular research and development project, have no alternative future uses, and are not required to be capitalized in accordance with the Company's capitalization policy, are expensed as research and development costs as incurred.

Fair Value of Financial Instruments

The carrying values of cash equivalents, accounts payable and accrued liabilities as of December 31, 2016, 2015 and 2014 approximated their fair values due to the short-term nature of these items.

The Company has categorized its financial instruments, based on the priority of the inputs used to value the investments, into a three-level fair value hierarchy. The fair value hierarchy gives the highest priority to quoted prices in active markets for identical assets or liabilities (Level 1), and lowest priority to unobservable inputs (Level 3). If the inputs used to measure the investments fall within different levels of the hierarchy, the categorization is based on the lowest level input that is significant to the fair value measurement of the investment. Financial instruments recorded in the accompanying consolidated balance sheet are categorized based on the inputs to valuation techniques as follows:

Level 1	-	Observable inputs that reflect unadjusted quoted market prices for identical assets or liabilities in active markets.
Level 2	-	Observable inputs other than Level 1 that are observable, either directly or indirectly in the marketplace for identical or similar assets and liabilities.
Level 3	-	Unobservable inputs that are supported by little or no market data, where values are derived from techniques in which one or more significant inputs are unobservable.

Due to the lack of market quotes relating to our preferred stock warrants, the fair value of the preferred stock warrants was determined using the Black-Scholes model, which is based on Level 3 inputs. For the year ended December 31, 2014, inputs used in the Black-Scholes model are presented below.

	Year Ended December 31, 2014
Estimated dividend yield	0.00%
Expected volatility	75.86% - 100%
Risk-free interest rate	0.02% - 0.13%
Expected term (years)	0.17 to 0.92
Fair value of preferred stock	$6.00 to $13.71
Exercise price	$ 6.00

Due to limited historical data, the Company estimates stock price volatility based on the actual volatility of comparable publicly traded companies over the expected life of the warrant.

The warrants expired in November 2014; as such, there was no preferred stock warrant liability at December 31, 2016, 2015 or 2014. The changes in the balances of Level 3 liabilities for the year ended December 31, 2014 were as follows:

	Fair Value Measurements Using Significant Unobservable Inputs (Level 3)				
	Beginning Balance	Revaluations Included In Earnings	Exercises	Expirations	Ending Balance
Warrant liability—December 31, 2014	$ 271	$ 641	$ (854)	$ (58)	$ —

For the years ended December 31, 2016, 2015 and 2014, there were no transfers between Levels 1, 2 and 3 liabilities.

Share-Based Compensation

Employees. The Company applies the fair value method of accounting for share-based compensation, which requires all such compensation to employees, including the grant of employee stock options, to be recognized in the statement of operations based on its fair value at the measurement date (generally the grant date). The expense associated with share-based compensation is recognized on a straight-line basis over the service period of each award. Share-based awards granted to non-employee directors as compensation for serving on the Company's Board of Directors are accounted for in the same manner as employee share-based compensation awards.

Non-employees. For share-based compensation granted to non-employees, other than non-employee directors, the measurement date is generally considered to be the date when all services have been rendered or the date that options are fully vested.

The fair value of each option grant is estimated using a Black-Scholes option-pricing model on the grant date using expected volatility, risk-free interest rate, expected life of options and fair value per share assumptions. Due to limited historical data, the Company estimates stock price volatility based on the actual volatility of comparable publicly traded companies over the expected life of the option. In evaluating similarity, the Company considered factors such as industry, stage of life cycle, financial leverage, size and risk profile.

The Company does not have sufficient history of exercise of stock options to estimate the expected term of employee stock options and thus continues to calculate expected life based on the mid-point between the vesting date and the contractual term, which is in accordance with the simplified method. The expected term for share-based compensation granted to non-employees is the contractual life. The risk-free rate is based on the U.S. Treasury yield curve during the expected life of the option.

For option grants occurring prior to the Company's IPO in September 2016, the fair value of common stock was estimated by a third-party valuation specialist and approved by the Board of Directors as of the grant date. For options granted to non-employee directors on September 20, 2016 in conjunction with the pricing of the IPO, pursuant to the non-employee director compensation policy, the fair value of common stock was equal to the public offering price of $11.00 per share. For option grants occurring subsequent to the Company's IPO in September 2016, the fair value of common stock will be based upon the closing stock price as of the grant date.

Income Taxes

Deferred tax assets and liabilities are determined based on the temporary differences between the financial statement carrying amounts and the tax bases of assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. In estimating future tax consequences, all expected future events are considered other than enactment of changes in the tax law or rates.

The Company recognizes the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities based on the technical merits of the position.

The Company's policy for recording interest and penalties is to record them as a component of interest expense and general and administrative expenses. As of December 31, 2016, 2015 and 2014, the Company accrued no interest or penalties related to uncertain tax positions.

Tax years that remain subject to examination by federal and state tax jurisdictions date back to the year ended December 31, 2008. The Company has not been informed by any tax authorities for any jurisdiction that any of its tax years are under examination.

The determination of recording or releasing a tax valuation allowance is made, in part, pursuant to an assessment performed by management regarding the likelihood that the Company will generate future taxable income against which benefits of its deferred tax assets may or may not be realized. This assessment requires management to exercise judgment and make estimates with respect to its ability to generate taxable income in future periods.

In accordance with Section 382 of the Internal Revenue Code of 1986, as amended, a change in equity ownership of greater than 50% within a three-year period results in an annual limitation on the Company's ability to utilize its net operating loss carryforwards created during the tax periods prior to the change in ownership. The Company has not determined whether ownership changes exceeding this threshold, including the Company's recent IPO, have occurred. If a change in equity ownership has occurred which exceeds the Section 382 threshold, a portion of the Company's net operating loss carryforwards may be limited.

Redeemable Convertible Preferred Stock

The carrying value of redeemable convertible preferred stock is increased so that the carrying amount is at least equal to the liquidation value. These increases are affected through changes against additional paid-in-capital, to the extent it is available, or the accumulated deficit.

Warrant Liability

Warrants to purchase the Company's convertible preferred stock are classified as liabilities and are recorded at their estimated fair value. In each reporting period, any change in fair value of the warrants is recorded as expense in the case of an increase in fair value and income in the case of a decrease in fair value.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. For the years ended December 31, 2016, 2015 and 2014, comprehensive loss was equal to net loss.

Net Loss Per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive for all periods presented.

The following securities, presented on a common stock equivalent basis, have been excluded from the calculation of weighted average common shares outstanding for the years ended December 31, 2016, 2015 and 2014 because the effect is anti-dilutive due to the net loss reported in each of those periods. All share amounts presented in the table below represent the total number outstanding as of the end of each period. The convertible preferred stock securities will no longer be potentially dilutive in future periods because, as discussed above, in September 2016, upon completion of the IPO, all outstanding shares of the convertible preferred stock were converted into shares of common stock at their conversion prices.

	December 31,		
	2016	2015	2014
Convertible preferred stock	—	8,776,269	5,658,942
Stock options outstanding	825,130	458,234	336,513

Segment Information

The Company has determined that it operates in one segment. The Company uses its nitric oxide-based technology to develop product candidates. The chief executive officer, who is the Company's chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance. The Company has only had limited revenue since its inception, but all of it was derived in the United States, and all of the Company's long-lived assets are maintained in the United States.

Recently Issued Accounting Standards

Accounting Pronouncements Adopted

In June 2014, the FASB issued ASU No. 2014-12, *Compensation—Stock Compensation (Topic 718): Accounting for Share-Based Payments When the Terms of an Award Provide That a Performance Target Could be Achieved after the Requisite Service Period*, which requires the Company to assess share-based awards with performance targets that could be achieved after the requisite service period for potential treatment as performance conditions. Under the ASU, compensation expense is to be recognized when the performance target is deemed probable and should represent the compensation expense attributable to the periods for which service has already been rendered. If the performance target is reached prior to achievement of the service period, the remaining unrecognized compensation cost should be recognized over the remaining service period. The ASU was effective for annual and interim periods beginning after December 15, 2015 with early adoption permitted. This standard was effective for the Company as of January 1, 2016. The adoption of this standard did not have a material impact on its financial statements.

In November 2014, the FASB issued ASU No. 2014-16, *Derivatives and Hedging (Topic 815): Determining Whether the Host Contract in a Hybrid Financial Instrument Issued in the Form of a Share Is More Akin to Debt or to Equity*. The guidance requires an entity to determine the nature of the host contract by considering all stated and implied substantive terms and features of the hybrid financial instrument, weighing each term and feature on the basis of the relevant facts and circumstances (commonly referred to as the whole-instrument approach). ASU 2014-16 applies to all entities and is effective for annual periods beginning after December 15, 2015, and interim periods thereafter. This ASU was effective for the Company as of January 1, 2016. Adoption of this standard did not have a material impact on its financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements – Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, which provides accounting guidance related to the evaluation of an entity's ability to continue as a going concern. ASU 2014-15 establishes management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern in connection with preparing financial statements for each annual and interim reporting period. The update also gives guidance to disclose information about relevant conditions and events when there is substantial doubt about an entity's ability to continue as a going concern. This guidance was effective for the annual periods ending after December 15, 2016 and annual and interim periods thereafter, with early adoption permitted. The Company has concluded that there is substantial doubt about its ability to continue as a going

concern and has presented the disclosures required by this ASU in the subsection titled "Liquidity and Ability to Continue as a Going Concern" in Note 1—Organization and Significant Accounting Policies.

In February 2015, the FASB issued ASU No. 2015-2, *Consolidation (Topic 810): Amendments to the Consolidation Analysis*, which provides clarification regarding the guidance surrounding consolidation of certain legal entities. This guidance is effective for annual and interim periods beginning after December 15, 2015. This standard was effective for the Company as of January 1, 2016. The adoption of this standard did not have a material impact on its financial statements.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes*. The new guidance requires that deferred tax assets and liabilities be classified as noncurrent in a classified statement of financial position. The new standard is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2016. Early adoption is permitted. The Company adopted this ASU for the annual period ended December 31, 2016 and has presented the disclosures required by this ASU in Note 10—Income Taxes.

Accounting Pronouncements Being Evaluated

In May 2014, the FASB and the International Accounting Standards Board issued a converged standard on the recognition of revenue from contracts with customers. The converged standard has been codified within Topic 606, *Revenue from Contracts with Customers* of the FASB Accounting Standard Codification (ASC). The objective of the new standard is to establish a single comprehensive revenue recognition model that is designed to create greater comparability of financial statements across industries and jurisdictions. Under the new standard, companies will recognize revenue to depict the transfer of goods or services to customers in amounts that reflect the consideration to which a company expects to be entitled in exchange for those goods or services. The new standard also will require expanded disclosures on revenue recognition and changes in assets and liabilities that result from contracts with customers. In July 2015, the FASB delayed the effective date of the new standard by one year. Early adoption as of January 1, 2017 is permitted. In March, April and May of 2016, the FASB issued additional ASUs to amend Topic 606 and to provide expanded or clarifying guidance associated with the application of certain principles within the revenue recognition model, including the areas of principle and agent, identification of performance obligations, licensing and other improvements and practical expedients.

The Company intends to adopt the Topic 606 guidance on January 1, 2018. While the Company has not reported material revenue from continuing operations in the historical periods presented, the Company is currently evaluating the impact that Topic 606 will have on anticipated reported revenues in 2017 and future periods associated with a recently executed licensing agreement (Note 14—Subsequent Events). The Company is also evaluating the impact that the adoption of Topic 606 will have on its recognition of costs related to obtaining contracts. The standard permits the use of either the full retrospective or modified retrospective transition method and the Company has not yet selected which transition method it will apply.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. This guidance revises the accounting related to leases by requiring lessees to recognize a lease liability and a right-of-use asset for all leases. The new lease guidance also simplifies the accounting for sale and leaseback transactions. This ASU is effective for annual reporting periods beginning after December 15, 2018 and early adoption is permitted. The Company is currently evaluating the impact of the adoption of this ASU on its financial statements.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting.* The FASB issued ASU 2016-09 to simplify several aspects of the accounting for share-based payment transactions, including the income tax consequences. This ASU is effective for annual and interim periods beginning after December 15, 2016, with early adoption permitted. The Company is currently evaluating the impact of the adoption of this ASU on the Company's financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments.* The FASB issued ASU 2016-09 to improve U.S. GAAP by providing guidance on the cash flow statement classification of eight specific areas where there is existing diversity in practice. The FASB expects that the guidance in this ASU will reduce the current and potential future diversity in practice in such areas. This ASU is effective for annual and interim periods beginning after December 15, 2017, with early

adoption permitted. The Company is currently evaluating the impact of the adoption of this ASU on its financial statements.

In October 2016, the FASB issued ASU No. 2016-17, *Consolidation (Topic 810): Interests Held through Related Parties That Are under Common Control,* which amends the consolidation guidance on how a reporting entity that is a single decision maker of a variable interest entity should treat indirect interests in the entity held through related parties that are under common control. This guidance is effective for annual periods beginning after December 15, 2016, including interim periods within those annual periods, with early adoption permitted. The Company is currently evaluating the impact of the adoption of this ASU on its financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash,* to improve U.S. GAAP by providing guidance on how to classify and present changes in restricted cash or restricted cash equivalents occurring due to transfers between cash, cash equivalents and restricted cash. This ASU is effective for annual and interim periods beginning after December 15, 2017, with early adoption permitted. The Company is currently evaluating the impact of the adoption of this ASU on its financial statements.

In January 2017, the FASB issues ASU No. 2017-01, B*usiness Combinations (Topic 805): Clarifying the Definition of a Business*, which clarifies the definition of a business to provide additional guidance with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. This ASU is effective for annual periods beginning after December 15, 2017, including interim periods within those periods. The Company plans to adopt this standard on January 1, 2018 and is currently evaluating the impact of the adoption of this ASU on its consolidated financial statements.

Note 2: Discontinued Operations

On December 14, 2015, the Board of Directors of Novan approved the separation of its non-dermatological assets and rights from Novan, Inc. through the Distribution. To consummate the Distribution, the Company's Board of Directors declared a pro rata dividend of KNOW Bio member units to Novan's stockholders of record as of the close of business on December 29, 2015 (the "Record Date"). Each Novan stockholder received one member unit of KNOW Bio for every share of Novan preferred or common stock held at the close of business on the Record Date. The Distribution occurred on December 30, 2015 (the "Distribution Date"). Immediately following the Distribution, KNOW Bio became an independent, privately-held company and the Company does not own an equity interest in KNOW Bio and has no significant influence by contract or other means. The results of KNOW Bio have been classified as discontinued operations in the consolidated statements of operations for all periods presented. Additionally, the related liabilities outstanding as of December 31, 2015 not assumed by KNOW Bio as part of the Distribution are classified as discontinued operations in the accompanying consolidated balance sheets.

At the Distribution Date, KNOW Bio had cash of $5,200 and equipment of $125. The cash included in the Distribution was recorded as a dividend distribution in the statement of cash flows. Certain intellectual property rights were licensed to KNOW Bio as further described in Note 4—Technology Agreement.

The financial results of KNOW Bio through the Distribution are presented as loss from discontinued operations in the consolidated statements of operations. The following table presents the financial results of KNOW Bio:

	Year Ended	
	2015	2014
Federal research contract and grant revenue	$ 229	$ 2,989
Other contract and grant revenue	—	53
Total revenue	229	3,042
Operating expenses:		
Research and development	1,826	1,319
General and administrative	677	8
Total operating expenses	2,503	1,327
Income (loss) from discontinued operations	$ (2,274)	$ 1,715

The following table presents the aggregate carrying amount of the classes of liabilities of discontinued operations of KNOW Bio as of December 31, 2015. There were no assets or liabilities of discontinued operations as of December 31, 2016.

	December 31, 2015
Accounts payable	$ 133
Accrued payroll	124
Total liabilities classified as discontinued operations in the consolidated balance sheets	$ 257

Note 3: Research and Development Licenses

The Company has entered into various licensing agreements with universities and other research institutions under which the Company receives the rights, and in some cases substantially all of the rights, of the inventors, assignee or co-assignee to produce and market technology protected by certain patents and patent applications. The Company's primary license agreement is with the University of North Carolina ("UNC") and has been described in further detail within the subsection below. The counterparties to the Company's various other licensing agreements are the University of Akron Research Foundation, Public Health Services, Hospital for Special Surgery, Strakan International S.A.R.L., which is a licensee of the University of Aberdeen, and KIPAX AB. The Company is generally required to make milestone payments based on development milestones and will be required to make royalty payments based on a percentage of future sales of covered products or a percentage of sublicensing revenue. Costs to acquire rights under license agreements and pre-commercialization milestone payments are classified as research and development expenses in the consolidated statements of operations. Research and development expense recognized in connection with the incurrence of such costs totaled $125, $260 and $60 during the years ended December 31, 2016, 2015 and 2014, respectively.

The Company is generally required by the various licensing agreements to reimburse the licensor for certain legal and other patent related costs. These costs are expensed as incurred and are classified as general and administrative expenses in the consolidated statements of operations. General and administrative expense recognized in connection with the incurrence of such costs totaled $87, $112 and $66 during the years ended December 31, 2016, 2015 and 2014, respectively.

These license arrangements could require the Company to make payments upon achievement of certain milestones by the Company. As future royalty payments are directly related to future revenues (either sales or sublicensing), future commitments cannot be determined. No accrual for future payments under these agreements has been recorded, as the Company cannot estimate if, when or in what amount payments may become due.

UNC License Agreement

The UNC License Agreement provides the Company with an exclusive license to issued patents and pending applications directed to the Company's library of Nitricil compounds, including patents issued in the U.S., Canada, Japan and Australia with claims intended to cover NVN1000, the new chemical entity ("NCE") for the Company's SB204, SB206 and SB208 product candidates. The UNC License Agreement requires the Company to pay UNC up to $425 in regulatory and commercial milestones on a licensed product by licensed product basis. Additionally, the Company is obligated to pay to UNC a running royalty percentage in the low single digits on net sales of licensed products. Unless earlier terminated, the UNC Agreement remains in effect on a country by country and licensed product by licensed product basis until the expiration of the last to expire issued patent covering such licensed product in the applicable country. The projected date of expiration of the last to expire of the patents issued under the UNC Agreement is 2033.

In connection with the UNC Agreement, the Company issued 115,865 shares of non-voting common stock to UNC and paid an upfront cash payment of $5 to UNC. During 2009, an additional 75,187 shares of non-voting common stock were issued to UNC in relation to the anti-dilution provision contained in the UNC Agreement. Upon

completion of the IPO in September 2016, all shares of UNC's non-voting common stock were converted to common stock.

See Note 14—Subsequent Events for discussion of contractual obligations associated with the UNC License Agreement that became effective subsequent to December 31, 2016.

Note 4: KNOW Bio Technology Agreement

In connection with the Distribution, the Company entered into exclusive license agreements and sublicense agreements with KNOW Bio, as described below. The agreements will continue for so long as there is a valid patent claim under the respective agreement, unless earlier terminated, and upon expiration, will continue as perpetual non-exclusive licenses. KNOW Bio has the right to terminate each such agreement, for any reason upon ninety days advance written notice to the Company.

License of existing and potential future intellectual property to KNOW Bio. The Company granted to KNOW Bio exclusive licenses, with the right to sublicense, to certain U.S. and foreign patents and patent applications controlled by the Company as of December 29, 2015. The Company also granted to KNOW Bio a non-exclusive license, with the right to sublicense, to any patents and patent applications that may become controlled by the Company during the three years immediately following the agreement's execution date related to nitric oxide-releasing compositions and methods of manufacturing thereof, including methods of manufacturing and other nitric oxide-based therapeutics.

Sublicense of UNC and other third party intellectual property to KNOW Bio. The Company also granted to KNOW Bio exclusive sublicenses, with the ability to further sublicense, under certain of the U.S. and foreign patents and patent applications exclusively licensed to the Company from UNC and another third party directed towards nitric oxide-releasing compositions, to develop and commercialize products utilizing the licensed technology. Under the exclusive sublicense to the UNC patents and applications, KNOW Bio is subject to the terms and conditions under the UNC License Agreement, including milestone and diligence payment obligations. There were no milestone or royalty payments required during the years ended December 31, 2016, 2015 and 2014.

Note 5: Property and Equipment, Net

Property and equipment consisted of the following:

	December 31,	
	2016	2015
Computer equipment	$ 500	$ 283
Furniture and fixtures	504	89
Laboratory equipment	5,723	2,995
Office equipment	106	36
Building related to facility lease obligation	10,557	—
Leasehold improvements	1,338	692
	18,728	4,095
Less: Accumulated depreciation and amortization	(2,438)	(1,751)
	$ 16,290	$ 2,344

Depreciation and amortization expense was $757, $631 and $462 for the years ended December 31, 2016, 2015 and 2014, respectively.

Note 6: Commitments and Contingencies

Lease Obligations

Operating Leases

The Company leases a facility under a non-cancelable operating lease with an expiration date of April 2017, following lease amendments made during the third and fourth quarters of 2016. Future minimum lease payments totaling $69 are due during the period of January to April 2017. This leased facility will contain a portion of the Company's research and development activities until April 2017. The Company has the option to extend the lease beyond April 2017 on a month-to-month basis.

Rent expense for operating leases totaled $525, $337 and $305 for the years ended December 31, 2016, 2015 and 2014, respectively.

Primary Facility Lease

In August 2015, the Company entered into a lease agreement for approximately 51,000 rentable square feet of facility space in Morrisville, North Carolina, commencing in April 2016. The initial term of the lease agreement extends through June 30, 2026. The Company has an option to extend the lease agreement by five years upon completion of the initial lease term. Current contractual base rent payments are $90 per month, subject to a three percent increase annually over the term of the lease agreement.

As a result of the nature of and the involvement in the renovations during the construction period of the leased space, the Company was the "deemed owner," for accounting purposes only, of the construction project and was required to capitalize the fair value of the building as well as the construction costs incurred by either the landlord or the Company on its consolidated balance sheet pursuant to FASB ASC 840, *Leases*, and the accounting policy described in Note 1—Organization and Significant Accounting Policies. The Company determined that the facility was substantially complete as of December 31, 2016 because the Company began to utilize the facility for all intended purposes, including primary research, development and drug compound manufacturing operations, in addition to administrative and corporate headquarters activities. Following the determination that the facility was substantially complete, the Company assessed the facility for sale-leaseback criteria qualification, which could result in a de-recognition of the building asset and the related financing obligation. The Company concluded that the facility did not meet the sale-leaseback criteria due to the Company's continuing involvement in the leased facility. As a result, the facility is being accounted for as an asset financing, with the building asset and related facility financing obligation remaining on the Company's balance sheet. The building asset will be depreciated over a 25 year period and the facility financing obligation will be amortized so that the net carrying value of the building asset and the facility financing obligation are equivalent at the end of the initial term of the lease agreement. Monthly rental payments will be allocated between principal and interest expense associated with the facility financing obligation, as well as grounds rent expense of $8 per month.

The Company has recorded an asset related to the building and construction costs within property and equipment of $10,557 as of December 31, 2016, which includes capitalized interest expense totaling $441. The non-current facility lease obligation on the Company's consolidated balance sheet is $7,998 as of December 31, 2016 and $0 as of December 31, 2015. During the year ended December 31, 2016, construction costs financed by the landlord totaled $8,157 and the Company made financing obligation principal payments to the landlord totaling $159.

Future minimum payments, including interest, required under the Company's primary facility lease agreement, accounted for as an asset financing, as of December 31, 2016 are as follows:

2017	$	1,103
2018		1,135
2019		1,170
2020		1,205
2021		1,241
Thereafter		6,062
Total minimum lease payments	$	11,916

Contingencies

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business activities. The Company accrues a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. The Company is not subject to any current pending legal matters or claims.

The Company has entered into, and expects to continue to enter into, contracts in the normal course of business with various third parties who support its clinical trials, preclinical research studies and other services related to its development activities. The scope of the services under these agreements can generally be modified at any time, and the agreement can be terminated by either party after a period of notice and receipt of written notice. There have been no contract terminations as of December 31, 2016.

Indemnification

In the ordinary course of business, the Company has entered into contractual arrangements under which it has agreed to provide indemnification of varying scope and terms to business partners and other parties with respect to certain matters, including, but not limited to, losses arising out of the Company's breach of such agreements and out of intellectual property infringement claims made by third parties. In these circumstances, payment may be conditional on the other party making a claim pursuant to the procedures specified in the particular contract.

The Company's obligations under these agreements may be limited in terms of time or amount, and in some instances, the Company may have recourse against third parties for certain payments. The terms of such obligations vary.

It is not possible to make a reasonable estimate of the maximum potential amount of future payments under these or similar agreements due to the conditional nature of the Company's obligations and the unique facts and circumstances involved in each particular agreement. No material indemnification liabilities were identified or accrued in the accompanying financial statements.

Other

See Note 14—Subsequent Events for discussion of additional contractual commitments the Company entered into subsequent to December 31, 2016.

Note 7: Convertible Debt

In February 2014, the Company entered into convertible note purchase agreements totaling $3,502 with various investors, including $2,836 with existing preferred stockholders and $300 with Board members. Principal and interest was due on the earlier of August 24, 2015 or the occurrence of a liquidating event. The notes accrued interest at 8% annually. In the event of a qualified financing, at the sole election of the Company, the entire principal balance and a minimum of one year of accrued interest converted into shares of Mezzanine A Preferred Stock at 90% of the per share price of the Mezzanine A Preferred Stock issued. In connection with the Mezzanine A

Preferred Stock issuance, a qualified financing, the Company elected in August 2014 to convert principal and interest totaling $3,782 into 306,484 shares of Mezzanine A Preferred Stock. The Company recognized $280 of interest expense related to the convertible notes during the year ended December 31, 2014. The Company recognized $420 in interest expense upon the conversion of the notes into shares of Mezzanine A Preferred Stock in 2014.

Note 8: Stockholders' Equity

Capital Structure

Authorized Shares. In conjunction with the completion of the IPO in September 2016, the Company amended its amended and restated certificate of incorporation and amended and restated bylaws. The amendment provides for 210,000,000 authorized shares of capital stock, of which 200,000,000 shares have been designated as $0.0001 par value common stock, and 10,000,000 shares have been designated as $0.0001 par value preferred stock.

Prior to the September 2016 amendment, the Company was authorized to issue 36,729,263 shares of capital stock, of which 22,000,000 shares were designated as $0.0001 par value common stock, 229,263 shares as $0.0001 par value non-voting common stock, and 14,500,000 shares of $0.0001 par value convertible preferred stock. The authorized shares of convertible preferred stock were designated as follows: 1,229,862 as Series 1 Convertible Preferred Stock ("Series 1"), 1,226,242 as Series 2 Convertible Preferred Stock ("Series 2"), 1,349,382 as Series 3 Convertible Preferred Stock ("Series 3"), 1,833,333 as Series 4 Preferred Stock ("Series 4"), 3,677,622 as Mezzanine A Convertible Preferred Stock ("Mezzanine A") and 5,000,000 as Mezzanine B Convertible Preferred Stock ("Mezzanine B").

Convertible Preferred Stock

The Company issued multiple series of convertible preferred stock between 2008 and 2015. In September 2016, in conjunction with the Company's IPO, all outstanding shares of convertible preferred stock automatically converted into an aggregate of 8,776,269 shares of common stock at their conversion prices. The significant features of the convertible preferred stock series in place immediately prior to the conversion to common shares are summarized in the subsection below.

Significant Features of Series 1, Series 2, Series 3, Series 4, Mezzanine A and Mezzanine B Convertible Preferred Stock

Voting. The holders of Series 1, Series 2, Series 3, Series 4, Mezzanine A and Mezzanine B were entitled to vote equally with the shares of common stock.

Dividends. Holders of preferred shares were entitled to dividends if and when declared by the Board of Directors. As of December 31, 2016, other than the Distribution (see Note 1—Organization and Significant Accounting Policies), no dividends had been declared.

Conversion. Each share of Series 1, Series 2, Series 3, Series 4, Mezzanine A and Mezzanine B were convertible at the option of the holder at any time after the date of issuance into such a number of common shares as is determined by dividing the original issue price by the conversion price in effect at the time of the conversion. The conversion prices were subject to adjustment for subdivisions, dividends, combinations, reclassifications, merger, sale, etc. As discussed in Note 1—Organization and Significant Accounting Policies, the Company's 1-for-1.2 reverse stock split of the Company's shares of common stock resulted in a proportional adjustment to the existing conversion ratio of each series of convertible preferred stock, effective September 7, 2016.

