# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**Washington, D.C. 20549**

# FORM 10-K

**(Mark One)**

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

**For the fiscal year ended December 31, 2018**

☐ **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 000-55764**

# EXICURE, INC.

**(Exact name of registrant as specified in its charter)**

| **Delaware** | **81-5333008** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification No.)** |

**8045 Lamon Avenue**
**Suite 410**
**Skokie, IL 60077**
**(Address of principal executive offices and Zip Code)**
**(847) 673-1700**
**(Registrant's telephone number, including area code)**

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

| **Common Stock, par value $0.0001 per share** | **None** |
|---|---|
| **(Title of each class)** | **(Name of each exchange on which registered)** |

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

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

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

Indicate by check mark whether the 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 ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). Yes ☒ 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. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting

company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

| | | | |
|---|---|---|---|
| ☐ | Large accelerated filer | ☐ | Accelerated filer |
| ☒ | Non-accelerated filer | ☒ | Smaller reporting company |
| | | ☒ | Emerging growth company |

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

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

Based on the closing price of the registrant's common stock on the last business day of the registrant's most recently completed second fiscal quarter, which was June 30, 2018, the aggregate market value of its shares (based on a closing price of $5.70 per share) held by non-affiliates was approximately $117.6 million. Shares of the registrant's common stock held by each executive officer and director and by each entity or person that owned five percent or more of the registrant's outstanding common stock were excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 5, 2019, the registrant had 44,358,000 shares of common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive Proxy Statement for the 2019 Annual Meeting of Stockholders, to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Form 10-K, are incorporated by reference in Part III, Items 10-14 of this Form 10-K. Except for the portions of the Proxy Statement specifically incorporated by reference in this Form 10-K, the Proxy Statement shall not be deemed to be filed as part hereof.

**EXICURE, INC.**

**ANNUAL REPORT ON FORM 10-K**

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## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, including the sections entitled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," contains express or implied "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical fact contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "could," "will," "would," "should," "expect," "plan,", "anticipate," "believe," "estimate," "intend," "predict," "seek," "contemplate," "project," "continue," "potential," "ongoing" or the negative of these terms or other comparable terminology. Forward-looking statements also include the assumptions underlying or relating to such statements.

Although we believe that the expectations reflected in the forward-looking statements contained herein are reasonable, such expectations or any of the forward-looking statements may prove to be incorrect and actual results could differ materially from those projected or assumed in the forward-looking statements. Our future financial condition and results of operations, as well as any forward-looking statements, are subject to inherent risks and uncertainties, including, but not limited to, the risk factors set forth in Part I, Item 1A "Risk Factors" below and for the reasons described elsewhere in this Annual Report on Form 10-K. All forward-looking statements and reasons why results may differ included in this report are made as of the date hereof and we do not intend to update any forward-looking statements except as required by law or applicable regulations.

- the initiation, timing, progress and results of our research and development programs, preclinical studies, clinical trials and Investigational New Drug, or IND, application, Investigational Medicinal Product Dossier, or IMPD, Clinical Trial Application, or CTA, New Drug Application, or NDA, or other regulatory submissions;
- our dependence on current and future collaborators for developing, obtaining regulatory approval for and commercializing therapeutic candidates in the collaboration;
- our receipt and timing of any milestone payments or royalties under any current or future research collaboration and license agreements or arrangements;
- our ability to identify and develop therapeutic candidates for treatment of additional disease indications;
- our or a current or future collaborator's ability to obtain and maintain regulatory approval of any of our therapeutic candidates;
- the rate and degree of market acceptance of any approved therapeutic candidates;
- the commercialization of any approved therapeutic candidates;
- our ability to establish and maintain collaborations and retain commercial rights for our therapeutic candidates in the collaborations;
- the implementation of our business model and strategic plans for our business, technologies and therapeutic candidates;
- our estimates of our expenses, ongoing losses, future revenue and capital requirements, including our expectations relating to the use of proceeds from our private placement offering, and our needs for additional financing;
- our ability to obtain additional funds for our operations;

- our ability to obtain and maintain intellectual property protection for our technologies and therapeutic candidates and our ability to operate our business without infringing the intellectual property rights of others;
- our reliance on third parties to conduct our preclinical studies and clinical trials;
- our reliance on third party supply and manufacturing partners to supply the materials and components for, and manufacture, our research and development, preclinical and clinical trial supplies;
- our ability to attract and retain qualified key management and technical personnel;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act;
- our financial performance;
- the impact of government regulation and developments relating to our competitors or our industry; and
- other risks and uncertainties, including those listed in Part I, Item 1A of this Annual Report on Form 10-K under the caption "Risk Factors."

These statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed in Part I, Item 1A of this Annual Report on Form 10-K under the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K.

Any forward-looking statement in this Annual Report on Form 10-K reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our business, results of operations, industry and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this Annual Report on Form 10-K and the documents that we reference herein and have filed with the SEC as exhibits thereto completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements. Except as required by law, we assume no, and specifically decline any, obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains or may contain estimates, projections and other information concerning our industry, our business and the markets for certain therapeutics, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which these data are derived.

Except where the context otherwise requires, in this Annual Report on Form 10-K, the "Company," "Exicure," "we," "us" and "our" refers to Exicure, Inc., a Delaware corporation, and, where appropriate, its subsidiary.

## TRADEMARKS

All trademarks, service marks and trade names appearing in this Annual Report on Form 10-K are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

## PART I

*Unless otherwise stated or the context otherwise indicates, references to "Exicure," the "Company," "we," "our," "us," or similar terms refer to Exicure, Inc. and our wholly-owned subsidiary, Exicure Operating Company. Exicure Operating Company, which we refer to as "Exicure OpCo," holds all material assets and conducts all business activities and operations of the Company.*

### Item 1. Business.

### Overview

We are a clinical-stage biotechnology company developing therapeutics for immuno-oncology, inflammatory diseases and genetic disorders based on our proprietary Spherical Nucleic Acid, or SNA, technology. SNAs are nanoscale constructs consisting of densely packed synthetic nucleic acid sequences that are radially arranged in three dimensions. We believe the design of our SNAs gives rise to distinct chemical and biological properties that may provide advantages over other nucleic acid therapeutics and enable therapeutic activity outside of the liver. Since our SNAs have shown in a Phase 1 clinical trial and in preclinical studies that they can cross certain biological barriers when administered locally, we believe that they have the therapeutic potential to target diseases not typically addressed with other nucleic acid therapeutics. We have demonstrated the ability to cross certain biological barriers in Phase 1 clinical trials of three therapeutic candidates, AST-008, XCUR17 and AST-005.

***Immuno-oncology***

AST-008 is an SNA consisting of toll-like receptor 9, or TLR9, agonists designed for immuno-oncology applications. TLR9 agonists bind to and activate TLR9 receptors. We believe AST-008 may be used for immuno-oncology applications as a monotherapy or in combination with checkpoint inhibitors. Checkpoint inhibitors are therapeutics that prevent tumors from evading destruction by the immune system. We have observed that administration of AST-008 as a monotherapy can have anti-tumor activity in mouse models of colon cancer, breast cancer, lymphoma and melanoma. We have also observed that, in preclinical studies in a variety of tumor models, AST-008, applied in combination with certain checkpoint inhibitors, exhibited anti-tumor responses and survival rates that were greater than those demonstrated by checkpoint inhibitors alone. We have also demonstrated that AST-008 was active when administered subcutaneously, intratumorally or intravenously, in both prevention and established mouse tumor models. The administration of AST-008 also produced localized as well as abscopal anti-tumor activity in mouse cancer models. Additionally, administration of AST-008 in combination with certain checkpoint inhibitors conferred adaptive immunity in breast and colon cancer mouse models.

During the fourth quarter of 2018 the FDA opened the IND for AST-008 and informed the Company that our proposed Phase1b/2 trial may proceed. Early in 2019, we opened four clinical sites and began dosing and recruiting patients in that trial. This is a Phase 1b/2, open-label, multi-center trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of intratumoral AST-008 injections alone and in combination with intravenous pembrolizumab in patients with advanced solid tumors. Conditions under study are planned to include advanced or metastatic: Merkel cell carcinoma, head and neck squamous cell carcinoma, cutaneous squamous cell carcinoma and melanoma. The primary outcome measure is the safety and tolerability of AST-008 alone and in combination with pembrolizumab. Secondary outcomes include the recommended Phase 2 dose and disease assessment with RECIST 1.1.

During the second quarter of 2017, we filed a CTA for a Phase 1 clinical trial of AST-008 in the United Kingdom. In the third quarter of 2017, we received an authorization from the MHRA, the competent health authority of the United Kingdom, to conduct a Phase 1 clinical trial with AST-008. We began subject dosing in our Phase 1 clinical trial for AST-008 in the fourth quarter of 2017. This trial was completed in the third quarter of 2018. Based on our initial analyses of the Phase 1 clinical trial results, AST-008 was shown to be safe and tolerable in all subjects, with no serious adverse events and no dose limiting toxicity. All AST-008-related adverse events were of short duration, reversible and consistent with TLR9 activation. In addition, AST-008 was shown to elicit high levels of certain cytokines as well as to activate important effector cells of the immune system, including T cells and natural killer cells which are the main drivers of an anti-tumor response.

***Inflammatory diseases***

*XCUR17*

XCUR17, is an SNA that targets the mRNA that encodes interleukin 17 receptor alpha, or IL-17RA, a protein that is considered essential in the initiation and maintenance of psoriasis. Although the availability of inhibitors of TNF revolutionized the systemic treatment of severe psoriasis, studies of disease pathogenesis have shifted attention to the IL-17 pathway, in which IL-17RA is a key driver of psoriasis. Our strategy is to reduce the levels of IL-17RA in the skin by topically applying XCUR17. In preclinical studies, XCUR17 inhibited IL-17RA in the keratinocytes of the skin.

We filed a CTA for a Phase 1 clinical trial of XCUR17 in patients with psoriasis in Germany in the third quarter of 2017. Our CTA was approved in February 2018 and we began dosing patients in our Phase 1 clinical trial in April 2018. The Phase 1 clinical trial, which had final patient visits in the fourth quarter of 2018, was a randomized, double-blinded, placebo-controlled trial in twenty-one patients with mild to moderate chronic plaque psoriasis designed to assess the safety of XCUR17 formulated as a topical gel, and to evaluate early signs of efficacy. All patients received three strengths of XCUR17 gel, a vehicle gel, and a positive comparator (Daivonex® cream), which were all applied on different areas of psoriatic skin within each individual patient.

In the fourth quarter of 2018 we reported results from the Phase 1 trial of XCUR17. In the case of XCUR17, of the twenty-one treated patients, eleven treated with the highest strength XCUR17 gel were observed to have a reduction in redness and improvement in healing as determined by blinded physician assessments. Further, the highest strength XCUR17 gel showed a statistically significant improvement in psoriasis symptoms versus the vehicle gel. By comparison, seventeen of the twenty-one patients treated with the positive comparator showed a clinical response, while four patients treated with the placebo vehicle had a clinical response.

There were no adverse safety events related to treatment with XCUR17 observed. In addition to the safety, tolerability and clinical assessments, the trial measured psoriatic infiltrate thickness over the 26-day treatment period. No relevant changes in mean psoriatic infiltrate thickness were observed for the three XCUR17 gels or the active ingredient-free vehicle gel. At this time, assessments of IL-17RA mRNA levels from skin biopsies collected from the treated areas in patients have not yet been correlated with the clinical or infiltrate thickness assessments.

*Dermelix License Agreement*

On February 17, 2019 Exicure entered into a License and Development Agreement, or the Dermelix License Agreement, with DERMELIX, LLC, d/b/a Dermelix Biotherapeutics. Under the terms of agreement, Dermelix licensed worldwide rights to research, develop, and commercialize Exicure's technology for the treatment of Netherton Syndrome and, at Dermelix's option, up to five additional rare skin indications.

Dermelix will initially develop a targeted therapy for the treatment of Netherton Syndrome (NS). NS is a rare and severe autosomal recessive disorder caused by loss-of-function mutations in the *SPINK5* gene, which encodes the serine protease inhibitor LEKT1 involved in skin barrier function. NS affects approximately 1 in 200,000 children born each year, and is characterized by severely inflamed, red, scaled, itchy skin, and patients are at increased risk of mortality in the first year of life due to recurrent infections and dehydration as a result of the impaired skin barrier. Currently, there are no approved treatments for NS patients and off-label use of standard of care treatments are of limited utility.

Under the terms of the Dermerlix License Agreement, Exicure received an upfront payment of $1 million at closing of the transaction and will receive an additional $1 million upon the exercise of each of the five options granted to Dermelix. Exicure will be responsible for conducting the early stage development for each indication up to IND enabling toxicology studies. Dermelix will undertake subsequent development, commercial activities and financial responsibility. For each of NS as well as any additional licensed product for which Dermelix exercises one of its options, Exicure is eligible to receive potential payments totaling up to $13.5 million upon achievement of certain development and regulatory milestones and up to $152.5 million upon achievement of certain sales milestones per indication in each of six indications. In addition, Exicure will receive low double-digit royalties on annual net sales for SNA therapeutics developed.

*Other Inflammatory Diseases*

We believe that one of the key strengths of our proprietary SNAs is that they have the potential to enter a number of different cells and organs. As a consequence, we are also conducting early stage research activities in ophthalmology, pulmonology, and gastroenterology.

We believe promising therapeutic targets for SNAs include antibody targets with confirmed therapeutic benefit. We envision inhibiting these targets with local application of SNAs in a variety of therapeutic areas. We believe that this approach combines the benefits of specifically inhibiting validated targets without the potential safety issues associated with systemic therapy.

***Genetic disorders***

We are investigating the utility of our SNA technology for the treatment of neurological conditions. In June 2018, the Company and researchers from The Ohio State University Wexner Medical Center presented a poster at the Cure SMA Annual Conference titled: "Nusinersen in spherical nucleic acid (SNA) format improves efficacy both in vitro in SMA patient fibroblasts and in Δ7 SMA mice and reduces toxicity in mice." It was observed in a preclinical study that nusinersen in SNA format prolonged survival by four-fold (maximal survival of 115 days compared to 28 days for nusinersen-treated mice) as well as doubled the levels of healthy full-length SMN2 mRNA and protein in SMA patient fibroblasts when compared to nusinersen.

Subsequently, in the fall of 2018, we completed a biodistribution study in rats comparing nusinersen to nusinersen in SNA format. We found that more nusinersen in SNA format was retained in the rats' brain and spinal cord compared to nusinersen retained in the rats' brain and spinal cord at 24, 72 and 168 hours.

We are now formulating our strategy for developing a pipeline of SNA therapeutics targeting neurological diseases. Preclinical research is underway in a number of indications including, spinal muscular atrophy, Huntington's Disease, spinocerebellar ataxia type 3 (SCA3), SCA2, SCA1, Friedreich's Ataxia, and Batten disease. We believe this preclinical research may lead to a therapeutic candidate for one of the above neurological indications.

***AST-005***

AST-005 is an SNA targeting TNF for the treatment of mild to moderate psoriasis. AST-005 is intended to be administered locally in a gel to psoriatic lesions. In a completed Phase 1 clinical trial, AST-005, when topically administered to the skin of patients with mild to moderate psoriasis, resulted in no drug associated adverse events, and demonstrated a reduction of TNF mRNA. The TNF mRNA reduction elicited by the highest strength of AST-005 gel was statistically significant when compared to the effects of the vehicle.

On December 2, 2016, we entered into a research collaboration, option and license agreement with Purdue Pharma L.P., referred to as the Purdue Collaboration. As part of our collaboration with Purdue, a Phase 1b clinical trial was conducted in Germany to evaluate the effect of AST-005 gel in patients with chronic plaque psoriasis. The trial demonstrated that AST-005 is safe and tolerable in patients at higher doses than were previously studied, however, the study did not result in a statistically significant decrease in echo lucent band thickness, one of the key indicators of efficacy in patients with psoriasis. In April 2018, Purdue notified the Company it had declined to exercise its option to develop AST-005 at that time, but that it also intended to retain rights relating to the TNF target, and Purdue reserved its right to continue joint development, with Exicure, of new anti-TNF drug candidates and to retain its exclusivity and other rights to AST-005. Purdue has not indicated that it has any plans to pursue AST-005 at this time and there no active therapeutic candidates in development.

***Intellectual property***

We believe that we have a strong intellectual property, or IP, position in the field of SNA therapeutics. As of December 31, 2018, our patent portfolio consists of over 60 issued patents and allowed patent applications and over 135 pending patent applications. We have licensed IP from Northwestern University and have also independently filed patents to protect our IP. Our license from Northwestern University is for exclusive worldwide rights to the use

of SNA technology for therapeutic applications. Any patents arising from AST-005, XCUR17 or AST-008 applications would expire by 2035, 2037, and 2034 or 2035, respectively.

**Our Strategy**

We intend to build a leading nucleic acid therapeutics company based on our proprietary SNA technology. The key elements of our strategy are:

- **Advance AST-008 through clinical development for immuno-oncology applications.** We have conducted preclinical studies of AST-008 in immuno-oncology applications including bladder, breast and colorectal cancer, lymphoma and melanoma. We believe AST-008 is applicable in two cancer treatment strategies: as a monotherapy or in combination with checkpoint inhibitors. We began our Phase 1 clinical trial for AST-008 in the United Kingdom in the fourth quarter of 2017. This trial was completed in the third quarter of 2018. During the fourth quarter of 2018 the FDA opened the IND for AST-008 and informed the Company that our proposed Phase1b/2 trial may proceed. We have now opened four clinical sites and are recruiting patients. We believe AST-008 may be an attractive partnership candidate and we continue to explore that possibility. We may seek to develop AST-008 through other clinical trial pathways, including investigator-initiated trials.

- **Continue research and development in neurological applications.** In June 2018, it was observed in a preclinical study that nusinersen in SNA format prolonged survival by four-fold as well as doubled the levels of healthy full-length SMN2 mRNA and protein in SMA patient fibroblasts when compared to nusinersen. Subsequently, in the fall of 2018, we completed a bio-distribution study comparing nusinersen to nusinersen in SNA format in rats. The concentration of nusinersen in the kidneys was significantly increased in comparison to nusinersen in SNA format while more nusinersen in SNA format was retained in the CNS (brain and spinal cord) compared to nusinersen at 24, 72 and 168 hours. We are now formulating our strategy for developing a pipeline of SNA therapeutics targeting neurological diseases. Preclinical research is underway in a number of indications including, spinal muscular atrophy, Huntington's Disease, spinocerebellar ataxia type 3 (SCA3), SCA2, SCA1, Friedreich's Ataxia, and Batten disease. We believe this preclinical research may lead to a therapeutic candidate for one of the above neurological indications.

- **Advance SNA platform in dermatological indications.** In the fourth quarter of 2018 we reported results from the Phase 1 trial of XCUR17, an SNA for the treatment of mild to moderate psoriasis. Of the twenty-one patients, eleven treated with the highest strength XCUR17 gel were observed to have a reduction in redness and improvement in healing as determined by blinded physician assessments. Informed by these results, on February 17, 2019, we entered into a License and Development Agreement with Dermelix. Under the terms of agreement, Dermelix licensed worldwide rights to research, develop, and commercialize Exicure's technology for the treatment of Netherton Syndrome and up to five additional rare skin indications.

- **Use our proprietary SNA technology to develop additional therapeutic candidates.** We have demonstrated in preclinical studies that in certain application, SNAs exhibit superior biodistribution properties compared to linear oligonucleotides being both more persistent and more stable in the tissue or organ of interest. As a consequence, SNAs may have potential applications in a variety of additional organs including the central nervous system, eye, gastrointestinal tract and lungs. We believe that we have the opportunity to take known oligonucleotides of clinical utility and enhance their therapeutic potential by incorporating them in our SNA platform. In addition, we may be able to develop novel therapeutic candidates targeting validated therapeutic targets.

- **Enter into additional partnerships to accelerate development and commercialization of our SNA therapeutic candidates.** We believe our proprietary SNA technology lends itself to license agreements or development partnerships with pharmaceutical companies that have development or commercial expertise in a particular therapeutic area of interest where it would be uneconomical or impractical for us to develop SNA therapeutics independently.