Automatic Conversion. Each share of Series 1, Series 2, Series 3, Series 4, Mezzanine A and Mezzanine B automatically converted into common stock at the then effective conversion prices for each series upon the completion of the IPO of the Company's common stock because gross proceeds from the IPO exceeded $40,000.

Consent Rights. Without consent of the holders of a majority of Series 1, Series 2, Series 3, Series 4, Mezzanine A and Mezzanine B shares, the Company could not take certain actions, including liquidation, dissolution, recapitalization or reorganization; increase or decrease the number of authorized shares of preferred or common stock; authorize or issue shares of capital stock with preferences or priorities over the existing shares of preferred stock; or effect any amendment to the certificate of incorporation or bylaws of the Company which would have had an adverse effect on the holders of Series 1, Series 2, Series 3, Series 4, Mezzanine A and Mezzanine B.

Liquidation Preference. Upon liquidation, dissolution, or winding up of the Company, holders of the Mezzanine B would have been entitled to receive, prior and in preference to any distribution of the assets to holders of Mezzanine A, Series 4, Series 3, Series 2, Series 1 or common stock, an amount equal to the greater of the original purchase price or the per share amount on an as converted basis. After such distribution to the holders of Mezzanine B, the holders of Mezzanine A would have been entitled to receive, prior and in preference to any distribution of the assets to holders of Series 4, Series 3, Series 2, Series 1 or common stock, an amount equal to the greater of the original purchase price or the per share amount on an as converted basis. After such distribution to the holders of Mezzanine A, the holders of the Series 4 would have been entitled to receive, prior and in preference to any distribution of the assets to holders of Series 3, Series 2, Series 1 or common stock, an amount equal to the greater of the original purchase price or the per share amount on an as converted basis. After such distribution to the holders of Series 4, the holders of Series 3 would have been entitled to receive, prior and in preference to any distribution of the assets to holders of Series 2, Series 1 or common stock, an amount equal to the greater of the original purchase price or the per share amount on an as converted basis. After such distribution to the holders of Series 3, the holders of Series 2 would have been entitled to receive, prior and in preference to any distribution of the assets to holders of Series 1 or common stock, an amount equal to the greater of the original purchase price or the per share amount on an as converted basis. After such distribution to the holders of Mezzanine B, Mezzanine A, Series 4, Series 3 and Series 2, the holders of Series 1 would have been entitled to receive, prior and in preference to any distribution of the assets to holders of common stock, an amount equal to the greater of the original purchase price or the per share amount on an as converted basis. Any assets remaining after such preferential distributions would be distributed to holders of common stock.

Anti-Dilution. Series 1, Series 2, Series 3, Series 4, Mezzanine A and Mezzanine B had a weighted average anti-dilution provision which protected against stock splits, stock dividends and recapitalizations. Prior to the IPO, in September 2016, the Company's Board of Directors and existing stockholders approved a waiver of the existing preferred stock holders' rights within the certificate of incorporation pertaining to (i) a notice requirement for the mandatory conversion of preferred stock to common stock in the IPO and (ii) the application of anti-dilution provisions with respect to issuance of common stock in the IPO.

Preferred Stock Warrants. In 2010 and 2011, in conjunction with the issuance of the Series 3 convertible preferred shares, the Company issued 149,931 warrants which were exercisable for an equal number of shares of Series 3 at a price of $6.00. The fair value of the warrants outstanding increased in 2014 resulting in a re-measurement loss in other expense of $641. During the year ended December 31, 2014, warrant holders exercised 114,946 warrants for an aggregate price of $550. Warrants exercised during 2014 include 23,322 warrants exercised through cashless exercise for 4,011 shares of Series 3. The liquidation value of Series 3 convertible preferred shares issued during 2014 was $478. In addition, 7,497 warrants expired unexercised. The Company recognized $58 of interest income during the year ended December 31, 2014 related to the expiration of these unexercised warrants. There were no warrants outstanding as of December 31, 2016, 2015 and 2014.

Related Party Stock Repurchase

In April 2016, the Company repurchased 9,500 shares of common stock for an aggregate price of $155 from an executive of the Company who is also a member of the Company's Board of Directors. The repurchase of these shares is recorded as treasury stock on the Company's consolidated balance sheet as of December 31, 2016.

Significant Features of Non-Voting Common Stock

Each share of non-voting common stock would have automatically been converted into one share of common stock, as adjusted for any dividends and stock-splits, upon the closing of a qualified public offering of the Company's common stock. As of December 31, 2016, other than the Distribution (see Note 1—Organization and Significant Accounting Policies), there were no previously declared dividends or stock-splits. As discussed in Note 1—Organization and Significant Accounting Policies, the Company's stockholders approved a 1-for-1.2 reverse stock split of the Company's shares of common stock, including all outstanding non-voting common stock, effective September 7, 2016. Subsequently, in conjunction with the Company's IPO, all outstanding shares of non-voting common stock were converted into an aggregate of 191,052 shares of common stock.

Preferred Stock

The Company's amended and restated certificate of incorporation provides the Company's Board of Directors with the authority to issue $0.0001 par value preferred stock from time to time in one or more series by adopting a resolution and filing a certificate of designations. Voting powers, designations, preferences, dividend rights, conversion rights and liquidation preferences shall be stated and expressed in such resolutions. There were 10,000,000 shares designated as preferred stock as of December 31, 2016 and zero shares designated as preferred stock as of December 31, 2015. There were no shares issued or outstanding as of December 31, 2016 and 2015.

Common Stock

Authorized, Issued and Outstanding Common Shares

The Company's common stock has a par value of $0.0001 per share and consists of 200,000,000 and 22,000,000 authorized shares as of December 31 2016 and 2015, respectively. There were 15,939,992 and 2,235,838 shares of voting common stock outstanding as of December 31, 2016 and 2015, respectively.

The Company has reserved shares of common stock for future issuance as follows:

	December 31,	
	2016	2015
Outstanding stock options	825,130	458,234
For possible future issuance under 2008 Stock Plan (Note 9)	—	405,893
For possible future issuance under 2016 Stock Plan (Note 9)	615,207	—
	1,440,337	864,127

Note 9: Stock Option Plan

2008 Stock Plan

During 2008, the Company adopted the 2008 Stock Plan (the "2008 Plan"). As amended, a total of 1,416,666 shares of common stock were reserved for issuance under the 2008 Plan. As of September 20, 2016, immediately prior to the IPO, 222,061 shares were available for future stock option grants. Eligible plan participants include employees, directors, and consultants. The 2008 Plan permitted the granting of incentive stock options, nonqualified stock options, and other stock-based awards. As further described below, as of September 20, 2016, no additional awards will be granted under the 2008 Plan.

2016 Stock Plan

Effective September 20, 2016 (the "Effective Date"), the Company adopted the 2016 Incentive Award Plan (the "2016 Plan"). The 2016 Plan is the successor to the 2008 Plan. As of the Effective Date, no additional awards will be granted under the 2008 Plan, but all stock awards granted under the 2008 Plan prior to the Effective Date will remain subject to the terms of the 2008 Plan. Any shares associated with stock awards previously granted under the 2008 Plan that are forfeited subsequent to the Effective Date of the 2016 Plan are not eligible for future issuance under the 2016 Plan. All awards granted on and after the Effective Date will be subject to the terms of the 2016

Plan. The 2016 Plan provides for the grant of the following awards: (i) incentive stock options, (ii) nonstatutory stock options, (iii) stock appreciation rights, (iv) restricted stock awards, (v) restricted stock unit awards and (vi) other stock awards. Eligible plan participants include employees, directors, and consultants. An aggregate of 833,333 shares of the Company's common stock were initially available for issuance under awards granted pursuant to the 2016 Plan, which shares may be authorized but unissued shares, treasury shares, or shares purchased in the open market.

Under both the 2008 Plan and the 2016 Plan, options to purchase the Company's common stock may be granted at a price no less than the fair value of a common stock share on the date of grant. The fair value shall be the closing sales price for a share as quoted on any established securities exchange for such grant date or the last preceding date for which such quotation exists. Vesting terms of options issued are determined by the board of directors or compensation committee of the board. The Company's stock options vest based on terms in the stock option agreements, generally at a rate of one-third for each anniversary of the vesting commencement date for three years. Stock options have a maximum term of ten years.

As of December 31, 2016, there were a total of 615,207 shares of common stock available for future issuance under the 2016 Plan.

Stock Compensation Expense

In December 2015, the Board of Directors approved the acceleration of each option holder's unvested options through the next annual anniversary of the grant's vesting commencement date provided that the option holder consents to the option acceleration in writing. As of December 31, 2015, 159,159 options were vested pursuant to this option acceleration and the Company recognized $1,312 of additional compensation expense.

During the years ended December 31, 2016, 2015 and 2014, the Company recorded employee share-based compensation expense from continuing operations of $1,573, $1,974 and $168, respectively. The Company recorded non-employee share-based compensation expense from continuing operations of $0 during the years ended December 31, 2016 and 2015, and $9 during the year ended December 31, 2014. Total share-based compensation expense included in the consolidated statements of operations is as follows:

	Year Ended December 31,		
	2016	2015	2014
Research and development	$ 477	$ 541	$ 98
General and administrative	1,096	1,433	79
Discontinued operations	—	410	—
	$ 1,573	$ 2,384	$ 177

The fair value of each option grant is estimated on the grant date using the Black-Scholes option-pricing model, using the following weighted average assumptions:

	Year Ended December 31,		
	2016	2015	2014
Estimated dividend yield	0.00%	0.00%	0.00%
Expected volatility	75.08%	65.96-102.77%	102.77%
Risk-free interest rate	1.32%	1.48-1.81%	1.88%
Expected life of options (in years)	5.72	5.1-5.9	6.00
Weighted-average fair value per share	$ 11.47	$ 6.83	$ 6.59 - 7.06

Stock option activity for the periods indicated is as follows:

	Shares Available for Grant	Shares Subject to Outstanding Options	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Options outstanding as of December 31, 2013	79,722	209,527	$ 0.63		
Additional shares reserved under plan	416,666	—			
Options granted	(211,500)	211,500	1.12		
Options forfeited	17,083	(17,083)	0.71		
Options exercised	—	(67,431)	0.70		
Options outstanding as of December 31, 2014	301,971	336,513	$ 0.91		
Additional shares reserved under plan	416,666	—			
Options granted	(366,909)	366,909	8.80		
Options forfeited	54,165	(54,165)	3.70		
Options exercised	—	(191,023)	2.45		
Options outstanding as of December 31, 2015	405,893	458,234	$ 6.26		
Additional shares reserved under plan	611,272	—			
Options granted	(405,624)	405,624	16.06		
Options forfeited	3,666	(7,395)	6.62		
Options exercised	—	(31,333)	1.11		
Options outstanding as of December 31, 2016	615,207	825,130	$ 11.27	8.54	$ 12,994
Vested and expected to vest as of December 31, 2014		279,505	$ 0.88	8.39	$ 1,996
Exercisable as of December 31, 2014		92,833	$ 0.54	6.44	$ 694
Vested and expected to vest as of December 31, 2015		430,730	$ 6.16	8.80	$ 5,102
Exercisable as of December 31, 2015		232,827	$ 4.27	8.38	$ 3,196
Vested and expected to vest as of December 31, 2016		766,402	$ 10.95	8.49	$ 12,314
Exercisable as of December 31, 2016		303,162	$ 7.32	7.53	$ 5,974

The total intrinsic value of options exercised during the years ended December 31, 2016, 2015 and 2014 was $543, $1,655 and $513, respectively.

As of December 31, 2016, there was $4,896 of total unrecognized compensation expense related to non-vested share based compensation arrangements, which is expected to be recognized over a weighted average period of 1.99 years. As of December 31, 2015, there was $1,649 of total unrecognized compensation expense related to non-vested share based compensation arrangements, which is expected to be recognized over a weighted average period of 2.3 years.

Note 10: Income Taxes

There was no income tax benefit recognized for the years ended December 31, 2016, 2015 and 2014 due to the Company's history of net losses combined with an inability to confirm recovery of the tax benefits from the Company's losses and other net deferred tax assets. The Company has established a valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets. The reasons for the difference between actual income tax benefit for the years ended December 31, 2016, 2015 and 2014, and the amount computed by applying the statutory federal income tax rate to losses before income tax benefit are as follows:

	Year Ended December 31,		
	2016	2015	2014
Income tax benefit at federal statutory rate	$ (20,298)	$ (9,540)	$ (3,872)
State income taxes, net of federal benefit	(1,204)	(741)	(376)
Non-deductible expenses	229	608	547
Distribution of intellectual property rights	—	657	—
Research and development tax credits	(1,692)	(767)	(478)
Other	(124)	283	(17)
Change in valuation allowance	23,089	9,500	4,196
Total income tax provision	$ —	$ —	$ —

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets and deferred tax liabilities are as follows:

	As of December 31,	
	2016	2015
Deferred tax assets:		
Deferred rent	$ —	$ 9
Accrued compensation	618	16
Accrued liabilities	700	83
Tax loss carryforwards	37,857	17,692
Intangible assets	361	351
Share-based compensation	412	304
Tax credits	3,930	2,237
Facility financing lease obligation	2,881	—
Other	120	53
Total deferred tax assets	46,879	20,745
Less valuation allowance	(43,800)	(20,711)
Net deferred tax asset	3,079	34
Deferred tax liabilities:		
Fixed assets	(3,079)	(34)
Net noncurrent deferred tax asset (liability)	$ —	$ —

As of December 31, 2016, the Company had federal and state net operating loss carryforwards of $105,051 and $106,671, respectively. The net operating loss carryforwards begin to expire in 2028 and 2023 for federal and state tax purposes, respectively. As of December 31, 2016, the Company had charitable contribution carryforwards of approximately $98 available to offset future federal taxable income which will begin to expire in 2017. As of December 31, 2016, the Company had government research and development tax credits of approximately $3,930 to offset future federal taxes which begin to expire in 2028.

The Company had no unrecognized tax benefits as of December 31, 2016 and 2015. The Company does not anticipate a significant change in total unrecognized tax benefits within the next 12 months.

The Tax Reform Act of 1986 contains provisions which limit the ability to utilize the net operating loss carryforwards in the case of certain events including significant changes in ownership interests. If the Company's net operating loss carryforwards are limited, and the Company has taxable income which exceeds the permissible yearly net operating loss carryforwards, the Company would incur a federal income tax liability even though net operating loss carryforwards would be available in future years.

Note 11: Retirement Plan

The Company maintains a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers all employees who meet minimum age requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. The Company makes a discretionary matching contribution, up to 3% of gross wages during 2016 and up to 2% of gross wages during 2015 and 2014. The Company contributed $170, $100 and $60, for the years ended December 31, 2016, 2015 and 2014, respectively.

Note 12: Related Party Transactions

During the years ended December 31, 2015 and 2014, the Company paid a former director $88 and $25, respectively, in conjunction with a research and development consulting agreement. No such payments were made during the year ended December 31, 2016. These costs were expensed as incurred and are classified as research and development expenses in the consolidated statements of operations.

Board members held 2,486,656 and 2,468,015 shares of convertible preferred stock as of December 31, 2015 and 2014, respectively. As discussed in Note 1—Organization and Significant Accounting Policies, all convertible preferred stock was converted into common stock in conjunction with the IPO in September 2016. As a result, Board members held zero preferred shares as of December 31, 2016. Board members held 1,561,916, 1,761,416 and 1,756,666 shares of the Company's common stock as of December 31, 2016, 2015 and 2014, respectively. See Note 7—Stockholders' Equity regarding a repurchase of common stock from a related party officer and director of the Company.

Note 13: Quarterly Results of Operations (Unaudited)

The following table contains quarterly financial information for 2016 and 2015. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	Three Months Ended (unaudited)			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
Total operating expenses	$ 11,272	$ 17,935	$ 17,481	$ 13,138
Operating loss	(11,272)	(17,935)	(17,481)	(13,138)
Other income, net	12	31	7	77
Loss from continuing operations	(11,260)	(17,904)	(17,474)	(13,061)
Loss from discontinued operations	—	—	—	—
Net loss and comprehensive loss	$ (11,260)	$ (17,904)	$ (17,474)	$ (13,061)
Loss per share, basic and diluted:				
Continuing operations	$ (4.60)	$ (7.31)	$ (5.76)	$ (0.82)
Discontinued operations	—	—	—	—
Net loss per share, basic and diluted	$ (4.60)	$ (7.31)	$ (5.76)	$ (0.82)
Weighted-average common shares outstanding, basic and diluted	2,445,351	2,448,747	3,033,967	15,938,941

	March 31, 2015	June 30, 2015	September 30, 2015	December 31, 2015
Total operating expenses	$ 5,349	$ 4,758	$ 5,626	$ 10,101
Operating loss	(5,349)	(4,758)	(5,626)	(10,101)
Other income, net	—	—	30	18
Loss from continuing operations	(5,349)	(4,758)	(5,596)	(10,083)
Loss from discontinued operations	(362)	(349)	(480)	(1,083)
Net loss and comprehensive loss	$ (5,711)	$ (5,107)	$ (6,076)	$ (11,166)
Loss per share, basic and diluted:				
Continuing operations	$ (2.39)	$ (2.11)	$ (2.45)	$ (4.37)
Discontinued operations	(0.16)	(0.16)	(0.21)	(0.47)
Net loss per share, basic and diluted	$ (2.55)	$ (2.27)	$ (2.66)	$ (4.84)
Weighted-average common shares outstanding, basic and diluted	2,238,471	2,249,666	2,281,001	2,306,476

Note 14: Subsequent Events

Licensing Arrangement

On January 12, 2017, the Company entered into a license agreement, and related amendment, with Sato Pharmaceutical Co., Ltd., or Sato, relating to SB204, its lead drug candidate for the treatment of acne vulgaris in Japan (the "Agreement"). Pursuant to the Agreement, the Company granted to Sato an exclusive, royalty-bearing, non-transferable license under certain of the Company's intellectual property rights, with the right to sublicense with the Company's prior written consent, to develop, use and sell products in Japan that incorporate SB204 in certain topical dosage forms for the treatment of acne vulgaris, and to make the finished form of such products. The rights granted to Sato do not include the right to manufacture the active pharmaceutical ingredient of SB204, which the Company will retain the rights to supply to Sato. The Company will also supply finished product to Sato for use in the development of SB204 in the licensed territory. During a specified time period, Sato has an exclusive option to negotiate the terms under which its license would be expanded to include certain additional territories within Asia, subject to Sato's payment of a specified option exercise fee. Under the terms of the Agreement, the Company also has exclusive rights to certain intellectual property that may be developed by Sato in the future, which the Company could choose to use for its own development and commercialization of SB204 outside of Japan.

In exchange for the licenses granted to Sato under the Agreement, Sato agreed to pay the Company an upfront payment, as well as additional milestone payments upon achievement of various future development, regulatory and commercial milestones. Pursuant to the terms of the Agreement, Sato is required to pay the Company an upfront payment of 1.25 billion Japanese Yen ("JPY"), and up to an aggregate of 2.75 billion JPY upon the achievement of various development and regulatory milestones. Under the Agreement, Sato also agreed to pay the Company up to an aggregate of 0.9 billion JPY in milestone payments upon the achievement of various commercial milestones. Sato must also pay the Company a royalty equal to a mid-single digit percentage of net sales of licensed products in the licensed territory, subject to a reduction in the royalty payments in certain circumstances.

The term of the Agreement and the period during which Sato must pay royalties under the Agreement expires, on a licensed product-by-licensed product basis, on the tenth anniversary of the first commercial sale of a licensed product in the licensed field in the licensed territory. The term of the Agreement may be renewed by mutual written agreement of the parties for additional two year periods following expiration of the initial term.

The Company is obligated pursuant to the Agreement to supply Sato with all quantities of licensed products required by Sato to develop the licensed products in the licensed field in the licensed territory. As part of the Agreement, the Company and Sato have also agreed to negotiate a commercial supply agreement pursuant to which the Company would be the exclusive supplier to Sato of the active pharmaceutical ingredient of licensed products for the manufacture of licensed products in the licensed territory.

Sato is responsible for funding the development and commercial costs for the program that are specific to Japan. The Company is obligated to perform certain oversight, review and supporting activities for Sato, including: (i) using commercially reasonable efforts to obtain marketing approval of SB204 in the U.S, (ii) sharing all future scientific information the Company may obtain during the term of the Agreement pertaining to SB204, (iii) performing certain additional pre-clinical studies if such studies are deemed necessary by the Japanese regulatory authority, up to and not to exceed a total cost of $1,000 and (iv) participating in a joint committee that oversees, reviews and approves Sato's development and commercialization activities under the Agreement. Additionally, the Company has granted Sato the option to use the Company's trademarks in connection with the commercialization of licensed products in the licensed territory for no additional consideration, subject to the Company's approval of such use.

On January 19, 2017, the Company received the upfront payment, which was equivalent to $10,813.

The Agreement may be terminated (i) by Sato without cause upon 120 days' advance written notice to the Company; (ii) by either party in the event of the other party's uncured material breach upon 60 days' advance written notice; (iii) force majeure; (iv) by either party in the event of the other party's dissolution, liquidation, bankruptcy or insolvency and (v) by the Company immediately upon written notice if Sato challenges the validity, patentability, or enforceability of any of the Company's patents or patent applications licensed to Sato under the Agreement.

The intellectual property rights granted to Sato under the Agreement include certain intellectual property rights which we have licensed from UNC. Under the Company's license agreement with UNC (Note 3), the Company is obligated to pay UNC a running royalty percentage in the low single digits on net sales of licensed products, including net sales that may be generated by Sato. Additionally, the Company made a payment to UNC in February 2017 representing the portion of the Sato upfront payment that was estimated to be directly attributable to the UNC intellectual property rights included in the license to Sato.

The Company also entered into an agreement with a third party to assist the Company in exploring the licensing opportunity which led to the execution of the Agreement with Sato. The Company paid a fee of $216 to the third party upon execution of the Agreement and is obligated to pay the third party a low-single-digit percentage of any future milestone payments the Company may receive from Sato under the Agreement.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Disclosure Controls and Procedures.

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934 is (i) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (ii) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of December 31, 2016, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934). Our 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. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of December 31, 2016, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting.

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies. We are an "emerging growth company" as defined in the JOBS Act. Commencing with the Annual Report on Form 10-K for our fiscal year ending December 31, 2017, we will include a report of management's assessment regarding internal control over financial reporting. For as long as we remain an "emerging growth company," we are exempt from the auditor attestation requirement in the assessment of the effectiveness of our internal control over financial reporting through the end of the fiscal year following the fifth anniversary of our IPO.

Changes in Internal Control over Financial Reporting

There were no changes in the Company's internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act) during the last quarter that have materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is incorporated herein by reference from our Proxy Statement, which will be filed with the SEC within 120 days after the end of our 2016 fiscal year pursuant to Regulation 14A for our 2017 Annual Meeting of Stockholders (the "Proxy Statement"), under the captions "Executive Officers of the Company," "Proposal 1—Election of Directors," "Section 16 Beneficial Ownership Reporting Compliance."

We have adopted a code of business conduct and ethics that applies to our directors, officers (including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions) and other employees. A copy of our Code of Business Conduct and Ethics is available on our website at www.novan.com under "Investors & Media—Corporate Governance." We intend to post on our website and (if required) file on Form 8-K all disclosures that are required by applicable law, the rules of the SEC, or the Nasdaq listing standards, concerning any amendment to, or waiver from, our Code of Business Conduct and Ethics.

Item 11. Executive Compensation.

The information required by this item is incorporated herein by reference from the Proxy Statement under the captions "Executive Compensation and Related Information."

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item is incorporated herein by reference from the Proxy Statement, under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information."

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item is incorporated herein by reference from the Proxy Statement, under the captions "Corporate Governance" and "Certain Relationships and Related Party Transactions."

Item 14. Principal Accounting Fees and Services.

The information required by this item will be set forth in our Proxy Statement under the caption "Principal Accountant Fees and Services."

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following financial statements are included in this Annual Report on Form 10-K:

(1) List of Financial Statements:

The financial statements required by this item are listed in Item 8, "Financial Statements and Supplementary Data" herein.

(2) List of Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or notes thereto.

(3) List of Exhibits.

The exhibits in the accompanying Exhibit Index following the signature page are filed or furnished as a part of this report and are incorporated herein by reference.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Novan, Inc.

Date: March 20, 2017

By: /s/ Nathan Stasko
Nathan Stasko
Chief Executive Officer
(Principal Executive Officer)

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

Name	Title	Date
/s/ Nathan Stasko Nathan Stasko	Chief Executive Officer and Director (Principal Executive Officer)	March 20, 2017
/s/ Richard Peterson **Richard Peterson**	Chief Financial Officer (Principal Financial and Accounting Officer)	March 20, 2017
/s/ Robert A. Ingram **Robert A. Ingram**	Chairman of the Board	March 20, 2017
/s/ W. Kent Geer **W. Kent Geer**	Director	March 20, 2017
/s/ Robert J. Keegan **Robert J. Keegan**	Director	March 20, 2017
/s/ G. Kelly Martin **G. Kelly Martin**	Director	March 20, 2017
/s/ Sean Murphy **Sean Murphy**	Director	March 20, 2017
/s/ John Palmour **John Palmour**	Director	March 20, 2017

EXHIBIT INDEX

EXHIBIT NO.		DESCRIPTION	FILED HEREWITH	INCORPORATED BY REFERENCE			
				FORM	FILE NO.	EXHIBIT	FILING DATE
3.1		Restated Certificate of Incorporation of Novan, Inc., effective September 26, 2016.		8-K	001-37880	3.1	September 27, 2016
3.2		Amended and Restated Bylaws of Novan, Inc., effective September 26, 2016.		8-K	001-37880	3.2	September 27, 2016
10.1	#	Form of Director and Executive Officer Indemnification Agreement.		S-1	333-213276	10.1	August 24, 2016
10.2	#	2008 Stock Plan, as amended, and form of option agreements thereunder.		S-1	333-213276	10.2	August 24, 2016
10.3	#	2016 Incentive Award Plan.		S-1	333-213276	10.3	August 24, 2016
10.4	#	Senior Executive Annual Incentive Plan.	X				
10.5	#	Form of Award Agreement Awarding Non-Qualified Stock Options to Employees under the Novan, Inc. 2016 Incentive Award Plan.		10-Q	001-37880	10.1	November 14, 2016
10.6	#	Form of Award Agreement Awarding Incentive Stock Options to Employees under the Novan, Inc. 2016 Incentive Award Plan.		10-Q	001-37880	10.2	November 14, 2016
10.7	#	Form of Award Agreement Awarding Non-Qualified Stock Options to Non-Employee Directors under the Novan, Inc. 2016 Incentive Award Plan.		10-Q	001-37880	10.3	November 14, 2016
10.8	#	Amended and Restated Employment Agreement, dated April 13, 2016, by and between Novan, Inc. and Nathan Stasko.		S-1	333-213276	10.4	August 24, 2016
10.9	#	Employment Agreement, dated April 13, 2016, by and between Novan, Inc. and Richard Peterson.		S-1	333-213276	10.5	August 24, 2016
10.10	#	Employment Agreement, dated April 13, 2016, by and between Novan, Inc. and Brian Johnson.		S-1	333-213276	10.6	August 24, 2016
10.11	#	Employment Agreement, dated August 25, 2016, by and between Novan, Inc. and M. Joyce Rico.	X				

EXHIBIT NO.		DESCRIPTION	FILED HEREWITH	INCORPORATED BY REFERENCE			
				FORM	FILE NO.	EXHIBIT	FILING DATE
10.12	#	Non-employee Director Compensation Policy	X				
10.13	†	Amended, Restated and Consolidated License Agreement between The University of North Carolina and Novan, Inc., dated as of June 27, 2012, and as amended on November 30, 2012.		S-1/A	333-213276	10,7	September 8, 2016
10.14	†	Second Amendment, dated April 12, 2016, to the Amended, Restated and Consolidated License Agreement between The University of North Carolina and Novan, Inc., dated as of June 27, 2012.		10-Q	001-37880	10.4	November 14, 2016
10.15	†	UNC Sublicense Agreement, dated December 29, 2015, by and between Novan, Inc. and KNOW Bio, LLC.		S-1	333-213276	10.8	August 24, 2016
10.16	†	Novan Patent and Know-How License Agreement, dated December 29, 2015, by and between Novan, Inc. and KNOW Bio, LLC.		S-1	333-213276	10.9	August 24, 2016
10.17	†	License Agreement, dated January 12, 2017, by and between Novan, Inc. and Sato Pharmaceutical Co. Ltd.	X				
10.18	†	First Amendment, dated January 12, 2017 to the License Agreement, dated January 12, 2017, by and between Novan, Inc. and Sato Pharmaceutical Co. Ltd.	X				
10.19		Lease, dated as of December 21st, 2010, by and between Novan, Inc. and Crown Royal Associates, LLC, as amended on August 27, 2013 and August 27, 2015.		S-1	333-213276	10.10	August 24, 2016
10. 20		Third Amendment, dated as of July 5, 2016, to the Lease, dated as of December 21, 2010, by and between Novan, Inc. and Durham Royal Center, LLC.		10-Q	001-37880	10.5	November 14, 2016
10.21		Fourth Amendment, dated as of September 28, 2016, to the Lease, dated as of December 21, 2010, by and between Novan, Inc. and Durham Royal Center, LLC.		10-Q	001-37880	10.6	November 14, 2016

EXHIBIT NO.	DESCRIPTION	FILED HEREWITH	INCORPORATED BY REFERENCE			
			FORM	FILE NO.	EXHIBIT	FILING DATE
10.22	Lease, dated as of August 17, 2015, by and between Novan, Inc. and Durham Hopson Road, LLC, as amended on January 6, 2015.		S-1	333-213276	10.11	August 24, 2016
10.23	Second Amendment, dated as of September 12, 2016, to the Lease, dated as of August 17, 2015, by and between Novan, Inc. and Durham Hopson Road, LLC.		10-Q	001-37880	10.7	November 14, 2016
10.24	Stock Sale and Purchase Agreement, dated April 13, 2016, by and between Novan, Inc. and Stasko Living Trust.		S-1	333-213276	10.12	August 24, 2016
23.1	Consent of PricewaterhouseCoopers LLP.	X				
31.1	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X				
31.2	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X				
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.	X				
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X				
101.INS	XBRL Instance Document.	X				
101.SCH	XBRL Taxonomy Extension Schema Document.	X				
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.	X				
101.DEF	XBRL Taxonomy Extension Definition Document.	X				

EXHIBIT NO.	DESCRIPTION	FILED HEREWITH	INCORPORATED BY REFERENCE			
			FORM	FILE NO.	EXHIBIT	FILING DATE
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.	X				
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.	X				

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment pursuant to Rule 24b-2 under the Securities Exchange Act of 1934.