- **Build, enhance and protect our proprietary SNA intellectual property.** We believe the three-dimensional structure of our SNAs provides novel technological and commercial opportunities. We have licensed IP from Northwestern University and have also filed patents independently to protect our IP. Our license from Northwestern University is for exclusive worldwide rights to the use of SNA technology for therapeutic

applications. We will continue to protect our IP and innovations arising from our research and development efforts, and prudently in-license technologies where appropriate for protection of our therapeutic pipeline and the broader SNA technology. Any patents arising from AST-005, XCUR17 or AST-008 applications would expire by 2035, 2037, and 2034 or 2035, respectively.

**Introduction to Nucleic Acid Therapeutics**

***Overview of nucleic acids as a therapeutic modality***

Historically, therapeutic development has been focused on small molecules and biologics, or protein-based therapeutics, including antibodies. Development of small molecule therapeutics often involves screening thousands of compounds, sometimes without a known protein structure or active site to which the small molecule can bind and affect its disease-related function. Protein-based therapeutics are also subject to limitations. For example, the choice of targets that antibodies can address is typically limited to extracellular protein targets. However, the majority of protein targets are located inside the cell, making them undruggable by antibodies.

Nucleic acid therapeutics represent a treatment approach differing in many important ways from small molecules and biologics. Nucleic acid therapeutics are based on the well-established scientific understanding that DNA in the nucleus of cells is converted into an intermediate molecule, called messenger RNA, or mRNA, that serves as the template for making proteins. Therapeutic gene regulation is the use of nucleic acid therapeutics to modulate the production of target proteins by changing the amount of mRNA that is converted to protein, thereby providing an approach to treating diseases at their genetic origin. Our SNAs are a type of nucleic acid therapeutic.

We believe the development timeline for nucleic acid therapeutic candidates will be shorter than that of small molecules and antibodies. Nucleic acid therapeutics can be directed against most mRNA, including the mRNA of proteins that cannot be targeted by small molecules or antibodies. Due to the detailed knowledge of mRNA sequences in humans, nucleic acid therapeutics can be engineered to be specific to a region of an mRNA sequence while interacting minimally with all other mRNA sequences. Moreover, due to the well-defined length and composition of mRNA sequences, a relatively small set of rationally designed therapeutic candidates, usually hundreds, can be synthesized and tested for activity against an mRNA target. This is in contrast to the small molecule drug development process that requires a much larger number of candidates to be screened.

***Challenges in developing nucleic acid therapeutics***

Significant progress has been made in the development of nucleic acid therapeutics. However, we believe there are ongoing technical challenges in the nucleic acid therapeutics field. Nucleic acids are molecules that, when administered without proper formulation, encounter a number of barriers to their bioavailability, biodistribution, and desired biological activity. These challenges have often been met by chemically modifying the oligonucleotide and by encapsulating or complexing it with a lipid or polymer carrier. Despite these advances in the delivery of oligonucleotides, the biodistribution of these molecules remains a challenge since oligonucleotides typically accumulate in the liver after subcutaneous or intravenous administration, thereby limiting their primary application to diseases of the liver. In an array of experiments, we have demonstrated that SNAs, administered locally without encapsulation or complexation, enter cells and organs. We believe the local administration of our gene regulatory SNAs will potentially enable safe and efficacious therapeutic applications to organs beyond the liver.

**Our Proprietary Technology: Spherical Nucleic Acids**

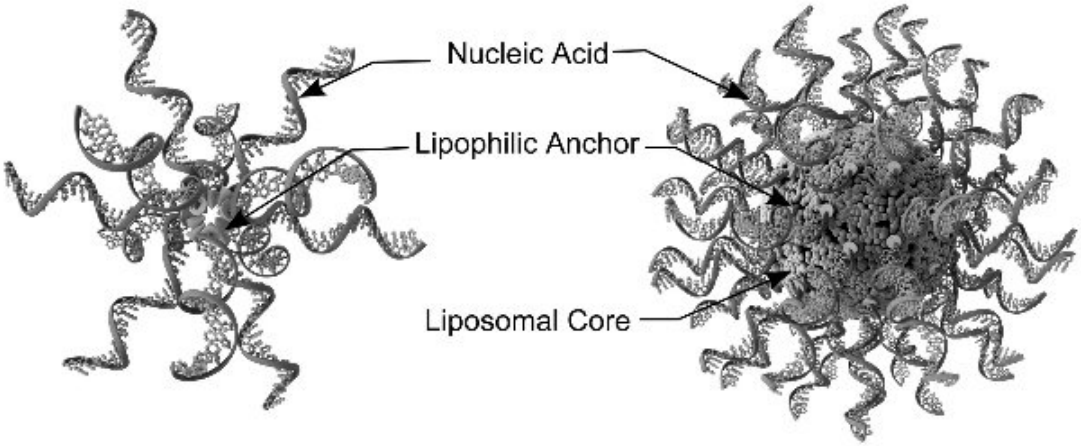
Our therapeutic discovery and development efforts rely on our proprietary SNA technology. SNAs are nanoscale constructs consisting of densely packed synthetic nucleic acid molecules that are radially arranged in three dimensions. We refer to these synthetic nucleic acid molecules in our SNAs as oligonucleotides and the radial orientation of the oligonucleotides without lipid or polymer encapsulation as our “inside out” or “3-D” approach. Our SNAs, unlike many other nucleic acid therapeutics, do not require lipid or polymer encapsulation or complexation in order to be delivered. Encapsulation is the process of confining the nucleic acids inside the cavities

of larger structures, typically liposomes, whereas complexation is the process of creating an assembly of nucleic acids bound together with other molecules, typically lipids or polymers.

This arrangement of oligonucleotides allows our proprietary SNAs to enter cells through class A scavenger receptors. Class A scavenger receptors are commonly found on the surface of cells throughout the body, which we believe provides a ubiquitous mechanism of cellular entry for the local administration of our SNA therapeutic candidates. This mechanism of cellular entry is different from many other nucleic acid therapeutics that typically bind to receptors found only in the liver.

The broad tissue penetration and biodistribution properties of SNAs potentially enable three distinct therapeutic approaches. SNAs may be designed to reduce target protein levels by reducing corresponding mRNA levels in cytoplasm. SNAs may also be designed to modulate splicing of pre-mRNA in the nucleus to enhance or alter the product of a target protein and mitigate a genetic defect. Finally, SNAs may be designed to potentially elicit an anti-tumor immune response by agonizing toll like receptors in the endosomes.

***Examples of our proprietary SNA constructs***




***All of our SNAs contain oligonucleotides that are densely packed and radially oriented.***

We believe the key advantages of our proprietary SNAs include:

- **SNAs cross certain biological barriers to deliver nucleic acid therapeutics .** Local delivery of nucleic acid therapeutics through biological barriers, such as the skin, has been a significant technical challenge. In a Phase 1 clinical trial of XCUR17 in patients with mild to moderate psoriasis, eleven of the twenty-one patients treated with the highest strength XCUR17 gel were observed to have a reduction in redness and improvement in healing as determined by blinded physician assessments. Further, in preclinical studies, we have demonstrated delivery and activity of our SNAs in the central nervous system, eye, lung, and gastrointestinal tract.
- **SNAs potentially exhibit superior biodistribution properties compared to linear oligonucleotides.** In the fall of 2018, we completed a biodistribution study in rats comparing nusinersen to nusinersen in SNA format. We found that more nusinersen in SNA format was retained in the rats' brain and spinal cord compared to nusinersen retained in the rats' brain and spinal cord at 24, 72 and 168 hours. We believe that we have the opportunity to take known oligonucleotides of clinical utility and enhance their therapeutic potential by incorporating them in our SNA platform. In addition, we may be able to develop novel therapeutic candidates.
- **SNAs are potentially well-tolerated.** In each of the Phase 1 clinical trials of AST-005 and XCUR17, we observed no drug associated adverse events when the SNA therapeutic candidate was applied topically to the skin of patients with mild to moderate psoriasis. No serious adverse events were observed in our Phase 1 trial

after injecting AST-008 subcutaneously into healthy volunteers. There are three key elements to our safety strategy. First, by administering SNAs locally, we expect to minimize systemic exposure thereby decreasing safety risk. Second, because SNAs enter cells and tissues without lipid or polymer encapsulation or complexation, we expect to avoid the toxicity risks associated with these delivery systems. Finally, due to the nuclease resistance attributable to the architecture of the SNA, we use fewer chemical modifications than are customary in nucleic acid therapeutic development.

- **SNAs can be administered locally into a number of different cell and tissue types.** SNAs enter cells through class A scavenger receptors, which are present on the surface of many cell types. We believe that by accessing this mechanism, our SNAs could have therapeutic applications in organs beyond the liver, such as the brain, eye, gastrointestinal tract, lung, and skin. In preclinical studies, more than 50 cell lines and primary cells have been shown to internalize SNAs.

- **Immuno-oncology SNAs may produce a powerful immune response against tumors.** In its Phase 1 trial, AST-008 was shown to elicit high levels of certain cytokines as well as activate important effector cells of the immune system, including T cells and natural killer cells which are the main drivers of an anti-tumor response. In preclinical studies, SNAs localized to endosomes and stimulated the immune system via TLRs. We have also observed in preclinical studies that SNAs can generate a cancer-specific adaptive immune response. In addition, in preclinical studies in a variety of cancer models, SNAs, in combination with certain checkpoint inhibitors, exhibited a greater anti-tumor response and increased survival than did such checkpoint inhibitors alone. Moreover, when administered as a monotherapy, AST-008 exhibited anti-tumor activity in mouse cancer models.

- **SNAs have shown greater resistance to nuclease degradation.** Nucleases are proteins that degrade oligonucleotides. In preclinical studies, SNAs have been shown to have an increased nuclease resistance compared to linear oligonucleotides. We believe this is a result of our 3-D approach, and as a consequence, we believe that smaller amounts of SNAs may be required to achieve therapeutic efficacy compared to linear oligonucleotides.

- **SNAs can be manufactured at commercial scale.** Based on our manufacturing work to date, we believe SNAs can be made in a low cost, high-throughput, scalable, and reproducible manner using cGMPs.

**Our Clinical Development Programs**

Our clinical development programs include the development of one SNA therapeutic candidate to address unmet medical needs in the treatment of solid tumors and one SNA therapeutic candidate to address unmet medical needs in the treatment of mild to moderate psoriasis. We are also conducting early stage research activities in neurology, ophthalmology, respiratory and gastrointestinal applications. These early stage research activities are described in more detail in the sections entitled "—Preclinical research programs."

The table below sets forth the stage of development of our SNA therapeutic candidates as of March 5, 2019:

| Therapeutic Area | Therapeutic Candidate/ Target | Indication | Development Stage | | | Status |
|---|---|---|---|---|---|---|
| | | | Preclinical Development | Phase 1 | Phase 2 | |
| Immuno-oncology | AST-008 (TLR9 agonist) | Solid Tumors | | | | • Phase 1b/2 opened late 2018[1]<br>• 4 clinical sites open<br>• Preliminary results in 2019 |
| Dermatology | XCUR17 (anti-IL17RA) | Psoriasis[2] | | | | • Phase 1 topline results announced late 2018 |

(1) In combination with checkpoint inhibitors (2) Mild to moderate

*TLR9 = Toll-like Receptor 9; IL17RA = Interleukin 17 Receptor Alpha*

Regulatory documents are prepared and submitted to the appropriate health authority to enable clinical trials in any given jurisdiction. In the United States, this document is called an IND application, while in other jurisdictions,

this document is often called an IMPD, which is submitted as part of a CTA. The content and scope of an IND and a CTA are similar.

**SNAs for immuno-oncology**

***Overview of immuno-oncology as a therapeutic modality***

In healthy individuals, the immune system fights off pathogens, such as bacteria and viruses. The immune system should also recognize cancer cells as foreign and eliminate them. However, cancers present a challenge because they have developed strategies to resist detection and clearance by the immune system. Immuno-oncology approaches help the patient's immune system identify a cancer as foreign and stimulate a tumor-clearing immune response. One of the greatest benefits of the immuno-oncology approach is the continuous, durable anti-tumor response that can be achieved long after discontinuation of treatment.

Current immuno-oncology therapeutic approaches generally fall into three broad categories. First, there are approaches that stimulate the immune system to detect and eliminate tumors. Examples include cytokines and toll-like receptor, or TLR, agonists. Second, some therapeutics make a cancer more readily visible to the immune system. These therapeutics include checkpoint inhibitors, such as those that target CTLA4, or cytotoxic T-lymphocyte-associated protein 4, PD-1, and PD-L1, or programmed death-ligand 1. Third, there are adoptive cell transfer therapies, including dendritic cell vaccines and chimeric antigen receptor T-cells, or CAR-Ts, that direct the immune system to target a specific type of cancer.

The knowledge of the TLR activation pathway is central to the understanding of how the immune system is stimulated to target cancer. TLRs are membrane- and endosome-bound receptors found on a number of cell types, including specialized immune cells. TLRs recognize specific molecular patterns ordinarily presented by pathogens. When cells recognize pathogens, they produce and release protein signals called cytokines that mobilize the immune system to fight invading pathogens. In addition, they activate antigen presenting cell and helper T-cells, which then coordinate the longer-term pathogen specific adaptive immune response, and as a result, confer long-term immunity to the host.

Checkpoint proteins, such as CTLA4 and PD-1, are expressed on the surface of T-cells and inhibit the function of activated T-cells. Cancers are difficult to treat because they have developed mechanisms to take advantage of these checkpoint proteins thereby evading detection and clearance by the immune system. Inhibiting these checkpoint proteins, especially PD-1 and PD-L1, has proven to be a highly effective anti-cancer therapy in some patients. Nevertheless, checkpoint inhibitors targeting the PD-1 pathway have limited clinical efficacy as monotherapy, with response rates of 20% or less in many common types of cancers, including breast and colon cancers. Emerging evidence suggests that checkpoint inhibitors are effective primarily in patients whose tumors already have pre-existent CD8 T-cell infiltrate, i.e. immune system is already capable of recognizing the tumors. We believe the challenge in the field is to increase the efficacy of checkpoint inhibitors in a broader cancer patient population by converting tumors that are non-T-cell inflamed to T-cell inflamed.

***AST-008 — an SNA for immuno-oncology***

AST-008, an SNA consisting of a TLR9 agonist, is being developed for the treatment of cancer. We believe AST-008 may be used for immuno-oncology applications as a monotherapy or in combination with checkpoint inhibitors.

Preclinical data suggest AST-008 delivered in combination with certain checkpoint inhibitors generate a greater anti-tumor activity than such checkpoint inhibitors alone. In mouse tumor models, administration of AST-008 with anti-PD-1 antibodies suppresses regulatory T-cells, or Tregs, and myeloid-derived suppressor cells, or MDSCs, and increases the levels of CD8 effector T-cells. We believe these important results suggest that the combination of immuno-oncology SNAs and checkpoint inhibitors could potentially treat a larger proportion of cancer patients than checkpoint inhibitors alone.

***Phase 1b/2 clinical development of AST-008***

During the fourth quarter of 2018 the FDA opened the IND for AST-008 and informed the Company that our

proposed Phase1b/2 trial may proceed. Early in 2019, we opened four clinical sites and began dosing and recruiting patients in that trial. This is a Phase 1b/2, open-label, multi-center trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of intratumoral AST-008 injections alone and in combination with intravenous pembrolizumab in patients with advanced solid tumors. Conditions under study are planned to include advanced or metastatic: Merkel cell carcinoma, head and neck squamous cell carcinoma, cutaneous squamous cell carcinoma and melanoma. The primary outcome measure is the safety and tolerability of AST-008 alone and in combination with pembrolizumab. Secondary outcomes include the recommended Phase 2 dose and disease assessment with RECIST 1.1.

***Phase 1 clinical development of AST-008***

The Phase 1 clinical trial was a first-in-human clinical trial of AST-008 evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of AST-008 in healthy volunteers. The trial was a randomized, single ascending dose, or SAD, trial. Sixteen healthy subjects were recruited and organized into four SAD cohorts. We began subject dosing in the fourth quarter of 2017 and announced our initial analyses of the results of the trial on September 20, 2018.

Based on our initial analyses of the Phase 1 clinical trial results, AST-008 was shown to be safe and tolerable in all subjects, with no serious adverse events and no dose limiting toxicity. AST-008 was well tolerated and all AST-008-related adverse events were of short duration, reversible and consistent with TLR9 activation. Such adverse events included flu-like symptoms, injections site reactions, and non-clinically significant lymphopenia and neutropenia.

In addition to the principal safety and tolerability endpoint, the trial screened for levels of select cytokines and markers of immune cell activation. AST-008 was shown to elicit high levels of certain cytokines as well as activate important effector cells of the immune system including T cells and natural killer cells.

For the four subjects receiving the trial's top dose of about 20 µg/kg of AST-008, initial analyses suggest that the average fold-increase above baseline for these cytokines is approximately as follows: IFN-gamma: 3 fold; IL-6: 57 fold; IL-12: 2 fold; IP-10: 32 fold; and MCP-1: 4 fold.

We believe that such cytokine induction has clinical importance because these cytokines play an important role in immune system activity. IL-12, is an important T cell-stimulating factor, involved in the differentiation of naive T cells into Th1 cells. IP-10, also known as CXCL10, acts as a chemo-attractant for macrophages, T cells, NK cells, and dendritic cells and in antitumor activity. IL-6 is a key player in the activation, proliferation and survival of lymphocytes during active immune responses and supports shifting the immune system from a suppressive to a responsive state that can effectively act against tumors. MCP-1, or CCL2, is a small cytokine which helps recruiting monocytes, memory T cells, and dendritic cells.

In addition to the cytokine response, AST-008 was shown to activate important effector cells of the immune system, including natural killer cells or NK cells which are cytotoxic lymphocytes critical to the innate immune system, and T cells which are key effector cells of the adaptive immune system. At the trial's top dose of about 20 µg/kg, AST-008 elicited 9.5 fold and 3.5 fold increases in the fraction of activated T cells and natural killer cells, respectively, compared to baseline. NK cells continually scan the body for abnormal cells to attack. T cells form the basis of a targeted and durable immune response and immunological memory. We believe that activation by AST-008 of the key effectors cells of both the innate and adaptive immune system makes AST-008 suitable for combination with checkpoint inhibitors.

***Historical TLR9 Agonist Healthy Volunteer Data***

In 2015, Mologen AG published results (European Journal of Cancer, 2015, volume 51, supplement 1, page S12) from a healthy volunteer trial. In a single cohort, 13 subjects each received one 60 mg dose (equivalent to 923 µg/kg for a 65 kg subject) of lefitolimod subcutaneously. On average, across the cohort, there was a 7 fold-increase in IP-10 expression above baseline. No cell activation data were reported. Lefitolimod is currently in a Phase 3 clinical trial.

In 2004, Coley Pharmaceutical Group (now Pfizer, Inc.) published results (Journal of Immunotherapy, 2004, Volume 27, pages 460-471) from a single ascending dose healthy volunteer trial. In that trial, their TLR9 agonist, PF-03512676, was administered subcutaneously to six subjects per dose level. For the 20 μg/kg dose level, the average fold-increase above baseline for these cytokines is as follows: IFN-gamma: no change from baseline; IL-6: 8 fold; IL-12: no change from baseline; IP-10: 9 fold; and MCP-1: 3 fold.

***Preclinical data for AST-008***

We have observed that administration of AST-008 as a monotherapy can have anti-tumor activity in colon cancer, breast cancer, lymphoma and melanoma mouse models. We have also observed that, in preclinical studies in a variety of tumor models, AST-008 applied in combination with certain checkpoint inhibitors exhibited anti-tumor responses and survival rates that were greater than those demonstrated by checkpoint inhibitors alone. Importantly, in an anti-PD-1 antibody-resistant breast cancer mouse model, administration of AST-008 with certain anti-PD-1, or programmed death 1, antibodies restored the anti-tumor activity of these antibodies. We have also demonstrated that AST-008 is active when administered subcutaneously, intratumorally or intravenously, in both prevention and established mouse tumor models. The administration of AST-008 also produced localized as well as abscopal anti-tumor activity in mouse cancer models. Additionally, administration of AST-008 in combination with certain checkpoint inhibitors confers adaptive immunity in breast and colon cancer mouse models.

Our preclinical data with AST-008 illustrate many of the important attributes of our proprietary SNA technology. Our immuno-oncology SNAs bind to class A scavenger receptors and are localized on the endosomes of immune cells. These same endosomes contain TLRs and are responsible for inducing an innate immune response. SNAs present their TLR agonists externally, in a 3-D configuration, which allows SNAs to bind to TLRs efficiently. We have designed and prepared SNAs which activate multiple classes of TLRs. Our preclinical data show that SNAs induce a broad immune response. We believe that such broad immune response includes the production of cytokines that induce a potent adaptive immune response, which in turn, may confer long-term immunity. In preclinical studies, local administration of AST-008 elicits systemic pro-inflammatory cytokine response. In mouse tumor models, administration of AST-008 with anti-PD-1 antibodies suppresses regulatory T-cells, or Tregs, and myeloid-derived suppressor cells, or MDSCs, and increases the levels of CD8 effector T-cells.

***AST-008 in combination with checkpoint inhibitors***

We have demonstrated that the combination of AST-008 with certain anti-PD-1 antibodies enhances therapeutic activity in a number of animal models, including breast and colorectal cancers, as well as lymphoma and melanoma.

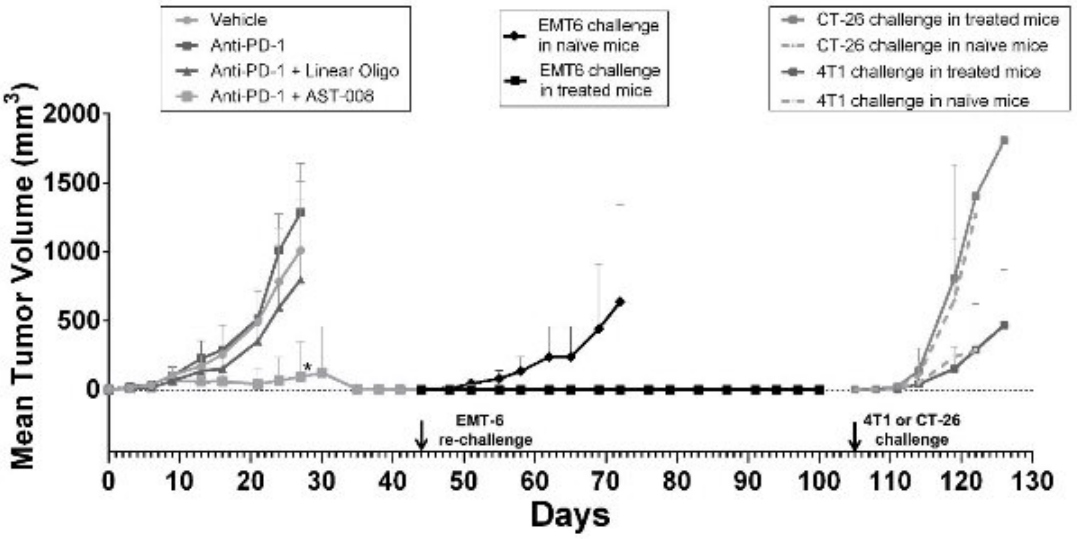
*Breast cancer mouse model.* We have demonstrated that administration of AST-008 with a selected anti-PD-1 antibody shows a durable anti-tumor response in an anti-PD-1 antibody insensitive mouse breast cancer model. This study was carried out with four groups, each consisting of eight mice per group. The four groups were vehicle treatment, antibody treatment alone, linear oligonucleotide plus antibody treatment, and AST-008 plus antibody treatment. Both the AST-008 and the linear oligonucleotide comparator treatments consisted of subcutaneous administration on days 3, 6, 9, 12, and 15 after tumor implantation at a dose of 0.8 mg/kg per injection. In the three groups where mice received anti-PD-1 antibody therapy, drug administration was performed intraperitoneally on days 3, 8 and 13 at a dose of 10 mg/kg per injection. The mice were monitored for mortality and their tumor volumes were periodically measured. The mice treated with the combination of AST-008 and the anti-PD-1 antibody had average tumor volume reductions of greater than 90% compared to anti-PD-1 antibody treatment alone. In addition, treatment with AST-008 resulted in an 88% average decrease in tumor volume compared to mice treated with linear oligonucleotides at the same dose. At the conclusion of the initial phase of the experiment, seven out of eight mice in the group treated with the combination of AST-008 and the anti-PD-1 antibody had no palpable tumors. In contrast, no mice treated with linear oligonucleotides and the anti-PD-1 antibody survived.

In the next phase of this study, we re-challenged the seven surviving mice from the combination group that was treated with AST-008 and anti-PD-1 with the same breast cancer tumor type. A new group of six mice that had never received any therapy, referred to here as naïve mice, was also inoculated with the same breast cancer tumor type for comparison. The tumor growth and survival were monitored in both groups of mice without further treatment with the AST-008 and anti-PD-1 antibody combination. No palpable tumors were observed in the surviving mice from the combination group through day 105 of the study, whereas naïve mice showed tumor growth. Finally, on day 105 of

the study, the mice from the combination group that had survived two rounds of tumor implantation were injected with different tumor types. The mouse colon cancer tumors grew in the animals that had survived two challenges with breast cancer cells. Taken together, we believe these data demonstrate an adaptive immune response and a systemic anti-cancer vaccination against the treated tumor type. We believe these data also demonstrate that AST-008 has the potential to synergize with checkpoint inhibitors for immuno-oncology applications.

Importantly, AST-008 in combination with selected anti-PD-1 antibodies shows significantly greater activity compared to the linear oligonucleotides of the same sequence and concentration. We believe this demonstrates the potential advantage of our proprietary SNA design compared to linear oligonucleotides for effecting a tumor clearing response.

*AST-008 in combination with a certain anti-PD-1 antibody in breast cancer mouse model resistant to anti-PD-1 treatment. Surviving mice from the experiment treated with anti-PD-1 and AST-008 survived when re-injected with the same EMT6 breast cancer cells, but did not survive when injected with unrelated CT-26 or 4T1 cancer cells. * $p < 0.0001$ versus vehicle treated group.*




**SNAs for inflammatory diseases**

***Overview of gene regulation utilizing oligonucleotides***

Gene regulation is the process of modulating target protein levels within cells. This could be a powerful approach for developing targeted therapies for diseases with known genetic origins. This approach may be for therapeutic targets that are identified as “undruggable” with small molecules or antibodies.

Gene regulation can be achieved with a number of approaches, three of which, siRNA-, miRNA-, and antisense-based therapeutics, have been the focus of commercial development. Small interfering RNAs, or siRNAs, are double-stranded RNA-like oligonucleotides that harness RNA interference, or RNAi, a potent and natural biological mechanism. When delivered into cells, siRNAs can lead to target mRNA degradation and a decrease in protein expression. miRNAs are naturally occurring small RNA molecules that modulate protein expression. Antisense therapeutics are short single-stranded oligonucleotides that bind to target mRNA and thus prevent its translation into protein.

***XCUR17—a topically applied anti-IL-17RA SNA***

***Overview***

XCUR17 targets the mRNA that encodes IL-17RA, a protein that is considered essential in the initiation and maintenance of psoriasis. Although the availability of inhibitors of TNF revolutionized the systemic treatment of severe psoriasis, studies of disease pathogenesis have shifted attention to the IL-17 pathway, in which IL-17RA is a key driver of psoriasis. IL-17 binding to IL-17RA on keratinocytes stimulates and perpetuates the inflammation cascade of psoriasis. IL-17RA-mediated inflammation can be inhibited by disrupting the protein's function. Brodalumab, an anti-IL-17RA monoclonal antibody, was approved by the FDA as an effective treatment for chronic moderate to severe plaque psoriasis. Our strategy is to reduce the levels of IL-17RA in the skin by topically applying XCUR17. In preclinical studies, XCUR17 showed inhibition of IL-17RA expression in the keratinocytes of the skin.

***Psoriasis market and current treatments***

According to a 2016 Global Report on Psoriasis issued by the World Health Organization, the prevalence of psoriasis in countries ranges between 0.09% and 11.43%, making psoriasis a serious global problem with at least 100 million individuals affected worldwide. According to LeadDiscovery, in 2009, over 4.5 million prescriptions were written for patients with psoriasis in the U.S., with approximately 3.9 million of these prescriptions written for topical therapies.

Patients suffering from severe psoriasis can benefit from antibody therapeutics, such as etanercept or adalimumab. These antibodies target TNF, a cytokine that plays a central role in the inflammation underlying psoriasis. When injected, the antibodies bind to TNF, diminishing TNF's ability to act as an inflammatory signal. Patients with limited disease, or mild to moderate psoriasis, can be treated with topical or oral anti-inflammatory therapeutic agents. These patients are generally not treated with systemic anti-TNF antibodies due to adverse health risks. According to the American Academy of Dermatology, patients with limited skin disease should not automatically be treated with systemic treatments if they do not improve, because treatment with systemic therapy may carry more risk than the disease itself.

Accordingly, topically applied agents, such as corticosteroids, are widely used to treat mild to moderate psoriasis. Unlike antibodies that target a specific pathway to treat psoriasis, topical therapies generally have a non-specific mechanism of action, which may cause skin thinning, skin irritation, and other side effects. Moreover, many of these therapies become less effective at treating the disease over time as patients become refractory to treatment. Findings from National Psoriasis Foundation surveys conducted between 2003 and 2011 indicate that 52.3% of patients with psoriasis were dissatisfied with their treatment.

We believe there is an unmet medical need in mild to moderate psoriasis for a locally administered therapeutic that combines the specificity of antibodies with the convenience of topical corticosteroids without the side effects of either class of therapeutics. To date, the skin has proven to be a barrier to the penetration of many potential therapies. Some approaches for delivering oligonucleotides directly into the skin require injections, which may be uncomfortable and painful.

*Our approach*

The clinical success of a systemically delivered anti-IL-17RA antibody has validated that target as a clinically relevant target for psoriasis. The IL-17 pathway is important for initiating and sustaining inflammatory responses. IL-17RA stimulation in the skin causes keratinocyte and T-cell proliferation as well as immune cell infiltration, which results in the formation of psoriatic lesions.

We are developing XCUR17, an SNA containing IL-17RA antisense oligonucleotides, for the treatment of mild to moderate psoriasis, which is often defined as psoriasis that affects less than 10% body surface area and is generally not treated with systemic antibody therapy. XCUR17 is intended to be applied locally as a topically applied gel to psoriatic lesions. We expect XCUR17 to enter into cells of the epidermis, especially keratinocytes, and modulate the production of IL-17RA.

***Phase 1 clinical development for XCUR17***

We filed a CTA for a Phase 1 clinical trial of XCUR17 in patients with psoriasis in Germany in the third quarter of 2017. Our CTA was approved in February 2018 and we began dosing patients in our Phase 1 clinical trial in April 2018. The Phase 1 clinical trial, which had final patient visits in the fourth quarter of 2018, was a randomized, double-blinded, placebo-controlled trial in twenty-one patients with mild to moderate chronic plaque psoriasis designed to assess the safety of XCUR17 formulated as a topical gel, and to evaluate early signs of efficacy. All patients received three strengths of XCUR17 gel, a vehicle gel, and a positive comparator (Daivonex® cream), which were all applied on different areas of psoriatic skin within each individual patient.

The clinical trial design allows for intra-patient comparisons of XCUR17 to a placebo and a currently approved therapeutic. A mask containing 5 holes is placed on the patient's skin, enabling the application of three different strengths of a gel containing XCUR17 as well as a placebo and a currently approved therapeutic within one psoriatic lesion. The drug is applied daily for 26 days in up to 25 patients. Over the course of the clinical trial, the safety and tolerability of XCUR17 is monitored. In addition, the severity of psoriasis in the treated areas is assessed. At the end of the clinical trial, biopsy samples from XCUR17- and vehicle-treated areas will be taken and interrogated for IL-17RA and downstream mRNA modulation to demonstrate that XCUR17 engages the target of interest and has an effect on inflammation in the skin. We believe our clinical trial design is consistent with the clinical trial design for other topically applied therapeutic candidates that have been accepted by the FDA and EMA.

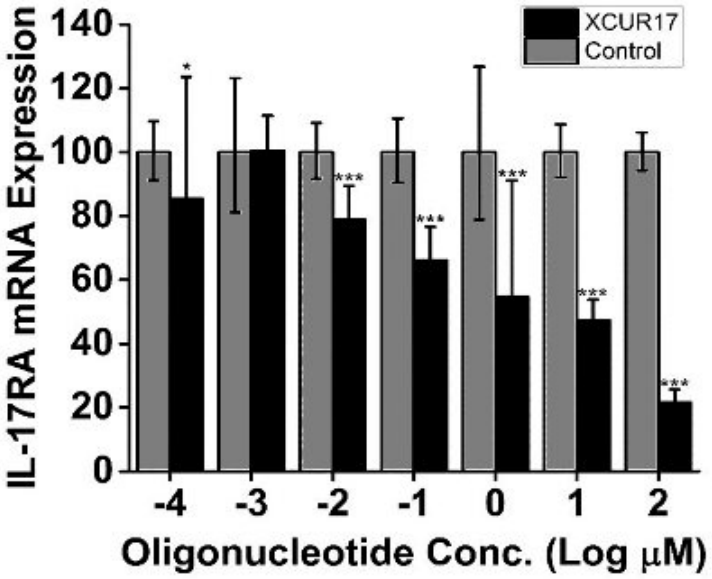
In the fourth quarter of 2018 we reported results from the Phase 1 trial of XCUR17. In the case of XCUR17, of the twenty-one treated patients, eleven treated with the highest strength XCUR17 gel were observed to have a reduction in redness and improvement in healing as determined by blinded physician assessments. Further, the highest strength XCUR17 gel showed a statistically significant improvement in psoriasis symptoms versus the vehicle gel. By comparison, seventeen of the twenty-one patients treated with the positive comparator showed a clinical response, while four patients treated with the placebo vehicle had a clinical response.

***Preclinical development of XCUR17***

We have gathered experimental evidence of the biological activity of XCUR17 in healthy human skin samples prior to undertaking a Phase 1 clinical trial. As a consequence, we believe we have a deeper understanding of how XCUR17 will perform during clinical trials than would be ordinarily possible with traditional therapeutic development.

XCUR17 exhibits cellular uptake and skin penetration properties. Specifically, XCUR17 enters into keratinocytes *in vitro* and enters into healthy human skin *ex vivo* after topical application. In addition, it also down-regulates the expression of IL-17RA mRNA and protein in keratinocytes *in vitro* . Further, XCUR17 gel down-regulates IL-17RA mRNA in healthy human skin *ex vivo* .

*Topical application of XCUR17 in a prototype gel to healthy human skin ex vivo results in a dose-dependent decrease in IL-17RA mRNA expression. * p < 0.05; *** p< 0.001 vs the controls*




***AST-005 — topically applied SNAs for psoriasis***

***Overview***

AST-005 is an SNA containing TNF antisense oligonucleotides and is intended to be applied in a gel to psoriatic lesions. We conducted a Phase 1 clinical trial to assess the safety, antipsoriatic efficacy and pharmacodynamic effect of AST-005 in 15 mild to moderate psoriasis patients in Germany. The primary endpoint of the clinical trial was the change in psoriatic infiltrate thickness compared to the start of the study, which is a method of measuring antipsoriatic effects. Secondary endpoints included evaluation of antipsoriatic efficacy by a clinical score, safety and tolerability assessments, and target mRNA reduction. The results of the clinical trial showed no adverse events related to treatment with AST-005. In addition, AST-005 application reduced the expression of TNF mRNA in a dose dependent manner in the psoriatic skin of the patients. The TNF mRNA reduction elicited by the highest strength of AST-005 gel was statistically significant when compared to the effects of the vehicle.

On December 2, 2016, we entered into the Purdue Collaboration for further development of AST-005 in mild to moderate psoriasis and in other indications. As part of our collaboration with Purdue, a Phase 1b clinical trial was conducted in Germany to evaluate the effect of AST-005 gel in patients with chronic plaque psoriasis. The trial evaluated the safety, tolerability, and plaque thickness following topical application of different strengths of AST-005 formulated as a topical gel. The trial demonstrated that AST-005 is safe and tolerable in patients at higher doses than were previously studied, however, the study did not result in a statistically significant decrease in echo lucent band thickness, one of the key indicators of efficacy in patients with psoriasis. In April 2018, Purdue notified the Company it had declined to exercise its option to develop AST-005 at that time, but that it also intended to retain rights relating to the TNF target, and Purdue reserved its right to continue joint development, with Exicure, of new anti-TNF drug candidates and to retain its exclusivity and other rights to AST-005.

***Preclinical research programs***

In addition to our named pipeline programs, a variety of early stage research efforts are ongoing in areas we believe will best leverage the properties of the SNA. Potential applications of the SNA include those in neurology, ophthalmology, pulmonology, and the gastroenterology.

***Neurology***

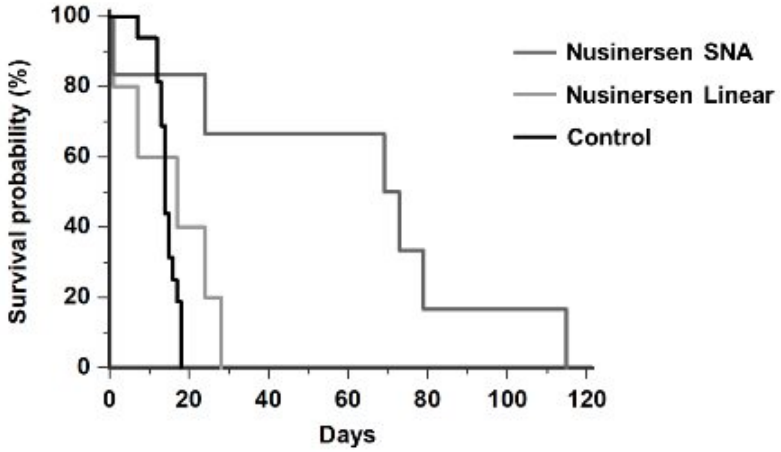
Despite delivery challenges, nucleic-acid based therapy has been successfully developed to treat a central nervous system, or CNS, disorder. Nusinersen, by Ionis Pharmaceuticals and Biogen Inc., was approved in late 2016 for the treatment of spinal muscular atrophy, or SMA by the FDA. SMA is a genetic disorder characterized by progressive muscle wasting and loss of muscle function due to motor neuron dysfunction. SMA is characterized by reduced amount of survival of motor neuron 1, or SMN1, protein. The severity of the disease depends on the amount of a related protein, SMN2, where lesser quantities of SMN2 are correlated to more severe disease. SMN2 is similar to SMN1, but leads to production of truncated protein, which is normally rapidly degraded.

Nusinersen is an antisense oligonucleotide designed to modulate splicing of SMN2 pre-mRNA in the nucleus to generate an alternative version of SMN2 mRNA that leads to production of a functional SMN protein. Nusinersen is designed to enhance the production of the full-length, more stable variant of SMN2, increasing the level of SMN2 protein, and thus improving motor function. In clinical trials, SMA patients treated with nusinersen achieved and sustained meaningful improvement in motor function and survival compared to untreated patients.

To evaluate the potential superiority of the SNA over linear oligonucleotides in directing the production of a more stable variant of the SMN2 protein, we compared the effects of nusinersen in linear format with nusinersen in SNA format in cells derived from SMA patients. The data showed that treatment with SNA format of nusinersen results in greater levels of the more stable variant of SMN2 mRNA compared with linear format. SNA format of nusinersen resulted in up to 45-fold increase in the more stable SMN2 mRNA variant versus controls, while a much smaller 2.5-fold increase was observed using nusinersen in the linear format.

We collaborated with The Ohio State University Wexner Medical Center to further study the pharmacology of our nusinersen SNA in mouse models. We tested nusinersen SNA in Δ7 SMA mouse model in which the untreated SMA-bearing mice have mean survival of approximately 15 days. New born Δ7 SMA mice were treated with a single dose of nusinersen SNA or nusinersen at 10, 20 or 30 µg by via intracerebroventricular injection on day 0. Following administration of compounds, mouse survival and body weights were recorded.