# Indicates management contract or compensatory plan.

NOVAN, INC.
SENIOR EXECUTIVE INCENTIVE BONUS PLAN

1. Purpose

This Senior Executive Incentive Bonus Plan (the "Bonus Plan") is intended to provide an incentive for superior work and to motivate eligible executives of Novan, Inc. (the "Company") and its subsidiaries toward even higher achievement and business results, to tie their goals and interests to those of the Company and its stockholders and to enable the Company to attract and retain highly qualified executives. The Bonus Plan is for the benefit of Covered Employees (as defined below).

2. Administration

The Compensation Committee of the Board of Directors of the Company (the "Compensation Committee") shall have the sole discretion and authority to administer and interpret the Bonus Plan.

3. Eligibility and Participation

The Compensation Committee shall select the persons eligible to participate in the Bonus Plan, which may include, without limitation, the executives of the Company and its subsidiaries who are or, as determined in the sole discretion of the Compensation Committee, may become "covered employees" (as defined in Section 162(m) of the Internal Revenue Code of 1986, as amended (the "Code")) of the Company and its subsidiaries for the applicable taxable year of the Company (such selected persons, the "Covered Employees").

4. Bonus Determinations

(a) A Covered Employee may receive a bonus payment under the Bonus Plan based upon the attainment of performance objectives which are established by the Compensation Committee and relate to financial, operational or other metrics with respect to the Company or any of its subsidiaries (the "Performance Goals"), including but not limited to: (i) net earnings or losses (either before or after one or more of the following: (A) interest, (B) taxes, (C) depreciation, (D) amortization and (E) non-cash equity-based compensation expense); (ii) gross or net sales or revenue or sales or revenue growth; (iii) net income (either before or after taxes); (iv) adjusted net income; (v) operating earnings or profit (either before or after taxes); (vi) cash flow (including, but not limited to, operating cash flow and free cash flow); (vii) return on assets or net assets; (viii) return on capital (or invested capital) and cost of capital; (ix) return on stockholders' equity; (x) total stockholder return; (xi) return on sales; (xii) gross or net profit or operating margin; (xiii) costs, reductions in costs and cost control measures; (xiv) funds from operations or funds available for distributions; (xv) expenses; (xvi) working capital; (xvii) earnings or loss per share; (xviii) adjusted earnings or loss per share; (xix) price per share or dividends per share (or appreciation in and/or maintenance of such price or dividends); (xx) economic value added models or similar metrics; (xxi) regulatory achievements or compliance (including, without limitation, regulatory

body approval for commercialization of a product); (xxii) implementation, completion or attainment of critical projects, processes or objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; (xxiii) sales, unit volume or market share; (xxiv) licensing revenue; (xxv) brand recognition/acceptance, (xxvi) inventory turns or cycle time, (xxvii) strategic initiatives (including, without limitation, with respect to market penetration and spending efficiency, geographic business expansion, manufacturing, commercialization, production and productivity, customer satisfaction and growth, employee satisfaction, recruitment and maintenance of personnel, human resources management, supervision of litigation and other legal matters, information technology, strategic partnerships and transactions (including acquisitions, dispositions, joint ventures, in-licensing and out-licensing of intellectual property, and establishment of relationships with commercial entities with respect to the marketing, distribution and sale of Company products, and factoring transactions, research and development and related activity, financial or other capital raising transactions, operating efficiency, and asset quality); (xxiii) financial ratios (including, without limitation, those measuring liquidity, activity, profitability or leverage); and (xxix) compound annual growth rate, any of which may be measured either in absolute terms or as compared to any incremental increase or decrease or as compared to results of a peer group or to market performance indicators or indices.

(b) Except as otherwise set forth in this Section 4(b): (i) any bonuses paid to Covered Employees under the Bonus Plan shall be based upon objectively determinable bonus formulas that tie such bonuses to one or more performance objectives relating to the Performance Goals; (ii) bonus formulas for Covered Employees shall be adopted in each performance period by the Compensation Committee (generally, for performance periods of one year or more, no later than 90 days after the commencement of the performance period to which the Performance Goals relate); and (iii) no bonuses shall be paid to Covered Employees unless and until the Compensation Committee makes a certification with respect to the attainment of the performance objectives. Notwithstanding the foregoing, the Company may pay bonuses (including, without limitation, discretionary bonuses) to Covered Employees under the Bonus Plan based upon such other terms and conditions as the Compensation Committee may in its sole discretion determine.

(c) The payment of a bonus to a Covered Employee with respect to a performance period shall be conditioned upon the Covered Employee's employment by the Company on the last day of the performance period; provided, however, that the Compensation Committee may make exceptions to this requirement, in its sole discretion, including, without limitation, in the case of a Covered Employee's termination of employment, retirement, death or disability.

5. Forfeiture and Claw-Back Provisions

The Compensation Committee may provide that any bonuses paid under the Bonus Plan shall be subject to the provisions of any claw-back policy implemented by the Company, including, without limitation, any claw-back policy adopted to comply with the requirements of the Dodd- Frank Wall Street Reform and Consumer Protection Act and any rules, regulations or interpretations thereunder, to the extent set forth in such claw-back policy.

6. Other Provisions

(a) Neither the establishment of the Bonus Plan nor the selection of any individual as a Covered Employee shall give any individual any right to be retained in the employ of the Company or any subsidiary thereof, or any right whatsoever under the Bonus Plan other than to receive bonus payments awarded by the Compensation Committee.

(b) No member of the Board of Directors of the Company or the Compensation Committee shall be liable to any individual in respect of the Bonus Plan for any act or omission of such member, any other member, or any officer, agent or employee of the Company or any of its subsidiaries.

(c) The Company and its subsidiaries shall be entitled to withhold such amounts as may be required by federal, state or local law from all bonus payments under the Bonus Plan.

(d) To the extent not preempted by federal law, the Bonus Plan shall be governed and construed in accordance with the internal laws of the State of Delaware, without regard to the principles of conflicts of law thereof or any other jurisdiction.

(e) The Bonus Plan is intended to meet the requirements of Section 409A of the Code and will be interpreted and construed in accordance with Section 409A of the Code and Department of Treasury Regulations and other interpretive guidance issued thereunder, including without limitation any such regulations or other guidance that may be issued after the Effective Date. Each bonus payable pursuant to the Bonus Plan shall be intended to comply with, or be exempt from, the requirements of Section 409A of the Code such that the bonus will not be subject to any penalty tax imposed under Section 409A of the Code and, unless otherwise determined by the Compensation Committee, each bonus under the Bonus Plan shall be paid subject to the applicable Covered Employee's continued employment through the date of payment of such bonus. Notwithstanding any provision of the Bonus Plan to the contrary, in the event that following the Effective Date the Company determines that any provision of the Bonus Plan could otherwise cause any person to be subject to the penalty taxes imposed under Section 409A of the Code, the Company may adopt such amendments to the Bonus Plan or adopt other policies and procedures (including amendments, policies and procedures with retroactive effect), or take any other actions, that the Company determines are necessary or appropriate to comply with the requirements of Section 409A of the Code and related Department of Treasury guidance and thereby avoid the application of any penalty taxes under Section 409A of the Code. Notwithstanding anything herein to the contrary, in no event shall any liability for failure to comply with the requirements of Section 409A of the Code be transferred from a Covered Employee or any other person to the Company or any of its affiliates, employees or agents pursuant to the terms of the Bonus Plan or otherwise.

7. Amendment and Termination

The Board of Directors of the Company reserves the right to amend or terminate the Bonus Plan at any time in its sole discretion. Any amendments to the Bonus Plan shall require stockholder approval only to the extent required by any applicable law, rule or regulation.

8. Stockholder Approval

No bonuses shall be paid under the Bonus Plan unless and until the Company's stockholders shall have approved the Bonus Plan. The Bonus Plan will be submitted for the approval of the Company's stockholders after the initial adoption of the Bonus Plan by the Board of Directors of the Company.

9. Term of Bonus Plan

The Bonus Plan shall become effective as of the day immediately prior to the first date upon which common stock of the Company is listed (or approved for listing) upon notice of issuance on any securities exchange or designated (or approved for designation) upon notice of issuance as a national market security on an interdealer quotation system (the "Effective Date"). The Bonus Plan shall expire on the earliest to occur of: (a) the first material modification of the Bonus Plan (as defined in Treasury Regulation Section 1.162-27(h)(1)(iii)); (b) the first meeting of the Company's stockholders at which members of the Board of Directors of the Company are to be elected that occurs after the close of the third calendar year following the calendar year in which occurred the first registration of an equity security of the Company under Section 12 of the Securities Exchange Act of 1934, as amended; or (c) such other date, if any, on which the "reliance period" described under Treasury Regulation 1.162-27(f)(2) expires pursuant to the terms of Section 162(m) of the Code, and the rules, regulations and interpretations thereunder. The Bonus Plan is intended to be subject to the relief set forth in Treasury Regulation Section 1.162-27(f)(1) and shall be interpreted accordingly.

* * * * *

I hereby certify that the Bonus Plan was duly authorized, approved and adopted by the Board of Directors of Novan, Inc. as of April 13, 2016, effective as of the Effective Date.

I hereby certify that the Bonus Plan was approved by the stockholders of Novan, Inc. as of September 6, 2016.

/s/ Jeff N. Hunter
Jeff N. Hunter

Corporate Secretary

EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is entered into as of August 25, 2016 (the "Effective Date") by and between Novan, Inc., a Delaware corporation with its principal place of business in Durham County, North Carolina (the "Company"), and M. Joyce Rico, a citizen and resident of Orange County, North Carolina ("Employee").

WITNESSETH:

WHEREAS, Employee commenced employment with the Company on August 7, 2012;

WHEREAS, the Company wishes to continue to employ Employee, and Employee desires to accept such continued employment with the Company, on the terms described herein; and

WHEREAS, effective as of the Effective Date, the parties desire to enter into this Agreement which shall supersede the offer letter dated July 18, 2012 ("Offer Letter") in its entirety.

NOW, THEREFORE, in consideration of the foregoing, the mutual promises herein contained, and other good and valuable consideration, including the employment of Employee by the Company and the compensation received by Employee from the Company from time to time, the receipt and sufficiency of which are hereby acknowledged, the parties hereto, intending to be legally bound, hereby agree as follows.

1. EMPLOYMENT. The Company hereby agrees to continue to employ Employee, and Employee hereby accepts such continued employment. Employee shall serve as the Company's Chief Medical Officer, reporting to the Chief Executive Officer (the "CEO"), upon the terms and conditions hereinafter set forth. The initial term of employment under this Agreement (the "Initial Term") shall be for the period beginning on the Effective Date and ending on the third (3rd) anniversary thereof, unless earlier terminated as provided in Section 4. This Agreement shall automatically be extended for successive one-year periods (each, an "Extension Term" and, collectively with the Initial Term, the "Term") unless either party gives notice of non-extension to the other no later than 90 days prior to the expiration of the then-applicable Term.

2. DUTIES; EXCLUSIVE SERVICE.

(a) During the Term, Employee shall faithfully discharge her responsibilities and perform all duties reasonably prescribed to her by the CEO consistent with her position, as well as any duties as are set forth in the Bylaws of the Company related to Employee's position. In addition, Employee expressly agrees that her services include but are not limited to attendance at scheduled meetings of the Company's Board of Directors (the "Board"), if and as requested by the CEO or the Board, and all other normal duties associated with the responsibilities of a Chief Medical Officer. Employee agrees to comply with all Company policies, standards and regulations now existing or hereafter promulgated of which she is aware. Employee further agrees to devote all of her working time and attention to the performance of her duties and responsibilities on behalf of the Company and in furtherance of its best interests. Notwithstanding the foregoing, Employee may serve on boards or advisory committees of non-profit or charitable organizations or, with the prior written consent of the CEO, boards or advisory committees of for-profit organizations or companies, in each case, so long as such service and obligations do not interfere with Employee's duties at the Company. Employee agrees to immediately resign from the board of any company that engages in any business that competes with or represents a conflict with the business of the Company as determined in the sole discretion of the Board.

3. COMPENSATION. Employee's compensation shall be paid as follows:

(a) Base Salary. During the Term, Employee shall receive as compensation a base salary at an annual rate of Three Hundred Fifty Thousand and Four Hundred Dollars ($350,400.00) (the "Base Salary"), less any federal, state and local payroll taxes and other withholdings legally required or properly requested by Employee. The Base Salary shall be payable semi-monthly in accordance with the Company's regular payroll practices and procedures. Employee's Base Salary shall be subject to annual review by the CEO. All full-time employees may be eligible for additional compensation based on performance and may receive additional stock option grants as approved by the Board in its sole discretion.

(b) Long-Term and Equity Incentive Compensation. During the Term, Employee shall be eligible to participate, at such level and on such terms as shall be approved by the Board in its sole discretion, in the Novan, Inc. 2016 Incentive Award Plan and such other long-term and/or equity-based incentive compensation plans or programs as may be approved by the Board from time to time.

(c) Annual Bonus. For calendar year 2016 and each subsequent calendar year that ends during the Term, Employee will be eligible to receive an annual performance-based cash bonus, upon achievement of the annual bonus objectives established by the President/CEO and/or Board of Directors or Compensation Committee thereof (the "Annual Bonus"), pursuant to the Company's Executive Annual Incentive Plan or another bonus plan established by the Company, with a target Annual Bonus equal to thirty-five percent (35%) of the Base Salary for achievement of 100% of the performance objectives. Employee's success in achieving the objectives and the amount of the Annual Bonus will be determined by the President, CEO and/or Board in their reasonable discretion. Upon the recommendation of the President and/or CEO, Employee's annual Bonus may exceed thirty-five percent (35%) of the Base Salary.

(d) Paid Leave. Employee shall be entitled to one hundred ninety-two (192) hours of paid time off ("PTO") each calendar year during the Term, to be used accrued and capped in accordance with the Company's then-existing policies at an accrual rate of eight (8) hours per pay period. Notwithstanding the Company's PTO policies providing otherwise, upon termination of Employee's employment other than for "Cause" (as hereinafter defined), Employee will receive pay for all PTO accrued and unused as of the termination date.

(e) Benefits. During the Term, Employee shall be entitled to participate in employee benefit plans, programs and arrangements of the Company as are provided generally from time to time to all other similarly situated employees of the Company, including, but not limited to sick leave arrangements. All such benefits are subject to the provisions of their respective plan documents in accordance with their terms and are subject to amendment or termination by the Company without Employee's consent.

(f) Business Expenses. During the Term, the Company will reimburse all reasonable expenses incurred by Employee in the performance of her duties to the Company, provided Employee complies with the Company's policies and procedures for reimbursement or advance of business expenses established by the Company. Traveling on behalf of the Company to professional meetings and participating in the dermatology community is expected of Employee in her role as Chief Medical Officer. The reasonable travel and related expenses incurred for such activities, as well as Employee's annual dues for two professional associations and fees for licensing in one state, shall be paid or reimbursed by the Company. Employee agrees to seek the Company's prior approval for any expenses in excess of One Thousand Dollars ($1,000.00).

(i) Life Insurance. During the Term, Company shall pay Employee's cost, or at Employee's election reimburse Employee for the cost required, to purchase term life insurance in the face amount of $700,800 to be effective as of the Effective Date or as soon thereafter as is reasonably practicable. The term of the policy will be for ten (10) years, with an annual payment term. The Company will pay the premium during the term of the agreement and any period during which Employee is receiving payments following separation from service under Section 6.

4. EMPLOYMENT AT WILL; TERMINATION. Subject to the terms of Section 6 of this Agreement, Employee's employment pursuant to this Agreement shall continue until terminated by either party. Employee's employment with the Company is at-will, and either party can terminate the employment relationship and/or this Agreement at any time, for any or no cause or reason, and with or without prior notice.

5. EFFECT OF TERMINATION. Upon termination of Employee's employment hereunder by either party regardless of the cause or reason, the Company shall pay Employee accrued, unpaid wages through the termination date. Such final payment, less any withholdings required by law or properly requested by Employee, shall be made on the next regular payday of the Company following the termination, in accordance with the Company's normal payroll procedures. Except as otherwise provided in Section 6 of this Agreement, no other payments, benefits or other remuneration shall be due or payable to Employee.

6. SEVERANCE PROVISIONS.

(a) Definitions. For the purposes of this Section 6, the following terms shall be defined as set out below:

i. "Base Salary" shall mean Employee's then current annual Base Salary.

ii. "Cause" shall be determined in good faith by the Board and shall mean:

a. Employee's conviction of, or plea of no contest to, any crime (whether or not involving the Company) that constitutes a felony in the jurisdiction in which Employee is charged, or that involves moral turpitude;

b. Any act of theft, fraud or embezzlement, or any other willful misconduct or materially dishonest behavior by Employee;

c. Employee's willful failure or refusal to perform her reasonably-assigned duties, provided that such failure or refusal is not corrected as promptly as practicable, and in any event within ten (10) calendar days after Employee shall have received written notice from the Company stating the nature of such failure or refusal;

d. Employee's willful or material violation of any of her obligations contained in any agreement between Employee and the Company, including but not limited to Confidentiality and Assignment of Inventions Agreement and Non-Competition Agreement executed by Employee (the "Restrictive Covenants Agreements") or material violation of any policies in the Company's Employee Handbook; and/or

e. Conduct by Employee that constitutes willful gross neglect or willful gross misconduct in carrying out her duties under this Agreement that results or that may result, as determined by the Company, in material harm to the Company, including harm to its reputation.

iii. A "Change In Control" shall be deemed to have occurred upon the consummation of a merger or consolidation in which the shareholders of the Company immediately prior to the merger or consolidation cease to own at least fifty percent (50%) of the combined entity immediately following the merger or consolidation; a sale of all or substantially all of the assets of the Company; the acquisition by any individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities and Exchange Act of 1934, as amended) of beneficial ownership of any capital stock of the Company, if, after such acquisition, such individual, entity or group owns more than fifty percent (50%) of either (A) the then-outstanding common stock of the Company or (B) the combined voting power of the then-outstanding securities of the Company entitled to vote in the election of directors; or during any period of 12 consecutive months, a majority of the members of the board of directors of the Company cease to be composed of individuals (i) who were members of that board on the first day of such period, (ii) whose election or nomination to that board was approved by individuals referred to in clause (i) above constituting at the time of such election or nomination at least a majority of that board or (iii) whose election or nomination to that board was approved by individuals referred to in clauses (i) and (ii) above constituting at the time of such election or nomination at least a majority of that board.

iv. "Disability" shall mean Employee's inability due to a physical or mental impairment to perform the essential functions of her job, with or without reasonable accommodation, for a period of at least ninety (90) consecutive or non-consecutive days in any twelve (12) month period.

v. "Effective Release" is defined as a general release of claims in favor of the Company in a form reasonably acceptable to the Company's counsel that is executed after the Separation Date and within any consideration period required by applicable law and that is not revoked by Employee within any legally-prescribed revocation period; provided, however, a release shall not be considered an Effective Release unless, in addition to the foregoing conditions, the release is executed and not revoked, and the legally-prescribed revocation period ends by the sixtieth (60th) day following the Separation Date; provided further that such release shall not impose material post-employment obligations on Employee other than those set forth herein or as agreed to by the parties, nor shall such release require Employee to release any rights under Sections 3(i) and 6 of this Agreement. Failure to provide and have in effect an Effective Release within the sixty (60)-day period following the Separation Date shall result in forfeiture of any benefits conditioned upon the existence of an Effective Release.

vi. "Good Reason" shall mean a material negative change to Employee in the service relationship with the Company as a result of one or more of the following conditions arising without the consent of Employee:

a. A decrease in Employee's Base Salary of greater than or equal to twenty percent (20%) of the then Base Salary;

b. A material diminution in Employee's authority, duties or responsibilities;

c. A material change in the geographic location at which Employee must perform services for the Company from her current work location in Durham, North Carolina, not to include regular business travel; or

d. Any other action or inaction that constitutes a material breach of the terms of this Agreement by the Company.

Notwithstanding the forgoing, "Good Reason" shall not include an event or condition unless (A) Employee notifies the Company within ninety (90) days of the initial existence of one of the adverse events described above, (B) Employee provides the Company with at least thirty (30) days' written notice of her intent to resign for Good Reason, and (C) the Company fails to correct the adverse event within thirty (30) days of such notice.

vii. "Separation from Service" shall mean Employee has a "separation from service" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code") and the regulations and other interpretive guidance thereunder ("Section 409A") from the Company and will not perform any additional services after a certain date for the Company (or a related entity) or that the level of bona fide services (whether performed as an employee or as a contractor) will permanently decrease to no more than 20% of the average level of bona fide services performed (whether performed as an employee or as a contractor) over the immediately preceding 36-month period (or, if less, the period the employee has rendered service to the Company).

viii. "Separation Date" shall mean the date that Employee has a Separation from Service from the Company.

(b) Compensation upon Separation without "Cause" or for "Good Reason." Upon Separation from Service by the Company without Cause or by Employee for Good Reason, conditioned upon the existence of an Effective Release and Employee's continued compliance with the Restrictive Covenants Agreements and the terms thereunder, and subject to Section 8, Employee shall be entitled to, in lieu of any other separation payment or severance benefit:

i. Payment of an amount equal to twelve (12) months of her Base Salary, minus applicable withholdings required by law or authorized by Employee, to be paid in installments pursuant to the Company's standard payroll practices and procedures, during the period beginning on the Company's next regular pay day occurring sixty (60) days following the Separation Date and ending on the twelve (12) month anniversary of the Separation Date;

ii. Vesting of the remaining options in the then current vesting year of any and all granted options to purchase Company common stock on the Separation Date, such options requiring exercise within ninety (90) days of the Separation Date and pursuant to the other terms and conditions of the applicable Company incentive award plan and individual award agreement; and

iii. Conditioned on Employee's proper and timely election to continue her health insurance benefits under COBRA after the Separation Date, reimbursement of Employee's applicable COBRA premiums for the lesser of eighteen (18) months following the Separation Date or until Employee becomes eligible for insurance benefits from another employer; provided, that the Company may discontinue the benefits under this paragraph and make a lump sum payment in lieu thereof to the extent reasonably necessary to avoid any penalty or excise taxes imposed on it in connection with the continued payment of premiums or other amounts by the Company under the Patient Protection and Affordable Care Act of 2010, as amended. Such lump sum payment shall be equal to the product of the current COBRA premium paid by the Company times the number of months remaining in the eighteen (18) month period if Employee is not at the time of the lump sum payment eligible for insurance benefits from another employer.

(c) Compensation upon Separation due to Change in Control. Upon Separation from Service by the Company without Cause or by Employee for Good Reason within six (6) months after a Change in Control, and conditioned upon the existence of an Effective Release and Employee's continued compliance with the Restrictive Covenants Agreements and the terms thereunder, Employee shall be entitled to, in lieu of any other separation payment or severance benefit (including but not limited to the severance benefits provided for in Section 6(b) hereof):

i. Payment of an amount equal to twelve (12) months of her Base Salary, minus applicable withholdings required by law or authorized by Employee, to be paid in installments pursuant to the Company's standard payroll practices and procedures during the period beginning on the Company's next regular pay day occurring sixty (60) days following the Separation Date and ending on the twelve (12) month anniversary of the Separation Date;

ii. Accelerated vesting of the remaining unvested portion of any and all granted options to purchase Company common stock on the Separation Date, such options requiring exercise within ninety (90) days of the Separation Date and pursuant to the other terms and conditions of the Novan Inc. 2008 Stock Plan and Employee's Notice(s) of Stock Option Grant; and

iii. Conditioned on Employee's proper and timely election to continue her health insurance benefits under COBRA after the Separation Date, reimbursement of Employee's applicable COBRA premiums for the lesser of eighteen (18) months following the Separation Date or until Employee becomes eligible for insurance benefits from another employer; provided, that the Company may discontinue the benefits under this paragraph and make a lump sum payment in lieu thereof to the extent reasonably necessary to avoid any penalty or excise taxes imposed on it in connection with the continued payment of premiums or other amounts by the Company under the Patient Protection and Affordable Care Act of 2010, as amended. Such lump sum payment shall be equal to the product of the current COBRA premium paid by the Company times the number of months remaining in the eighteen (18) month period if Employee is not at the time of the lump sum payment eligible for insurance benefits from another employer.

(d) Other Separation from Service. Notwithstanding any Change in Control, upon Separation from Service by Employee other than for Good Reason or due to Employee's death or Disability, or by the Company for Cause, Employee shall not be entitled to additional compensation under this Agreement beyond that earned and accrued as of the Separation Date.

7. SECTION 409A.

(a) The parties hereby acknowledge and agree that all benefits or payments provided by the Company to Employee pursuant to this Agreement are intended either to be exempt from Section 409A of the Code, or to be in compliance with Section 409A, and the Agreement shall be interpreted to the greatest extent possible to be so exempt or in compliance and to incorporate the terms and conditions required by Section 409A. If there is an ambiguity in the language of the Agreement, or if Section 409A guidance indicates that a change to the Agreement is required or desirable to achieve exemption or compliance with Section 409A, notwithstanding any provision of this Agreement to the contrary, the Company reserves the right (without any obligation to do so or to indemnify Employee for failure to do so) to (i) adopt such amendments to this Agreement and or adopt such other policies and procedures, including amendments, policies and procedures with retroactive effect, that the Company determines to be necessary or appropriate to preserve the intended tax treatment of the benefits provided by this Agreement, to preserve the economic benefits of this Agreement and to avoid less favorable accounting or tax consequences for the Company and/or (ii) take such other actions as the Company determines to be necessary or appropriate to exempt the amounts payable hereunder from Section 409A or to comply with the requirements of Section 409A and thereby avoid the application of penalty taxes thereunder. No provision of this Agreement shall be interpreted or construed to transfer any liability for failure to comply with the requirements of Section 409A from the Employee or any other individual to the Company or any of its affiliates, employees or agents.

(b) If any severance or other payments that are required by the Agreement are to be paid in a series of installment payments, each individual payment in the series shall be considered a separate payment for purposes of Section 409A. To the extent that any reimbursement of expenses or in-kind benefits constitutes "deferred compensation" under Section 409A, such reimbursement or benefit shall be provided no later than December 31 of the year following the year in which the expense was incurred. The amount of expenses reimbursed in one year shall not affect the amount eligible for reimbursement in any subsequent year. The amount of any in-kind benefits provided in one year shall not affect the amount of in-kind benefits provided in any other year.