*Nusinersen in SNA format prolonged survival compared to linear nusinersen in Δ7 SMA mice. The 20 µg treatment group is shown below.*




In June 2018, the Company and researchers from The Ohio State University Wexner Medical Center presented a poster at the Cure SMA Annual Conference titled: “Nusinersen in spherical nucleic acid (SNA) format improves efficacy both in vitro in SMA patient fibroblasts and in Δ7 SMA mice and reduces toxicity in mice.” It was observed in a preclinical study that nusinersen in SNA format prolonged survival by four-fold (maximal survival of 115 days compared to 28 days for nusinersen-treated mice) as well as doubled the levels of healthy full-length SMN2 mRNA

and protein in SMA patient fibroblasts when compared to nusinersen. Based on the results of this preclinical study, we intend to further pursue our early stage research activities in neurological applications.

Subsequently, in the fall of 2018, we completed a biodistribution study in rats comparing nusinersen to nusinersen in SNA format. We found that more nusinersen in SNA format was retained in the rats' brain and spinal cord compared to nusinersen retained in the rats' brain and spinal cord at 24, 72 and 168 hours.

We are now formulating our strategy for developing a pipeline of SNA therapeutics targeting neurological diseases. Preclinical research is underway in a number of indications including, spinal muscular atrophy, Huntington's Disease, spinocerebellar ataxia type 3 (SCA3), SCA2, SCA1, Friedreich's Ataxia, and Batten disease. We believe this preclinical research may lead to a therapeutic candidate for one of the above neurological indications.

***Gastroenterology***

A variety of gastrointestinal disorders, including ulcerative colitis and Crohn's disease, collectively referred to as irritable bowel disease, or IBD, are inadequately treated with existing therapies such as immunosuppressive steroids and anti-TNF antibodies.

We believe that orally applied SNAs may provide the opportunity to treat diseases such as IBD by taking advantage of the local tissue penetration of the SNA technology. Accordingly, the effect of oral SNA treatment was assessed in an induced IBD mouse model. After the induction of colitis, the mice were treated with anti-TNF SNAs on day 1, 2, 3 and 4, for a total four doses, at 200 or 1000 µg/dose/mouse by oral gavage. Control mice were treated with vehicle only. The mice were monitored for mortality and scored clinically for seven days. On day 7, the surviving animals were sacrificed. Gross pathology assessment was performed on the proximal colon.

Clinical scores for the mice during the course of the study were assigned by considering the body weight, stool consistency, bleeding and any abnormalities observed in fur coat and abdomen. Gross pathology scores were assigned on the last day of study from the colons removed from the animals after euthanization. Gross pathology scores ranging from 0 to 5, indicating no abnormalities and multiple ulcers, respectively, were assigned based on the severity of the inflammation and ulceration in the colon.

The results showed statistically significant improvement in clinical score and gross pathology for animals treated with 1000 µg/dose of anti-TNF SNAs compared to those treated with vehicle only. Overall, the results suggest that oral administration of SNA had a positive effect on disease symptoms as reflected by lower clinical and pathology scores.

***Ophthalmology***

Ophthalmic therapies, such as antibodies, peptides or aptamers, are typically injected into the eye to reach their target tissues and achieve therapeutic effects. We believe that the penetration properties of the SNA may result in the delivery of therapeutically relevant concentrations of oligonucleotides to certain tissues in the eye. We have observed in preclinical studies the delivery of SNAs into the eye either through eyedrops or intravitreal injections.

In one study, to assess penetration into the eye, Dutch belted rabbits were given either eyedrops containing no SNAs, referred to as vehicle, or an SNA in a formulation targeting an ocular gene of interest. The eyedrops were administered to the animals 18 times over the course of five days. On the fifth day, the rabbit eyes were analyzed for SNA content. The results indicate that SNAs were detected in tissues at the surface of the eye, where the application occurred, but also in the retina and vitreous humor, indicating that the SNA had penetrated into the eye.

We believe these results are a promising step in demonstrating that SNAs may be used to treat ophthalmic diseases.

***Pulmonology***

Altering the immunological state of the lung has promising therapeutic implications for the treatment of allergic diseases, such as asthma. In a preliminary assessment, we demonstrated an alteration of the immunological state

both locally in the lung and systemically in mice after the inhalation of SNAs. An intranasal dose of PBS or nebulized formulation of AST-008 was administered to mice at 7.5 mg/kg to assess the pharmacodynamic effects of SNA delivery to the lungs. Four mice per group were used. At 4, 10, 16, or 24 hours following administration, serum was collected from the animals and bronchoalveolar lavage, or BAL, was performed to produce fluid from the lung surface. Finally, lung tissue was also collected from the animals. The fluids and tissue were subjected to cytokine concentration analysis. The results show that nebulized SNAs can produce a cytokine response in the lung tissue and BAL fluid, as well as systemically, as measured in the mouse serum. We believe these results have implications for the potential treatment of allergic diseases of the lung.

***Dermelix License Agreement***

On February 17, 2019 Exicure entered into a License and Development Agreement, or the Dermelix License Agreement, with DERMELIX, LLC, d/b/a Dermelix Biotherapeutics. Under the terms of agreement, Dermelix licensed worldwide rights to research, develop, and commercialize Exicure's technology for the treatment of Netherton Syndrome and, at Dermelix's option, up to five additional rare skin indications.

Dermelix will initially develop a targeted therapy for the treatment of Netherton Syndrome (NS). NS is a rare and severe autosomal recessive disorder caused by loss-of-function mutations in the *SPINK5* gene, which encodes the serine protease inhibitor LEKT1 involved in skin barrier function. NS affects approximately 1 in 200,000 children born each year, and is characterized by severely inflamed, red, scaled, itchy skin, and patients are at increased risk of mortality in the first year of life due to recurrent infections and dehydration as a result of the impaired skin barrier. Currently, there are no approved treatments for NS patients and off-label use of standard of care treatments are of limited utility.

Under the terms of the Dermerlix License Agreement, Exicure received an upfront payment of $1 million at closing of the transaction and will receive an additional $1 million upon the exercise of each of the five options granted to Dermelix. Exicure will be responsible for conducting the early stage development for each indication up to IND enabling toxicology studies. Dermelix will undertake subsequent development, commercial activities and financial responsibility. For each of NS as well as any additional licensed product for which Dermelix exercises one of its options, Exicure is eligible to receive potential payments totaling up to $13.5 million upon achievement of certain development and regulatory milestones and up to $152.5 million upon achievement of certain sales milestones per indication in each of six indications. In addition, Exicure will receive low double-digit royalties on annual net sales for SNA therapeutics developed.

***Purdue Collaboration***

Pursuant to the Purdue Collaboration we entered into with Purdue on December 2, 2016, Purdue has the option to obtain from us the full worldwide development and commercial rights to AST-005, an option to obtain three additional collaboration targets and a further option to obtain from us the full worldwide development and commercial rights to any therapeutic candidates developed targeting the three additional collaboration targets. In connection with the Purdue Collaboration, we received a non-refundable development fee of $10.0 million. In addition, we are eligible to potentially receive additional payments for certain research, regulatory and commercial sales milestones if a program under the collaboration was pursued and the milestones were successfully completed . In April 2018, Purdue notified the Company it had declined to exercise its option to develop AST-005 at that time and there are currently no active therapeutic candidates in development under the Purdue Collaboration. There can be no assurance that any research, regulatory and commercial sales milestones or royalties will be achieved as they are subject to highly significant risks and uncertainties, many of which are outside of our control.

Purdue is entitled to terminate the Purdue Collaboration by providing the Company with advance written notice. The agreement also provides termination provisions for material breaches of contract provisions that are customary for agreements of this type.

**Our Intellectual Property**

***Proprietary Protection***

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our therapeutic candidates, manufacturing and process discoveries and other know-how, to operate without infringing the proprietary rights of others, and to prevent others from infringing on our proprietary rights. We have been building and continue to build our intellectual property portfolio relating to our AST-005, XCUR17 and AST-008 therapeutic candidates and our SNA technology platform. Our policy is to seek to protect our proprietary position by, among other methods, filing and licensing U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also intend to rely on trade secrets, know-how, and technological innovation to develop and maintain our proprietary position. We cannot be sure that patents will be granted with respect to any of our owned or licensed pending patent applications or with respect to any patent applications filed or licensed by us in the future, nor can we be sure that any of our existing owned or licensed patents or any patents that may be granted or licensed to us in the future will be commercially useful in protecting our technology.

***Patent Rights***

Our patent portfolio includes pending patent applications and issued patents in the United States and in foreign countries. As of December 31, 2018, our patent portfolio consists of over 60 issued patents and allowed patent applications and over 135 pending patent applications. Our general practice is to seek patent protection in major markets worldwide, including the U.S., Canada, China, Japan, Australia, certain members of the European Union, among others. Majority of the issued patents and allowed patent applications are licensed from Northwestern University. Among the pending patent applications, we license over 45 from NU, we exclusively own 80, and we jointly own 8 with Northwestern University.

Our license from Northwestern University is for royalty bearing worldwide exclusive rights to the use of SNAs for therapeutic applications. Pursuant to the license, we are allowed to manufacture, use, offer for sale, sell and import products covered by the licensed patent rights.

Our AST-008 patent portfolio includes one allowed and 39 pending U.S. nonprovisional and foreign patent applications. Foreign jurisdictions where we are seeking patent protection for our AST-008 patent portfolio include Canada, China, Japan, Australia, the European Union, India, South Korea and Mexico. Each of these applications is a composition of matter and method of use type application. The claims of these applications are directed to certain nanoscale constructs, liposomal particles, and multivalent nanostructures, and their methods of use for treating cancer and other disorders. Any patents that may issue from these applications would expire by 2034 or 2035. The expiration dates do not take into consideration any potential patent term adjustment that may be applied by the U.S. Patent Office upon issuance of the patent, any terminal disclaimers that may be filed in the future or any regulatory extensions that may be obtained.

Our XCUR17 patent portfolio includes 8 pending U.S. nonprovisional and foreign patent applications. The pending applications are composition of matter and

method of use type applications and include claims to one or more oligonucleotides that are 18 nucleotides in length, and methods of use for treating dermal and other disorders. Any patents that may issue from this application would expire by 2037. The expiration date does not take into consideration any potential patent term adjustment that may be applied by the U.S. Patent Office upon issuance of the patent, any terminal disclaimers that may be filed in the future or any regulatory extensions that may be obtained.

Our AST-005 patent portfolio includes one allowed U.S. patent application and corresponding pending applications in 7 foreign jurisdictions. The applications are composition of matter and method of use type applications and include claims to an oligonucleotide that is 18 nucleotides in length, and methods of use for treating

dermal and other disorders. Any patents that may issue from these applications would expire by 2035. The expiration dates do not take into consideration any potential patent term adjustment that may be applied by the U.S. Patent Office upon issuance of the patent, any terminal disclaimers that may be filed in the future or any regulatory extensions that may be obtained.

Upon receiving FDA approval for AST-008, XCUR17 or AST-005, we intend to list applicable patents in the FDA's Orange Book.

Patent life determination depends on the date of filing of the application and other factors as promulgated under the patent laws. In most countries, including the United States, the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country.

***Trade Secret and Other Protection***

In addition to patented intellectual property, we also rely on trade secrets and proprietary know-how to protect our technology, especially when we do not believe that patent protection is appropriate or can be obtained. It is our policy to require our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive confidential information from us to execute confidentiality agreements upon the commencement of employment or consulting relationships. These agreements provide that all confidential information developed or made known to these individuals during the course of the individual's relationship with the company is to be kept confidential and is not to be disclosed to third parties except in specific circumstances. The agreements provide that all inventions conceived by an employee shall be the property of our Company. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

***Other Intellectual Property Rights***

We seek trademark protection in the United States when appropriate. We have filed for trademark protection for the following marks: LIFE HAPPENS IN 3D, LIFE IN 3D, and EXICURE. We currently have one registered trademark, EXICURE.

From time to time, we may find it necessary or prudent to obtain licenses from third party intellectual property holders.

***Northwestern University License Agreements***

In September 2009, Northwestern University and AuraSense LLC, or ASLLC, one of our significant stockholders, entered into a license agreement under which Northwestern University granted ASLLC an exclusive, worldwide license under certain Northwestern University patents and patent applications to exploit products and processes in the field of the use of nanoparticles, nanotechnology, microtechnology or nanomaterial-based constructs as or accompanying therapeutics or theradiagonostics and in or for intracellular diagnostic applications and intracellular research. On December 12, 2011, ASLLC assigned to us all of its worldwide rights and interests under the Northwestern University-ASLLC license in the field of the use of nanoparticles, nanotechnology, microtechnology or nanomaterial-based constructs as therapeutics or accompanying therapeutics as a means of delivery, but expressly excluding diagnostics (the "assigned field"). In accordance with the terms and conditions of this assignment, we assumed all liabilities and obligations of ASLLC to Northwestern University as set forth Northwestern University its license agreement in the assigned field and in August 2015 we entered into a restated license agreement with Northwestern University. In February 2016, we obtained exclusive license as to Northwestern University's rights in certain SNA technology we jointly own with Northwestern University. Our license to Northwestern University's rights is limited to the assigned field, however we have no such limitation as to our own rights in this jointly owned technology. In June 2016, we entered into an exclusive license with Northwestern University to obtain worldwide rights to certain inhibitors of glucosylceramide synthase and their use in wound healing in diabetes. Our rights and obligations in these 2016 agreements are substantially the same as in the restated license agreement from August 2015. For purposes of the assigned field, therapeutic uses means the use of products and processes that are covered by the patents and patent applications licensed from Northwestern University for the purpose of providing a therapy or course of medical treatment to address a medical condition or

disease. The Northwestern University license agreements provide to us the exclusive, worldwide right to make, have made, use, modify, sell, offer for sale and import any product or process that is covered by any claim in the licensed Northwestern University patents and patent applications. We have the right to sublicense these rights to third parties. The Northwestern University license agreements require us to use commercially reasonable efforts, consistent with demand in the marketplace, regulatory procedures and industry conditions and development timelines, to research, develop, market and manufacture the licensed products.

Our rights under the Northwestern University license agreements are subject to a variety of material limitations. First, the license specifically excludes use of the licensed patent rights to perform qualitative or quantitative *in vitro* analysis, testing, or measurement as well as detection of a variety of combinations of biodiagnostics field subsets and targets. Second, the license specifically prohibits us from using the licensed patent rights with regard to diagnostics, including without limitation, theradiagnostics. Third, though the license is otherwise exclusive in the assigned field, Northwestern University retains the right to use the licensed patent rights for research, teaching, and other educational purposes, including the right to distribute and publish materials related to the licensed patent rights. Fourth, the license is subject to the rights of the U.S. government under any and all applicable laws including substantially manufacturing all licensed products in the U.S. unless such requirement is waived by the U.S. government. Fifth, other than in certain circumstances, the Northwestern University license agreements are non-transferable without the consent of Northwestern University. Under the terms of the Northwestern University license agreements, depending on the circumstances, either we or Northwestern University can sue to enforce the patent rights against third party infringers.

In order to secure the assignment of the Northwestern University-ASLLC license in the field, we assumed the obligation to pay Northwestern University an annual license fee, which may be credited against any royalties based on sales of licensed products that are due to Northwestern University in the same year, and to reimburse Northwestern University for expenses associated with the prosecution and maintenance of the licensed patent rights. In addition, we assumed the obligation to pay Northwestern University royalties at a low single-digit percentage of any net revenue generated by our sale or transfer of any licensed product. In the event we grant a sublicense under the licensed patent rights, we also assumed the obligation to pay Northwestern University, on a quarterly basis, the greater of a mid-teen percentage of all sublicensee royalties or a low single-digit percent of any net revenue generated by a sublicensee's sale or transfer of any licensed product.

We may terminate our license agreements with Northwestern University at any time by providing 90 days written notice to Northwestern University. Northwestern University may terminate the agreements or, alternatively, convert our exclusive rights to non-exclusive rights if we fail to comply with certain prescribed timelines for research, development, marketing and manufacturing milestones for the licensed products. Northwestern University may also terminate the agreements if we sue, or do not terminate all agreements with a sublicensee who sues Northwestern University, in a matter not arising from the agreements themselves. Either party may terminate the agreements in the event of a material breach by the other that remains uncured for a period of 30 days after the non-breaching party provides notice to the breaching party. The agreements will automatically terminate if we reach specified thresholds of financial distress. In the event of termination, all rights immediately revert to Northwestern University. The agreements will automatically expire upon the expiration of the last to expire patent rights. In the event of expiration, the license automatically becomes a non-exclusive, irrevocable, fully-paid license to use or sublicense the use of know-how to make and sell products in each country where the license had previously been in effect.

***Our technology licenses and assignments***

Our strategy around protection of our proprietary technology, including any innovations and improvements, is to obtain worldwide patent coverage with a focus on jurisdictions that represent significant global pharmaceutical markets. Generally, patents have a term of twenty years from the earliest priority date, assuming that all maintenance fees are paid, no portion of the patent has been terminally disclaimed and the patent has not been invalidated. In certain jurisdictions, and in certain circumstances, patent terms can be extended or shortened. We are pursuing worldwide patent protection for at least novel molecules, compositions of matter, pharmaceutical formulations, methods of use, including treatment of disease, methods of manufacture and other novel uses for the inventive molecules originating from our research and development efforts. We continuously assess whether it is strategically

more favorable to maintain confidentiality for the "know-how" regarding a novel invention rather than pursue patent protection. For each patent application that is filed we strategically tailor our claims in accordance with the existing patent landscape around a particular technology.

There can be no assurance that an issued patent will remain valid and enforceable in a court of law through the entire patent term. Should the validity of a patent be challenged, the legal process associated with defending the patent can be costly and time consuming. Issued patents can be subject to oppositions, interferences and other third party challenges that can result in the revocation of the patent or limit patent claims such that patent coverage lacks sufficient breadth to protect subject matter that is commercially relevant. Competitors may be able to circumvent our patents. Development and commercialization of pharmaceutical products can be subject to substantial delays and it is possible that at the time of commercialization any patent covering the product has expired or will be in force for only a short period of time following commercialization. We cannot predict with any certainty if any third party U.S. or foreign patent rights, or other proprietary rights, will be deemed infringed by the use of our technology. Nor can we predict with certainty which, if any, of these rights will or may be asserted against us by third parties. Should we need to defend ourselves and our partners against any such claims, substantial costs may be incurred. Furthermore, parties making such claims may be able to obtain injunctive or other equitable relief, which could effectively block our ability to develop or commercialize some or all of our products in the U.S. and abroad, and could result in the award of substantial damages. In the event of a claim of infringement, we or our partners may be required to obtain one or more licenses from a third party. There can be no assurance that we can obtain a license on a reasonable basis should we deem it necessary to obtain rights to an alternative technology that meets our needs. The failure to obtain a license may have a material adverse effect on our business, results of operations and financial condition.

We also rely on trade secret protection for our confidential and proprietary information. No assurance can be given that we can meaningfully protect our trade secrets on a continuing basis. Others may independently develop substantially equivalent confidential and proprietary information or otherwise gain access to our trade secrets.

It is our policy to require our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive confidential information from us to execute confidentiality agreements upon the commencement of employment or consulting relationships. These agreements provide that all confidential information developed or made known to these individuals during the course of the individual's relationship with the company is to be kept confidential and is not to be disclosed to third parties except in specific circumstances. The agreements provide that all inventions conceived by an employee shall be the property of the company. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Our success will depend in part on our ability to obtain and maintain patent protection, preserve trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others, both in the U.S. and other territories worldwide.

**Manufacturing and Supply**

We do not currently own or operate manufacturing facilities for the production of preclinical, clinical or commercial quantities of any of our therapeutic candidates. We currently contract with two therapeutic substance and two drug product manufacturers for the supply of SNAs and we expect to continue to do so to meet the preclinical and any clinical requirements of our therapeutic candidates. We do not have a long-term agreement with these third parties.

We have agreements for the supply of such therapeutic materials with manufacturers or suppliers that we believe have sufficient capacity to meet our demands. In addition, we believe that adequate alternative sources for such supplies exist. However, there is a risk that, if supplies are interrupted, it would materially harm our business. We typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our contract manufacturing organizations manufacture our therapeutic candidates

subject to cGMP conditions. cGMPs are regulatory requirements for the production of therapeutics that will be used in humans.

**Competition**

We believe that our scientific knowledge and expertise in SNA-based therapies provide us with competitive advantages over the various companies and other entities that are attempting to develop oligonucleotide based-therapeutics. However, we face competition at the technology and therapeutic indication levels from both large and small biotechnology companies, academic institutions, government agencies and public and private research institutions. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our success will be based in part upon our ability to identify, develop and manage a portfolio of therapeutics that are safer and more effective than competing products in the treatment of our targeted patients. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient or are less expensive than any therapeutics we may develop.

***Competition in oligonucleotide-based therapeutics***

There is intense and rapidly evolving competition in the biotechnology, pharmaceutical and oligonucleotide therapeutics fields. We believe that while our SNA technology, its associated intellectual property and our scientific and technical know-how gives us a competitive advantage in this space, competition from many sources remains. Our competition includes larger and better funded pharmaceutical, biotechnological and oligonucleotide therapeutic firms. Moreover, we not only compete with other firms, but also with current and future therapeutics.

We are aware of several companies that are developing oligonucleotide delivery platforms and oligonucleotide based therapeutics. These competitors include Ionis Pharmaceuticals, Inc., Alnylam Pharmaceuticals, Inc., Dicerna Pharmaceuticals, Inc., Arbutus Biopharma Corp., Wave Life Sciences Ltd., Arrowhead Pharmaceuticals, Inc., ProQR Therapeutics N.V., Dynavax Technologies Corp., Idera Pharmaceuticals, Inc., Mologen AG, and Checkmate Pharmaceuticals, Inc. These and other competitors compete with us in recruiting scientific and managerial talent, and for the finite funding available from biotechnology and pharmaceutical companies.

Our success will partially depend on our ability to develop and protect therapeutics that are safer and more effective than competing products. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective, or less expensive than the therapeutics we develop.

If our lead therapeutic candidates are approved for the indications for which we undertake clinical trials, they will compete with therapies that are either in development or currently marketed, such as the following:

***Competition in immuno-oncology***

There are a number of competitive products to SNAs for immuno-oncology on the market and in development. Ipilimumab and nivolumab from Bristol-Myers Squibb Company, atezolizumab from the Roche Group, as well as pembrolizumab from Merck & Co., Inc., are now marketed for the treatment of advanced melanoma or other cancers, and these and other therapeutic products are in development for other immuno-oncology applications. A number of our competitors are already conducting clinical trials testing combination of TLR9 agonists with checkpoint inhibitors in cancer patients. In addition, adoptive cell therapies such as CAR-T cells are showing great promise for the treatment of B-cell malignancies in clinical trials.

***Competition in psoriasis***

There are currently a number of therapeutics on the market for the treatment of psoriasis. Over the counter medications such as salicylic acid and zinc pyrithione are used for treating mild to moderate psoriatic lesions.

Prescription medications such as corticosteroids, calcipotriene, retinoids are available and can be applied topically. Oral therapeutics like cyclosporine and methotrexate are also used. Finally, injectable antibody-based therapies are used to decrease psoriasis-associated inflammation and thus reduce the symptoms of the disorder in the case of severe psoriasis.

**Government Regulation and Product Approval**

Governmental authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing, sales, and export and import of products such as those we are developing. Our therapeutic candidates must be approved by the FDA through the NDA process before they may be legally marketed in the U.S. and will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

***U.S. government regulation***

*NDA approval processes* **.** In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act of 1938, or the FDCA, and implementing regulations. If we fail to comply with applicable FDA or other requirements at any time during the product development or approval process, or after approval, we may become subject to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- license suspension or revocation;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning or untitled letters;
- seizures or administrative detention of product;
- product recalls;
- total or partial suspension of production or distribution; or
- injunctions, fines, disgorgement, or civil or criminal penalties.

The process required by the FDA before a therapeutic candidate may be marketed in the U.S. generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices, or GLPs, and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCPs, to establish the safety and efficacy of the therapeutic candidate for its intended use;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the therapeutic candidate is produced to assess readiness for commercial manufacturing and conformance to the manufacturing-related elements of the application, to conduct a data integrity audit, and to assess compliance with cGMPs to assure that the facilities, methods and controls are adequate to preserve the therapeutic candidate’s identity, strength, quality and purity; and

- FDA review and approval of the NDA.

The testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain any approvals for our therapeutic candidates will be granted on a timely basis, if at all.

Once a therapeutic candidate is identified for development, it enters the preclinical or nonclinical testing stage. Nonclinical tests include laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some nonclinical testing may continue even after the IND is submitted. In addition to including the results of the nonclinical studies, the IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. Currently, the IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may result in the FDA not allowing the clinical trials to commence or not allowing the clinical trials to commence on the terms originally specified in the IND. A separate submission to an existing IND must also be made for each successive clinical trial conducted during drug development, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol, and any subsequent material amendment to the protocol, must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors also must report to the FDA serious and unexpected adverse reactions in a timely manner, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation brochure or any findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the therapeutic. An IRB at each institution participating in the clinical trial must review and approve the protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each research subject or the subject's legal representative, monitor the trial until completed and otherwise comply with IRB regulations. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trials results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined.

- Phase 1-The therapeutic candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some therapeutic candidates for severe or life-threatening diseases, such as cancer, especially when the therapeutic candidate may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- Phase 2-Clinical trials are performed on a limited patient population intended 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 are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling.

Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or 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 therapeutic candidate has been associated with unexpected serious harm to patients.

A drug being studied in clinical trials may be made available to individual patients, in certain circumstances. Pursuant to the 21st Century Cures Act, or Cures Act, which was signed into law in December 2016, the manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug.

During the development of a new therapeutic candidate, sponsors are given opportunities to meet with the FDA at certain points; specifically, prior to the submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support the approval of the new therapeutic.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies and also develop additional information about the chemistry and physical characteristics of the therapeutic candidate and finalize a process for manufacturing commercial quantities of the therapeutic candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the therapeutic candidate and the manufacturer must develop methods for testing the quality, purity and potency of the therapeutic candidate. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the therapeutic candidate does not undergo unacceptable deterioration over its proposed shelf-life.

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual product fee for products and an annual establishment fee on facilities used to manufacture prescription drug products. Fee waivers or reductions are available in certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the applicant is a small business submitting its first human therapeutic application for review. Within 60 days following submission of the application, the FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is 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. NDAs receive either standard or priority review. A therapeutic representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product 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 will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements. To assure cGMP and GCP compliance, an applicant must incur significant expenditures of time, money and effort in the areas of training, record keeping, production and quality control.

During the product approval process, the FDA also will determine whether a REMS plan is necessary to assure the safe use of the product. If the FDA concludes a REMS plan is needed, the sponsor of the NDA must submit a proposed REMS plan. The FDA will not approve an NDA without a REMS plan, if required. The FDA has authority to require a REMS plan under the Food and Drug Administration Amendments Act of 2007, or FDAAA, when necessary to ensure that the benefits of a therapeutic outweigh the risks. In determining whether a REMS plan is necessary, the FDA must consider the size of the population likely to use the therapeutic, the seriousness of the disease or condition to be treated, the expected benefit of the therapeutic, the duration of treatment, the seriousness of known or potential adverse events, and whether the therapeutic is a new molecular entity. A REMS plan may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the risks, limitations on who may prescribe or dispense the therapeutic, or other measures that the FDA deems necessary to assure the safe use of the therapeutic. In addition, the REMS plan must include a timetable to assess the strategy at 18 months, three years, and seven years after the strategy's approval.

The FDA may also require a REMS plan for a therapeutic that is already on the market if it determines, based on new safety information, that a REMS plan is necessary to ensure that the product's benefits outweigh its risks.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the NDA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the NDA in its present form, the FDA will issue a complete response letter that describes all of the specific deficiencies in the NDA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if the NDA is resubmitted, FDA may again decide that the resubmitted NDA does not satisfy the criteria for approval.

Even if a product receives regulatory approval, the approval may be significantly limited to specific indications and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. In addition, the FDA may require post-marketing clinical trials, sometimes referred to as "Phase 4" clinical trials, designed to further assess a product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

*Companion Diagnostics* . The FDA has issued a final guidance document addressing the agency's policy in relation to in vitro companion diagnostic tests. The guidance explains that for some therapeutics, the use of a companion diagnostic test is essential for the safe and effective use of the product, such as when the use of a product is limited to a specific patient subpopulation that can be identified by using the test. According to the guidance, the FDA generally will not approve such a product if the companion diagnostic is not also approved or cleared for the appropriate indication, and accordingly the therapeutic product and the companion diagnostic should be developed and approved or cleared contemporaneously. However, the FDA may decide that it is appropriate to approve such a product without an approved or cleared in vitro companion diagnostic device when the therapeutic is intended to treat a serious or life-threatening condition for which no satisfactory alternative treatment exists and the FDA determines that the benefits from the use of a product with an unapproved or uncleared in vitro companion diagnostic device are so pronounced as to outweigh the risks from the lack of an approved or cleared in vitro companion diagnostic device. The FDA encourages sponsors considering developing a therapeutic product that requires a companion diagnostic to request a meeting with both relevant device and therapeutic product review divisions to ensure that the product development plan will produce sufficient data to establish the safety and effectiveness of both the therapeutic product and the companion diagnostic. Because the FDA's policy on companion diagnostics is set forth only in guidance, this policy is subject to change and is not legally binding.

*Expedited review and approval.* The FDA has various programs, including Fast Track, priority review, accelerated approval and breakthrough therapy, which are intended to expedite or simplify the process for reviewing

therapeutic candidates, or provide for the approval of a therapeutic candidate on the basis of a surrogate endpoint. Even if a therapeutic candidate qualifies for one or more of these programs, the FDA may later decide that the therapeutic candidate no longer meets the conditions for qualification or that the time period for FDA review or approval will be lengthened. Generally, therapeutic candidates that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of therapeutic candidates to treat serious or life-threatening diseases or conditions and fill unmet medical needs. Priority review is designed to give a therapeutic candidate that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness, an initial review within eight months as compared to a standard review time of twelve months.

Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated therapeutic candidate and expedite review of the application for a therapeutic candidate designated for priority review. Accelerated approval, which is described in Subpart H of 21 CFR Part 314, provides for an earlier approval for a new therapeutic candidate that is intended to treat a serious or life-threatening disease or condition, generally provides a meaningful advantage over available therapies and demonstrates 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, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a therapeutic candidate receiving accelerated approval perform post-marketing clinical trials to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the product may be subject to accelerated withdrawal procedures.

In the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was signed into law in July 2012, the U.S. Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of therapeutic candidates under accelerated approval. The law required the FDA to issue related guidance and also promulgate confirming regulatory changes. In May 2014, the FDA published a final Guidance for Industry titled “Expedited Programs for Serious Conditions—Drugs and Biologics,” which provides guidance on FDA programs that are intended to facilitate and expedite development and review of new therapeutic candidates as well as threshold criteria generally applicable to concluding that a therapeutic candidate is a candidate for these expedited development and review programs.

In addition to the Fast Track, accelerated approval and priority review programs discussed above, the FDA also provided guidance on a new program for Breakthrough Therapy Designation, established by FDASIA to subject a new category of drugs to accelerated approval. A sponsor may seek FDA designation of a therapeutic candidate as a “breakthrough therapy” if the therapeutic is intended, alone or in combination with one or more other therapeutics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapeutic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A request for Breakthrough Therapy designation should be submitted concurrently with, or as an amendment to, an IND, but ideally no later than the end of the Phase 2 meeting.

Similar to FDASIA, the Cures Act, which was signed into law in December 2016, includes numerous provisions intended to accelerate the development of new products regulated by the FDA. As an example, the Cures Act provides that the FDA may allow the sponsor of an NDA for a genetically targeted drug or variant protein targeted drug to rely upon data and information previously developed by the same sponsor (or another sponsor that has provided the sponsor with a contractual right of reference to such data and information) and submitted by the sponsor in support of one or more previously approved applications submitted to the FDA for a drug that incorporates or utilizes the same or similar genetically targeted technology or the same variant protein targeted drug.

*Patent term restoration and marketing exclusivity.* Depending upon the timing, duration and specifics of FDA approval of the use of our therapeutic candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-

Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the therapeutic candidate's approval date. The patent term restoration period is generally one half of the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved therapeutic candidate is eligible for the extension and the application for extension must be made prior to expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity. A therapeutic candidate is a new chemical entity if the FDA has not previously approved any other new therapeutic candidate containing the same active moiety, which is the molecule or ion responsible for the action of the therapeutic candidate substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such therapeutic candidate where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing therapeutic candidate. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for therapeutic candidates containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

*Orphan drug designation.* Under the Orphan Drug Act, the FDA may grant orphan drug designation to therapeutic candidates intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S. or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a therapeutic candidate for this type of disease or condition will be recovered from sales in the U.S. for that therapeutic candidate. Orphan drug designation must be requested before submitting a marketing application for the therapeutic for that particular disease or condition. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. The FDA may revoke orphan drug designation, and if it does, it will publicize the drug is no longer designated as an orphan drug.

If a therapeutic candidate with orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the therapeutic candidate is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same therapeutic candidate for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our therapeutic candidates for seven years if a competitor obtains approval of the same therapeutic candidate as defined by the FDA or if our therapeutic candidate is determined to be contained within the competitor's therapeutic candidate for the same indication or disease.

*Pediatric exclusivity and pediatric use.* Under the Best Pharmaceuticals for Children Act, or BPCA, certain therapeutic candidates may obtain an additional six months of exclusivity if the sponsor submits information requested in writing by the FDA, referred to as a Written Request, relating to the use of the active moiety of the therapeutic candidate in children. The FDA may not issue a Written Request for studies on unapproved or approved

indications where it determines that information relating to the use of a therapeutic candidate in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for most therapeutic candidates and biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, BLAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the therapeutic candidate for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the therapeutic candidate is safe and effective. The sponsor or the FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. The FDA must send a noncompliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation. The FDA also must post the PREA noncompliance letter and sponsor's response.

As part of the FDASIA, the U.S. Congress made a few revisions to BPCA and PREA, which were slated to expire on September 30, 2012, and made both laws permanent.

*Post-approval requirements.* Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the therapeutic candidate reaches the market. Later discovery of previously unknown problems with a therapeutic candidate may result in restrictions on the therapeutic candidate or even complete withdrawal of the therapeutic candidate from the market. After approval, some types of changes to the approved therapeutic candidate, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may under some circumstances require testing and surveillance programs to monitor the effect of approved therapeutic candidates that have been commercialized, and the FDA under some circumstances has the power to prevent or limit further marketing of a therapeutic candidate based on the results of these post-marketing programs.

Any therapeutic candidates manufactured or distributed by us or our collaborators pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences associated with the therapeutic candidate;
- providing the FDA with updated safety and efficacy information;
- therapeutic sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes; and
- complying with FDA promotion and advertising requirements, which include, among other things, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved labeling, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet.

Therapeutic manufacturers, their subcontractors, and other entities involved in the manufacture and distribution of approved therapeutic candidates are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMPs and other laws. The FDA periodically inspects manufacturing facilities to assess compliance with ongoing regulatory requirements, including cGMPs, which impose extensive procedural, substantive and record-keeping requirements upon us and any third-party manufacturers that we may decide to use if our therapeutic candidates are approved. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require FDA approval before being implemented. FDA regulations would also require investigation and correction of any deviations from cGMPs and impose reporting and documentation

requirements upon us and the third-party manufacturers. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMPs and other aspects of regulatory compliance. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory actions, such as warning letters, suspension of manufacturing, seizures of products, injunctive actions or other civil penalties. We cannot be certain we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If we or our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials or require us to recall a product from distribution.

*New Legislation and Regulations* . From time to time, legislation is drafted, introduced and passed in the U.S. Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations will be changed or what the effect of such changes, if any, may be.

***Regulation outside of the U.S.***

In addition to regulations in the U.S., we will be subject to regulations of other countries governing any clinical trials and commercial sales and distribution of our therapeutic candidates. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the U.S. before we can commence clinical trials in such countries and approval of the regulators of such countries or economic areas, such as the European Union, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

The currently applicable Clinical Trials Directive 2001/20/EC and Commission Directive 2005/28/EC on GCP setting out the system for the approval of clinical trials in the European Union, or EU, have been implemented through national legislation in the EU Member States. Under this system, an applicant must obtain approval from the national competent authorities in all EU Member States in which the clinical trials are to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site once approved by the competent ethics committee.

In 2014, a new Clinical Trials Regulation 536/2014, replacing the current Clinical Trials Directive, was adopted. The new Regulation will become directly applicable in all EU Member States (without national implementation) once the EU Portal and Database are fully functional. The Regulation was expected to apply by October 2018. However, due to technical difficulties with the development of the IT systems, it is currently expected that the new Regulation will come into application during 2019. The new Regulation seeks to simplify and streamline the approval of clinical trials in the EU. For example, the sponsor shall submit a single application for approval of a clinical trial via the EU Portal. As part of the application process, the sponsor shall propose a reporting Member State, who will coordinate the validation and evaluation of the application. The reporting Member State shall consult and coordinate with the other concerned Member States. If an application is rejected, it can be amended and resubmitted through the EU Portal. If an approval is issued, the sponsor can start the clinical trial in all concerned Member States. However, a concerned Member State can in limited circumstances declare an “opt-out” from an approval. In such a case, the clinical trial cannot be conducted in that Member State. The Regulation also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU Database.

In the EU, a company may submit a marketing authorization application either: (i) at the national level with the national competent authorities in one EU Member State, or the national procedure; (ii) via mutual recognition of a national authorization in other EU Member States, or the mutual recognition procedure; (iii) at the national level in several EU Member States, or the decentralized procedure; or (iv) at centralized level with the European Medicines Agency, or EMA, referred to as the centralized procedure. The national procedure allows sponsor to choose the EU Member State in which he wishes to first submit an application. The mutual recognition procedure allows a marketing authorization granted in one EU Member State via the national procedure to be recognized in other EU

Member States. The decentralized procedure allows a medicine that has not yet been authorized in the EU to be authorized in several EU Member States. The centralized procedure, whereby a medicine receives marketing authorization in all EU Member States, is compulsory for certain medicines and is optional for other types of medicines if the applicant can show eligibility.

As in the U.S., we may apply for designation of a therapeutic candidate as an orphan drug for the treatment of a specific indication in the EU before the application for marketing authorization is made. Orphan drugs in the EU enjoy economic and marketing benefits, including up to ten (10) years of market exclusivity for the approved indication unless certain exceptions apply.

***Healthcare Reform***

In March 2010, Congress passed the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of health 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 policy reforms. The ACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes, and fraud and abuse, impacting existing government healthcare programs and resulting in the development of new programs, including Medicare payment for performance initiatives, and improvements to the physician quality reporting system and feedback program. Other aspects of the ACA include, but are not limited to:

- Increases in pharmaceutical manufacturer rebate liability under the Medicaid Drug Rebate Program due to an increase in the minimum basic Medicaid rebate on most branded prescription drugs, and the application of Medicaid rebate liability to drugs used in risk-based Medicaid managed care plans.
- Expansion of the 340B Drug Pricing Program to require discounts for “covered outpatient drugs” sold to certain children’s hospitals, critical access hospitals, freestanding cancer hospitals, rural referral centers, and sole community hospital.
- Requirements on pharmaceutical companies to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the “Donut Hole.”
- Requirements on pharmaceutical companies to pay an annual non-tax-deductible fee to the federal government based on each company’s market share of prior year total sales of branded drugs to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs, and Department of Defense.
- Establishment of the Independent Payment Advisory Board, which, since 2014, has had authority to recommend certain changes to the Medicare program to reduce expenditures by the program when spending exceeds a certain growth rate and such changes could result in reduced payments for prescription drugs. Under certain circumstances, these recommendations will become law unless Congress enacts legislation achieving the same or greater Medicare cost savings. However, as of early 2017, the President has yet to nominate anyone to serve on the board.
- Establishment of the Patient-Centered Outcomes Research Institute to identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.
- Establishment the Center for Medicare and Medicaid Innovation within the Centers for Medicare and Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

From time to time, legislation is drafted, introduced, and passed in Congress that could significantly change the statutory provisions governing the sale, marketing, coverage, and reimbursement of products regulated by CMS or

other government agencies. In addition to new legislation, CMS regulations and policies are often revised or interpreted by the agency in ways significantly affecting our business and our products.