(c) If any severance compensation or other benefit provided to Employee pursuant to this Agreement that constitutes "nonqualified deferred compensation" within the meaning of Section 409A is considered to be paid on account of "separation from service" within the meaning of Section 409A, and Employee is a "specified employee" within the meaning of Section 409A, no payments of any of such severance or other benefit shall made for six (6) months plus one (1) day after the Separation Date (the "New Payment Date"). Amounts payable under this Agreement shall be deemed not to be "nonqualified deferral of compensation" subject to Section 409A to the extent provided in the exceptions in Treasury Regulation §§ 1.409A-1(b)(4) ("short-term deferrals") and (b)(9) ("separation pay plans," including the exception under subparagraph (iii)) and other applicable provisions of Section 409A. The aggregate of any such payments that would have otherwise been paid during the period between the Separation Date and the New Payment Date shall be paid to Employee in a lump sum on the New Payment Date.

8. EXCESS PARACHUTE PAYMENTS.

(a) If any payments or benefits received or to be received by Employee pursuant to this Agreement or any other Company plan, program or arrangement, including those made in connection with or contingent on a change in ownership or control, (collectively, the "Company Payments") would be deemed to be an "excess parachute payment" within the meaning of Section 280G of the Code ("Excess Parachute Payment"), and if the Company has no publicly-traded stock, the Company, with the consent of Employee, will use commercially reasonable efforts to obtain "shareholder approval" within the meaning of Section 280G(b)(5) of the Code of such payments or benefits in order to exempt such payments or benefits from being considered an Excess Parachute Payment. Employee's consent to shareholder approval shall include a waiver by Employee of any such payments or benefits that are not approved by the shareholders. If Employee does not consent to subjecting such payments or benefits to shareholder approval, then, at Company's election, such payments under this Agreement shall either be paid in full or reduced to the extent necessary to avoid being considered an Excess Parachute Payment, based upon Company's determination, in its sole discretion, as to which alternative results in the better tax consequences for Employee.

(b) If the Company has publicly traded stock, then Employee will be entitled to receive either (i) the full amount of the Company Payments, or (ii) a portion of the Company Payments having a value equal to $10 less than three (3) times Employee's "base amount" (as such term is defined in Section 280G(b)(3)(A) of the Code), whichever of clauses (i) and (ii), after taking into account applicable federal, state, and local income taxes and the excise tax imposed by Section 4999 of the Code, results in the receipt by Employee on an after-tax basis, of the greatest portion of the Company Payments. Any determination required under this Section 8 shall be made in writing by the independent public accountant of the Company (the "Accountants"), whose determination shall be conclusive and binding for all purposes upon the Company and Employee. For purposes of making any calculation required by this Section 8, the Accountants may make reasonable assumptions and approximations concerning applicable taxes and may rely on reasonable, good-faith interpretations concerning the application of Sections 280G and 4999 of the Code. If there is a reduction of the Company Payments pursuant to this Section 8, such reduction shall occur in the following order: (A) any cash severance payable by reference to Employee's Base Salary or Annual Bonus, (B) any other cash amount payable to Employee, (C) any employee benefit valued as a "parachute payment," and (D) acceleration of vesting of any outstanding equity award.

9. NOTICES. Any notice required or permitted hereunder shall be made in writing (a) either by actual delivery of the notice into the hands of the party thereto entitled, by messenger, by fax or by over-night delivery service or (b) by the mailing of the notice in the United States mail, certified or registered mail, return receipt requested, all postage pre-paid and addressed to the party to whom the notice is to be given at the party's respective address set forth below, or such other address as the parties may from time to time designate by written notice as herein provided.

If to Employee:	M. Joyce Rico 306 W. Barbee Chapel Road Chapel Hill, North Carolina 27517
If to the Company:	Novan, Inc. 4222 Emperor Boulevard Suite 200 Durham, North Carolina 27703 (Fax) (919) 237-9212 Attn: Chief Financial Officer

The notice shall be deemed to be received, if sent per subsection (a), on the date of its actual receipt by the party entitled thereto and, if sent per subsection (b), on the third day after the date of its mailing.

10. RETURN OF COMPANY PROPERTY. Upon Employee's Separation from Service from the Company for any reason, Employee shall return to Company all personal property belonging to Company ("Company Property") that is in Employee's possession or control as of the date of such Separation from Service, including, without limitation, all records, papers, drawings, notebooks, specifications, marketing materials, software, reports, proposals, equipment, or any other device, document or possession, however obtained, whether or not such Company Property contains confidential information belonging to the Company. Such Company Property shall be returned in the same condition as when provided to Employee, reasonable wear and tear excepted.

11. EMPLOYEE REPRESENTATIONS.

(a) Employee represents that her performance of all of the terms of this Agreement does not and will not breach any arrangement to keep in confidence information acquired by Employee in confidence or in trust prior to Employee's employment by the Company. Employee represents that she has not entered into, and agrees not to enter into, any agreement either oral or written in conflict herewith.

(b) Employee understands as part of the consideration for this Agreement and for Employee's employment or continued employment by the Company, that Employee has not brought and will not bring with Employee to the Company, or use in the performance of Employee's duties and responsibilities for the Company or otherwise on its behalf, any materials or documents of a former employer or other owner which are generally not available to the public, unless Employee has obtained written authorization from the former employer or other owner for their possession and use and has provided the Company with a copy thereof.

(c) Employee understands that during her employment for the Company she is not to breach any obligation of confidentiality that Employee has to a former employer or any other person or entity and agrees to comply with such understanding.

12. INDEMNIFICATION. Employee agrees to indemnify and hold harmless the Company, its directors, officers, agents and employees against any liabilities and expenses, including amounts paid in settlement, incurred by any of them in connection with any claim by any of Employee's prior employers that the termination of Employee's employment with such employer, Employee's employment by the Company, or use of any skills and knowledge by the Company is a violation of contract or law or otherwise violates the rights thereof.

13. SEVERABILITY. Employee hereby agrees that each provision herein shall be treated as a separate and independent clause, and the unenforceability of any one clause shall in no way impair the enforceability of any of the other clauses herein.

14. WAIVER. Any waiver by the Company of a breach of any provision of this Agreement shall not operate or be construed as a waiver of any subsequent breach of such provision or any other provision hereof.

15. AFFILIATES; ASSIGNMENT; BINDING EFFECT. The term "Company" shall also include any of the Company's subsidiaries, subdivisions or affiliates. The Company shall have the right to assign this Agreement to its successors and assigns, and all covenants and agreements hereunder shall inure to the benefit of and be enforceable by said successors or assigns. Employee may not assign any of her rights or delegate any of her duties under this Agreement. This Agreement shall be binding upon and shall inure to the benefit of each of the parties hereto, and to their respective heirs, representatives, successors and permitted assigns.

16. ENTIRE AGREEMENT. The terms of this Agreement (together with any other agreements and instruments contemplated hereby or referred to herein) are intended by the parties hereto to be the final expression of their agreement with respect to the employment of Employee by the Company and may not be contradicted by evidence of any prior or contemporaneous agreement (including, without limitation, the Offer Letter, any term sheet or offer letter). The parties hereto further intend that this Agreement shall constitute the complete and exclusive statement of its terms and that no extrinsic evidence whatsoever may be introduced in any judicial, administrative or other legal proceeding to vary the terms of this Agreement. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, will be effective unless in writing and signed by each of the parties hereto.

17. GOVERNING LAW; VENUE. This Agreement shall be governed by and construed in accordance with the laws of the State of North Carolina, without regard to that body of law known as choice of law. Any litigation under this Agreement shall be brought by either party exclusively in Durham County, North Carolina. As such, the parties irrevocably consent to the jurisdiction of the courts in Durham County, North Carolina (whether federal or state) for all disputes related to this Agreement.

18. COUNTERPARTS. This Agreement may be executed in separate counterparts, each of which is deemed to be an original and all of which taken together constitute one agreement. Counterparts may be transmitted and/or signed by facsimile or electronic mail. The effectiveness of any such documents and signatures shall have the same force and effect as manually signed originals and shall be binding on the parties to the same extent as a manually signed original thereof.

[Signature Page Follows]

IN WITNESS WHEREOF, the parties have executed this Employment Agreement effective as of the day and year first above written.

NOVAN, INC.

/s/ Nathan Stasko

NATHAN STASKO
President and Chief Executive Officer

EMPLOYEE

/s/ M. Joyce Rico

M. JOYCE RICO

Exhibit 10.12

NOVAN, INC.

NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

Non-employee members of the board of directors (the ***"Board"***) of Novan, Inc. (the ***"Company"***) shall be eligible to receive cash and equity compensation as set forth in this Non-Employee Director Compensation Policy (this ***"Policy"***). The cash and equity compensation described in this Policy shall be paid or be made, as applicable, automatically and without further action of the Board, to each member of the Board who is not an employee of the Company or any parent or subsidiary of the Company (each, a ***"Non-Employee Director"***), who may be eligible to receive such cash or equity compensation, unless such Non-Employee Director declines the receipt of such cash or equity compensation by written notice to the Company. This Policy shall become effective on the date (the ***"Effective Date"***) of the Company's initial public offering (the ***"IPO"***) and shall remain in effect until it is revised or rescinded by further action of the Board. This Policy may be amended, modified or terminated by the Board at any time in its sole discretion. The terms and conditions of this Policy shall supersede any prior cash and/or equity compensation arrangements for service as a member of the Board between the Company and any of its Non-Employee Directors and between any subsidiary of the Company and any of its non-employee directors. No Non-Employee Director shall have any rights hereunder, except with respect to equity awards granted pursuant to the Policy.

1. Cash Compensation.

(a) Annual Retainers. Each Non-Employee Director shall receive an annual retainer of $35,000 for service on the Board.

(b) Additional Annual Retainers. In addition, a Non-Employee Director shall receive the following annual retainers:

(i) Chairman of the Board. A Non-Employee Director serving as Chairman of the Board shall receive an additional annual retainer of $25,000 for such service.

(ii) Audit Committee. A Non-Employee Director serving as Chairperson of the Audit Committee shall receive an additional annual retainer of $15,000 for such service. A Non-Employee Director serving as a member of the Audit Committee (other than the Chairperson) shall receive an additional annual retainer of $7,500 for such service.

(iii) Compensation Committee. A Non-Employee Director serving as Chairperson of the Compensation Committee shall receive an additional annual retainer of $12,500 for such service. A Non-Employee Director serving as a member of the Compensation Committee (other than the Chairperson) shall receive an additional annual retainer of $6,250 for such service.

(iv) Nominating and Corporate Governance Committee. A Non-Employee Director serving as Chairperson of the Nominating and Corporate Governance Committee shall receive an additional annual retainer of $10,000 for such service. A Non-Employee Director serving as a member of the Nominating and Corporate Governance Committee (other than the Chairperson) shall receive an additional annual retainer of $5,000 for such service.

(c) Payment of Retainers. The annual retainers described in Sections 1(a) and 1(b) shall be earned on a quarterly basis based on a calendar quarter and shall be paid by the Company in arrears not later than the fifteenth day following the end of each calendar quarter. In the event a Non-Employee Director does not serve as a Non-Employee Director, or in the applicable positions described in Section 1(b), for an entire calendar quarter, such Non-Employee Director shall receive a prorated portion of the retainer(s) otherwise payable to such Non-Employee Director for such calendar quarter pursuant to Section 1(b), with such prorated portion determined by multiplying such otherwise payable retainer(s) by a fraction, the numerator of which is the number of days during which the Non-Employee Director serves as a Non-Employee Director or in the applicable positions described in Section 1(b) during the applicable calendar quarter and the denominator of which is the number of days in the applicable calendar quarter.

2. Equity Compensation. Non-Employee Directors shall be granted the equity awards described below. The awards described below shall be granted under and shall be subject to the terms and provisions of the Company's 2016 Incentive Award Plan or any other applicable Company equity incentive plan then-maintained by the Company (the ***"Equity Plan"***) and shall be granted subject to the execution and delivery of award agreements, including attached exhibits, in substantially the forms previously approved by the Board. All applicable terms of the Equity Plan apply to this Policy as if fully set forth herein, and all equity grants hereunder are subject in all respects to the terms of the Equity Plan.

(a) IPO Awards. Each Non-Employee Director who (i) serves on the Board as of the date the IPO price of the shares of the Company's common stock, par value $0.0001 per share (***"Common Stock"***) is established in connection with the Company's IPO (the "Pricing Date") and (ii) will continue to serve as a Non-Employee Director immediately following the Pricing Date shall be automatically granted, on the Pricing Date, an option to purchase the number of shares of the Company's common stock (at a per-share exercise price equal to the IPO price) that have an aggregate fair market value on the date of grant of $100,000 (as determined in accordance with FASB Accounting Standards Codification Topic 718 (***"ASC 718"***)) (with the number of shares of Common Stock underlying each such award subject to adjustment as provided in the Equity Plan). The awards described in this Section 2(a) shall be referred to herein as the ***"IPO Awards"***).

(b) Annual Awards. A Non-Employee Director who (i) serves on the Board as of the date of any annual meeting of the Company's stockholders (an ***"Annual Meeting"***) after the Effective Date and (ii) will continue to serve as a Non-Employee Director immediately following such Annual Meeting shall be automatically granted, on the date of such Annual Meeting, an option to purchase the number of shares of the Company's common stock (at a per-share exercise price equal to the closing price per share of the Company's common stock on the date of such annual meeting (or on the last preceding trading day if the date of the annual meeting is not a trading day) that have an aggregate fair value on the date of grant of $100,000 (as determined in accordance with ASC 718) (with the number of shares of Common Stock underlying each such award subject to adjustment as provided in the Equity Plan). The awards described in this Section 2(b) shall be referred to as the ***"Annual Awards."*** Notwithstanding the foregoing, the Board in its sole discretion may determine that the Annual Awards for any year be granted in the form of restricted stock units with equivalent value on the date of grant (with the number of shares of Common Stock underlying each such award subject to adjustment as provided in the Equity Plan). For the avoidance of doubt, a Non-Employee Director elected for the first time to the Board at an Annual Meeting shall only receive an Annual Award in connection with such election, and shall not receive any Initial Award (as defined below) on the date of such Annual Meeting as well.

(c) Initial Awards. Except as otherwise determined by the Board, each Non-Employee Director who is initially elected or appointed to the Board after the Pricing Date on any date other than the date of an Annual Meeting shall be automatically granted, on the date of such Non-Employee Director's initial election or appointment (such Non-Employee Director's ***"Start Date"***), an option to purchase shares of the Company's common stock (at a per-share exercise price equal to the [closing price per share of the Company's common stock on the date of such annual meeting (or on the last preceding trading day if the date of the annual meeting is not a trading day)] that have an aggregate fair value on such Non-Employee Director's Start Date equal to the product of (i) $100,000 (as determined in accordance with ASC 718), and (ii) a fraction, the numerator of which is (x) 365 minus (y) the number of days in the period beginning on the date of the Annual Meeting immediately preceding such Non-Employee Director's Start Date (or, if no such Annual Meeting has occurred, the effective date of the Company's IPO) and ending on such Non-Employee Director's Start Date and the denominator of which is 365 (with the number of shares of Common Stock underlying each such award subject to adjustment as provided in the Equity Plan). The awards described in this Section 2(c) shall be referred to as ***"Initial Awards."*** Notwithstanding the foregoing, the Board in its sole discretion may determine that the Initial Award for any Non-Employee Director be granted in the form of restricted stock units with equivalent value on the date of grant (with the number of shares of Common Stock underlying each such award subject to adjustment as provided in the Equity Plan). For the avoidance of doubt, no Non-Employee Director shall be granted more than one Initial Award.

(d) Termination of Service of Employee Directors. Members of the Board who are employees of the Company or any parent or subsidiary of the Company who subsequently terminate their service with the Company and any parent or subsidiary of the Company and remain on the Board will not receive an Initial Award pursuant to Section 2(c) above, but to the extent that they are otherwise eligible, will be eligible to receive, after termination from service with the Company and any parent or subsidiary of the Company, Annual Awards as described in Section 2(b) above.

(e) Vesting of Awards Granted to Non-Employee Directors . Each IPO Award, Annual Award and Initial Award shall vest and become exercisable in four equal quarterly installments, such that each such award shall be fully vested and exercisable on the first anniversary of the date of grant, subject to the Non-Employee Director's continued service on the Board as a Non-Employee Director through each applicable vesting date. No portion of an IPO Award, Annual Award or Initial Award that is unvested or unexercisable at the time of a Non-Employee Director's termination of service on the Board as a Non-Employee Director shall become vested and exercisable thereafter. All of a Non-Employee Director's IPO Awards, Annual Awards and Initial Awards shall vest in full immediately prior to the occurrence of a Change in Control (as defined in the Equity Plan), to the extent outstanding at such time.

* * * * *

[***] Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

January 12, 2017

Novan, Inc
(as Licensor)

and

Sato Pharmaceutical Co., Ltd
(as Licensee)

LICENSE AGREEMENT

CONTENTS

LICENSE AGREEMENT

This License Agreement is entered into by and between Novan, Inc., a Delaware corporation having an address at 4105 Hopson Roac Morrisville, North Carolina 27560, USA ("**Novan**") and Sato Pharmaceutical Co., Ltd, a Japanese corporation having an address at 1-5-27, Moto-Akasaka Minato-ku, Tokyo 107-0051, Japan ("**Sato**"). Novan and Sato are also referred to individually as a "**Party**" and together as the "**Parties**".

WITNESSETH THAT:

WHEREAS, Novan is developing a pharmaceutical product in the United States known as SB204 for the treatment of acne vulgaris, and owns o controls certain proprietary technology, know-how and information relating to such product; and

WHEREAS, Sato desires to obtain from Novan a license to develop and commercialize such product in Japan, and Novan desires to grant such license and option to Sato.

NOW, THEREFORE, it is agreed between the Parties as follows:

1. DEFINITIONS

The following terms as used in this Agreement (as hereinafter defined) shall have the meanings set forth in this Section (which meanings shall be applicable both to the singular and the plural forms of such terms):

1.1 "**Accountant**" has the meaning set forth in Section 15.8.

1.2 "**Additional License Agreement**" has the meaning set forth in Section 2.10(ii).

1.3 "**Additional Licensed Territories**" shall mean China (including Hong Kong), South Korea, Taiwan, Singapore, Indonesia Thailand, Philippines, Vietnam, Malaysia, Cambodia, Brunei, Myanmar, or Laos.

1.4 "**Affiliate**" means with respect to each Party, any Person that directly or indirectly is controlled by, controls or is under common control with a Party. For the purposes of this definition only, the term "control" (including, with correlative meanings, the terms "controlled by" and "under common control with") as used with respect to a Person means (a) in the case of a corporate entity, direct or indirect ownership of voting securities entitled to cast at least fifty percent (50%) of the votes in the election of directors or (b) in the case of a non-corporate entity, direct or indirect ownership of at least fifty percent (50%) of the equity interests with the power to direct the management and policies of such entity; provided that, if local Laws restrict foreign ownership, control shall be established by direct or indirect ownership of the maximum ownership percentage that may, under such local Laws, be owned by foreign interests, but only if such lower percentage provides such Person with the power to direct the management and policies of such entity.

1.5 "**Agreement**" means this License Agreement, including all of its Annexes.

1.6 "**[***]**" means the **[***]**, and shall include **[***]**. Such **[***]** shall be in accordance with U.S. GAAP, consistently applied. **[***]** shall not include **[***]**.

1.7 "**Approved Label**" means the label included in the Marketing Approval for the Licensed Product in the Licensed Field in the Licensed Territory.

1.8 "**Bankruptcy Laws**" has the meaning set forth in Section 20.3.

1.9 "**Base Price**" has the meaning set forth in Section 5.4.

1.10 "**Business Day**" means a day other than Saturday, Sunday or any day on which commercial banks located in the State of North Carolina, U.S., or in Tokyo, Japan are authorized or obligated by Laws to close.

1.11 "**CEO**" has the meaning set forth in Section 24.1.

1.12 "**Commercial Supply Agreement**" has the meaning set forth in Section 5.4.

1.13 "**Commercially Reasonable Efforts**" means, with respect to a Party's obligation under this Agreement to develop, manufacture, commercialize or seek intellectual property protection for the Licensed Product, the level of efforts required to carry out such obligation in a sustained manner consistent with the efforts that a similarly situated company devotes to a product of similar market potential, profit potential, or strategic value at a similar stage in its development or product life within its portfolio. For purposes of illustration, Commercially Reasonable Efforts requires, with respect to such an obligation, that a Party reasonably and in good faith: (a) promptly assign responsibility for such obligation to specific employee(s) who are held accountable for progress and monitor such progress on an on-going basis, (b) set and seek to achieve reasonable objectives for carrying out such obligation, and (c) reasonably make and implement decisions and allocate resources designed to advance progress with respect to such objectives, all taking into account issues of available intellectual property coverage, safety and efficacy information, targeted product profile, the competitiveness of the marketplace, other technical, legal, scientific and/or medical factors and the pricing and reimbursement status for the relevant product. In evaluating whether a Party has used Commercially Reasonable Efforts, due consideration will be given to any delays by the other Party in performing its obligations under this Agreement that adversely impact the first Party's ability to perform its obligations under this Agreement.

1.14 "**Competing Product**" means **[***]** product for **[***]**.

1.15 "**Compound**" means the substance known as NVN1000, which is the subject of Investigational New Drug Application **[***]**.

1.16 "**Confidentiality Agreement**" means that certain confidentiality agreement between Sato and Novan dated **[***]**.

1.17 "**Control**" means possession of the ability to grant a license, sublicense or access as provided for under this Agreement without (a) violating the terms of any agreement or other arrangement with any Third Party or (b) increasing at any time the amount of any payments required under any such agreement or arrangement that is entered into after the Effective Date, provided that this subsection (b) shall not apply if the other Party elects in writing to be responsible for all such increased payments as provided in Section 2.9.

1.18 "**Conversion Rate**" means the average conversion rate from JPY to USD during the **[***]** prior to the Effective Date, as published in *The Wall Street Journal*.

1.19 "**Cover**", "**Covered**" or "**Covering**" means, with reference to a Patent and a product, composition, article of manufacture, or method, that the manufacture, practice, use, offer for sale, sale or importation of the product, composition, article of manufacture, or method, would infringe a Valid Claim of such Patent in the country in which such activity occurs without a license thereto (or ownership thereof).

1.20 "**Damages**" has the meaning set forth in Section 16.1.

1.21 "**Development Plan**" has the meaning set forth in Section 4.2.

1.22 "**Dispute**" has the meaning set forth in Section 24.1.

1.23 "**Drug Approval Application**" means an application for Marketing Approval required before commercial sale or use of the Licensed Product as a drug in a regulatory jurisdiction or country.

1.24 "**Effective Date**" means January 12, 2017.

1.25 "**[***]**" has the meaning set forth in Section 2.3(v).

1.26 "**Election Time Period**" has the meaning set forth in Section 16.3(i).

1.27 "**FCPA**" has the meaning set forth in Section 10.3(iii).

1.28 "**First Commercial Sale**" means the first arm's length commercial sale of a Licensed Product by Sato or an Affiliate of Sato to a Third Party (including without limitation any final sale to a distributor or wholesaler under any non-conditional sale arrangement) in a country where Marketing Approval of such Licensed Product has been obtained by Sato or an Affiliate of Sato.

1.29 "**Force Majeure**" has the meaning set forth in Section 21.1.

1.30 "**Fully Burdened Manufacturing Cost**" means, as applicable to Study Materials manufactured by Novan or its Third Party supplier, Novan's or its Affiliate's cost of manufacturing such Study Material, which is equal to (a) **[***]** for the Study Material (or components thereof) made by Novan, **[***]**, in each case for the manufacture of the Study Material, (b) **[***]**, and (c) for Study Materials (or components thereof) made by Novan's Third

Party supplier, **[***]** to the extent such costs in (a) and (c) are **[***]**. Fully Burdened Manufacturing Cost shall be calculated in a manner consistent with U.S GAAP, consistently applied.

1.31 "**Goods**" means the Compound, Study Materials and/or the Licensed Product.

1.32 "**Government or Public Official**" has the meaning set forth in Section 10.3(iii).

1.33 "**ICDR**" has the meaning set forth in Section 24.1.

1.34 "**Improvement**" means any **[***]**.

1.35 "**Information**" means all data, materials and documents necessary for the development or commercialization of the Licensed Product within the Licensed Field, including without limitation those relating to or comprising inventions; practices; methods; knowledge; know-how skill; experience; compositions of matter; assays; medical, toxicological, pharmacological, pre-clinical, clinical and chemical data; specifications; medical uses; adverse reactions; formulations; bioanalytical metrics; analytical and quality control data and methods; and all proprietary information submitted to relevant Regulatory Authorities to support a Drug Approval Application for and Marketing Approval of the Licensed Product in the Licensed Field.

1.36 "**Indemnification Claim Notice**" has the meaning set forth in Section 16.3(i).

1.37 "**Indemnified Party**" has the meaning set forth in Section 16.3(i).

1.38 "**Indemnifying Party**" has the meaning set forth in Section 16.3(i).

1.39 "**Invention**" means any and all discoveries, developments, improvements, modifications, formulations, materials, compositions of matter, cell lines, processes, machines, manufactures and other inventions (whether patentable or not patentable) made in the course of activities performed under this Agreement by or on behalf of either Party or both Parties.

1.40 "**JNDA**" has the meaning set forth in Section 3.1(i).

1.41 "**Joint Committee**" or "**JC**" has the meaning set forth in Section 2.4(i).

1.42 "**Joint Inventions**" has the meaning set forth in Section 7.2.

1.43 "**Joint Patent**" has the meaning set forth in Section 7.4(iii).

1.44 "**JPY**" means a Japanese yen.

1.45 "**Law**" means all applicable laws, statutes, rules, regulations, ordinances and other pronouncements having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, domestic or foreign.

1.46 "**Licensed Field**" means the treatment of acne vulgaris in humans.

1.47 "**Licensed Product**" means any topical finished dosage form that (i) contains the Compound and (ii) meets the Specifications or, subject to Section 4.3, the Modified Specifications.

1.48 "**Licensed Rights**" means the rights granted by Novan to Sato pursuant to Section 2.1.

1.49 "**Licensed Territory**" means Japan.

1.50 "**Licensee Efficacy Data**" means Licensee Scientific Information relating to the efficacy of the Licensed Product including, without limitation, **[***]** and **[***]**. For clarity, Licensee Efficacy Data excludes **[***]**, including, without limitation, **[***]**.

1.51 "**Licensee Scientific Information**" means the Scientific Information **[***]** that is **[***]**, that is **[***]**.

1.52 "**Litigation Conditions**" has the meaning set forth in Section 16.3(i).

1.53 "**Marketing Approval**" means, with respect to a particular country or regulatory jurisdiction, all necessary authorizations and approvals by the Regulatory Authorities required to manufacture, use, import, market, distribute and promote the Licensed Product in the Licensed Field in such country or regulatory jurisdiction, including, but not limited to, any importation or manufacturing licenses, marketing authorization (health registration), labeling approval, and NHI Price and reimbursement approval, if applicable.

1.54 "**Marketing Exclusivity**" means, with respect to the Licensed Territory, the period of data exclusivity as provided under local Laws during which Third Parties do not have the right, in connection with seeking or obtaining Marketing Approval of a pharmaceutical product that contains the same or substantially similar active ingredient(s) or the same active moiety(ies) as a Licensed Product, (i) to reference the Licensed Product's clinical dossier without an express right of reference from the dossier holder, or (ii) to rely on previous Regulatory Authority determinations of safety and effectiveness with respect to the Licensed Product to support the submission, review or approval of a Drug Approval Application or similar regulatory submission filed with the applicable Regulatory Authority for such pharmaceutical product, as well as any other exclusivity periods available under local Laws (e.g. with respect to orphan drugs, new chemical entity exclusivity and pediatric exclusivity) during which Third Parties are prevented from filing or having accepted by Regulatory Authorities a Drug Approval Application for, or obtaining Marketing Approval of, a pharmaceutical product that contains the same or substantially similar active ingredient(s) or the same active moiety(ies) as a Licensed Product in the Licensed Field in the Licensed Territory.

1.55 "**Modified Specifications**" has the meaning set forth in Section 4.3.