In particular, we expect that the new administration and the U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the U.S. healthcare reform legislation. Since taking office, President Trump has continued to support the repeal of all or portions of the ACA. President Trump has also issued an executive order in which he stated it is his administration's policy to seek the prompt repeal of the ACA and directed executive departments and federal agencies to waive, defer, grant exemptions from, or delay the implementation of the provisions of the ACA to the maximum extent permitted by law. There is still uncertainty with respect to the impact President Trump's administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold. Such reforms could have an adverse effect on anticipated revenues from therapeutic candidates we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop therapeutic candidates. However, we cannot predict the ultimate content, timing, or effect of any healthcare reform legislation or the impact of potential legislation on us.

Furthermore, political, economic, and regulatory influences frequently subject the healthcare industry in the U.S. to fundamental change. For example, initiatives to reduce the federal budget and debt and to reform healthcare coverage are increasing cost-containment efforts. We anticipate federal agencies, Congress, state legislatures, and the private sector will continue to review and assess alternative healthcare benefits, controls on healthcare spending, and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit coverage for or the amounts federal and state governments will pay for health care products and services, which could also result in reduced demand for our products or additional pricing pressures, and limit or eliminate our spending on development projects and affect our ultimate profitability.

***Third-Party Payor Coverage and Reimbursement***

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the U.S., sales of any products for which we may receive regulatory marketing approval will depend, in part, on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities such as Medicare, Medicaid, TRICARE, and the Veterans Administration, managed care providers, private health insurers, and other organizations.

The Medicaid Drug Rebate Program, which is part of the federal Medicaid program (a program for financially needy patients, among others), requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for receiving federal reimbursement for the manufacturer's outpatient drugs furnished to Medicaid patients.

In order for a pharmaceutical product to (i) receive federal reimbursement under Medicaid and Medicare Part B (the part of the federal Medicare program covering outpatient items and services for the aged and disabled) or (ii) be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program, which is a federal program that requires manufacturers to provide discounts to certain statutorily defined safety-net providers. The required 340B discount on a given product is calculated based on certain Medicaid Drug Rebate Program metrics the manufacturer is required to report to CMS. The failure to report or the misreporting of such pricing metrics could result in significant civil monetary penalties and fines, including up to $178,156 (adjusted for inflation) for each item of false or omitted information and $17,816 (adjusted for inflation) per day per labeler code for each day the submission of such pricing information is late beyond the due date.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, imposed requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities, which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and

class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The process for determining whether a payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate a payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list or formulary, which may not include all FDA-approved products for a particular indication. Also, third-party payors may refuse to include a particular branded product on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. Furthermore, a payor's decision to provide coverage for a product does not imply an adequate reimbursement rate will be available. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of therapeutics have been a focus in this effort. The U.S. government, state legislatures, and foreign governments have shown significant interest in 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. Our drug candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover an approved product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

Further, the American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by the Department of Health and Human Services, the Agency for Healthcare Research and Quality, or AHRQ, and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to the U.S. Congress. In addition, the ACA requires, among other things, that AHRQ broadly disseminate findings from federally funded comparative clinical effectiveness research. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our therapeutic candidates if any such therapeutic, or the condition that it is intended to treat, is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our therapeutic candidates.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by the U.S. Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, started in April 2013, and, due to subsequent legislative amendments, will stay in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which among other things, also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that additional federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will

pay for healthcare drugs and services, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability.

Finally, in some foreign countries, the proposed pricing for a therapeutic candidate must be approved before it may be lawfully marketed. The requirements governing therapeutic pricing vary widely from country to country. For example, in the EU, pricing and reimbursement of pharmaceutical products are regulated at a national level under the individual EU Member States' social security systems. Some foreign countries provide options to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A country may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our therapeutic candidates. Even if approved for reimbursement, historically, therapeutic candidates launched in some foreign countries such as some countries in the EU do not follow price structures of the U.S. and prices generally tend to be significantly lower.

***Other Healthcare Laws and Regulations***

If we obtain regulatory approval of our products, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales and marketing strategies. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. These laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, and physician sunshine laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or paying remuneration (a term interpreted broadly to include anything of value, including, for example, gifts, discounts and credits), 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, an item or reimbursable, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. Violations of the federal Anti-Kickback Statute can result in significant civil monetary and criminal penalties, including $21,916 (adjusted annually for inflation) per kickback plus three times the amount of remuneration and a five year prison term per violation. Further, violation of the federal Anti-Kickback Statute can also form the basis for False Claims Act liability (discussed below). The Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the Anti-Kickback Statute to reach large settlements with healthcare companies based on allegedly inappropriate consulting, discounting and other financial arrangements with physicians and others in a position to refer patients to receive items or services reimbursable by a federal healthcare program. 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. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only government programs.

Additionally, the civil False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in very significant monetary penalties, including $10,957-$21,916 (adjusted annually for inflation) for each false claim and treble the amount of the government's damages. The federal government continues to use the False Claims Act, and the accompanying threat of significant liability, in its investigations and prosecutions of pharmaceutical and biotechnology companies throughout the U.S. Such investigations and prosecutions frequently involve, for example, the alleged promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with the False Claims Act and other applicable fraud and abuse laws.

The U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, includes a fraud and abuse provision referred to as the HIPAA All-Payor Fraud Law, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services. 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.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by HITECH, and its implementing regulations, including the final omnibus rule published on January 25, 2013, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. Penalties include up to $55,010 per violation (with a maximum fine of $1,650,300 per violation category per year) (adjusted for inflation) and ten years in prison.

We may also be subject to federal transparency laws, including the federal Physician Payment Sunshine Act, which was part of the ACA and requires manufacturers of certain drugs and biologics, among others, to track and disclose payments and other transfers of value they make to U.S. physicians and teaching hospitals, as well as physician ownership and investment interests in the manufacturer. This information is subsequently made publicly available in a searchable format on a CMS website. Failure to disclose required information may result in civil monetary penalties of up to an aggregate of $163,117 per year (or up to an aggregate of $1,087,450 per year for "knowing failures") (adjusted for inflation), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians and/or other healthcare providers.

Finally, as noted above, analogous state laws and regulations, such as, state anti-kickback and false claims laws may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. Similarly, many states also have laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

***Environment***

Our third party manufacturers are subject to inspections by the FDA for compliance with cGMP and other U.S. regulatory requirements, including U.S. federal, state and local regulations regarding environmental protection and hazardous and controlled substance controls, among others. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. We have incurred, and may continue to incur, significant expenditures to ensure we are in compliance with these laws and regulations. We would be subject to significant penalties for failure to comply with these laws and regulations.

**Sales and Marketing**

Our current focus is on the development of our existing portfolio, the initiation and completion of clinical trials and, if and where appropriate, the registration of our therapeutic candidates. We currently do not have marketing, sales and distribution capabilities. If we receive marketing and commercialization approval for any of our therapeutic candidates, we intend to market the product through strategic alliances and distribution agreements with

third parties. The ultimate implementation of our strategy for realizing the financial value of our therapeutic candidates is dependent on the results of clinical trials for our therapeutic candidates, the availability of funds and the ability to negotiate acceptable commercial terms with third parties.

**Advisors**

We seek advice from our advisory board, which consists of a number of leading executive officers, scientists and physicians, on strategic direction, scientific and medical matters. Our advisory board may provide advice regarding

- our research and development programs;
- the design and implementation of our clinical programs;
- our patent and publication strategies;
- new technologies relevant to our research and development programs; and
- specific scientific and technical issues relevant to our business.

The current members of our advisory board are as follows.

| Name | Position and Institutional Affiliation |
|---|---|
| Freddy Boey, Ph.D. | Deputy President and Provost, Nanyang Technological University |
| Michael Hodges, MBBS | Chief Medical Officer, Amplyx Pharmaceuticals |
| Amy S. Paller, M.D. | Walter J. Hamlin Professor and Chair Department of Dermatology, Northwestern University Feinberg School of Medicine |
| Steven T. Rosen, M.D., F.A.C.P. | Provost/Chief Scientific Officer, City of Hope |
| Robert P. Schleimer, Ph.D. | Chief, Division of Medicine-Allergy-Immunology, Northwestern University |
| Oliver von Stein, Ph.D. | Founder & CEO, iModia Biotech GmbH |
| John J. Renger, Ph.D. | Head of Clinical R&D/Translational Medicine, Purdue Pharma, L.P. |

**Employees**

As of December 31, 2018, we have 27 full time employees, of whom 20 are engaged in research and development activities and 7 are engaged in finance, legal, human resources, business development and general management. We have no collective bargaining agreement with our employees and we have not experienced any work stoppages. We consider our relations with our employees to be good.

**Corporate Information**

We were originally incorporated in the State of Delaware on February 6, 2017 under the name “Max-1 Acquisition Corporation.” Prior to the Merger, Max-1 was a “shell” company registered under the Securities Exchange Act of 1934, as amended, or the Exchange Act, with no specific business plan or purpose until it began operating the business of Exicure OpCo through the Merger transaction on September 26, 2017. Exicure OpCo was originally formed as a limited liability company under the name AuraSense Therapeutics, LLC in the State of Delaware in June 2011 and was a clinical-stage biotechnology company developing gene regulatory and immuno-oncology therapeutics based on its proprietary SNA technology. AuraSense Therapeutics, LLC was subsequently converted into AuraSense Therapeutics, Inc., a Delaware corporation, on July 9, 2015, and changed its name on the same date to Exicure, Inc. Immediately after giving effect to the Merger and the initial closing of the 2017 Private Placement, the business of Exicure OpCo became our business.

Our corporate headquarters are located at 8045 Lamon Avenue, Suite 410, Skokie, IL 60077, and our telephone number is (847) 673-1700.

All trademarks, service marks and trade names appearing in this prospectus are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

**Available Information**

We maintain a website at www.exicuretx.com, to which we regularly post copies of our press releases as well as additional information about us. Our filings with the SEC will be available free of charge through the website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Information contained in our website is not a part of, nor incorporated by reference into, this prospectus or our other filings with the SEC, and should not be relied upon.

**Item 1A. Risk Factors.**

*We are providing the following cautionary discussion of risk factors, uncertainties and assumptions that we believe are relevant to our business. These are factors that, individually or in the aggregate, we think could cause our actual results to differ materially from expected and historical results and our forward-looking statements. We note these factors for investors as permitted by Section 21E of the Exchange Act and Section 27A of the Securities Act. You should understand that it is not possible to predict or identify all such factors. Consequently, you should not consider this section to be a complete discussion of all potential risks or uncertainties that may substantially impact our business. Moreover, we operate in a competitive and rapidly changing environment. New factors emerge from time to time and it is not possible to predict the impact of all of these factors on our business, financial condition or results of operations.*

**Risks Related to Our Business**

***We are a clinical-stage biotechnology company with a history of losses. We expect to continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability, which could result in a decline in the market value of our common stock.***

We are a biotechnology company developing gene regulatory and immuno-oncology therapeutics based on our proprietary SNA technology. We have a limited operating history. Since our inception in June 2011, we have devoted our resources to the development of SNA technology. We have had significant operating losses since our inception. As of December 31, 2018, we have generated an accumulated deficit of $73.8 million . For the years ended December 31, 2018 and 2017, our net loss was $22.4 million and $11.0 million , respectively. Substantially all of our losses have resulted from expenses incurred in connection with our research programs and from general and administrative costs associated with our operations. Our technology and therapeutic candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of therapeutic candidates based on novel technologies.

We have not generated, and do not expect to generate, any product revenue for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, preclinical studies, clinical trials, and the regulatory approval process for therapeutic candidates. The amount of future losses is uncertain. Our ability to achieve profitability, if ever, will depend on, among other things, us, or any current or future collaborators, successfully developing therapeutic candidates, obtaining regulatory approvals to market and commercialize therapeutic candidates, manufacturing any approved products on commercially reasonable terms, establishing a sales and marketing organization or suitable third party alternatives for any approved product and raising sufficient funds to finance business activities. If we, or any current or future collaborators, are unable to develop and commercialize one or more of our therapeutic candidates or if sales revenue from any therapeutic candidate that receives approval is insufficient, we will not achieve profitability, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

***Our approach to the discovery and development of innovative therapeutic treatments based on our technology is unproven and may not result in marketable products.***

We plan to develop a pipeline of therapeutic candidates using our proprietary SNAs as therapeutic agents. We believe that therapeutic candidates identified with our therapeutic discovery technology may offer an improved therapeutic approach to small molecules and antibodies, as well as several advantages over linear oligonucleotide-based therapeutics. However, the scientific research that forms the basis of our efforts to develop therapeutic candidates based on our SNAs and the identification and optimization of SNAs is relatively new. Further, the scientific evidence to support the feasibility of developing therapeutic treatments based on SNAs is both preliminary and limited.

Therapeutic candidates based on SNA technology have not been extensively tested in humans, and a number of clinical trials conducted by other companies using oligonucleotide technologies have not been successful. We may discover that the SNAs do not possess certain properties required for therapeutic treatment to be effective, such as the ability to remain stable in the human body for the period of time required for the therapeutic candidate to reach the target tissue or the ability to cross the cell membrane and enter into cells within the target tissue for effective delivery. We currently have only limited data, and no conclusive evidence, to suggest that we can introduce these necessary drug-like properties into SNAs. We may spend substantial funds attempting to introduce these properties and may never succeed in doing so. In addition, therapeutic candidates based on SNAs may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies. Even if therapeutic candidates have successful results in animal studies, they may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective or harmful ways. As a result, we may never succeed in developing a marketable therapeutic, we may not become profitable and the value of our common stock would decline.

Further, the U.S. Food and Drug Administration (the "FDA"), has limited experience with SNA-based therapeutics. No regulatory authority has granted approval to any person or entity, including us, to market and commercialize therapeutics using SNAs, which may increase the complexity, uncertainty and length of the regulatory approval process for our therapeutic candidates. We and any current or future collaborators may never receive approval to market and commercialize any therapeutic candidate. Even if we or a future collaborator obtain regulatory approval, the approval may be for disease indications or patient populations that are not as broad as we intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We or a future collaborator may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post-marketing testing requirements to maintain regulatory approval. If our SNA technology proves to be ineffective, unsafe or commercially unviable, our technology and pipeline would have little, if any, value, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

***Our therapeutic candidates are in early stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability.***

We have no therapeutics on the market and all of our therapeutic candidates are in early stages of development. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals, including an institutional review board ("IRB"), approval to conduct clinical trials at particular sites for, and successfully commercializing, our therapeutic candidates, either alone or with third parties. Before obtaining regulatory approval for the commercial distribution of our therapeutic candidates, we or an existing or a future collaborator must conduct extensive preclinical studies and clinical trials to demonstrate the safety and efficacy in humans of our therapeutic candidates. Preclinical studies and clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. The start or end of a clinical trial is often delayed or halted due to changing regulatory requirements, manufacturing challenges, required clinical trial administrative actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative therapeutic or required prior therapy, clinical outcomes or financial constraints. For instance, delays or difficulties in patient enrollment or difficulties in retaining trial participants can result in increased costs, longer development times or termination of a clinical trial. Clinical trials of a new therapeutic candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the therapeutic candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the eligibility criteria for the clinical trial, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites and the availability of effective treatments for the relevant disease.

A therapeutic candidate can unexpectedly fail at any stage of preclinical and clinical development. In our completed Phase 1 trial, AST-005 did not show an antipsoriatic effect. There is no guarantee that AST-005 will show an antipsoriatic effect in future clinical trials of longer duration. The historical failure rate for therapeutic candidates is high due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. The results from preclinical studies or early clinical trials of a therapeutic candidate may not predict the results that will be obtained in later phase clinical trials of the therapeutic candidate. We, the FDA, an IRB, an independent ethics committee, or other applicable regulatory authorities may suspend clinical trials of a therapeutic candidate at any time for various reasons, including a finding that subjects participating in such trials are being exposed to unreasonable and significant risk of illness or injury. Similarly, an IRB or ethics committee may suspend a clinical trial at a particular trial site. We may not have the financial resources to continue development of, or to enter into collaborations for, a therapeutic candidate if we experience any problems or other unforeseen events that delay or prevent regulatory approval of, or our ability to commercialize, therapeutic candidates, including:

- negative or inconclusive results from our clinical trials or the clinical trials of others for therapeutic candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- therapeutic-related side effects experienced by participants in our clinical trials or by individuals using therapeutics similar to our therapeutic candidates;
- delays in submitting INDs or CTAs, or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or IRBs to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign authorities, such as the European Medicines Agency ("EMA"), or European Union national competent authorities, regarding the scope or design of our clinical trials;

- delays in enrolling research subjects in clinical trials;
- high drop-out rates of research subjects;
- inadequate supply or quality of therapeutic candidate components or materials or other supplies necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- poor effectiveness of our therapeutic candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- failure of our third party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular, especially in light of the novelty of our therapeutic candidates;
- varying interpretations of data by the FDA and similar foreign regulatory agencies; or
- refusal of the FDA to accept data from clinical trials conducted outside the United States, or acceptance of these data subject to certain conditions by the FDA.

***Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical studies and clinical trials may not be predictive of future clinical trial results.***

Clinical testing is expensive and generally takes many years to complete, and the outcome is inherently uncertain. Failure can occur at any time and at any stage during the clinical trial process. The results of preclinical studies and early clinical trials of our therapeutic candidates may not be predictive of the result of any subsequent clinical trials. Therapeutic candidates that have shown promising results in early stage clinical trials may still suffer significant setbacks in subsequent clinical trials. We will have to conduct trials in our proposed indications to verify the results obtained to date and to support any regulatory submissions for further clinical development. A number of companies in the biopharmaceutical industry have suffered significant setbacks in clinical trials due to lack of efficacy or adverse safety profiles despite promising results in earlier clinical trials. Moreover, clinical data is often susceptible to varying interpretations and analyses. We do not know whether Phase 1, Phase 2, Phase 3, or other clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety with respect to the proposed indication for use sufficient to receive regulatory approval or market our therapeutic candidates. If we experience delays in the completion of, or termination of, any clinical trial of our therapeutic candidates, the commercial prospects of our therapeutic candidates may be harmed, and our ability to generate product revenues from any of these therapeutic candidates will be delayed. In addition, any delays in completing clinical trials will increase our costs, slow down our therapeutic candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences could materially and adversely affect our business, financial condition, results of operations or prospects.

***We will need substantial additional funds to advance the development of our therapeutic candidates, and we cannot guarantee that we will have sufficient funds available in the future to develop and commercialize our current or future therapeutic candidates.***

If our existing therapeutic candidates or our future therapeutic candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand our development, regulatory, manufacturing, marketing, and sales capabilities or contract with other organizations to provide these capabilities for us. We have used substantial funds to develop our therapeutic candidates and will require significant funds to conduct further research and development and preclinical studies and clinical trials of our therapeutic candidates, to seek regulatory approvals for our therapeutic candidates and to manufacture and market products, if any, that are approved for commercial sale. As of December 31, 2018 and 2017, we had $26.3 million and $25.8 million in cash and cash equivalents, respectively. Based on the Company's current operating plans, we believe that existing working capital at December 31, 2018 is sufficient to fund our current operating plans into January 2020. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing development and corporate activities. Since the length of time

and activities associated with successful development of our therapeutic candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. To execute our business plan, we will need, among other things:

- to obtain the human and financial resources necessary to develop, test, obtain regulatory approval for, manufacture and market our therapeutic candidates;
- to build and maintain a strong intellectual property portfolio and avoid infringing the intellectual property of third parties;
- to establish and maintain successful licenses, collaborations and alliances;
- to satisfy the requirements of clinical trial protocols, including patient enrollment;
- to establish and demonstrate the clinical efficacy and safety of our therapeutic candidates;
- to obtain regulatory approvals;
- to manage our spending as costs and expenses increase due to preclinical studies and clinical trials, regulatory approvals, and commercialization;
- to obtain additional capital to support and expand our operations; and
- to market our products to achieve acceptance and use by the medical community in general.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, reduce or terminate our research and development programs and preclinical studies or clinical trials, if any, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technology or therapeutic candidates that we would otherwise pursue on our own. We do not expect to realize revenue from product sales, milestone payments or royalties in the foreseeable future, if at all. Our revenue sources are, and will remain, extremely limited unless and until our therapeutic candidates are clinically tested, approved for commercialization and successfully marketed. To date, we have primarily financed our operations through the sale of equity securities, payments received in connection with our research collaboration, license, and option agreement with Purdue Pharma L.P., or Purdue, or as a primary contractor or as a subcontractor on government grants, and proceeds from our loan agreement with Hercules Technology Growth Capital, or Hercules. We will be required to seek additional funding in the future and intend to do so through either collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, may involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of equity securities received any distribution of corporate assets.

***Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.***

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

- variations in the level of expense related to our therapeutic candidates or future development programs;
- results of clinical trials, or the addition or termination of clinical trials or funding support by us, or a future collaborator or licensing partner;
- our execution of any collaboration, licensing or similar arrangement, and the timing of payments we may make or receive under such existing or future arrangements or the termination or modification of any such existing or future arrangements;

- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- whether or not any of our therapeutic candidates receives regulatory approval, market acceptance and demand for such therapeutic candidates;
- regulatory developments affecting our therapeutic candidates or those of our competitors; and
- changes in general market and economic conditions.

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

***We may not successfully engage in strategic transactions, including any additional collaborations we seek, which could adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expense and present significant distractions to our management.***

From time to time, we may consider strategic transactions, such as collaborations, acquisitions of companies, asset purchases and out- or in-licensing of product candidates or technologies. In particular, in addition to our current arrangements with Dermelix, which began in February 2019 and is in its early stages, and Purdue, with which there no active therapeutic candidates in development and which has not indicated any further interest in development, we will evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or pharmaceutical companies. The competition for collaborators is intense, and the negotiation process is time-consuming and complex. Any new collaboration may be on terms that are not optimal for us, and we may be unable to maintain any new or existing collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product do not meet expectations or the collaborator terminates the collaboration. Any such collaboration, or other strategic transaction, may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and have a material adverse effect on our business, results of operations, financial condition and prospects. Conversely, any failure to enter any collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market.

***If third parties on which we depend to conduct our preclinical studies and clinical trials do not perform as contractually required, fail to satisfy regulatory or legal requirements, or miss expected deadlines, our development program could be delayed with materially adverse effects on our business, financial condition, results of operations and prospects.***

We rely on third party clinical investigators, contract research organizations ("CROs"), clinical data management organizations and consultants to design, conduct, supervise and monitor preclinical studies and clinical trials for our therapeutic candidates. Because we rely on third parties and do not have the ability to conduct preclinical studies or clinical trials independently, we have less control over the timing, quality and other aspects of preclinical studies and clinical trials than we would if we conducted them on our own. These investigators, CROs and consultants are not our employees and we have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may

draw time and resources away from our programs. The third parties with which we contract might not be diligent, careful or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. The FDA requires preclinical studies to be conducted in accordance with applicable Good Laboratory Practices ("GLPs"), and clinical trials to be conducted in accordance with applicable FDA regulations and Good Clinical Practices ("GCPs"), including requirements for conducting, recording and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any adverse development or delay in our preclinical studies or clinical trials could have a material adverse effect on our business, financial condition, results of operations and prospects.

***Because we rely on third party manufacturing and supply partners, our supply of research and development, preclinical studies and clinical trial materials may become limited or interrupted or may not be of satisfactory quantity or quality.***

We rely on third party partners to manufacture and supply the materials and components for our research and development, preclinical study and clinical trial supplies. We do not own manufacturing facilities or supply sources for such components and materials. Our manufacturing requirements include oligonucleotides and lipids. We procure our nonclinical toxicology and clinical development materials from a single source supplier on a purchase order basis. There can be no assurance that our supply of research and development, preclinical study and clinical trial therapeutic candidates and other materials will not be limited, interrupted, restricted in certain geographic regions or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our drug product manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a therapeutic candidate is subject to oversight by the FDA and foreign regulatory authorities. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory requirements, such as current Good Manufacturing Practices ("cGMPs"). In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our therapeutic candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our therapeutic candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop therapeutic candidates in a timely manner or within budget.

We expect to continue to rely on third party manufacturers if we receive regulatory approval for any therapeutic candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third party manufacturing for therapeutic candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our therapeutic candidates successfully. Our or a third party's failure to execute on our manufacturing requirements and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue preclinical studies or clinical trials of our therapeutic candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for therapeutic candidates;

- loss of the cooperation of a future collaborator;
- subjecting manufacturing facilities of our therapeutic candidates to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our therapeutic candidates; and
- in the event of approval to market and commercialize a therapeutic candidate, an inability to meet commercial demands for our therapeutics.

***We face competition from entities that have developed or may develop therapeutic candidates for our target disease indications, including companies developing novel treatments and technology platforms based on modalities and technology similar to ours. If these companies develop technologies, including delivery technologies, or therapeutic candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize therapeutic candidates may be adversely affected.***

The development and commercialization of therapeutic candidates is highly competitive. We compete with a number of multinational pharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or will develop therapeutic candidates and processes competitive with our therapeutic candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We believe that a significant number of therapeutics are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop therapeutic candidates. There is intense and rapidly evolving competition in the biotechnology, pharmaceutical and oligonucleotide therapeutics fields. While we believe that our SNA technology, its associated intellectual property and our scientific and technical know-how give us a competitive advantage in this space, competition from many sources remains. Our competitors include larger and better funded pharmaceutical, biotechnology and oligonucleotide therapeutics companies. Moreover, we also compete with current and future therapeutics developed at universities and other research institutions.

We are aware of several companies that are developing oligonucleotide delivery platforms and oligonucleotide-based therapeutics. These competitors include Ionis Pharmaceuticals, Inc., Alnylam Pharmaceuticals, Inc., Dicerna Pharmaceuticals, Inc., Arbutus Biopharma Corp., Wave Life Sciences Ltd., Dynavax Technologies Corp., Idera Pharmaceuticals, Inc., Mologen AG, and Checkmate Pharmaceuticals, Inc. These and other competitors compete with us in recruiting scientific and managerial talent, and for funding from pharmaceutical companies.

Our success will partially depend on our ability to develop and protect therapeutics that are safer and more effective than competing therapeutics. Our commercial opportunity and success will be reduced or eliminated if competing therapeutics are safer, more effective, or less expensive than the therapeutics we develop.

If our therapeutic candidates are approved for the indications we are currently pursuing, they will compete with a range of therapeutic treatments that are either in development or currently marketed. A number of therapeutics for treating psoriasis and cancers are on the market or in clinical development. For the treatment of psoriasis, marketed therapies range from small molecules like topical steroids to biologics, such as AbbVie Inc.'s adalimumab. In addition, numerous compounds are in clinical development for psoriasis treatment. With respect to immunogenic cancers such as melanoma, the most common treatments are chemotherapeutic compounds, radiation therapy and now immunotherapeutic antibodies such as ipilimumab, atezolizumab and pembrolizumab.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any therapeutic candidate, we will face competition based on many different factors, including the safety and effectiveness of our therapeutics, the ease with which our therapeutics can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these therapeutics, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing therapeutics could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any therapeutics we may develop. Competitive therapeutics may make any therapeutics we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our therapeutic candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

***The market may not be receptive to our therapeutic candidates based on a novel therapeutic modality, and we may not generate any future revenue from the sale or licensing of therapeutic candidates.***

Even if approval is obtained for a therapeutic candidate, we may not generate or sustain revenue from sales of the product due to factors such as whether the product can be sold at a competitive cost and otherwise accepted in the market. The therapeutic candidates that we are developing are based on our SNA technology. Market participants with significant influence over acceptance of new treatments, such as physicians and third party payors, may not adopt a treatment based on SNA technology, and we may not be able to convince the medical community and third party payors to accept and use, or to provide favorable reimbursement for, any therapeutic candidates developed by us or any current or future collaborators. Market acceptance of our therapeutic candidates will depend on, among other factors:

- the timing of our receipt of any marketing and commercialization approvals;
- the terms of any approvals and the countries in which approvals are obtained;
- the safety and efficacy of our therapeutic candidates;
- the prevalence and severity of any adverse side effects associated with our therapeutic candidates;
- limitations or warnings contained in any labeling approved by the FDA or other regulatory authority;
- relative convenience and ease of administration of our therapeutic candidates;
- the willingness of patients to accept any new methods of administration;
- the success of our physician education programs;
- the availability of adequate government and third party payor reimbursement;
- the pricing of our products, particularly as compared to alternative treatments; and
- availability of alternative effective treatments for indications our therapeutic candidates are intended to treat and the relative risks, benefits and costs of those treatments.

With our focus on SNAs, these risks may increase to the extent the space becomes more competitive or less favored in the commercial marketplace. Additional risks apply in relation to any disease indications we may pursue which are classified as rare diseases and allow for orphan drug designation by regulatory agencies in major commercial markets, such as the U.S., Europe and Japan. Because of the small patient population for a rare disease, if pricing is not approved or accepted in the market at an appropriate level for an approved product with orphan drug designation, such therapeutic may not generate enough revenue to offset costs of development, manufacturing, marketing and commercialization despite any benefits received from the orphan drug designation, such as market exclusivity, assistance in clinical trial design or a reduction in user fees or tax credits related to development expense. Market size is also a variable in disease indications not classified as rare. Our estimates regarding potential market size for any indication may be materially different from what we discover to exist at the time we commence commercialization, if any, for a therapeutic, which could result in significant changes in our business plan and have a material adverse effect on our business, financial condition, results of operations and prospects.

If a therapeutic candidate that has orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the therapeutic candidate is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same therapeutic candidate for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our therapeutic candidates for seven years if a competitor obtains approval of the same therapeutic candidate as defined by the FDA or if our therapeutic candidate is determined to be contained within the competitor's therapeutic candidate for the same indication or disease.

As in the U.S., we may apply for designation of a therapeutic candidate as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Sponsors of orphan drugs in the European Union can enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication. During such period, marketing applications for similar medicinal products will not be accepted, unless certain exceptions apply. In the EU, a "similar medicinal product" is a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication.

***Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.***

Our success largely depends on the continued service of key management and other specialized personnel, including David A. Giljohann, Ph.D., our Chief Executive Officer, David S. Snyder, our Chief Financial Officer, and Matthias G. Schroff, our Chief Operating Officer. The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs and materially harm our business, financial condition, results of operations and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly technical nature of our therapeutic candidates and our technology and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance policies on any of our management team members or key employees. Our future success will depend in large part on our continued ability to attract and retain highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

***If our therapeutic candidates advance into clinical trials, we may experience difficulties in managing our growth and expanding our operations.***

We have limited experience in therapeutic development and limited experience with clinical trials of therapeutic candidates. As our therapeutic candidates enter and advance through preclinical studies and clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

***If any of our therapeutic candidates are approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own or enter into agreements with third parties to perform these functions on acceptable terms, we will be unable to successfully commercialize any such future therapeutics.***

We currently have no sales, marketing or distribution capabilities or experience. If any of our therapeutic candidates is approved, we will need to develop internal sales, marketing and distribution capabilities to appropriately commercialize such therapeutics, which would be expensive and time-consuming, or enter into collaborations with third parties to perform these services. If we decide to market our approved therapeutics directly, we will need to commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration and compliance capabilities. If we rely on third parties with such capabilities to market our approved therapeutics or decide to co-promote therapeutics with collaborators, we will need to establish and maintain compliant marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable terms or at all. In entering into third party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and there can be no assurance that such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved therapeutic. If we are not successful in commercializing any therapeutic approved in the future, either on our own or through third parties, our business, financial condition, results of operations and prospects could be materially and adversely affected.

***If we fail to comply with U.S. or foreign regulatory requirements, regulatory authorities could withhold marketing or commercialization approvals, limit or withdraw any marketing or commercialization approvals we may receive and subject us to other penalties that could materially harm our business.***

We and our therapeutic candidates, as well as our suppliers, contract manufacturers, distributors, and contract testing laboratories are subject to extensive regulation by governmental authorities in the European Union, the U.S., and other countries, with the regulations differing from country to country.

If we or current or future collaborators, manufacturers or service providers fail to comply with applicable requirements, these regulatory authorities could refuse to issue necessary approvals for marketing and commercialization. Even if we receive marketing and commercialization approval of a therapeutic candidate, we and our third party service

providers will be subject to continuing regulatory requirements, including a broad array of regulations related to establishment, registration and product listing, manufacturing processes, risk management measures, quality and pharmacovigilance systems, pre- and post-approval clinical data, labeling, advertising and promotional activities for such therapeutic, record keeping, distribution, and import and export of therapeutics for any therapeutic for which we obtain marketing approval. We are required to submit safety and other post market information and reports and are subject to continuing regulatory review, including in relation to adverse patient experiences with the therapeutic and clinical results that are reported after a therapeutic is made commercially available, both in the U.S. and any foreign jurisdiction in which we seek regulatory approval. The FDA and certain foreign regulatory authorities, such as the EMA, have significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a therapeutic or to require withdrawal of the therapeutic from the market. The FDA also has the authority to require a Risk Evaluation and Mitigation Strategies, or REMS, plan either before or after approval, which may impose further requirements or restrictions on the distribution or use of an approved therapeutic. The EMA now routinely requires risk management plans, or RMPs, as part of the marketing authorization application process, and such plans must be continually modified and updated throughout the lifetime of the product as new information becomes available. In addition, for nationally authorized medicinal products, the relevant governmental authority of any European Union member state can request an RMP whenever there is a concern about the risk/benefit balance of the product.

The manufacturer and manufacturing facilities we use to make a future therapeutic, if any, will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with cGMP requirements. The discovery of any new or previously unknown problems with our third party manufacturers, manufacturing processes or facilities may result in restrictions on the therapeutic, manufacturer or facility, including withdrawal of the therapeutic from the market. If we rely on third party manufacturers, we will not have control over compliance with applicable rules and regulations by such manufacturers. Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. If we or our future collaborators, manufacturers or service providers fail to comply with applicable continuing regulatory requirements in the U.S. or foreign jurisdictions in which we seek to market our therapeutics, we or they may be subject to, among other things, fines, warning and untitled letters, clinical holds, delay or refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications, suspension, refusal to renew or withdrawal of regulatory approval, recalls, seizures or administrative detention of products, refusal to permit the import or export of therapeutics, operating restrictions, inability to participate in government programs including Medicare and Medicaid, and total or partial suspension of production or distribution, injunction, restitution, disgorgement, debarment, civil and criminal penalties and criminal prosecution.

***Price controls imposed in foreign markets may adversely affect our future profitability.***

In some countries, particularly member states of the European Union, the pricing of prescription drugs is subject to governmental control at the national level, and in some cases also at the regional level. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a therapeutic. 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 and reimbursement negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or current or future collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our SNA therapeutic candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any therapeutic candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be adversely affected.

***Our business entails a significant risk of product liability and our inability to obtain sufficient insurance coverage could have a material adverse effect on our business, financial condition, results of operations or prospects.***

Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing therapeutics, such claims could result in an investigation by certain regulatory authorities, such as the FDA or foreign regulatory authorities, of the safety and effectiveness of our therapeutics, our manufacturing processes and facilities or our marketing programs and potentially a recall of our therapeutics or more

serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our therapeutics, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources, substantial monetary awards to trial participants or patients and a decline in our stock price. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels of product liability insurance prior to marketing any of our therapeutic candidates. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material adverse effect on our business.

***Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements which could have an adverse effect on our business.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include, but is not limited to, intentional failures to comply with FDA, the Centers for Medicare and Medicaid Services ("CMS"), the Department of Health and Human Services ("HHS"), Office of Inspector General ("OIG") or other agency regulations, applicable laws, regulations, guidance or codes of conduct set by foreign governmental authorities or self-regulatory industry organizations, or provide accurate information to any governmental authorities, such as the FDA, comply with manufacturing standards we may establish, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws, regulations, guidance and codes of conduct intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws, regulations, guidance and codes of conduct may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, including, fines, debarment, or disqualification of those employees from participation in certain government-regulated activities, and serious harm to our reputation. This could include violations of the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive.

It is not always possible to identify and deter employee misconduct, 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, regulations, guidance or codes of conduct. 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, including exclusion from participation in the U.S. federal healthcare programs, the imposition of significant fines or other sanctions.

***Compliance with governmental regulations regarding the treatment of animals used in research could increase our operating costs, which would adversely affect the commercialization of our technology.***

The Animal Welfare Act, or AWA, is the federal law that covers the treatment of certain animals used in research. Currently, the AWA imposes a wide variety of specific regulations that govern the humane handling, care, treatment and transportation of certain animals by producers and users of research animals, most notably relating to personnel, facilities, sanitation, cage size, and feeding, watering and shipping conditions. Third parties with whom we contract are subject to registration, inspections and reporting requirements under the AWA. Furthermore, some states have their own regulations, including general anti-cruelty legislation, which establish certain standards in handling animals. Comparable rules, regulations, and or obligations exist in many foreign jurisdictions. If we or our contractors fail to comply with regulations concerning the treatment of animals used in research, we may be subject to fines and penalties and adverse publicity, and our operations could be adversely affected.

***Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our therapeutic development programs.***

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such events could cause interruptions of our operations. For

instance, the loss of preclinical study or clinical trial data involving our therapeutic candidates could result in delays in our development and regulatory filing efforts and significantly increase our costs. In addition, theft or other exposure of data may interfere with our ability to protect our intellectual property, trade secrets, and other information critical to our operations. We can provide no assurances that certain sensitive and proprietary information relating to one or more of our therapeutic candidates has not been, or will not in the future be, compromised. Although we have invested resources to enhance the security of our computer systems, there can be no assurances we will not experience additional unauthorized intrusions into our computer systems, or those of our CROs and other contractors and consultants, that we will successfully detect future unauthorized intrusions in a timely manner, or that future unauthorized intrusions will not result in material adverse effects on our financial condition, reputation, or business prospects. Payments related to the elimination of ransomware may materially affect our financial condition and results of operations.

Certain data breaches must also be reported to affected individuals and the government, and in some cases to the media, under provisions of HIPAA, as amended by HITECH, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive. Financial penalties may also apply in some data breaches where noncompliance with the applicable law is identified.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of our therapeutic candidates could be delayed.

***We are subject to European data protection laws, including the new EU General Data Protection Regulation 2016/679, or GDPR. If we fail to comply with existing or future data protection regulations, our business, financial condition, results of operations and prospects may be materially adversely affected.***

By virtue of our clinical trial activities in the United Kingdom and Germany, we are subject to European data protection laws, including GDPR. The GDPR which came into effect on May 25, 2018, establishes new requirements applicable to the processing of personal data ( *i.e* ., data which identifies an individual or from which an individual is identifiable), affords new data protection rights to individuals (e.g., the right to erasure of personal data) and imposes penalties for serious breaches of up to 4% annual worldwide turnover or €20 million, whichever is greater. Individuals ( *e.g* ., study subjects) also have a right to compensation for financial or non-financial losses ( *e.g* ., distress). There may be circumstances under which a failure to comply with GDPR, or the exercise of individual rights under the GDPR, would limit our ability to utilize clinical trial data collected on certain subjects. The GDPR will likely impose additional responsibility and liability in relation to our processing of personal data. This may be onerous and materially adversely affect our business, financial condition, results of operations and prospects.

***If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.***

Our research, development and manufacturing involve the use of hazardous materials and various chemicals. We maintain quantities of various flammable and toxic chemicals in our facilities in Skokie, Illinois that are required for our research, development and manufacturing activities. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We believe our procedures for storing, handling and disposing these materials in our Skokie facilities comply with the relevant guidelines of Skokie, the state of Illinois, and the Occupational Safety and Health Administration of the U.S. Department of Labor. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of animals and biohazardous materials. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

***Our information technology systems could face serious disruptions that could adversely affect our business.***

Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the Internet, face the risk of systemic failure that could disrupt our operations. A significant

disruption in the availability of our information technology and other internal infrastructure systems could cause interruptions and delays in our research and development work.