1.56 "**Net Sales**" means the gross amounts invoiced or otherwise billed by Sato or its Affiliates on account of sales or any other commercial disposition of the Licensed Product to Third Parties, including without limitation wholesalers, hospitals, distributors and/or other intermediate Third Parties, in the Licensed Territory (hereinafter the "**Gross Sales**"), less the following to the extent specifically related to the Licensed Product and actually allowed, incurred or paid during such period according to Japanese GAAP:

(i) **[***]** and **[***]**, **[***]** and other **[***]** directly related to the sale to the extent applicable and not reimbursable, but **[***]**;

(ii) amounts **[***]** or **[***]** (including without limitation **[***]** and **[***]**), **[***]**, **[***]** or **[***]** with respect to the Licensed Product;

(iii) **[***]**, **[***]**, **[***]**, **[***]** or **[***]** and **[***]** to the **[***]**;

(iv) charges incurred in connection with the **[***]** or **[***]** of the Licensed Product, to the extent not deducted pursuant to subsection (i) or subsection (iii) above;

(v) **[***]** in connection with the Licensed Product (it being understood that "**Net Sales**" will include all amounts received for any **[***]**); and

(vi) **[***]** and **[***]** on account of the sale of the Licensed Product to the extent actually allowed and common within the pharmaceutical industry in the Licensed Territory;

provided that all of the foregoing deductions are incurred in the ordinary course and calculated in accordance with Japanese GAAP, consistently applied, during the applicable calculation period throughout the selling party's organization.

All such discounts, allowances, credits, rebates, and other deductions granted for a range of products shall be fairly and equitably allocated to the Licensed Product and other products of Sato and its Affiliates such that the Licensed Product does not bear a disproportionate portion of such deductions.

1.57 "**[***]**" means the **[***]** for **[***]** as approved by relevant Regulatory Authorities.

1.58 "**Novan Confidential Information**" has the meaning set forth in Section 11.1(i).

1.59 "**Novan Indemnitees**" has the meaning set forth in Section 16.2.

1.60 "**Novan Know-How**" means Information that (i) is necessary for the development, manufacture, use, sale, offer for sale and/or importation of Licensed Product in the Licensed Field, and (ii) is within the Control of Novan during the Term of this Agreement.

Notwithstanding anything herein to the contrary, Novan Know-How shall exclude Novan Patents, but shall include the Novan Scientific Information.

1.61 "**Novan License**" has the meaning set forth in Section 2.3.

1.62 "**Novan Licensee**" means any Third Party to which Novan has granted a sublicense or other rights under the Novan Patents or Novan Know-How for development or commercialization of the Licensed Product in the Licensed Field outside of the Licensed Territory.

1.63 "**Novan Patent**" means a Patent which claims inventions necessary for the development, manufacture, use, sale, offer for sale and/or importation of Licensed Products within the Licensed Field, and that is Controlled by Novan during the Term of this Agreement, including without limitation Novan's interest in any Joint Patents. Novan Patents include without limitation the patents listed in Annex 2.

1.64 "**Novan Scientific Information**" means such Scientific Information generated and/or compiled by or on behalf of Novan as of the Effective Date and listed in Annex 1 as well as Scientific Information generated and/or compiled by or on behalf of Novan that is Controlled by Novan during the Term of this Agreement, and that is necessary for the development, manufacture, use, sale, offer for sale and/or importation of Licensed Product in the Licensed Field.

1.65 "**Novan Trademarks**" means the trademarks set forth on Annex 4, as updated from time to time to reflect trademarks obtained by Novan for use with Licensed Products in the Licensed Field (excluding for clarity trademarks generally used by Novan in its business or for use with products that are not Licensed Products).

1.66 "**Option**" has the meaning set forth in Section 2.10(i).

1.67 "**Option Exercise Fee**" means **[***]**.

1.68 "**Option Period**" means the period starting on the date that is **[***]** and ending **[***]**.

1.69 "**Patent**" means (a) letters patent (or other equivalent legal instrument), including without limitation utility and design patents, and including without limitation any extension, substitution, registration, confirmation, reissue, re-examination or renewal thereof, (b) applications for letters patent, including without limitation a provisional application, non-provisional application, reissue application, a re-examination application, a continuation application, a continued prosecution application, a continuation-in-part application, a divisional application or any equivalent of the foregoing applications that is pending at any time during the Term of this Agreement before a government patent authority and (c) all foreign or international equivalents of any of the foregoing in any country.

1.70 "**Patent Family**" means any and all nonprovisionals, continuations, continuations-in-part, divisions, substitutions, extensions, reissues, reexaminations, and/or foreign counterparts of a Patent, all of which claim priority from a common Patent.

1.71 "**Patent Term Extensions**" has the meaning set forth in Section 7.8.

1.72 "**Paying Party**" has the meaning set forth in Section 15.6.

1.73 "**Person**" means any individual, firm, corporation, partnership, limited liability company, trust, business trust, joint venture, governmental authority, association or other entity.

1.74 "**PMDA**" means Japan's Pharmaceuticals and Medical Devices Agency.

1.75 "**Product Infringement**" has the meaning set forth in Section 7.5(ii)(a).

1.76 "**Prosecuting Party**" has the meaning set forth in Section 7.4(iii).

1.77 "**Publications**" has the meaning set forth in Section 11.3.

1.78 "**Recipient Party**" has the meaning set forth in Section 15.6.

1.79 "**Regulatory Authority**" means any national or supranational governmental authority, including without limitation the MHLW (i.e., the Japanese Ministry of Health, Labour and Welfare, or any successor agency thereto), or other governmental body that has responsibility in a given country or jurisdiction over the development, manufacture and/or commercialization of the Licensed Product.

1.80 "**Remaining Novan Patent**" means **[***]**.

1.81 "**Repeat Studies**" has the meaning set forth in Section 4.4.

1.82 "**Rules**" has the meaning set forth in Section 24.1.

1.83 "**Sales Report**" means with respect to each calendar quarter a report detailing:

(i) the number and description of Licensed Products sold or otherwise disposed of;

(ii) the relevant Gross Sales in the Licensed Territory invoiced by Sato or its Affiliates to Third Parties, including wholesalers, hospitals or other intermediate Third Parties, indicating the breakdown of sales by each type of the Licensed Product;

(iii) the deductions from Gross Sales used to calculate Net Sales;

(iv) the Net Sales in the Licensed Territory;

(v) the currency exchange rate used, if applicable; and

(vi) the sum of royalties due pursuant to Section 15.1.

1.84 "**Sato Confidential Information**" has the meaning set forth in Section 12.1(i).

1.85 "**Sato Efficacy Data**" means Sato Scientific Information relating to the efficacy of the Licensed Product, including, without limitation, all efficacy data and information included in all draft and final reports of any test, study or trial of Licensed Product. For clarity, Sato Efficacy Data excludes Sato Scientific Information relating to the safety of the Licensed Product, including, without limitation, the safety data and information included in all draft and final reports of any test, study or trial of Licensed Product.

1.86 "**Sato Improvements**" has the meaning set forth in Section 7.1.

1.87 "**Sato Indemnitees**" has the meaning set forth in Section 16.1.

1.88 "**Sato Scientific Information**" means the Scientific Information generated and/or compiled by or on behalf of Sato that is Controlled by Sato during the Term of this Agreement, that is necessary for the development, manufacture, use, sale, offer for sale and/or importation of Licensed Product in the Licensed Field.

1.89 "**Sato Know-How**" means Information that (i) is necessary for the development, manufacture, use, sale, offer for sale and/or importation of Licensed Product in the Licensed Field, and (ii) is within the Control of Sato during the Term of this Agreement or thereafter (if Section 20.1 applies). Notwithstanding anything herein to the contrary, Sato Know-How shall exclude Sato Patents, but shall include Sato Scientific Information.

1.90 "**Sato Patent**" means a Patent that claims inventions necessary for the development, manufacture, use, sale, offer for sale and/or importation of Licensed Product within the Licensed Field, and that is Controlled by Sato during the Term of this Agreement or thereafter (if Section 20.1 applies), including without limitation Sato's interest in any Joint Patents.

1.91 "**Sato Trademarks**" has the meaning set forth in Section 8.1.

1.92 "**Scientific Information**" means all Information relating to or comprising medical, toxicological, pharmacological, pre-clinical, clinical and chemical data; specifications; medical uses; adverse reactions; formulations; bioanalytical metrics; analytical and quality control data and methods; and all proprietary information submitted to relevant Regulatory Authorities to support a Drug Approval Application for and Marketing Approval of the Licensed Product in the Licensed Field in any country of the world.

1.93 "**Sole Inventions**" has the meaning set forth in Section 7.2.

1.94 "**Specifications**" means the specifications set forth in Annex 3 or, if applicable, the Modified Specifications.

1.95 "**Study Materials**" means any supplies of Licensed Product as well as placebos for use in developing the Licensed Product in the Licensed Field.

1.96 "**Term**" shall have the meaning set forth in Section 18.1.

1.97 "**Third Party**" means any person or corporation or unincorporated body other than Novan and Sato and their respective Affiliates, including, without being limited to, governmental bodies and authorities.

1.98 "**Third-Party Licensee**" has the meaning set forth in Section 2.10(i).

1.99 "**Third-Party Territory**" has the meaning set forth in Section 2.10(i).

1.100 "**Trademark Infringement**" has the meaning set forth in Section 8.2(v).

1.101 "**UNC**" means The University of North Carolina at Chapel Hill.

1.102 "**UNC IP**" has the meaning set forth in Section 2.7.

1.103 "**UNC License Agreement**" means that certain Amended, Restated and Consolidated License Agreement between Novan and UNC with an effective date of June 27, 2012 and as amended on November 30, 2012 and April 12, 2016, and as may be further amended from time to time.

1.104 "**USD**" means a United States Dollar.

1.105 "**U.S.**" means the United States of America, its territories and possessions.

1.106 "**Valid Claim**" means, for a country, a claim of an issued and unexpired Patent, or a Patent application filed in good faith, in each case, that is within the Novan Patents (including the Joint Patents), and that has not been held unpatentable, invalid, or unenforceable by a final unappealable decision of a court or other government agency of competent jurisdiction, in an unappealed or unappealable decision, admitted to be invalid or unenforceable through reissue, re-examination, disclaimer, or otherwise.

1.107 "**Withholding Taxes**" has the meaning set forth in Section 15.6.

2. GRANT OF LICENSE; RIGHT OF FIRST NEGOTIATION

2.1 License Grant to Sato. Subject to the terms and conditions of this Agreement, Novan hereby grants to Sato, and Sato accepts, an exclusive, royalty-bearing, non-transferable (except pursuant to Section 22.1) right and license under Novan Know-How and Novan Patents, with the right to grant sublicenses solely with Novan's prior written consent (not to be unreasonably withheld, delayed or conditioned), to develop, manufacture (but excluding

the manufacture of Compound as set forth in Section 5.4), use, sell, offer for sale, import, market, distribute and promote the Licensed Product in the Licensed Field and in the Licensed Territory. For clarity, the license granted under this Section 2.1 does not grant Sato any right to manufacture or have manufactured the Compound, or any right to use, sell, offer for sale or import the Compound except in connection with the development, manufacture or commercialization of Licensed Product in the Licensed Field in the Licensed Territory.

2.2 No Practice of Novan Patents and Novan Know-How Outside Scope of License Sato shall not, directly or through its Affiliates or sublicensees, practice the Novan Patents and Novan Know-How outside the scope of the license granted to it in Section 2.1.

2.3 License Grant to Novan Subject to the terms and conditions of this Agreement, Sato hereby grants to Novan and Novan accepts, an exclusive, fully paid-up, royalty-free, non-transferable (except pursuant to Section 22.1) right and license under Sato Know-How and Sato Patents, with the right to, subject to Sections 2.3(i) through 2.3(vii), grant sublicenses through multiple tiers of sublicensees, develop, manufacture, use, sell, offer for sale, import, market, distribute and promote the Licensed Product in the Licensed Field outside the Licensed Territory and within the Licensed Territory to manufacture Goods for sale outside the Licensed Territory (the "**Novan License**").

Each agreement between Novan and a sublicensee, or between Novan's sublicensees and their further sublicensees, granting a sublicense under the Novan License:

(i) shall be in writing and subject and subordinate to, and consistent with, the terms and conditions of this Agreement;

(ii) shall not diminish, reduce or eliminate any of Novan's obligations under this Agreement;

(iii) shall require the sublicensee(s) to comply with all applicable terms of this Agreement;

(iv) shall require further sublicensing to be done only on terms consistent with this Section 2.3, with Novan being responsible for the performance of each such sublicensee and ensuring that each sublicensee complies with all relevant provisions of this Agreement;

(v) for any sublicense to a Third Party, shall provide that such sublicense **[***]**, including, without limitation, the **[***]** unless and until either (a) **[***]**, or (b) **[***]**;

(vi) for any sublicense to a Third Party, shall provide that **[***]**, provided that the Novan Know-How shall include all Information **[***]** with respect to the Licensed Product; and

(vii) if Novan grants to any Third Party a sublicense under the license granted to Novan in this Section 2.3 or in Section 7.4(iii), other than with respect to **[***]** or with

respect to safety data (which is to be made available as set forth in Section 2.3(vi)), **[***]** based on (a) **[***]**, (b) **[***]**, and (c) **[***]**.

2.4 Joint Committee.

(i) **Membership**. Within **[***]** after the Effective Date, each Party shall appoint three (3) of its senior employees with appropriate expertise related to the then-ongoing activities in connection with Licensed Product in the Licensed Field to serve on the Joint Committee ("**JC**"). Each Party may replace its JC representatives by written notice to the other Party. For the first **[***]** following the Effective Date, a JC member appointed by Novan shall serve as chairperson of the JC. In each subsequent year commencing upon an anniversary of the Effective Date, the chairperson shall be appointed by the Party that did not appoint the chairperson for the immediately preceding year.

(ii) **Responsibilities**. The JC shall oversee the research, development, and commercialization of the Licensed Products in the Licensed Territory. In particular, the JC shall:

(a) coordinate the Parties' communications and exchange of Scientific Information and data regarding development and marketing activities pursuant to the Agreement as further specified in Articles 3, 4, 6, 7 and 9;

(b) review and serve as a forum for discussing the Development Plan and review and approve amendments thereto;

(c) review and approve any proposed changes to the Specifications for Licensed Products in the Licensed Territory in the Licensed Field; and

(d) perform such other functions as are set forth herein or as the Parties may mutually agree in writing, except where in conflict with any provision of this Agreement.

(iii) **JC Meetings**. The JC shall meet at least once every **[***]** prior to the First Commercial Sale of the Licensed Product in the Licensed Field in the Licensed Territory and at least **[***]** every year thereafter, in each case at times mutually agreed upon by the Parties. At least **[***]** of such meetings per calendar year shall be held in person, and all other such meetings may be held by teleconference or videoconference. The location of the meetings of the JC to be held in person shall be agreed upon by the Parties. Each Party shall bear all the expenses of its representatives on the JC.

(iv) **JC Decision-Making** The JC shall operate by unanimous consent of its members. Any disagreement between the representatives of the Parties on the JC as to matters within the JC's jurisdiction that remain unresolved for **[***]** shall, at the election of either Party's JC members, be submitted to the Parties' designated officers for resolution in accordance with Section 24.1. The JC shall not have the power to amend or waive compliance with this Agreement.

(v) **JC Meeting Agendas.** The JC chairperson shall be responsible for preparing and circulating an agenda in advance of each meeting of the JC, and preparing and issuing minutes of each meeting within **[***]** thereafter. Such minutes will not be finalized until both Parties' representatives on the JC review and confirm the accuracy of such minutes in writing. Sato shall provide a summary of its technical and other efforts made towards the First Commercial Sale of the Licensed Product in the Licensed Field in the Licensed Territory at each meeting of the JC and shall provide the JC with any updates that have occurred since the last meeting. Each Party will disclose to the other Party any other proposed agenda items along with appropriate information at least **[***]** in advance of each meeting of the JC; provided that, under exigent circumstances requiring the JC's input, a Party may provide its agenda items to the other Party within a lesser period of time in advance of the meeting so long as such other Party consents to such later addition of such agenda items for such JC meeting.

(vi) **Disbandment**. The JC shall continue to exist until the first to occur of (1) the Parties mutually agreeing in writing to disband the JC or (2) the expiration or termination of this Agreement.

2.5 No Other Licenses. Neither Party grants to the other Party any rights, licenses or covenants in or to any intellectual property, whether by implication, estoppel, or otherwise, other than the license rights that are expressly granted under this Agreement.

2.6 Retained Rights. Novan will at all times retain the exclusive and absolute right to practice and license the Novan Know-How and Novan Patents for any and all uses outside of the Licensed Field in the Licensed Territory, and for all uses outside the Licensed Territory.

2.7 Upstream Agreement. Sato hereby acknowledges and agrees that all licenses granted by Novan under this Article 2, to the extent they constitute sublicenses under intellectual property rights owned or controlled by UNC and licensed to Novan under the UNC License Agreement (the **"UNC IP"**), are subject to the limitations set forth in, and other relevant terms and conditions of, the UNC License Agreement.

2.8 Non-Compete. During the Term of this Agreement, Sato and its Affiliates shall not, directly or indirectly (by itself or with or through any Third Party), conduct outside the scope of this Agreement any commercialization of any Competing Product in the Licensed Territory.

2.9 Third-Party Information, Scientific Information or Patents If, after the Effective Date, either Party enters into an agreement or other arrangement to obtain a license or other rights to or under Information or Patents that are owned or controlled by a Third Party and that would, solely but for the operation of Section 1.17, in the case of Novan be included in the Novan Know-How or Novan Patents or, in the case of Sato, be Sato Know-How or Sato Patents, then the Party obtaining such license or rights shall promptly notify the other Party and shall specify in such notice the type and amount of payments that would be due to such Third Party by reason of the practice or use of, or access to, such Information or Patents by the other Party pursuant to the license set forth in Section 2.1 or 2.3, as applicable (but not by reason of the

practice or use of, or access to, such Information or Patents outside the scope of such license). The Party receiving such notice may elect in writing to bear the responsibility for such additional payments, and upon such receiving Party's written election to bear such responsibility, the Information, Scientific Information, or Patents as applicable, shall thereafter be deemed "**Controlled**" by the Party originally obtaining such license or rights (notwithstanding Section 1.17), and shall be subject to the license under Section 2.1 or 2.3, as applicable.

2.10 Exclusivity Period; Exclusive Option for Negotiation of Additional Licensed Territories.

(i) **Option**. Subject to the terms and conditions of this Agreement, Novan hereby grants to Sato the exclusive option to elect by written notice to Novan during the Option Period to negotiate to acquire an exclusive license under Novan Know-How and Novan Patents with the right to grant sublicenses solely with Novan's prior written consent (not to be unreasonably withheld, delayed or conditioned), to develop (including to obtain relevant Marketing Approvals), manufacture, use, sell, offer for sale, import, market, distribute and promote the Licensed Product in the Licensed Field in one or more countries in the Additional Licensed Territories (the "**Option**"). In consideration for the grant of the Option, Sato shall pay to Novan the Option Exercise Fee within **[***]** after **[***]**. For clarity, prior to the Option Period, Novan shall retain the right to license the Novan Know-How and Novan Patent to a Third Party (a "**Third-Party Licensee**") to develop, manufacture, use, sell, offer for sale, import, market, distribute and promote the Licensed Product in the Licensed Field in one or more countries in the Additional Licensed Territories (the "**Third-Party Territory**"). In the event Novan enters into such an agreement with a Third-Party Licensee, Sato's Option hereunder shall not be exercisable with respect to that Third-Party Territory.

(ii) **Exercise of Option** Subject to Section 2.10(i), Sato may, in its sole discretion, exercise the Option at any time during the Option Period by written notice of such exercise to Novan prior to the expiration of the Option Period. If Sato so exercises the Option, the Parties shall negotiate in good faith until the expiration of the Option Period or until the Parties enter into the Additional License Agreement, whichever is earlier the terms pursuant to which Sato would obtain an exclusive license to develop and commercialize the Licensed Product in the Licensed Field in the Additional Licensed Territories (excluding the Third-Party Territory) (such license, the "**Additional License Agreement**"). If the Parties do not enter into an Additional License Agreement within the Option Period, then Novan shall be free to grant such rights to one or more Third Parties with no further obligation to Sato**.**

3. DILIGENCE

3.1 Diligence of Sato. Sato shall (a) use Commercially Reasonable Efforts to develop the Licensed Product in the Licensed Field in the Licensed Territory in accordance with the Development Plan, and (b) shall develop the Licensed Product in the Licensed Field in the Licensed Territory in accordance with the requirements of this Agreement and in conformity with all applicable Laws. Sato's obligations under this Section 3.1 shall include, but not be limited to, the following:

(i) using Commercially Reasonable Efforts to submit a New Drug Application for the Licensed Product in th Licensed Field with the PMDA (a "**JNDA**") as soon as reasonably practical after the Effective Date; and

(ii) using Commercially Reasonable Efforts to obtain, and once obtained, to maintain, Marketing Approval for the Licensed Product in the Licensed Field in the Licensed Territory.

3.2 Diligence of Novan Novan shall use Commercially Reasonable Efforts to obtain Marketing Approval for the Licensed Product in the Licensed Field in the U.S. Novan shall also use Commercially Reasonable Efforts to provide Sato, at Sato's request, with reasonable assistance **[***]**, relating to Sato's development of the Licensed Product and obtainment of Marketing Approvals for the Licensed Product in the Licensed Field in th Licensed Territory; provided that if the assistance required by Sato pursuant to the immediately preceding sentence requires **[***]**, then Novan shall be obligated to **[***]**.

4. DEVELOPMENT AND COMMERCIALIZATION OF LICENSED PRODUCT

4.1 PMDA Consultation Within **[***]** after Sato's receipt of Novan Scientific Information pursuant to Section 6.1, Sato shall use Commercially Reasonable Efforts to visit and start consultation with PMDA with respect to development of and obtainment of the Marketing Approval for the Licensed Product in the Licensed Field in the Licensed Territory. Novan shall, at Sato's request, reasonably cooperate with Sato in such PMDA consultation (including but not limited to by attending such PMDA consultation) at Novan's expense.

4.2 Development Plan Within **[***]** after the completion of the PMDA consultation described in Section 4.1, Sato shall submit a development plan ("**Development Plan**") to the JC for review and approval. The Development Plan shall, at all times, contain (a) detailed plans of Sato's studies to support obtaining or maintaining Marketing Approval of the Licensed Product in the Licensed Field in the Licensed Territory, including study designs, CMC/process development protocols, summaries of nonclinical study protocols, and summaries of clinical study protocols, summaries of post-approval study protocols; and (b) a detailed timeline for achieving each key milestone in the development of the Licensed Product in the Licensed Field in the Licensed Territory and target dates for regulatory submissions to a Regulatory Authority with respect to the Licensed Product in the Licensed Field. The Development Plan shall be reviewed **[***]** after the first submission by Sato to Novan, and any material amendment to the Development Plan shall be subject to the JC's prior written approval, which approval shall not be unreasonably withheld.

4.3 Modified Specifications. Sato may propose modifications to the Specifications for the Licensed Product in the Licensed Field. The JC shall discuss any such proposed modifications and the bases therefor. If the JC approves such modification, then the Specifications shall be updated as approved by the JC ("**Modified Specifications**"). For clarity, Novan shall have no obligation to modify the specifications for Licensed Product in the Licensed

Field outside the Licensed Territory if any Modified Specifications are adopted for the Licensed Product in the Licensed Field in the Licensed Territory.

4.4 JNDA. During the Term, Sato will be responsible for conducting all activities necessary to support the submission of the JNDA. Sato will submit the JNDA utilizing pre-clinical information included in the Novan Scientific Information. In the event that the PMDA determines, documented in official, written correspondence with Sato, that the applicable Pre-Clinical Studies are not sufficient for approval of the JNDA, then the JC sha decide whether the applicable Pre-Clinical Studies should be repeated. If the JC determines that such Pre-Clinical Studies should be repeated (such repeate Pre-Clinical Studies, the "**Repeat Studies**"), Novan shall perform such Repeat Studies at Novan's expense, provided that in no event shall Novan be required to spend more than one million ($1,000,000) USD with regard to all Repeat Studies in the aggregate. Sato agrees that Novan owns the data and results of any such Repeat Study. Other studies for Licensed Product in the Licensed Field, including the implementation of, cost sharing for, and ownership of data resulting from such studies, shall be discussed by the JC. Novan may, at its discretion, elect to participate in the funding and conduct of any such studies.

4.5 Costs. Sato shall have full responsibility for all development and commercialization activities for the Licensed Product in the Licensed Field in the Licensed Territory, including, without limitation, all activities in Sections 4.4 and 4.7, at Sato's expense (unless otherwise provided in this Agreement) and risk and in accordance with the terms of this Agreement and in conformity with all applicable Laws.

4.6 Marketing. Sato shall commence the marketing of the Licensed Product in the Licensed Field under either the Nova Trademark or another trademark selected and owned or Controlled by Sato, as Sato in its sole discretion shall decide and as set forth in Article 8, in the Licensed Territory within **[***]** after the first **[***]** of the Licensed Product in the Licensed Field is listed. Sato shall notify Novan promptly of the date of Firs Commercial Sale of the Licensed Product in the Licensed Field in the Licensed Territory.

4.7 Launch. After receiving Marketing Approval of the Licensed Product in the Licensed Field in the Licensed Territory, Sat shall use Commercially Reasonable Efforts to market, sell and promote the Licensed Product in the Licensed Field in the Licensed Territory.

Specifically, and without limiting any of Sato's obligations under Sections 4.6 or 4.7, Sato shall (a) launch commercially a Licensed Product in the Licensed Field in the Licensed Territory no later than **[***]** after receipt of Marketing Approval for such Licensed Product in the Licensed Field in the Licensed Territory, and (b) not withdraw a Licensed Product from sale or abandon for more than **[***]** the sale of a Licensed Product, provided that Sato shall not be in breach of the foregoing obligations to the extent that Sato's failure to launch or abandonment of the Licensed Product as described above results from a **[***]**, as applicable, including without limitation if **[***]**, and further provided that to the extent that Section 21.1 applies to prevent Sato from complying with its obligations under this Section 4.7, then Sato shall not be deemed in breach of this Section 4.7 and the Parties shall have the rights and obligations set forth in Section 21.1.

4.8 Communications. The JC will coordinate communications regarding certain aspects of the Parties' marketing efforts for Licensed Product in the Licensed Field as follows. Through the JC:

(i) Novan shall share with Sato **[***]** any and all of the marketing information in the Control of Novan with respect to the Licensed Product in the Licensed Field, including without limitation, complete promotion plans and strategies, as well as all promotional and sales materials used for the launch and marketing of the Licensed Product in the Licensed Field outside the Licensed Territory.

(ii) Sato shall share with Novan **[***]** any and all of marketing information in the Control of Sato with respect to Licensed Product in the Licensed Field, including without limitation, complete promotion plans and strategies, as well as all promotional and sales activities and materials used for the launch and marketing of the Licensed Product in the Licensed Field in the Licensed Territory.

4.9 Approvals. Sato shall (i) use Commercially Reasonable Efforts not to abandon or allow to lapse any Drug Approval Application for a Licensed Product in the Licensed Field in the Licensed Territory, and (ii) not abandon or allow to lapse any Marketing Approval for the Licensed Product in the Licensed Field in the Licensed Territory.

5. MANUFACTURING & SUPPLY

5.1 Development Supply. Novan shall, by itself or through its Third Party contract manufacturer, supply to Sato, and Sato shall purchase from Novan, all quantities of Study Materials required by Sato to develop the Licensed Product in the Licensed Field in the Licensed Territory.

5.2 Pricing. Sato will purchase the Study Materials at a price equal to the Fully Burdened Manufacturing Cost thereof. The other terms concerning sales and purchase of the Study Material shall be separately determined after the completion of the PMDA consultation pursuant to Section 4.1 and set forth in a clinical supply agreement between the Parties.

5.3 Payment. Novan will invoice Sato for each delivery of Study Materials. Payment is due **[***]** after the date of receipt of invoice by Sato. All payments under this Section 5.3 shall be made in USD.

5.4 Commercial Supply. Within **[***]** after the conclusion of the PMDA consultation described in Section 4.1, the Parties shall commence negotiations of a commercial supply agreement that shall govern Novan's supply of Compound to Sato for Sato's manufacture of the Licensed Product (the "**Commercial Supply Agreement**"). The Parties shall use Commercially Reasonable Efforts to conclude negotiations of such Commercial Supply Agreement within **[***]** after they commence such negotiations. Both Parties understand that the Commercial Supply Agreement shall be modified, if necessary, consistent with the conditions of the Marketing Approval in the Licensed Territory. Pursuant to the Commercial Supply Agreement, Novan shall be obligated, by itself or through its Third Party contract

manufacturer, to supply to Sato, and Sato shall be required to purchase Compound at a price [***] equal to [***] of Licensed Product in the Licensed Territory, provided that such price per gram shall not be less than an amount equal to the Base Price (as defined below). The "**Base Price**" shall mean the USD value of [***] of Compound supplied, calculated using the Conversion Rate. For example, if [***] of Licensed Product in the Licensed Territory is [***], then Sato shall be required to purchase Compound at a price [***] of [***], provided that such price [***] is not less than an amount equal to the Base Price at the time such payment is due. All payments under the Commercial Supply Agreement shall be made in JPY.

5.5 Negotiations for Supply of Licensed Products At any time, Sato may propose in writing to negotiate the terms and conditions pursuant to which it would purchase from Novan necessary volumes of the finished Licensed Products to be sold in the Licensed Field in the Licensed Territory, and the Parties shall negotiate in good faith such terms and conditions; provided that no such terms and conditions shall become effective without the mutual written consent of the Parties (the agreement with such effective terms and conditions, the "**Product Supply Agreement**").

5.6 Appointment of Distributors; No Delivery or Sale for Use Outside Licensed Territory Sato may at its discretion appoint distributors or wholesalers for the Licensed Product in the Licensed Field in the Licensed Territory. Throughout the Term, Sato shall not, and shall use Commercially Reasonable Efforts (consistent with any applicable Law) to obligate its distributors or wholesalers to not, deliver or cause to be delivered including via the Internet or mail order, Licensed Product either outside the Licensed Field in the Licensed Territory, or outside the Licensed Territory, and to not sell any Licensed Product to a purchaser if in either case Sato, its approved distributors or wholesalers knows, or has reason to believe, that such purchaser intends to sell such Licensed Product outside the Licensed Field in the Licensed Territory or to remove such Licensed Product from the Licensed Territory for the purpose of sales or use by patients of the Licensed Product outside the Licensed Territory.

6. EXCHANGE OF SCIENTIFIC INFORMATION

6.1 Technology Transfer. Within [***] after the Effective Date, Novan shall deliver to Sato a copy of all Novan Scientific Information listed in Annex 1 that is available in tangible form as of the Effective Date. Novan shall deliver to Sato copies of Novan Scientific Information that is necessary for the development, manufacture or commercialization of the Licensed Product in the Licensed Field in the Licensed Territory becomes available in tangible or written form after the Effective Date, as may be mutually agreed upon by the Parties.

6.2 Communication by Novan Relating to Material Events Whenever any material event occurs in the course of the development of the Licensed Product in the Licensed Field by Novan or Novan Licensees of which Novan becomes aware, but in no event less than [***] until such time as Sato receives Marketing Approval for the Licensed Product in the Licensed Field in the Licensed Territory, Novan shall disclose to Sato all Novan Scientific Information resulting from all development activities with respect to the Licensed Product in the Licensed Field conducted by Novan or its Affiliates as may be necessary or useful for

development of the Licensed Product in the Licensed Field in the Licensed Territory, and a description of the status of such development efforts.

6.3 Communication by Sato Relating to Material Events Whenever any material event occurs in the course of the development of the Licensed Product by Sato, but in no event less than **[***]** during the Term of this Agreement, Sato shall disclose to Novan all Sato Scientific Information resulting from all development activities with respect to the Licensed Product in the Licensed Field conducted by Sato or its Affiliates, and a description of the status of such development efforts.

6.4 Use of Scientific Information Each Party shall have the right, at no additional expense, to use all Scientific Information disclosed to it pursuant to Section 6.2 or Section 6.3, as applicable, for the development and commercialization of the Licensed Product pursuant to the license granted to it in Sections 2.1 and 2.3.

6.5 Right of Cross-Reference Novan, its Affiliates and Novan Licensees shall have the right to cross-reference, for purposes of developing Licensed Products outside of the Licensed Territory or in the Licensed Territory outside the Licensed Field, all Drug Approval Applications and other filings with Regulatory Authorities made by Sato for Licensed Products, subject to Section 2.3 (for clarity, for **[***]**, this Section 6.5 applies, as to **[***]**). Sato shall have the right to cross-reference, for purposes of developing Licensed Products in the Licensed Field in the Licensed Territory, all Drug Approval Applications and other filings with Regulatory Authorities made by Novan or, to the extent Controlled by Novan and as long as Novan would not incur costs to grant such a right to cross-reference to Sato, the Novan Licensees.

6.6 Communication Through Joint Committee The JC shall coordinate the Parties' sharing of Scientific Information as required under this Agreement. Through the JC:

(i) Novan shall share with Sato, **[***]**, any and all Novan Scientific Information generated or compiled during the Term of this Agreement for use in development and commercialization of the Licensed Product in the Licensed Field in the Licensed Territory.

(ii) Sato shall share with Novan, **[***]**, any and all Sato Scientific Information generated or compiled during the Term of this Agreement for use in development and commercialization of the Licensed Product outside of the Licensed Territory or within the Licensed Territory outside the Licensed Field.

6.7 Ownership of Novan Scientific Information Sato agrees that all Novan Scientific Information delivered by Novan or any of its Affiliates or Novan Licensees hereunder shall, as between the Parties, at all times be and remain sole and exclusive property of Novan, or its Affiliates or Novan Licensees, respectively.

6.8 Ownership of Sato Scientific Information Novan agrees that all Sato Scientific Information delivered by Sato or any of its Affiliates hereunder shall, as between the Parties, at all times be and remain sole and exclusive property of Sato or its Affiliates, respectively.

7. INVENTIONS; ACCESS TO IMPROVEMENTS; PATENTS

7.1 Improvements. Novan shall have the right to grant sublicenses under Section 2.3 according to the terms therein with respect to Sato Know-How and Sato Patents that constitute Improvements ("**Sato Improvements**").

7.2 Ownership of Inventions. Inventorship shall be determined in accordance with U.S. patent laws. Any Invention made solely by employees, agents, or independent contractors of a Party in the course of performing activities under this Agreement, together with all intellectual property rights therein ("**Sole Inventions**") shall be owned by such Party. Any Invention made jointly by employees, agents, or independent contractors of each Party, together with all intellectual property rights therein ("**Joint Inventions**") shall be owned jointly by the Parties in accordance with joint ownership interests of co-inventors under U.S. patent laws, with each joint Party having, unless otherwise set forth in this Agreement, the unrestricted right to license and grant rights to sublicense any such Joint Invention without any duty of accounting to the other Party.

7.3 Disclosure of Inventions. Each Party shall promptly disclose to the other Party in writing any Invention disclosures, or other similar documents, submitted to it by its employees, agents, or independent contractors describing each and every Invention that may be either a Sole Invention or a Joint Invention, and all Information relating to such Invention.

7.4 Prosecution of Patents.

(i) **Novan Patents Other than Joint Patents**. Novan shall have the sole right and authority to file, prosecute, and maintain Novan Patents other than Joint Patents on a worldwide basis at its sole discretion and at its own cost. Novan shall provide Sato with a copy of material communications from patent authorities in the Licensed Territory regarding the Novan Patents, and shall provide drafts of any material filings or responses to be made to such Patent authorities in a timely manner. Novan may **[***]** a Novan Patent in the Licensed Territory **[***]**. For any Novan Patent that Novan is filing, prosecuting or maintaining, Novan shall do so at its own cost.

(ii) **Sato Patents Other than Joint Patents** Sato shall have the first right and authority to file, prosecute, and maintain Sato Patents other than Joint Patents on a worldwide basis at its sole discretion and at its own cost. Sato shall provide Novan with a copy of material communications from patent authorities in the Licensed Territory regarding the Sato Patents, and shall provide drafts of any material filings or responses to be made to such Patent authorities in a timely manner. Notwithstanding the foregoing, if Sato determines in its sole discretion to abandon or not maintain a Sato Patent other than a Joint Patent, Sato shall provide Novan with **[***]** prior written notice of such determination and, if Novan so requests, shall provide Novan with the opportunity to prosecute and maintain such Sato Patent in the name of Sato. Thereafter, Novan shall bear all expenses of filing, prosecuting and maintaining such Sato Patent.

(iii) **Joint Patents**. Subject to this Section 7.4(iii) and (a) unless otherwise agreed by the Parties Sato will prosecute and maintain any Patent applications Covering a Joint Invention (any such Patent application and any Patents issuing therefrom, a "**Joint Patent**") in the Licensed Territory and (b) Novan shall have the first right to prosecute and maintain the Joint Patents outside the Licensed Territory, with Sato having a backup right to do so if Novan elects to cease such prosecution and maintenance on **[***]** prior written notice to Sato. The Parties shall coordinate their efforts as appropriate to make such prosecution activities as efficient, convenient, and harmonious as possible. The Parties shall share equally all expenses of filing, prosecuting and maintaining such Joint Patents in the Licensed Territory. **[***]** of filing, prosecuting and maintaining such Joint Patents outside the Licensed Territory. **[***]** of filing, prosecuting and maintaining the Joint Patents outside the Licensed Territory pursuant to this Section 7.4(iii), Sato hereby grants Novan an exclusive, fully paid-up, royalty-free, non-transferable (except pursuant to Section 22.1) license, with the right to grant sublicenses through multiple tiers of sublicensees, under Sato's interest in the Joint Patents for all purposes outside of those within the scope of the rights granted to Novan under Section 2.3, subject to the last sentence of this Section 7.4(iii). The Party that prosecutes a Joint Patent (the "**Prosecuting Party**") in the Licensed Territory shall provide the other Party the opportunity to review and comment on any and all such prosecution efforts regarding the applicable Joint Patent in the Licensed Territory, provided that the Prosecuting Party shall have final control over such prosecution efforts after reasonably considering the other Party's comments, if any. The Prosecuting Party for a Joint Patent in any jurisdiction shall provide the other Party with a copy of all material communications from any Patent authority in the applicable jurisdictions regarding the Joint Patent being prosecuted by such Party, and shall provide drafts of any material filings or responses to be made to such patent authorities a reasonable amount of time in advance of submitting such filings or responses. In particular, each Party agrees to provide the other Party with all information necessary or desirable to enable the other Party to comply with any duty of candor and/or duty of disclosure requirements of any Patent authority. Notwithstanding anything to the contrary, the Prosecuting Party shall not take any action while prosecuting or maintaining the applicable Joint Patent that could reasonably be expected to have a materially detrimental effect on the other Party's interest in such Joint Patent or any Novan Patent. Except to the extent a Party is restricted by the licenses granted by such Party to the other Party under the terms of this Agreement, and/or the other covenants contained in this Agreement, each Party shall be entitled to practice, and grant licenses to Third Parties and Affiliates of such Third Parties to practice, the Joint Patents and all Joint Inventions without restriction or an obligation to account to the other Party, and the other Party shall consent and hereby consents, without additional consideration, to any and all such licenses. Notwithstanding the foregoing, if Novan grants a sublicense under the license granted to Novan pursuant to this Section 7.4(iii), then Section 2.3(vii) will apply.

(iv) **Cooperation in Prosecution** Each Party shall provide the other Party all reasonable assistance and cooperation in the Patent prosecution efforts described above in this Section 7.4, including without limitation providing any necessary power of attorney and executing any other required documents or instruments for such prosecution.

7.5 Infringement of Patents by Third Parties.

(i) **Notification**. Each Party shall promptly notify the other Party in writing of any existing or threatened infringement of the Novan Patents (including Joint Patents) of which it becomes aware in the Licensed Territory, and shall provide to the other Party any and all evidence and information available to such Party regarding such alleged infringement.

(ii) **Product Infringement of Novan Patents (Including Joint Patents) in the Licensed Field in the License Territory**.

(a) If a Party becomes aware of any actual or alleged existing or threatened infringement by a Third Party of any Novan Patent, including any Joint Patent, by making, using, importing, offering for sale, or selling the Licensed Product in the Licensed Field (such activities, "**Product Infringement**") in the Licensed Territory, such Party shall notify the other Party as provided in Section 7.5(i).

(b) With respect to Product Infringement of Novan Patents excluding Joint Patents, subject to Section 7.11, **[***]** an appropriate suit or other action against any Person engaged in such Product Infringement in the Licensed Territory, subject to Section 7.5(ii)(d), provided that if **[***]**, it shall **[***]**. **[***]** shall provide to **[***]** reasonable assistance in any such enforcement, including without limitation joining an action as a party plaintiff if so required by Laws to pursue such action. **[***]** shall keep **[***]** regularly informed of the status and progress of such enforcement efforts, and shall reasonably consider **[***]**'s comments on any such efforts. **[***]** shall **[***]** in connection with each Party's activities under this Section 7.5(ii)(b), provided that **[***]** pursuant to this Agreement, **[***]**, **[***]** and **[***]** shall **[***]**. **[***]** may **[***]** under this Section 7.5(ii)(b) **[***]**, provided that **[***]** pursuant to this Agreement.

(c) With respect to Product Infringement of Joint Patents, Sato shall have a period of **[***]** (or any such shorter period described in Section 7.5(ii)(b)) after the notification to or by Sato pursuant to Section 7.5(ii)(a), to elect to so enforce such Joint Patent in the Licensed Territory, subject to Section 7.5(ii)(d). If Sato does not so elect, Sato shall so notify Novan in writing during such **[***]** period, but in no event later than **[***]** prior to any deadline relating to loss of any rights with respect to the Product Infringement, whichever is earlier, in which case Novan shall have the right, but not the obligation, to commence a suit or take action to enforce such Joint Patent against the Third Party(ies) allegedly perpetrating such Product Infringement. Each Party shall provide to the Party enforcing any such rights under this Section 7.5(ii)(c) reasonable assistance in such enforcement, including without limitation joining an action as a party plaintiff if so required by Laws to pursue such action. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts, and shall reasonably consider the other Party's comments on any such efforts. The Parties shall equally bear and be responsible for all costs incurred in connection with enforcing the Joint Patents under this Section 7.5(ii)(c).

(d) The Party not bringing an action with respect to Product Infringement under this Section 7.5 shall be entitled to separate representation in such matter by

counsel of its own choice and at its own expense, but such Party shall at all times cooperate fully with the Party bringing such action. Additionally, the Party not bringing an action under this Section 7.5 may have an opportunity to participate in such action to the extent that the Parties may mutually agree at the time the other Party elects to bring an action hereunder.

(iii) **Other Infringement of Novan Patents (Including Joint Patents) Outside the Licensed Field in th Licensed Territory and Outside the Territory**.

(a) For any and all infringement of Novan Patents other than Joint Patents anywhere outside the Licensed Territory, and for any and all infringement other than Product Infringement of the Novan Patents (other than Joint Patents) in the Licensed Territory Novan shall have the sole and exclusive right, but not the obligation, to bring an appropriate suit or other action against any person or entity engaged in such infringement of such Patents, in its sole discretion, and as between the Parties Novan shall bear all related expenses and retain all related recoveries. If Novan brings a suit or other action against such infringement, Novan shall periodically make a report to Sato about the state of the progress of the suit or action.

(b) If a Third Party infringes a Joint Patent outside the Licensed Territory, Novan shall have the sole and exclusive right, but not the obligation, to bring an appropriate suit or other action against any person or entity engaged in such infringement of such Joint Patent, in its sole discretion, and as between the Parties Novan shall bear all related expenses and retain all related recoveries. Sato shall provide to Novan reasonable assistance in such enforcement, at Novan's request and expense, including without limitation joining such action as a party plaintiff if so required by Laws to pursue such action.

(iv) **Settlement**. Subject to Section 7.11, Sato shall not settle any claim, suit, or action that it brings under this Section 7.5 involving Novan Patents (excluding Joint Patents) in any manner that would negatively impact Novan, including settlements involving the ownership validity or enforceability of any of the Novan Patents, or that do not include a full and unconditional release from all liability of Novan, without the prior written consent of Novan, which shall not be unreasonably withheld, delayed or conditioned. Novan shall not settle any claim, suit, or action that it brings under this Section 7.5 involving Novan Patents (excluding Joint Patents) in the Licensed Territory in any manner that would negatively impact Sato, or that do not include a full and unconditional release from all liability of Sato, without the prior written consent of Sato, which shall not be unreasonably withheld, delayed or conditioned. Moreover, any settlement by Sato involving Novan Patents (excluding Joint Patents), or by Novan involving Novan Patents (excluding Joint Patents) in the Licensed Territory, that (i) results in cross-licensing or (ii) results in sublicenses to Third Parties, shall require the other Party's written consent, which shall not be unreasonably withheld, delayed or conditioned. Neither Party shall settle any claim, suit, or action that it brings under this Section 7.5 involving Joint Patents in any manner that would negatively impact the other Party, including settlements on the ownership, validity or enforceability of any of the Joint Patents, or if the settlement does not include a full and unconditional release from all liability of the other Party, without the prior written consent of such other Party.

(v) **Allocation of Proceeds**. Except as otherwise provided herein, if either Party recovers monetary damages from any Third Party in a suit or action brought under this Section7.5, whether such damages result from the infringement of Sato Patents or Novan Patents, such recovery shall be **[***]** in such litigation (excluding expenses of internal counsel), and any **[***]**.

7.6 Infringement of Third Party Rights in the Licensed Territory.

(i) **Notice**. If the development, manufacture, use, sale, offer for sale, import or export of the Licensed Product in the Licensed Field and in the Licensed Territory results in a claim for Patent infringement by a Third Party, the Party first having notice of such claim shall promptly notify the other Party in writing of such a claim. Following such notice, the Parties agree to enter into either a joint defense or common interest agreement, under which agreement the Parties can share the known facts of such infringement in reasonable detail, if they are advised to do so by counsel.

(ii) **Third Party Claims**. Sato shall assume control of the defense of any claims brought by Third Parties alleging infringement of Third Party intellectual property rights in connection with the development, manufacture, use, sale, offer for sale, import or export of the Licensed Product in the Licensed Field in the Licensed Territory, represented by its own counsel. If requested by Sato, Novan agrees to cooperate reasonably with Sato with respect to such litigation, at Sato's expense. Sato shall have the exclusive right to settle any such claim without the consent of Novan, unless such settlement could negatively impact Novan, including without limitation settlements on the ownership, validity or enforceability of any Novan Patents (for which Novan's consent shall be required). Any expenses incurred in defending any such claims and any damages awarded to or settlement agreed with such Third Parties shall be **[***]**, provided that **[***]**, provided that **[***]**.

7.7 Patent Oppositions and Other Proceedings.

(i) **By the Parties**. If either Party desires to bring an opposition, action for declaratory judgment, nullity action, interference, declaration for non-infringement, reexamination, or other attack upon the validity, title, or enforceability of a Patent owned or controlled by a Third Party that Covers, in the Licensed Territory, the Licensed Product in the Licensed Field, or the manufacture, use, sale, offer for sale, or importation of the Licensed Product in the Licensed Field (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, a Third Party's claim or assertion of infringement under Section 7.6, in which case the provisions of Section 7.6 shall govern), such Party shall so notify the other Party, and the Parties shall promptly confer to determine whether to bring such action or the manner in which to settle such action. **[***]** shall have the first right, but not the obligation, to bring in its sole control and at its sole expense such action in the Licensed Territory. If **[***]** does not bring such action within **[***]** of notification thereof pursuant to this Section 7.7 (or earlier, if required by the nature of the proceeding), then **[***]** shall have the right, but not the obligation, to bring, in **[***]** sole control and at its sole expense, such action. The Party not bringing an action under this Section 7.7 shall join the action as a joint party plaintiff if required to enable the other Party to bring such action, at the other Party's expense. Additionally, if

appropriate, the Party not bringing an action under this Section 7.7 shall be entitled to separate representation, at its sole expense, in such proceeding by counsel of its own choice, and shall cooperate fully with the Party bringing such action. Any awards or amounts received in bringing any such action shall **[***]**, and any **[***]**.

(ii) **By Third Parties**.

(a) If a Novan Patent (excluding a Joint Patent) becomes the subject of any proceeding commenced by a Third Party in the Licensed Territory in connection with an opposition, reexamination request, action for declaratory judgment, nullity action, interference, or other attack upon the validity, title or enforceability thereof (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, an action for infringement against a Third Party under Section 7.5, in which case the provisions of Section 7.5 shall govern), then **[***]** shall control such defense at its sole cost. Upon **[***]** request, **[***]** shall reasonably cooperate with **[***]** in such defense at **[***]** cost. Subject to Section 7.11, **[***]** shall permit **[***]** to participate in the proceeding to the extent permissible under Laws, and to be represented by its own counsel in such proceeding, at **[***]** sole expense.

(b) If a Joint Patent becomes the subject of any proceeding commenced by a Third Party in the Licensed Territory in connection with an opposition, reexamination request, action for declaratory judgment, nullity action, interference, or other attack upon the validity, title or enforceability thereof (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, an action for infringement against a Third Party under Section 7.5, in which case the provisions of Section 7.5 shall govern), then **[***]** shall control such defense at its sole cost. Upon **[***]** request, **[***]** shall reasonably cooperate with **[***]** in such defense at **[***]** cost. Subject to Section 7.11, **[***]** shall permit **[***]** to participate in the proceeding to the extent permissible under Laws, and to be represented by its own counsel in such proceeding, at **[***]** sole expense.

(c) Except as set forth in Sections 7.7(ii)(a) or 7.7(ii)(b) above, all expenses incurred by the Parties in an applicable action under Sections 7.7(ii)(a) or 7.7(ii)(b) shall **[***]**. Any awards or amounts received in defending any such Third Party action, if any, shall **[***]**, as if the **[***]**.

7.8 Patent Term Extensions in the Territory. The patent counsel of each Party shall discuss and recommend for which, if any, of the Novan Patents in the Licensed Territory the Parties should seek any term extensions, supplementary protection certificates, and equivalents thereof offering Patent protection beyond the initial term with respect to any issued Patents ("**Patent Term Extensions**") in the Licensed Territory. Subject to Section 7.11, Sato shall have the final decision-making authority with respect to applying for any such Patent Term Extensions in the Licensed Territory, provided that Sato shall not unreasonably fail or refuse to do so, and shall have the sole right to apply for any such Patent Term Extensions Sato decides to seek, at its expense. Novan shall cooperate fully with Sato, at Sato's expense, in making such filings or taking any related actions, for example and without limitation, making available all required regulatory data and information and executing any required authorizations to apply for such Patent Term Extension.

7.9 Orange Book Equivalent. Upon request of Sato and at Sato's expense, to the extent that Sato shall not have the right to itself do so, Novan shall file appropriate information with Regulatory Authorities in the Licensed Territory listing any Novan Patents with such Regulatory Authorities in the equivalent of the U.S. Orange Book, if any, as a Patent related to the Licensed Product. Novan shall use Commercially Reasonable Efforts to maintain such listing, at Sato's expense.

7.10 Patent Marking. Sato agrees to mark or have marked with the Novan Patents to the extent consistent with applicable Laws any Licensed Product sold by Sato in accordance with the statutes of the Licensed Territory relating to the marketing of patented articles.

7.11 Rights and Obligations Under UNC License Agreement Notwithstanding anything to the contrary in this Article 7, to the extent the provisions of this Article 7 conflict with Novan's rights and obligations under the UNC License Agreement with respect to UNC IP, the terms and conditions of the UNC License Agreement shall prevail. In such case, the Parties shall discuss in good faith to determine a reasonable solution that may best reflect the Parties original intentions under Article 7.

8. TRADEMARKS

8.1 General. Sato shall be responsible for the selection, registration and maintenance of all trademarks which it employs in connection with the commercialization of any Licensed Product in the Licensed Field in the Licensed Territory under this Agreement, other than the Novan Trademarks (the "**Sato Trademarks**"). Sato shall solely own the Sato Trademarks and pay all relevant costs thereof. Sato shall not select, register or otherwise use any trademark that is the same as or confusingly similar to, misleading or deceptive with respect to or that dilutes any of the Novan Trademarks. Novan shall not use any trademark that is the same as or confusingly similar to, misleading or deceptive with respect to or that dilutes any of the Sato Trademarks. Sato shall have the sole right to initiate at its own discretion legal proceedings against any infringement or threatened infringement of any Sato Trademark.

8.2 Election to Use Novan Trademarks. Sato shall inform Novan in writing if Sato elects to use the Novan Trademarks, or equivalent thereof, in the Licensed Territory, in connection with the commercialization of the Licensed Product in the Licensed Field in the Licensed Territory, and Novan shall have the right to approve, at its sole discretion, such use of the Novan Trademarks, including approval of the size, position, and location thereof on the Licensed Product or its components. If Novan so provides its approval, the Parties shall enter into an agreement setting forth the terms and conditions of Sato's use of such Novan Trademarks, subject to Section 8.1, which agreement shall include the following:

(i) Novan shall and hereby does grant to Sato an exclusive, royalty-free license to use the Novan Trademarks on or in connection with the commercialization of the Licensed Product in the Licensed Territory in the Licensed Field. Novan shall not grant to any Third Party license to use the Novan Trademarks on or in connection with the commercialization of any products outside the Licensed Field in the Licensed Territory.

(ii) Sato shall not use any trademark that is confusingly similar to, misleading or deceptive with respect to or that dilutes any of the Novan Trademarks.

(iii) Sato shall properly designate the Novan Trademarks on the packaging of the final Licensed Product, to the extent required or permissible by the applicable Marketing Approvals and Sato agrees that all Licensed Products with which the Novan Trademarks are used shall conform to all requirements of any applicable Laws and any Regulatory Authorities in the Licensed Territory and shall be of a level of quality commensurate to Novan's Licensed Products outside of the Territory, but in no event less than a reasonable level of quality.

(iv) Except as otherwise provided in this Section 8.2, if Sato elects to use the Novan Trademarks, Novan shall have an obligation to register and maintain the Novan Trademarks in the Licensed Territory (subject to this Section 8.2(iv)) at Sato's expense. Novan shall provide Sato reasonable opportunity to review and comment on such registration efforts regarding the Novan Trademarks. Novan shall provide Sato with a copy of material communications from any governmental authority in the Licensed Territory regarding the Novan Trademark, and shall provide drafts of any material filings or responses to be made to such authorities in a timely manner. Notwithstanding the foregoing, if Novan determines in its sole discretion to abandon or not maintain any Novan Trademark in the Licensed Territory, Novan shall provide Sato with **[***]** prior written notice of such determination and, if Sato so requests, shall transfer to Sato such Novan Trademark in the Licensed Territory. Sato shall bear all costs of such transfer and maintenance of such Novan Trademark in the Licensed Territory.

(v) If a Party becomes aware of any actual or alleged threatened or existing infringement of any Novan Trademark or of any unfair trade practices, trade dress imitation, passing off of counterfeit goods, or like offenses, against such Novan Trademark by a Third Party in the Licensed Territory (such activities, "**Trademark Infringement**"), such Party shall notify the other Party, and shall provide to the other Party any and all evidence and information available to such Party regarding such alleged infringement. Sato shall have the first right, but not the obligation, to bring an appropriate suit or other action against any person or entity engaged in such Trademark Infringement, at its sole expense, subject to this Section 8.2(v). Sato shall have a period of **[***]** after such notification to or by Sato, to elect to so enforce such Novan Trademark. If Sato does not so elect, Sato shall so notify Novan in writing during such **[***]** period, or **[***]** prior to any deadline relating to loss of any rights with respect to the Trademark Infringement, whichever is earlier, and Novan shall have the right, but not the obligation, to commence a suit or take action to enforce such Novan Trademark against such Third Party, at its sole expense. Each Party shall provide to the Party enforcing any such rights under this Section 8.2(v) reasonable assistance in such enforcement, at such enforcing Party's request and expense, including without limitation joining an action as a party plaintiff if so required by Laws to pursue such action. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts, and shall reasonably consider the other Party's comments on any such efforts.

(vi) The Party not bringing an action with respect to Trademark Infringement under this Section 8.2 shall be entitled to separate representation in such matter by

counsel of its own choice and at its expense, but such Party shall at all times cooperate fully with the Party bringing such action. Additionally, the Party not bringing an action under this Section 8.2 may have an opportunity to participate in such action to the extent that the Parties may mutually agree at the time the other Party elects to bring an action hereunder.

8.3 Infringement of Sato Trademarks by Third Parties. With respect to any Sato Trademarks associated with Licensed Products in the Licensed Territory, each Party shall notify the other Party promptly upon learning of any actual or alleged threatened or existing infringement of any trademark or of any unfair trade practices, trade dress imitation, passing off of counterfeit goods, or like offenses, against such trademark. Sato shall have the sole right, in its own discretion and at its own expense, to bring an action to address such infringement.

9. SERIOUS ADVERSE EVENT REPORTING

9.1 Serious Adverse Event Reporting by the Parties Each Party shall (i) notify the other Party within **[***]** (or any such shorter period required by applicable Law) of its becoming aware of any information relating to the occurrence of any serious adverse event in connection with the Licensed Product or concerning any and all charges, complaints or claims reportable to any Regulatory Authority relating to the Licensed Product and (ii) promptly provide to the other Party all such information.

9.2 Recall or Market Withdrawal of Licensed Product; "Dear Doctor" Letters In the event that: (i) Sato determines that an event, incident, or circumstance has occurred which may result in the need for a recall, market withdrawal or other removal of the Licensed Product or any lot or lots thereof from the market in the Licensed Territory, or Novan determines that an event, incident, or circumstance that could reasonably adversely affect the Licensed Product in the Licensed Territory has occurred which is reasonably likely to result in the need for a recall, market withdrawal or other removal of the Licensed Product, or any lot or lots thereof from the market; (ii) either Party becomes aware that a Regulatory Authority is threatening or has initiated an action to remove the Licensed Product from the market in the Licensed Territory or, if such event could reasonably adversely affect the Licensed Product in the Licensed Territory, any Regulatory Authority is threatening or has initiated an action to remove the Licensed Product from the market; or (iii) either Party is required by any Regulatory Authority to distribute a "**Dear Doctor**" letter or its equivalent regarding use of the Licensed Product in the Licensed Territory or, if such event could reasonably adversely affect Licensed Product in the Licensed Territory, any Regulatory Authority has required distribution of a "**Dear Doctor**" letter or its equivalent regarding use of the Licensed Product, it shall promptly advise the other Party in writing with respect thereto, and shall provide to the other Party copies of all relevant correspondence, notices, and the like in the possession or Control of such Party. In such event, Sato shall have the sole authority to determine if a recall or other removal of the Licensed Product is required in the Licensed Territory, and shall be responsible for conducting any such recall or other removal of the Licensed Product in the Licensed Territory, whether voluntary or involuntary, or taking such other remedial action required by applicable Laws in the Licensed Territory. At Sato's request, Novan shall assist Sato, at Sato's expense, with respect to any such recall or remedial action, and shall provide Sato with all information that Sato may request in connection with its dealings with a Regulatory Authority in connection with such recall or

remedial action. Expenses incurred in connection with such recall or remedial action shall be **[***]** except to the extent (i) **[***]**, or (ii) such recall or remedial action is **[***]**. For avoidance of doubt, Novan shall have the sole authority to determine if a recall or other removal of the Licensed Product is required outside of the Licensed Territory.

9.3 Pharmacovigilance. At least **[***]** before the First Commercial Sale of the Licensed Product in the Licensed Territory the Parties shall enter into a pharmacovigilance agreement to specify in detail each Party's respective obligations with respect to adverse event reporting, monitoring, maintenance of safety databases and related submissions to Regulatory Authorities and other similar obligations with respect to the commercialized Licensed Product in the Licensed Field in the Licensed Territory, which shall be consistent with this Article 9. Both Parties understand that the pharmacovigilance agreement shall be modified, if necessary, consistent with the conditions of the Marketing Approval in the Licensed Territory.

10. REPRESENTATIONS AND WARRANTIES

10.1 The Parties' Representations and Warranties. Each Party hereby represents and warrants to the other Party, as of the Effective Date, as set forth below.

(i) Such Party (a) is a corporation duly organized and subsisting under the applicable Laws of its jurisdiction of organization, and (b) has full power and authority and the legal right to own and operate its property and assets and to carry on its business as it is now being conducted and as it is contemplated to be conducted by this Agreement.

(ii) Such Party has the power, authority and legal right, and is free to enter into this Agreement and, in so doing, will not violate any other agreement to which such Party is a party as of the Effective Date.

(iii) This Agreement has been duly executed and delivered on behalf of such Party and constitutes a legal, valid, and binding obligation of such Party and is enforceable against it in accordance with its terms, subject to the effects of bankruptcy, insolvency, or other applicable Laws of general application affecting the enforcement of creditor rights and judicial principles affecting the availability of specific performance and general principles of equity.

(iv) Such Party has taken all corporate action necessary to authorize the execution and delivery of this Agreement.

(v) Except with respect to Marketing Approvals for the Licensed Product or as otherwise described in this Agreement, such Party has obtained all necessary consents, approvals, and authorizations of all Regulatory Authorities and other Third Parties required to be obtained by such Party in connection with the execution and delivery of this Agreement and the performance of its obligations hereunder.

(vi) The execution and delivery of this Agreement and the performance of such Party's obligations hereunder (i) do not conflict with or violate any requirement of applicable Laws or any provision of the articles of incorporation, bylaws, limited partnership agreement, or any similar instrument of such Party, as applicable, in any material way, and

(ii) do not conflict with, violate, or breach or constitute a default or require any consent under, any applicable Laws or any contractual obligation or court or administrative order by which such Party is bound.

(vii) All of such Party's employees, officers, independent contractors, consultants, and agents have executed agreements requiring assignment to such Party of all Inventions made during the course of and as a result of their association with such Party and obligating the individual to maintain as confidential the confidential information of such Party.

(viii) Neither such Party, nor any of such Party's employees, independent contractors, consultants, agents or officers: (i) has ever been debarred or is subject to debarment or, to such Party's knowledge, convicted of a crime for which a Person could be debarred before a Regulatory Authority under applicable Laws, or (ii) to such Party's knowledge, has ever been under indictment for a crime for which a Person could be debarred under such Laws.

(ix) All documents, information and know-how furnished or transferred by such Party to the other Party under this Agreement shall be, to its knowledge, free of errors in any material respect.

10.2 Novan's Representations and Warranties. Novan hereby represents and warrants to Sato, as of the Effective Date as set forth below:

(i) Novan has sufficient legal and/or beneficial title under its intellectual property rights necessary to grant the licenses contained in this Agreement.

(ii) Novan has the right to transfer to Sato a copy of the Novan Know-How set forth in Annex 1 in accordance with this Agreement.

(iii) There is no pending or, to Novan's knowledge, threatened claim, litigation or any other proceeding brought by a Third Party against Novan challenging the validity of the Novan Patent Rights in the Licensed Territory, or claiming that the development, manufacture or commercialization of the Licensed Product in the Licensed Field in the Licensed Territory constitutes or would constitute infringement of such Third Party's intellectual property right(s).

(iv) Novan has not received any written communications alleging that it has violated or that it would violate, in any material manner, through the manufacture, use, import, export, sale, and/or offer for sale of the Licensed Product in the Licensed Field and in the Licensed Territory, any intellectual property rights of any Third Party.

(v) Novan has (1) the sole and exclusive ownership of or (2) a license (with the right to grant sublicenses thereunder) to the Novan Patents, Novan Trademarks (if used with the Licensed Product), Novan Study Materials and Novan Scientific Information.

10.3 The Parties' Covenants. Each Party hereby covenants throughout the Term of this Agreement as set forth below:

(i) Such Party shall not enter into any agreement with a Third Party that will conflict with the rights granted to the other Party under this Agreement.

(ii) If during the Term of this Agreement, a Party has reason to believe that it or any of its employees, officers, independent contractors, consultants, or agents rendering services relating to the Licensed Product: (x) is or will be debarred or convicted of a crime for which such Person could be debarred before a Regulatory Authority under applicable Laws, or (y) is or will be under indictment under such Laws, then such Party promptly shall notify the other Party of the same in writing.

(iii) In connection with this Agreement, and without limiting anything in this Article 10, each Party represents, warrants and covenants that it has not given or promised to give, and will not make, offer, agree to make or authorize any payment or transfer anything of value, directly or indirectly, to (i) any Government or Public Official (as defined below); (ii) any political party, party official or candidate for public or political office; (iii) any person while knowing or having reason to know that all or a portion of the value will be offered, given, or promised, directly or indirectly, to anyone described in items (i) or (ii) above; or (iv) any owner, director, employee, representative or agent of any actual or potential customer of such Party (if any such transfer of value would be a violation of any applicable Laws). Each Party agrees to comply with all applicable anti-bribery laws in the countries where the Parties have their principal places of business and where they conduct activities under this Agreement. Additionally, each Party represents, warrants and covenants that such Party shall comply with the U.S. Foreign Corrupt Practices Act ("**FCPA**") and the UK Anti-Bribery Act, both as revised from time to time, as well as similar applicable Laws of the country where a Party has its principal place of business and where such Party conducts activities under this Agreement, and to take no action that would reasonably be deemed to cause the other Party to be in violation of the FCPA, the UK Anti-Bribery Act or similar applicable Laws of the country where a Party has its principal place of business and where it conducts activities under this Agreement. Additionally, each Party will make reasonable efforts to comply with requests for information, including answering questionnaires and narrowly tailored audit inquiries, to enable the other Party to ensure compliance with applicable anti-bribery Laws. For purposes of this Agreement, "**Government or Public Official**" means any officer or employee or anyone acting in an official capacity on behalf of: a government or any department or agency thereof; a public international organization (such as the United Nations, the International Monetary Fund, the International Red Cross, and the World Health Organization), or any department, agency or institution thereof; or a government-owned or controlled company, institution, or other entity, including a government-owned hospital or university.

10.4 No Off-Label Uses Sato hereby covenants throughout the Term that it shall not (by itself or with or through a Third Party) develop, sell, offer for sale, import, market, distribute or promote the Licensed Product in the Licensed Field in the Licensed Territory for uses or indications outside of the scope of the Approved Label. If Sato becomes aware of any

activities in contravention of the immediately preceding sentence Sato shall immediately notify Novan and provide to Novan relevant information.

11. CONFIDENTIALITY OBLIGATIONS OF SATO

11.1 Confidentiality Obligations. During the Term of this Agreement and for a period of **[***]** thereafter, or **[***]** from the Effective Date, whichever is longer, Sato:

(i) shall hold in strict confidence any and all information disclosed to it by Novan, including, without limitation Novan Scientific Information, (collectively "**Novan Confidential Information**") and shall not use, nor disclose or supply to any Third Party, nor permit any Third Party, to have access to the Novan Confidential Information, without first obtaining the written consent of Novan, except as expressly permitted in this Agreement;

(ii) shall take all reasonable precautions necessary or prudent to prevent material in its possession or control that contains or refers to Novan Confidential Information from being destroyed or lost, or discovered, received, used, intercepted or copied by any Third Party; and

(iii) may disclose the Novan Confidential Information only to its employees, consultants, independent contractors, agents, Affiliates, and actual or potential acquirers, provided that such employees, consultants, independent contractors, agents, Affiliates, and actual or potential acquirers are bound by terms and conditions of confidentiality no less protective than the terms and conditions that bind Sato hereunder.

For the avoidance of doubt, it is understood that Sato shall be liable for any breach of the confidentiality obligation under this Section 11.1 by any Person to whom the Novan Confidential Information is disclosed by Sato.

11.2 Exceptions. Sato's obligations of confidentiality and non-use under Section 11.1 shall not apply and Sato shall have no further obligations with respect to any of the Novan Confidential Information, to the extent Sato can establish by competent proof that such Novan Confidential Information:

(i) is or becomes part of the public domain without breach by Sato of this Agreement;

(ii) was in Sato's possession before disclosure by Novan and was not acquired directly or indirectly from Novan;

(iii) is obtained from a Third Party with no obligation of confidentiality to Novan, who has a right to disclose it to Sato;

(iv) is developed by Sato without using any Novan Confidential Information; or

(v) is required to be revealed in response to a court decision or administrative order, or to comply with applicable Laws, in which case Sato shall inform Novan immediately by written notice and cooperate with Novan using Commercially Reasonable Efforts either to enabl Novan to seek protective measures for such Novan Confidential Information, or to seek confidential treatment of such Novan Confidential Information, and i such case Sato shall disclose only such portion of the Novan Confidential Information which is so required to be disclosed.

11.3 Disclosure for Marketing Approvals; Publications. Nothing herein shall prevent Sato from disclosing any Novar Confidential Information to the extent that such Novan Confidential Information is required to be used or disclosed for the purposes of seeking or obtainin Marketing Approvals of Licensed Products in the Licensed Field in the Licensed Territory or seeking patent protection for Inventions it owns or ha responsibility for prosecuting under Article 7. Sato shall further have the right to present Novan Scientific Information at conferences or to publish Novar Scientific Information in journals (collectively "**Publications**"), provided such Publication is subject to Novan's prior written consent, not to be unreasonably withheld, delayed or conditioned.

12. CONFIDENTIALITY OBLIGATIONS OF NOVAN

12.1 Confidentiality Obligations. During the Term of this Agreement and for a period of **[***]** thereafter, or **[***]** from the Effective Date, whichever is longer, Novan:

(i) shall hold in strict confidence any and all information disclosed to it by Sato, including without limitation the Satc Scientific Information, (collectively "**Sato Confidential Information**") and shall not use, nor disclose or supply to any Third Party nor permit any Third Party to have access to the Sato Confidential Information, without first obtaining the written consent of Sato, except as expressly permitted in this Agreement;

(ii) shall take all reasonable precautions necessary or prudent to prevent material in its possession or control that contains or refers to Sato Confidential Information from being destroyed or lost, or discovered, received, used, intercepted or copied by any Third Party; and

(iii) may disclose the Sato Confidential Information only to its employees, consultants, independent contractors, agents, Affiliates, actual and potential Novan Licensees and actual and potential acquirers, provided that such employees, consultants, independent contractors, agents, Affiliates, actual and potential Novan Licensees and actual and potential acquirers are bound by terms and conditions of confidentiality no less protective than the terms and conditions that bind Novan hereunder.

For the avoidance of doubt, it is understood that Novan shall be liable for any breach of the confidentiality obligation under this Section 12.1 by any person or corporation to whom the Sato Confidential Information is disclosed by Novan.

12.2 Exceptions. Novan's obligations of confidentiality and non-use under Section 12.1 shall not apply and Novan shall have no further obligations with respect to any of the Sato Confidential Information as far as Novan can establish by competent proof that such Sato Confidential Information:

(i) is or becomes part of the public domain without breach by Novan of this Agreement;

(ii) was in Novan's possession before disclosure by Sato to Novan and was not acquired directly or indirectly from Sato;

(iii) is obtained from a Third Party with no obligation of confidentiality to Sato, who has a right to disclose it to Novan;

(iv) is developed by Novan without using any Sato Confidential Information; or

(v) is required to be revealed in response to a court decision or administrative order, or to comply with applicable Laws of a governmental authority or rules of a securities exchange, in which case Novan shall inform Sato immediately by written notice and cooperate with Sato using Commercially Reasonable Efforts either to enable Sato to seek protective measures for such Sato Confidential Information, or to seek confidential treatment of such Sato Confidential Information, and in such case Novan shall disclose only such portion of the Sato Confidential Information which is so required to be disclosed.

12.3 Disclosure for Marketing Approvals; Publications. Nothing herein shall prevent Novan from disclosing any Sato Confidential Information to the extent that such Sato Confidential Information is required to be used or disclosed for the purposes of seeking or obtaining Marketing Approvals of Licensed Products outside the Licensed Territory, obtaining Marketing Approvals of Licensed Products in the Licensed Territory outside the Licensed Field, or seeking patent protection for Inventions it owns or has responsibility for prosecuting under Article 7. Novan, its Affiliates and Novan Licensees shall further have the right to disclose any Sato Scientific Information in a Publication, provided that if the Sato Scientific Information concerned has not been previously published, such Publication is subject to Sato's prior written consent, not to be unreasonably withheld, delayed or conditioned.

13. PRESS RELEASES

13.1 Press Releases. Subject to Articles 11 or 12 as applicable, either Party may issue a press release or public announcement concerning any aspect of the development or commercialization of the Licensed Product in the Licensed Field in the Licensed Territory, provided that it provides to the other Party a copy of such press release or public announcement at least **[***]** in advance of its intended publication or release thereof and obtains the written consent, not to be unreasonably withheld, delayed or conditioned, of such other Party to such publication or release. Notwithstanding the foregoing, subject to Sections 11.2(v) or 12.2(v) as applicable, either Party may issue any public announcement that it is advised by legal counsel is

required under applicable Laws or rules of a securities exchange, provided that such Party provides to the other Party a copy of such press release or public announcement promptly after its release thereof.

13.2 No Disclosure of Terms and Conditions. No press release or public announcement shall be made by either Party concerning the execution of this Agreement or the terms and conditions hereof, without the prior written consent of the other Party which shall not be unreasonably withheld, delayed or conditioned. Notwithstanding the foregoing, either Party may disclose the existence of this Agreement and the terms and conditions hereof without the prior written consent of the other pursuant to Section 11.2(v) or Section 12.2(v), as applicable, or in connection with a due diligence process associated with any future financing by either Party or the negotiation or exploration of a possible strategic transaction involving such Party, provided that such disclosure is made in the course of such diligence, negotiation or exploration pursuant to confidentiality obligations consistent with those set forth in this Agreement.

14. PAYMENT

14.1 Payments. In consideration of the licenses and other rights granted to Sato herein, Sato shall pay to Novan a total o 4.00 billion JPY, payable in equal annual installments over fifteen (15) years after the Effective Date of this Agreement; provided that such payment condition (for clarity, the amount of payment is not included) may be changed under the mutual consent of the Parties. In addition to such payment, Sato shall pay to Novan the following sales milestone payments.

SALES MILESTONE PAYMENTS

One-time sales milestone payments shall be made by Sato to Novan upon the first achievement of each of the following annual Net Sales milestones:

Annual Net Sales of **[***]**	**[***]**
Annual Net Sales of **[***]**	**[***]**
Annual Net Sales of **[***]**	**[***]**

14.2 Currency. All payments under Section 14.1 shall be made in JPY.

14.3 Notification. Sato shall notify Novan of the achievement of each of the sales milestones set forth in Section 14.1 within **[***]** after Sato closes its books for the relevant annual period in which such sales milestone payment becomes due. All payments under Section 14.1 shall be made within **[***]** after Sato receives the relevant invoice from Novan. All payments under Section 14.1 shall be made without setoff or deduction of any kind, other than pursuant to Sections **[***]**.

14.4 **Account**. All payments to be made to Novan under this Agreement shall be made by wire transfer to the following account:

For all wire payments denominated in JPY	Payments should be remitted to **[***]**
	Any such payments to **[***]** should be remitted **[***]**
For all other wire payments	Recipient US Bank: **[***]**

or such other account as may be specified by Novan in writing to Sato.

15. ROYALTY PAYMENT; AUDITS

15.1 **Royalty**. In consideration of the rights granted to Sato herein, Sato shall pay to Novan a royalty of **[***]** of annual Net Sales in the Licensed Territory during the Term, subject to Section 15.2.

15.2 **Royalty Term; Reduction**. Royalties shall be payable in the Licensed Territory, on a product-by-product basis, for the duration of the Term. If, on a product-by-product basis, during the Term (i) no Valid Claim exists in the Licensed Territory Covering the Licensed Product or its manufacture, use or sale, or (ii) the Marketing Exclusivity with respect to such Licensed Product in the Licensed Territory has expired, then the royalty rate shall be reduced to **[***]** of annual Net Sales for the remainder of the Term in the Licensed Territory for such Licensed Product.

15.3 **Significant Value of Novan Know-How** The Parties acknowledge that the Novan Know-How is of significant value for the development and commercialization of Licensed Product in the Licensed Field in the Licensed Territory, and have determined the royalty rate and royalty term set forth herein on the basis of this assumption.

15.4 **Payment**. Sato shall provide to Novan a good faith estimate of the royalties payable to Novan under Section 15.1 within **[***]** after the end of the calendar quarter in which such royalties are due, and shall pay to Novan all royalties payable to Novan under Section 15.1 within **[***]** after the end of the applicable calendar quarter. Payment of royalties under Section 15.1 shall be made in JPY. All payments under Section 15.1 shall be made without setoff or deduction of any kind, other than pursuant to Sections **[***]**. Royalties payable under Section 15.1 shall be payable only once with respect to a particular unit of Licensed Product and shall be paid only once regardless of the number of Patents applicable to such Licensed Product.

15.5 **Maintenance of Records**. Sato shall keep true, correct and complete records of all royalties and other amounts payable to Novan under Section 15.1 hereof, including without limitation all financial information needed to calculate Net Sales for such periods of time as are required under applicable Law, provided that in no event shall Sato retain such books and

records for less than **[***]** after the date of relevant payment made to Novan. Sato shall deliver to Novan a preliminary Sales Report **[***]** after the end of each calendar quarter and a final Sales Report **[***]** after the end of each calendar quarter. All financial terms and standards (including any calculation of Net Sales and financial payments due under this Agreement) shall be governed by and determined in accordance with Japanese GAAP and shall be consistent with Sato's audited consolidated financial statements.

15.6 **Taxes**. All payments under this Agreement shall be made without any deduction or withholding for or on account of any tax, except as set forth in this Section 15.6. The Parties agree to cooperate with one another and use reasonable efforts to minimize obligations for any and all income or other taxes required by Law to be withheld or deducted from any of the royalty and other payments made by or on behalf of a Party hereunder ("**Withholding Taxes**"). The applicable paying Party under this Agreement (the "**Paying Party**") shall, if required by Law, deduct from any amounts that it is required to pay to the recipient Party hereunder (the "**Recipient Party**") an amount equal to such Withholding Taxes, provided that the Paying Party shall give the Recipient Party reasonable notice prior to paying any such Withholding Taxes. Such Withholding Taxes shall be paid to the proper taxing authority for the Recipient Party's account and, if available, evidence of such payment shall be secured and sent to recipient within **[***]** of such payment. The Paying Party shall, at the Recipient Party's cost and expense, do all such lawful acts and things and sign all such lawful deeds and documents as the Recipient Party may reasonably request to enable the Paying Party to avail itself of any applicable legal provision or any double taxation treaties with the goal of paying the sums due to the Recipient Party hereunder without deducting any Withholding Taxes.

15.7 **[***]**. All payments due from Sato to Novan under Section 15.1 **[***]**, provided that **[***]**.

15.8 **Audits**. Novan shall have the right, no more than **[***]** during each calendar year during the Term of this Agreement and for **[***]** after its termination, to have an independent certified public accountant ("**Accountant**") of its own selection (subject to Sato's acceptance of such Accountant, such acceptance not to be unreasonably withheld, delayed or conditioned) and at its own expense audit the relevant books and records of account of Sato in connection with the payment of royalties and any other amounts under this Agreement during normal business hours, and upon reasonable prior notice, to determine whether appropriate accounting has been performed and payments have been made to Novan hereunder; provided that such Accountant shall be bound to treat all information reviewed during such audit as confidential, and does not disclose to Novan any information other than information which shall have previously been given to Novan pursuant to any provision of this Agreement or information regarding the payments due to or by Novan as a result of such audit. Notwithstanding the foregoing, such Accountant may support its audit conclusions with underlying Sato Confidential Information if challenged by Sato, provided that all such disclosures shall be maintained as confidential by such Accountant and Novan with respect to Third Parties, except that Novan may disclose such Sato Confidential Information to UNC as part of Novan's reporting obligations under the UNC License Agreement.

If the Accountant determines that the Sales Report has not been true or accurate, then Sato shall refund Novan for the costs of the Accountant if Sato has underpaid such royalties by more than **[***]**, and the royalties shall be re-calculated on the basis of the Accountant's findings. Such Accountant's findings shall be binding for both Parties absent manifest error.

15.9 Late Payments. If Novan does not receive payment of any sum due to it under Section 14.1 or Section 15.1 on or before the due date, simple interest shall thereafter accrue on the sum due to Novan from the due date until the date of payment at the USD LIBOR plus **[***]** or the maximum rate allowable by applicable Law, whichever is less.

16. INDEMNIFICATION

16.1 By Novan Novan shall defend, indemnify and hold harmless Sato and its Affiliates and their respective directors, officers, agents, successors, assignees and employees (the "**Sato Indemnitees**") from and against any and all claims, liabilities, losses, costs, actions, suits, damages and expenses, including reasonable attorneys' fees (collectively "**Damages**") to the extent arising from any claim, action or proceeding made or brought against Sato Indemnitees by a Third Party in connection with (i) the gross negligence, recklessness, or intentional wrongful acts or omissions of Novan, its Affiliates, and/or Novan Licensees and its or their respective employees, officers, independent contractors, consultants, or agents, in connection with the performance by or on behalf of Novan of Novan's obligations or exercise of its rights under this Agreement; (ii) any breach by Novan, or its Affiliates, Novan Licensees or independent contractors of any representation, warranty, covenant, or obligation of Novan set forth in this Agreement, and (iii) the development, manufacture, use, handling, storage, commercialization, transfer, importation, exportation or labeling, of the Licensed Product by or for Novan, its Affiliates or Novan Licensees either prior to the Effective Date anywhere in the world, or on or after the Effective Date outside the Licensed Territory or outside the Licensed Field in the Licensed Territory; except in any such case to the extent such Damages are reasonably attributable to any negligence, willful misconduct or breach of this Agreement by Sato or a Sato Indemnitee.

16.2 By Sato. Sato shall defend, indemnify and hold harmless Novan and its Affiliates, directors, officers, agents, successors, assignees and employees (the "**Novan Indemnitees**") from and against any and all Damages to the extent arising from any claim, action or proceeding made or brought against Novan Indemnitees by a Third Party in connection with (i) the gross negligence, recklessness, or intentional wrongful acts or omissions of Sato, its Affiliates, and its or their respective employees, officers, independent contractors, consultants, or agents, in connection with the performance by or on behalf of Sato of Sato's obligations or exercise of its rights under this Agreement; (ii) any breach by Sato, or its Affiliates or independent contractors of any representation, warranty, covenant, or obligation of Sato set forth in this Agreement; and (iii) the development, manufacture (other than by Novan or its contract manufacturers), use, handling, storage, commercialization, transfer, importation, exportation or labeling of the Licensed Product by or for Sato or any of its Affiliates, agents, and independent contractors; except in any such case to the extent such Damages are reasonably attributable to any negligence, willful misconduct, or breach of this Agreement by Novan or an Novan Indemnitee.

16.3 Indemnification Procedure.

(i) Each Party shall notify the other in the event it becomes aware of a claim for which indemnification may be sought pursuant to this Article 16. In case any proceeding (including any governmental investigation) shall be instituted involving any Party in respect of which indemnity may be sought pursuant to this Article 16, such Party (the "**Indemnified Party**") shall promptly notify the other Party (the "**Indemnifying Party**") in writing (an "**Indemnification Claim Notice**"). The Indemnifying Party and Indemnified Party shall promptly meet to discuss how to respond to any claims that are the subject matter of such proceeding. At its option, the Indemnifying Party may assume the defense of any Third Party claim subject to indemnification as provided for in this Section 16.3 by giving written notice to the Indemnified Party within **[***]** (or until such time provided in any applicable extension to appropriately answer any complaint, if any, but no longer than **[***]** (the "**Election Time Period**"); with the Indemnified Party being obligated to make all reasonable efforts to obtain any such extension) after the Indemnifying Party's receipt of an Indemnification Claim Notice, solely for claims, (i) that solely seek monetary damages and (ii) as to which the Indemnifying Party expressly agrees in writing that, as between the Indemnifying Party and the Indemnified Party, the Indemnifying Party shall be solely obligated to satisfy and discharge the claim in full (the matters described in (i) and (ii), the "**Litigation Conditions**"). The Indemnified Party may assume responsibility for such defense if the Litigation Conditions are not satisfied, by written notice to the Indemnifying Party within the Election Time Period. If the Indemnified Party fails to promptly provide an Indemnification Claim Notice, and such failure materially prejudices the defense of such claim, then the Indemnifying Party shall be relieved of its responsibility to indemnify the Indemnified Party.

(ii) Upon assuming the defense of a Third Party claim in accordance with this Section 16.3, the Indemnifying Party shall be entitled to appoint lead and any local counsel in the defense of the Third Party claim. Should the Indemnifying Party assume and continue the defense of a Third Party claim, except as otherwise set forth in this Section 16.3, the Indemnifying Party will not be liable to the Indemnified Party for any legal expense subsequently incurred by such Indemnified Party after the date of assumption of defense in connection with the analysis, defense, countersuit or settlement of the Third Party claim. Without limiting this Section 16.3, any Indemnified Party will be entitled to participate in, but not control, the defense of a Third Party claim for which it has sought indemnification hereunder and to engage counsel of its choice for such purpose; provided, however, that such engagement will be at the Indemnified Party's own expense unless (a) the engagement thereof has been specifically requested by the Indemnifying Party in writing, or (b) the Indemnifying Party has failed to assume and actively further the defense and engage counsel in accordance with this Section 16.3 (in which case the Indemnified Party will control the defense), or (c) the Indemnifying Party no longer satisfies the Litigation Conditions.

(iii) Subject to the Litigation Conditions being satisfied, the Indemnifying Party will have the sole right to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Damages, on such terms as the Indemnifying Party, in its reasonable discretion, will deem appropriate (provided, however that such terms shall include a complete and unconditional release of the Indemnified Party from all liability with

respect thereto), and will transfer to the Indemnified Party all amounts which such Indemnified Party will be liable to pay pursuant to such settlement or disposa of such claim prior to the time such payments become due by the Indemnified Party. With respect to all other Damages in connection with Third Party claims where the Indemnifying Party has assumed the defense of the Third Party claim in accordance with this Section16.3, the Indemnifying Party will have authority to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Damages, provided it obtains the prior written consent of the Indemnified Party, not to be unreasonably withheld, delayed or conditioned.

(iv) The Indemnifying Party that has assumed the defense of the Third Party claim in accordance with this Sectio 16.3 will not be liable for any settlement or other disposition of any Damages by an Indemnified Party that is reached without the written consent of such Indemnifying Party. The Indemnified Party will not admit any liability with respect to, or settle, compromise or discharge, any Third Party claim without firs offering to the Indemnifying Party the opportunity to assume the defense of the Third Party claim in accordance with this Section 16.3. If the Indemnifying Part chooses to defend or prosecute any Third Party claim, the Indemnified Party will cooperate in the defense or prosecution thereof and will furnish such records information and testimony, provide such witnesses including to the extent possible, former employees and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection with such Third Party claim. Such cooperation will include access during norma business hours afforded to the Indemnifying Party to, and reasonable retention by the Indemnified Party of, records and information that are reasonably relevan to such Third Party claim, and making employees and agents available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder. The Indemnifying Party will reimburse the Indemnified Party for all its reasonable out-of-pocket expenses incurred in connectio with such cooperation.

16.4 Insurance. During the Term of this Agreement and for **[***]** thereafter, Novan shall keep and maintain the following insurance with a reputable carrier **[***]** reasonably acceptable to Sato: comprehensive public liability, including products liability coverage and clinical trial coverage, with limits of (a) before receipt of Marketing Approval for any Licensed Product, not less than**[***]** USD per event and (b) after receipt o Marketing Approval for any Licensed Product, not less than**[***]** USD per event or any such greater mutually agreed amount and type of insurance determined by the board of directors of the each Party, naming Sato as an additional insured from the Effective Date forward with respect to Novan's performance hereof. Sato shall keep and maintain the following insurance with a reputable carrier **[***]** reasonably acceptable to Novan, naming Novan as an additional insured with respect to Sato's performance hereof: (i) from no later than the start of a clinical study of the Licensed Product in the Licensed Territory until **[***]** after the expiration or termination of this Agreement, comprehensive public liability including clinical trial coverage, with limits of not less than **[***]** USD per event, and (ii) from no later than the first commercial sale of the Licensed Product in the Licensed Territory until**[***]** after the expiration or termination of this Agreement, comprehensive public liability including products liability coverage, with limits of not less than **[***]** USD per event. The type and amount of insurance maintained by the Parties pursuant to this Section 16.4 may be modified upon mutual written agreement of the Parties. Both Parties agree to provide the other Party certificate evidencing such coverage within **[***]** after the date on which such Party purchases

the relevant insurance pursuant to the terms and conditions of this Section 16.4 and at least annually thereafter. If such insurance is canceled or materially altered, the each Party shall provide prompt written notice to the other Party.

16.5 Except as expressly provided in this Article 16, neither Party shall have any liability to indemnify the other Party against any Third Party claims.

17. LIMITATION OF LIABILITY; EXCLUSION OF DAMAGES; DISCLAIMER

17.1 EXCEPT IN THE CASE OF A BREACH OF ARTICLES 11 OR 12, AND WITHOUT LIMITING THE PA OBLIGATIONS UNDER ARTICLE 16 OR LIABILITY OF A PARTY FOR INFRINGEMENT OR MISAPPROPRIATION INTELLECTUAL PROPERTY RIGHTS OF THE OTHER PARTY OR FOR FRAUD OR WILLFUL MISCONDUCT, NEITHER PARTY S LIABLE TO THE OTHER PARTY FOR SPECIAL, INDIRECT, INCIDENTAL, PUNITIVE, OR CONSEQUENTIAL DAMAGES (IN WITHOUT LIMITATION DAMAGES RESULTING FROM LOSS OF USE, LOSS OF PROFITS, INTERRUPTION OR LOSS OF BUS OTHER ECONOMIC LOSS) ARISING OUT OF THIS AGREEMENT OR WITH RESPECT TO A PARTY'S PERFORMANCE C PERFORMANCE HEREUNDER.

17.2 EXCEPT AS EXPRESSLY PROVIDED IN THIS AGREEMENT, NEITHER PARTY PROVIDES WARRANTIES, WHETHER WRITTEN OR ORAL, EXPRESS OR IMPLIED, REGARDING THE LICENSED PRODUCT AND EAC HEREBY DISCLAIMS ALL OTHER WARRANTIES, WHETHER WRITTEN OR ORAL, EXPRESS AND IMPLIED, INCLUDING LIMITATION THE IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, AND FREEDO INFRINGEMENT OF THIRD PARTY RIGHTS.

18. TERM

18.1 **Term**. The term of this Agreement shall commence as of the Effective Date and, unless sooner terminated as specifically provided in this Agreement, shall continue in effect until the tenth (10th) anniversary of the First Commercial Sale of the Licensed Product in the Licensed Fiel in the Licensed Territory (the "**Term**"), unless terminated earlier pursuant to Section 19. This Agreement may be renewed by mutual written agreement of the Parties for additional two (2) year periods following expiration of the Term.

18.2 **Effect of Expiration**. Upon expiration of this Agreement in accordance with Section 18.1:

(i) the Licensed Rights shall continue in full force and effect and be considered to be fully paid-up;

(ii) subject to Section 18.2(i) hereof, Sato's confidentiality obligation under Section 11 shall continue to be in full force and effect for a period of **[***]** following expiration of this Agreement;

(iii) Novan shall have the right to freely use and license all Novan Scientific Information and all Sato Scientifi Information disclosed by Sato to Novan hereunder;

(iv) The licenses granted by Sato to Novan pursuant to Section 2.3 and other provisions of this Agreement shal continue in effect in addition to those sections that also survive pursuant to Section 18.3 and shall be expanded to include the Licensed Field in the Licensec Territory;

(v) Sato shall transfer and assign to Novan all of Sato's right, title and interest in and to all Drug Approva Applications, Marketing Approvals, and regulatory dossiers with respect to any and all Licensed Products in the Licensed Field in the Licensed Territory; and

(vi) subject to Sections 18.2(iii) and 18.2(iv) hereof, Novan's confidentiality obligation under Section 12 shal continue to be in full force and effect for a period of **[***]** following expiration of this Agreement.

18.3 Survival. For the avoidance of doubt, it is understood that provisions under Sections 6.7 (*Ownership of Novan Scientific Information*), 6.8 (*Ownership of Sato Scientific Information*), 7.1 (*Improvements*), 7.2 (*Ownership of Inventions*), 8.1 (*Trademarks*), 9 (*Serious Adverse Event Reporting*), 11 (*Confidentiality Obligations of Sato*), 12 (*Confidentiality Obligations of Novan*), 15.5 (*Maintenance of Records*), 15.6 (*Taxes*), 15.8 (*Audits*), 16 (*Indemnification*), 17 (*Limitation of Liability; Exclusion of Damages; Disclaimer*), 18.2 (*Effect of Expiration*) 18.3 (*Survival*), 20 (*Obligations Upon Early Termination*), 22 (*General Provisions*), 23 (*Governing Law*) and 24 (*Dispute Resolution; Jurisdiction*) shall survive the expiration of this Agreement.

18.4 Other Remedies. Termination or expiration of this Agreement for any reason shall not release any Party from any liability or obligation that has accrued prior to such expiration or termination, nor affect the survival of any provision hereof to the extent it is expressly stated to survive termination. Termination or expiration of this Agreement for any reason shall not constitute a waiver or release of, or otherwise be deemed to prejudice or adversely affect, any rights, remedies, or claims, whether for damages or otherwise, that a Party may have hereunder or that may arise out of or in connection with such termination or expiration.

19. EARLY TERMINATION

19.1 At Sato's Convenience. Sato may terminate this Agreement at-will on one hundred twenty (120) calendar days' written notice to Novan.

19.2 Material Breach. Without prejudice and in addition to any other contractual remedy the non-defaulting Party may have under this Agreement, either Party may terminate this Agreement in writing, if the other Party commits a material breach of any provision of this Agreement and such breach is not cured within sixty (60) calendar days after written notice of the breach is received by the other Party.

19.3 **Force Majeure**. The Agreement may be terminated by either Party in the event of a Force Majeure (as hereinafter defined) pursuant to Section 21.2.

19.4 **Insolvency**. Either Party may terminate this Agreement upon written notice if the other Party is dissolved or liquidated, files or has filed against it a petition under any bankruptcy or insolvency law that is not dismissed within sixty (60) calendar days, makes an assignment for the benefit of its creditors or has a receiver or trustee appointed for all or substantially all of its property.

19.5 **Patent Challenge**. In the event that Sato or any of its Affiliates commences or otherwise, directly or indirectly, pursues (or, other than as required by Law or legal process, voluntarily assists any Third Party to pursue in any material respect where Sato has knowledge that its assistance will be used by the Third Party to pursue) any proceeding seeking to have any of the Novan Patents revoked or declared invalid, unpatentable, or unenforceable, Novan may declare a material breach hereunder, terminate this Agreement on written notice to Sato and shall then have the right to exercise the remedies available under Section 20.1 with immediate effect.

20. OBLIGATIONS UPON EARLY TERMINATION

20.1 **Early Termination by Novan; Termination for Convenience by Sato**. In the event of termination of this Agreement by Novan in accordance with Sections 19.2, 19.3, 19.4 or 19.5 or by Sato under Section 19.1:

(i) all Licensed Rights shall revert to Novan without any compensation to be paid by Novan;

(ii) Sato shall return to Novan any and all Novan Scientific Information;

(iii) Sato shall transfer to Novan or its nominee any and all Marketing Approvals and all other filings and submissions with and to Regulatory Authorities with respect to the Licensed Product. To this end Sato shall make Commercially Reasonable Efforts to file for transfer with the relevant Regulatory Authorities and to give all other notifications and approvals necessary under law for the transfer of Marketing Approvals and such other filings and submissions;

(iv) Sato shall grant to Novan a worldwide, fully-paid, royalty-free license, with the right to sublicense, to use the Sato Trademarks (including, without limitation, the goodwill symbolized by such Sato Trademarks) used to brand the Licensed Product, and a license to reproduce, distribute, perform, display and prepare derivative works of Sato's copyrights used to brand or promote the Licensed Product, in each case solely to the extent necessary or useful for commercializing the Licensed Product;

(v) The licenses granted by Sato to Novan pursuant to Section 2.3 and other provisions of this Agreement shall continue in effect in addition to those sections that also

survive pursuant to Section 18.3 and shall be expanded to include the Licensed Field in the Licensed Territory;

(vi) Sato shall furnish Novan with reasonable cooperation, at Sato's expense, to assure a smooth transition of any clinical or other studies in progress related to the Licensed Products which Novan determines to continue in compliance with applicable Laws and ethical guidelines applicable to the transfer or termination of any such studies. In the event that Novan informs Sato that it does not intend to continue specific development activities then in progress, costs incurred in closing out such activities shall be borne by Sato; and

(vii) Sato shall not withdraw or cancel any Marketing Approval or Drug Approval Application, unless expressly instructed so by Novan in writing.

20.2 Early Termination by Sato. In the event of termination of this Agreement by Sato in accordance with Sections 19.2, 19.3 or 19.4:

(i) If such termination is pursuant to Section 19.2 or 19.4 for Novan's material breach or Novan's insolvency that in either case does not result in Novan's material failure to supply Compound or Licensed Product pursuant to then-existing obligations under the Commercial Supply Agreement or any Product Supply Agreement, Sato may elect by written notice to Novan provided concurrently with the relevant termination notice to have the Licensed Rights survive for the remainder of the Term (such Term determined as if the early termination had not occurred) subject to payment by Sato to Novan of (a) **[***]** and (b) all **[***]**; provided that **[***]**;

(ii) If such termination is pursuant to Section 19.2 or 19.4 for Novan's material breach or Novan's insolvency that in either case results in Novan's material failure to supply Compound or Licensed Product pursuant to then-existing obligations under the Commercial Supply Agreement or any Product Supply Agreement, or if Sato does not elect for the Licensed Rights to survive as provided in Section 20.2(i) concurrently with the relevant termination notice, the Licensed Rights shall terminate upon the effective date of termination, and Sato may pursue all rights and remedies it may have at law or in equity with respect to the early termination of this Agreement; and

(iii) Novan's obligations and Sato's rights under Articles 5, 6, 7, and 8 shall continue in addition to those sections that also survive pursuant to Section 18.3, including without limitation Sato's obligation to indemnify Novan pursuant to Section 16.2.

20.3 Bankruptcy Laws. All rights and licenses granted under or pursuant to this Agreement by Novan or Sato are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the United States Bankruptcy Code and of any similar provisions of applicable Laws under any other jurisdiction (collectively, the "**Bankruptcy Laws**"), licenses of right to "**intellectual property**" as defined under the Bankruptcy Laws. Each Party agrees that the other Party, as a licensee of rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the Bankruptcy Laws.

21. FORCE MAJEURE

21.1 Force Majeure. No failure or delay by either Party in the performance of any obligation hereunder shall be deemed a breach of this Agreement nor create any liability for any damages, increased cost or losses which the other Party may sustain by reason of such failure or delay of performance, if the same shall arise from any cause or causes beyond the control of that Party, such as earthquake, storm, flood, fire, other acts of nature, epidemic, war, riot, hostility, public disturbance, cessation of transport, act of public enemies, prohibition or act by a government or public agency, strike or other labor dispute or work stoppage (collectively "**Force Majeure**"); provided, however, that the Party so prevented shall continue to take all commercially reasonable actions within its power to comply with its obligations hereunder as fully as possible and to mitigate possible damages.

The Party so prevented shall without undue delay notify the other Party in writing thereof.

21.2 Continued Force Majeure. Should the event of Force Majeure continue for more than **[***]**, the Parties shall promptly discuss their further performance under this Agreement and whether to modify or terminate this Agreement in view of the effect of the event of Force Majeure. If no agreement can be reached within **[***]** after expiration of such **[***]**, either Party may terminate this Agreement effective immediately upon written notice to the other Party.

22. GENERAL PROVISIONS

22.1 Assignment. This Agreement is binding upon and will inure to the benefit of the Parties and their respective permitted assignees or successors in interest, including without limitation those that may succeed by assignment, transfer or otherwise to the ownership of either of the Parties or of the assets necessary to the conduct of the business to which this Agreement relates. This Agreement may not be assigned or otherwise transferred by either Party without the prior written consent of the other Party, which consent shall not be unreasonably withheld, delayed or conditioned; provided, however, that either Party may, without such consent, assign this Agreement together with all of its rights and obligations hereunder to its Affiliates, or to a successor in interest in connection with the transfer or sale of all or substantially all of its business to which this Agreement relates, or in the event of its merger or consolidation or similar transaction, subject to the assignee agreeing to be bound by the terms of this Agreement. Any purported assignment in violation of the preceding sentences shall be void. Any permitted successor shall assume and be bound by all obligations of its assignor or predecessor under this Agreement.

22.2 Headings. Headings are inserted for convenience and shall not affect the meaning or interpretation of this Agreement.

22.3 Waiver. No waiver of any default hereunder by either Party or any failure to enforce any rights hereunder shall be deemed to constitute a waiver of any subsequent default with respect to the same or any other provision hereof.

22.4 **Notices**. Any and all notices given by one Party to the other Party under this Agreement must be in writing and shall be deemed effectively given (i) upon personal delivery to the Party to be notified, (ii) when sent by confirmed email or facsimile if sent during normal business hours of the recipient, if not, then on the next Business Day, (iii) one day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt, or (iv) on the second Business Day after the date deposited if mailed by certified mail, return receipt requested, postage prepaid. All notices shall be sent to the other Party's address as set out at the beginning of this Agreement or to the latest address of such Party as shall have been communicated to the other Party.

Notices sent to Novan shall be directed to:

Novan, Inc.
4105 Hopson Road
Morrisville, North Carolina 27560
USA

Attn: **[***]**

Notices sent to Sato shall be directed to:

Sato Pharmaceutical Co. Ltd.
AHC Building 1-5-27
Moto-Akasaka, Minato-ku, Tokyo 107-0051
Japan

Attn: **[***]**

22.5 **Severability**. Should any part of this Agreement be held unenforceable or in conflict with the applicable Laws of any jurisdiction, the invalid or unenforceable part or provision shall be replaced with a provision which accomplishes, to the extent possible, the original business purpose of such part or provision in a valid and enforceable manner, and the remainder of this Agreement shall remain binding upon the Parties hereto.

22.6 **Entire Agreement**. This Agreement, together with all Annexes attached hereto, constitute the whole agreement between the Parties and shall cancel and supersede any and all prior and contemporaneous negotiations, correspondence, understandings and agreements, whether oral or written, between the Parties respecting the subject matter hereof, including without limitation the Confidentiality Agreement, provided, however, that all Confidential Information (as defined therein) exchanged between the Parties under the Confidentiality Agreement shall be deemed Confidential Information under this Agreement and shall be governed by the terms of this Agreement.

22.7 **Amendment**. Any amendment or modification to this Agreement shall only be made in writing and shall only be valid when signed by the due representatives of the Parties.

22.8 **Counterparts**. This Agreement may be executed in more than one (1) counterpart, each of which shall be deemed an original, but all of such counterparts taken together shall constitute one (1) and the same agreement.

22.9 Agency. Neither Party is, nor shall be deemed to be, an employee, agent, co-venturer, or legal representative of the other Party for any purpose. Neither Party shall be entitled to enter into any contracts in the name of, or on behalf of the other Party, nor shall either Party be entitled to pledge the credit of the other Party in any way or hold itself out as having the authority to do so.

22.10 Further Actions. Each Party agrees to execute, acknowledge, and deliver such further instruments, and to do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

22.11 Compliance with Laws. Each Party will comply with all Laws in performing its obligations and exercising its rights hereunder, including without limitation all Laws relating to the export, re-export or other transfer of any Information transferred pursuant to this Agreement or the Licensed Product.

22.12 Performance by Affiliates. Sato may perform some or all of its obligations under this Agreement through Affiliates, provided, however, that Sato shall remain responsible for the performance by its Affiliates and shall use Commercially Reasonable Efforts to cause its Affiliates to comply with the provisions of this Agreement in connection with such performance.

23. GOVERNING LAW

23.1 Governing Law. The construction, validity and performance of this Agreement shall be governed in all respects by the laws of the state of Delaware, excluding its provisions regarding conflicts of law, except that Article 24 and any arbitration thereunder shall be governed by the Federal Arbitration Act, Chapters 1 and 2. The United Nations Convention on the International Sale of Goods shall not apply. This Agreement shall be written and executed in, and all other communications under or in connection with this Agreement shall be in, the English language. Any translation into any other language shall not be an official version thereof, and in the event of any conflict in interpretation between the English version and such translation, the English version shall control.

24. DISPUTE RESOLUTION; JURISDICTION

24.1 Resolution by CEOs. In the event of any dispute, claim, question, or disagreement arising from or relating to this Agreement or the breach thereof ("**Dispute**"), the Chief Executive Officers of each Party ("**CEOs**") shall attempt to reach a solution satisfactory to both Parties. If the CEOs do not reach such solution within a period of **[***]** or such longer period as the Parties may mutually agree upon, then, upon notice by either Party to the other, all Disputes shall be finally settled by arbitration administered by the International Centre for Dispute Resolution ("**ICDR**") in accordance with the International Arbitration Rules ("**Rules**").

24.2 Arbitration. The arbitration shall be held in London, United Kingdom. The language of the arbitration shall be English. The arbitration shall be conducted by three (3) arbitrators; provided, however, that the arbitration may be conducted by only one arbitrator if the

Parties so agree in advance of the arbitration and are able to agree upon a single, mutually acceptable individual who is knowledgeable in the subject matter at issue in the dispute. If the arbitration is to be conducted by three (3) arbitrators, within **[***]** after the commencement of arbitration, each Party shall appoint one (1) arbitrator, and within **[***]** of their appointment, the two appointed arbitrators shall select a third arbitrator who shall act as the chair of the tribunal. If any of the arbitrators are not appointed within the deadline, the ICDR shall appoint the arbitrator.

24.3 Award. The award shall be made within **[***]** of the filing of the notice of arbitration, and the arbitrator(s) shall agree to comply with this schedule before accepting appointment. However, this time limit may be extended by agreement of the Parties or by the arbitrator(s) if necessary. Judgment on the award rendered by the arbitrator(s) may be enforced in any court having competent jurisdiction thereof.

24.4 Attorneys' Fees and Costs. The arbitrator(s) shall award to the prevailing Party, if any, as determined by the arbitrators, all of its attorneys' fees and costs.

24.5 Confidentiality. The Parties undertake to keep confidential all awards in their arbitration, together with all materials in the proceedings created for the purpose of the arbitration and all other documents produced by another Party in the proceedings not otherwise in the public domain, save and to the extent that disclosure may be required of a Party by legal duty, to protect or pursue a legal right or to enforce or challenge an award in legal proceedings before a court or other judicial authority.

24.6 Disputes Relating to Patent Rights Notwithstanding the provisions of this Section 24, disputes relating to the inventorship, enforceability, validity or scope of patent rights shall be submitted for resolution to a court of competent jurisdiction.

IN WITNESS WHEREOF, the Parties hereto have caused this Agreement to be executed in duplicate by their respective duly authorized office or representatives.

Novan, Inc.

/s/ Nathan Stasko

By: **Nathan Stasko, President and CEO**

Date: January 12, 2017

Sato Pharmaceutical Co., Ltd.

/s/ Seiichi Sato

By: **Seiichi Sato, President and CEO**

Date: January 12, 2017

Overview of Annexes (to be attached):

Annex 1: Novan Scientific Information

Annex 2: Patent List

Annex 3: Specifications

Annex 4: Novan Trademarks

Annex 1: Novan Scientific Information (CTD)

[***] Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

Annex 2: Patent List

Application No.	Title	Filing Date; Licensed Territory Numbers	Countries where Application was Filed & Status
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]

[***] Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

Annex 3: Specifications

[***]

[***] Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

Annex 4: Novan Trademarks

[***] Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

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FIRST AMENDMENT TO LICENSE AGREEMENT BETWEEN NOVAN, INC. AND SATO PHARMACEUTICAL CO., LTD.

This First Amendment to the License Agreement (the "**Amendment**") is made and entered into as of January 12, 2017 (the "**Amendment Effective Date**") by and between Novan, Inc., a Delaware corporation having an address at 4105 Hopson Road, Morrisville, North Carolina 27560, USA ("**Novan**") and Sato Pharmaceutical Co., Ltd., a Japanese corporation having an address at 1-5-27, Moto-Akasaka, Minato-ku, Tokyo 107-0051, Japan ("**Sato**"), and amends that certain License Agreement between Novan and Sato, dated as of January 12, 2017 (the "**Agreement**").

RECITALS

WHEREAS, Novan and Sato are parties to the Agreement; and

WHEREAS, Novan and Sato desire to amend certain payment terms and conditions of the Agreement as provided below.

NOW THEREFORE, in consideration of the mutual covenants contained herein, the Parties hereto agree as follows:

AGREEMENT

1. **Defined Terms.** All capitalized terms used herein but not defined herein shall have the meanings given to such terms in the Agreement.

2. **Section 14.1.** Section 14.1 shall be amended and restated in its entirety to read as follows:

14.1 Payments. In consideration of the licenses and other rights granted to Sato herein, Sato shall pay to Novan the following one-time, lump sum payments on occurrence of the corresponding events.

UPFRONT PAYMENT (the "**Upfront Payment**")

Upon the Effective Date	1.25 billion JPY

DEVELOPMENT MILESTONE PAYMENTS

Upon [***]	[***]
Upon [***]	[***]
Upon [***]	[***]
Upon [***]	[***]
Upon [***]	[***]

SALES MILESTONE PAYMENTS

One-time sales milestone payments shall be made by Sato to Novan upon the first achievement of each of the following annual Net Sales milestones:

Annual Net Sales of **[***]**	**[***]**
Annual Net Sales of **[***]**	**[***]**
Annual Net Sales of **[***]**	**[***]**

For avoidance of doubt, if two or more of the foregoing milestones shall be achieved in the same calendar year, the payments corresponding to each such milestone shall be payable to Novan with respect to such calendar year.

3. **Section 14.3.** Section 14.3 shall be amended and restated in its entirety to read as follows:

14.3 Notification. Sato shall notify Novan of the achievement of each of the development milestones set forth in Section 14.1 within **[***]** of its achievement, and each of the sales milestones set forth in Section 14.1 within **[***]** after Sato closes its books for the relevant annual period in which such sales milestone payment becomes due. All payments under Section 14.1 shall be made within **[***]** after Sato receives the relevant invoice from Novan, except that the Upfront Payment due pursuant to Section 14.1 shall be made within **[***]** after the Effective Date. All payments under Section 14.1 shall be made without setoff or deduction of any kind, other than pursuant to **[***]**.

4. **Effective Date.** This Amendment is effective as of the Amendment Effective Date immediately after the Agreement becomes effective (the "**Effective Time**"), and the terms and conditions of this Amendment shall govern after such Effective Time.

[***] Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

5. **Reaffirmation of Other Terms and Conditions.** The Agreement shall remain in full force and effect, as amended hereby, and as so amended, the Parties hereby reaffirm their respective rights and obligations thereunder.

6. The Parties may execute this Amendment in multiple counterparts, each of which shall be an original and all of which together shall constitute, together with the Agreement, one legal instrument.

IN WITNESS WHEREOF, the Parties have signed and delivered this Amendment as of the date first written above.

Novan, Inc.	**Sato Pharmaceutical Co., Ltd.**
/s/ Nathan Stasko	/s/ Seiichi Sato
By: **Nathan Stasko, President and CEO**	By: **Seiichi Sato, President and CEO**
Date: January 12, 2017	Date: January 12, 2017

[***] Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-213854) of Novan, Inc. of our report dated March 20, 2017 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Raleigh, North Carolina
March 20, 2017

Exhibit 31.1

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302
OF THE SARBANES-OXLEY ACT OF 2002

I, Nathan Stasko, certify that:

1. I have reviewed this annual report on Form 10-K of Novan, Inc. (the "registrant");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

    (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

March 20, 2017

By: /s/ Nathan Stasko
Nathan Stasko
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302
OF THE SARBANES-OXLEY ACT OF 2002

I, Richard Peterson, certify that:

1. I have reviewed this annual report on Form 10-K of Novan, Inc. (the "registrant");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

March 20, 2017

By: /s/ Richard Peterson
Richard Peterson
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002

I, Nathan Stasko, President and Chief Executive Officer of Novan, Inc. (the "Company"), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) the Annual Report on Form 10-K of the Company for the year ended December 31, 2016 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the periods presented therein.

Date: March 20, 2017

/s/ Nathan Stasko
Nathan Stasko
President and Chief Executive Officer
(Principal Executive Officer)

This certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the Company for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and shall not be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Report, irrespective of any general incorporation language contained in such filing.

A signed original of this written statement required by Section 906 of the Sarbanes-Oxley Act of 2002 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002

I, Richard Peterson, Chief Financial Officer of Novan, Inc. (the "Company"), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) the Annual Report on Form 10-K of the Company for the year ended December 31, 2016 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the periods presented therein.

Date: March 20, 2017

/s/ Richard Peterson
Richard Peterson
Chief Financial Officer
(Principal Financial Officer)

This certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the Company for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and shall not be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Report, irrespective of any general incorporation language contained in such filing.

A signed original of this written statement required by Section 906 of the Sarbanes-Oxley Act of 2002 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.