***Our current operations are concentrated in one location and any events affecting this location may have material adverse consequences.***

Our current operations are located in our facilities situated in Skokie, Illinois. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or man-made accidents or incidents that result in us being unable to fully utilize the facilities, may have a material adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our therapeutic candidates or interruption of our business operations. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material adverse effect on our business, financial position, results of operations and prospects.

***The investment of our cash, cash equivalents and fixed income marketable securities is subject to risks which may cause losses and affect the liquidity of these investments.***

As of December 31, 2018 and 2017, we had $26.3 million and $25.8 million in cash and cash equivalents, respectively. We historically have invested excess cash in certificates of deposit or money market mutual funds that invest in U.S. government or U.S. government agency securities, floating rate and variable rate demand notes of U.S. and foreign corporations, and commercial paper. These investments are subject to general credit, liquidity, market and interest rate risks, including potential future impacts similar to the impact of U.S. sub-prime mortgage defaults that have affected various sectors of the financial markets and caused credit and liquidity issues. We may realize losses in the fair value of these investments, an inability to access cash in these investments for a potentially meaningful period, or a complete loss of these investments, which would have a negative effect on our financial statements.

In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. The market risks associated with our investment portfolio may have an adverse effect on our results of operations, liquidity and financial condition.

***Changes in accounting rules and regulations, or interpretations thereof, could result in unfavorable accounting charges or require us to change our compensation policies.***

Accounting methods and policies for biotechnology companies, including policies governing revenue recognition, research and development and related expenses, and accounting for stock-based compensation, are subject to review, interpretation and guidance from our auditors and relevant accounting authorities, including the SEC. Changes to accounting methods or policies, or interpretations thereof, may require us to reclassify, restate or otherwise change or revise our historical financial statements, including those contained in this Annual Report on Form 10-K.

***We previously identified a material weakness in our internal control over financial reporting, and if we are unable to implement and maintain effective internal control over financial reporting in the future, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock may be adversely effected, and we may become subject to litigation and regulatory investigation.***

During the quarter ended March 31, 2018, we identified a material weakness in internal control over financial reporting related to a deficiency in the Company's information and communication controls, which led to ineffectively designed controls over management's review of certain research and development contracts to ensure expenses were recognized as incurred by third-party contract research organizations. Those ineffectively designed controls arose in a prior period and resulted in an immaterial error. The immaterial error has been corrected in previously issued financial statements as disclosed in Note 1 to the accompanying consolidated financial statements for the period ended December 31, 2018.

As further described above and in Part II, Item 9A "Controls and Procedures," of this Form 10-K, management has implemented applicable remedial controls, believes those remedial controls have operated for a sufficient period of time and has concluded that the material weakness discussed above is remediated at December 31, 2018. If the additional

controls and procedures we have implemented are not effective, or if we identify new material weaknesses in the future in our internal controls over financial reporting, we may not detect errors in a timely manner and our consolidated financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. We may also fail to report our financial results on a timely and accurate basis, which could result in sanctions, lawsuits, or other adverse consequences that would materially harm our business. In addition, we could become subject to investigations by the national stock exchange on which our securities are eventually listed, the SEC, or other regulatory authorities, and become subject to litigation from investors and stockholders, which could harm our reputation and our financial condition, or divert financial and management resources from our core business.

***We have incurred significant losses since our inception and expect to incur continued losses in the future. We must obtain additional funds to finance our operations and to remain a going concern.***

Our recurring losses from operations raise substantial doubt about our ability to continue as a going concern. As a result, we included an explanatory paragraph in our consolidated financial statements for the period ended December 31, 2018 with respect to this uncertainty. Our ability to continue as a going concern will require us to obtain additional funding. Based on the Company's current operating plans, we believe that existing working capital at December 31, 2018 is sufficient to fund our current operating plans into January 2020. We have based these estimates, however, on assumptions that may prove to be wrong, and we could spend our available financial resources much faster than we currently expect and need to raise additional funds sooner than we anticipate. The perception of our ability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate our research and development programs and commercialization efforts.

***Our business may be affected by litigation and government investigations.***

We may from time to time receive inquiries and subpoenas and other types of information requests from government authorities and others and we may become subject to claims and other actions related to our business activities. While the ultimate outcome of investigations, inquiries, information requests and legal proceedings is difficult to predict, defense of litigation claims can be expensive, time-consuming and distracting, and adverse resolutions or settlements of those matters may result in, among other things, modification of our business practices, costs and significant payments, any of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

**Risks Related to Intellectual Property**

***If we are not able to obtain and enforce patent protection for our technology or therapeutic candidates, development and commercialization of our therapeutic candidates may be adversely affected.***

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our therapeutic candidates, methods used to manufacture our therapeutic candidates and methods for treating patients using our therapeutic candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. As of December 31, 2018, our patent portfolio consists of over 60 issued patents and allowed patent applications and over 135 pending patent applications. We may not be able to apply for patents on certain aspects of our therapeutic candidates in a timely fashion or at all. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing therapeutics and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable or that any issued or granted patents will include claims that are sufficiently broad to cover our therapeutic candidates or to provide meaningful protection from our competitors. Moreover, the patent position of pharmaceutical and biotechnology companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and therapeutic candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market.

The U.S. Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There

are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary therapeutics and technology. While we will endeavor to try to protect our therapeutic candidates with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time-consuming, expensive and sometimes unpredictable.

In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the USPTO, which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the Leahy-Smith America Invents Act enacted in 2011, involves significant changes in patent legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. The 2013 decision by the Supreme Court in *Association for Molecular Pathology v. Myriad Genetics, Inc.* precludes a claim to a nucleic acid having a stated nucleotide sequence that is identical to a sequence found in nature and unmodified. We currently are not aware of an immediate impact of this decision on our patents or patent applications because we are developing oligonucleotide therapeutics which contain modifications that we believe are not found in nature. However, this decision has yet to be clearly interpreted by courts and by the USPTO. We cannot assure you that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. 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 decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that may weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such initial grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether. In addition, there can be no assurance that:

- Others will not or may not be able to make, use or sell compounds that are the same as or similar to our therapeutic candidates but that are not covered by the claims of the patents that we own or license.
- We or our licensors, or any current or future collaborators, are the first to make the inventions covered by each of our issued patents and pending patent applications that we own or license.
- We or our licensors, or any current or future collaborators, are the first to file patent applications covering certain aspects of our inventions.
- Others will not independently develop similar or alternative technologies or duplicate any of our technology without infringing our intellectual property rights.
- A third party will not challenge our patents and, if challenged, a court may not hold that our patents are valid, enforceable and infringed.
- Any issued patents that we own or have licensed will provide us with any competitive advantages, or will not be challenged by third parties.
- We will develop additional proprietary technologies that are patentable.
- The patents of others will not have an adverse effect on our business.
- Our competitors will not conduct research and development activities in countries where we lack enforceable patent rights and then use the information learned from such activities to develop competitive therapeutics for sale in our major commercial markets.

***We currently license patent rights from Northwestern University and may in the future license patent rights from third party owners or licensees. If Northwestern University or such other owners or licensees do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, or if they retain or license to others any competing rights, our competitive position and business prospects may be adversely affected.***

We do, and will continue to, rely on intellectual property rights licensed from third parties to protect our technology. We are a party to a number of licenses that give us rights to third party intellectual property that is necessary or useful for our business. In particular, we have a license from Northwestern University, which provides us the exclusive worldwide right under certain patents and patent applications owned by Northwestern University to exploit therapeutics and processes using nanoparticles, nanotechnology, microtechnology and nanomaterial-based constructs as therapeutics or accompanying therapeutics as a means of administration. We may also license additional third party intellectual property in the future. Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, and in particular, for those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications licensed to us. Even if patents issue or are granted, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue litigation less aggressively than we would. Further, we may not obtain exclusive rights, which would allow for third parties to develop competing therapeutics. Without protection for, or exclusive rights to, the intellectual property we license, other companies might be able to offer substantially identical therapeutics for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, the U.S. government has certain rights to the inventions covered by the patent rights licensed to us by third parties and Northwestern University, as an academic research and medical center, has reserved the right to practice the patent rights it has licensed to us (i) for research, teaching and/or other educationally related purposes (including the right to distribute materials for such purposes) and (ii) for use in the field of diagnostics (including theradiagnostics) and in any field other than the field of use licensed to us.

***Other companies or organizations may challenge our or our licensors' patent rights or may assert patent rights that prevent us from developing and commercializing our therapeutic candidates.***

Oligonucleotide and SNA-based therapeutics are a relatively new scientific field. We have obtained grants and issuances of SNA therapeutic patents and have licensed many of these patents from a third party on an exclusive basis for therapeutics applications. The issued patents and pending patent applications in the U.S. and in key markets around the world that we own or license claim many different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of SNA therapeutics. Specifically, we own and have licensed a portfolio of patents, patent applications and other intellectual property covering SNA compositions of matter as well as their methods of use.

As the field of SNA therapeutics matures, patent applications are being processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material adverse effect on our business and our ability to successfully compete.

There are many issued and pending patents that claim aspects of oligonucleotide chemistry and modifications that we may need to apply to our SNA therapeutic candidates. There are also many issued patents that claim targeting genes or portions of genes that may be relevant for SNA therapeutics we wish to develop. Thus, it is possible that one or more organizations will hold patent rights to which we will need a license. If those organizations refuse to grant us a license to such patent rights on reasonable terms, we may not be able to market therapeutics or perform research and development or other activities covered by these patents.

***We may be unable to protect our intellectual property rights throughout the world.***

Obtaining a valid and enforceable issued or granted patent covering our technology in the U.S. and worldwide can be extremely costly. In jurisdictions where we have not obtained patent protection, competitors may use our technology to develop their own therapeutics and, further, may export otherwise infringing therapeutics to territories where we have patent protection, but where it is more difficult to enforce a patent as compared to the U.S. Competitor therapeutics may compete with our future therapeutics in jurisdictions where we do not have issued or granted patents or where our issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce

patents and such countries may not recognize other types of intellectual property protection, particularly that relating to biotechnology and pharmaceuticals. This could make it difficult for us to prevent the infringement of our patents or marketing of competing therapeutics in violation of our proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

We generally file a provisional patent application first, also known as a priority filing, at the USPTO. An international application under the Patent Cooperation Treaty, or PCT, is usually filed within twelve months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in the U.S., European Union, Japan, Australia and Canada and, depending on the individual case, also in any or all of, *inter alia* , China, India, South Korea, and Mexico. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant registration authorities, while granted by others. It is also quite common that depending on the country, various scopes of patent protection may be granted on the same therapeutic candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the U.S., and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business and results of operations may be adversely affected.

***We or our licensors, or any current or future strategic partners, may become subject to third party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights, and we may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which could be costly, time consuming, delay or prevent the development and commercialization of our therapeutic candidates, or put our patents and other proprietary rights at risk.***

We or our licensors, or any current or future strategic partners, may be subject to third party claims for infringement or misappropriation of patent or other proprietary rights. We are generally obligated under our license agreements to indemnify and hold harmless our licensors for damages arising from intellectual property infringement by us. If we or our licensors, or any current or future strategic partners, are found to infringe a third party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have willfully infringed. In addition, we or our licensors, or any current or future strategic partners, may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we or any current or future collaborator may be unable to effectively market therapeutic candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our therapeutics or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the U.S., 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, for example, lack of novelty, obviousness or non-enablement. 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. The outcome following legal assertions of invalidity and unenforceability during patent litigation 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 one or more of our therapeutics or certain aspects of our technology. Such a loss of patent protection could have a material adverse impact on our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

It is also possible that we have failed to identify relevant third party patents or applications. For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the U.S. remain confidential until patents issue. Patent applications in the U.S. and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our therapeutics or technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our SNA technology, our therapeutics or the use of our therapeutics. Third party intellectual property right holders may also actively bring infringement claims against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable and time-consuming litigation and may be prevented from or experience substantial delays in marketing our therapeutics. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our therapeutic candidates that are held to be infringing. We might, if possible, also be forced to redesign therapeutic candidates so that we no longer infringe the third party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

***If we fail to comply with our obligations under any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our therapeutic candidates or we could lose certain rights to grant sublicenses.***

Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, 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 therapeutics that are covered by the licensed technology or could enable a competitor to gain access to the licensed technology. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights in such unlicensed intellectual property. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future therapeutics, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in therapeutics that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize therapeutics, we may be unable to achieve or maintain profitability.

***If we are unable to pr otect the con fidentiality of our trade secrets, our business and competitive position would be harmed.***

In addition to seeking patent protection for certain aspects of our therapeutic candidates, we also consider trade secrets, including confidential and unpatented know-how important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us. 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 in the U.S. and certain foreign jurisdictions 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 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 harmed.

Under the terms of the Northwestern University License Agreements, Northwestern University could publish research findings relating to the patent rights licensed to us by Northwestern University, which could have a material adverse effect on our business.

We are also subject both in the U.S. and outside the U.S. to various regulatory schemes regarding requests for the information we provide to regulatory authorities, which may include, in whole or in part, trade secrets or confidential commercial information. While we are likely to be notified in advance of any disclosure of such information and would likely object to such disclosure, there can be no assurance that our challenge to the request would be successful.

***We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel.***

Many of our employees were previously employed at universities or pharmaceutical or biotechnology companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper our ability to commercialize, or prevent us from commercializing, our therapeutic candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

***If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.***

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

***Third parties may independently develop similar or superior technology.***

There can be no assurance that others will not independently develop, or have not already developed, similar or more advanced technologies than our technology; or that others will not design around, or have not already designed around, aspects of our technology and/or our trade secrets developed therefrom. If third parties develop technology similar or superior to our technology, or they successfully design around our current or future technology, our competitive position, business prospects, and results of operations could be materially and adversely affected.

***The intellectual property which we have licensed from Northwestern University was discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.***

We have licensed certain intellectual property from Northwestern University pursuant to the Northwestern University License Agreements. The Northwestern University License Agreements indicate that the rights licensed to us by Northwestern University are subject to the obligations to and the rights of the U.S. government, including those set forth in the Bayh-Dole Act of 1980, or the Bayh-Dole Act. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future therapeutics based on the licensed Northwestern University intellectual property. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or nonexclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights." While the U.S. government has sparingly used, and to the Company's knowledge never successfully exercised, such march-in rights, any exercise of the march-in rights by the U.S. government could harm our competitive position, business, financial condition, results of operations, and prospects. If the U.S. government exercises such march-in rights,

we may receive compensation that is deemed reasonable by the U.S. government in its sole discretion, which may be less than what we might be able to obtain in the open market. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources.

In addition, the U.S. government requires that any therapeutics embodying any invention generated through the use of U.S. government funding be manufactured substantially in the U.S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. therapeutic manufacturers for therapeutics covered by such intellectual property.

**Risks Related to Government Regulation**

***We may be unable to obtain U.S. or foreign regulatory approval and, as a result, unable to commercialize our therapeutic candidates.***

Our therapeutic candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing, sampling, and distribution of therapeutics. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required to be successfully completed in the U.S. and in many foreign jurisdictions before a new therapeutic can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the therapeutic candidates we may develop will obtain the regulatory approvals necessary for us or any current or future collaborators to begin selling them.

We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA as well as foreign regulatory authorities, such as the EMA and European Union national competent authorities. The time required to obtain FDA and foreign regulatory approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity and novelty of the therapeutic candidate. The standards that the FDA and its foreign counterparts use when regulating us are not always applied predictably or uniformly and can change. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in the policy of the FDA or foreign regulatory authorities during the period of therapeutic development, clinical trials and regulatory review by the FDA or foreign regulatory authorities. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign laws, regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

Because the therapeutics we are developing may represent a new class of therapeutic, the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines in relation to these therapeutics. While we believe the therapeutic candidates that we are currently developing are regulated as new drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, the FDA could decide to regulate them or other therapeutics we may develop as biologics under the Public Health Service Act. The lack of policies, practices or guidelines may hinder or slow review by the FDA or foreign regulatory authorities of any regulatory filings that we may submit. Moreover, the FDA may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the clinical development of our therapeutic candidates. In addition, because there may be therapeutic candidates approved for some of the diseases for which we may seek approval, in order to receive regulatory approval, we may need to demonstrate through clinical trials that the therapeutic candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products.

Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular therapeutic candidate for which we are seeking approval. Furthermore, any regulatory approval to market a therapeutic may be subject to limitations on the approved uses for which we may market the therapeutic or the labeling or other restrictions. Regulatory authorities also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the therapeutic. In addition, the FDA has the authority to require a REMS plan as part of a NDA or a Biologics License Application, or BLA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug or

biologic, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for the therapeutic and affect coverage and reimbursement by third party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the U.S. and vice versa.

***Certain of our therapeutic candidates may require companion diagnostics in certain indications. Failure to successfully develop, validate and obtain regulatory clearance or approval for such tests could harm our product development strategy or prevent us from realizing the full commercial potential of our therapeutic candidates.***

Certain of our therapeutic candidates may require companion diagnostics to identify appropriate patients for those therapeutic candidates in certain indications. Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as a medical device and may require separate regulatory authorization prior to commercialization. We may rely on third parties for the design, development, testing and manufacturing of these companion diagnostics, the application for and receipt of any required regulatory authorization, and the commercial supply of these companion diagnostics. If these parties are unable to successfully develop companion diagnostics for these therapeutic candidates, or experience delays in doing so, the development of our therapeutic candidates may be adversely affected and we may not be able to obtain marketing authorization for these therapeutic candidates. Furthermore, our ability to market and sell, as well as the commercial success, of any of our therapeutic candidates that require a companion diagnostic will be tied to, and dependent upon, the receipt of required regulatory authorization and the continued ability of such third parties to make the companion diagnostic commercially available on reasonable terms in the relevant geographies. Any failure to develop, validate, obtain and maintain marketing authorization for a companion diagnostic and supply such companion diagnostic will harm our business, results of operations and financial condition

***If we or current or future collaborators, manufacturers or service providers fail to comply with healthcare laws and regulations, we or they could be subject to enforcement actions, which could affect our ability to develop, market and sell our therapeutics and may harm our reputation.***

Although we do not currently have any products on the market, once our therapeutic candidates or clinical trials are covered by federal health care programs, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal, state and foreign governments of the jurisdictions in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any therapeutic candidates for which we obtain marketing approval. Our arrangements with third-party payors and customers 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 or distribute our therapeutic candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, but are not limited to, the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons from soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made, in whole or in part, under a federal healthcare program, such as Medicare or Medicaid;
- the U.S. federal False Claims Act, which imposes 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 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 federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- HIPAA includes a fraud and abuse provision referred to as the HIPAA All-Payor Fraud Law, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program (i.e., not just federal healthcare programs), or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially

false statement in connection with the delivery of or payment for healthcare benefits, items or services; 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 HITECH, and its implementing regulations, which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- the federal Physician Payment Sunshine Act and the implementing regulations, also referred to as "Open Payments," issued under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the ACA, which require that manufacturers of pharmaceutical and biological drugs reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program report to the Department of Health and Human Services all consulting fees, travel reimbursements, research grants, and other payments, transfers of value or gifts made to U.S.-licensed physicians and U.S. teaching hospitals with limited exceptions; and
- analogous state laws and regulations, such as, state anti-kickback and false claims laws potentially applicable to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and state transparency laws that require the reporting of certain pricing information; among other state laws.

Ensuring that our future business arrangements with third-parties comply with applicable healthcare laws and regulations could involve substantial costs. If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely affect our financial results. Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

If we or current or future collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our therapeutics successfully and could harm our reputation and lead to reduced acceptance of our therapeutics by the market. These enforcement actions include, among others:

- adverse regulatory inspection findings;
- warning or untitled letters;
- voluntary product recalls or public notification or medical product safety alerts to healthcare professionals;
- restrictions on, or prohibitions against, marketing our therapeutics;
- restrictions on, or prohibitions against, importation or exportation of our therapeutics;
- suspension of review or refusal to approve pending applications or supplements to approved applications;
- exclusion from participation in government-funded healthcare programs;
- exclusion from eligibility for the award of government contracts for our therapeutics;
- FDA debarment;

- suspension or withdrawal of therapeutic approvals;
- seizures or administrative detention of therapeutics;
- injunctions; and
- civil and criminal penalties and fines.

***Any therapeutics we develop may become subject to unfavorable pricing regulations, third party coverage and reimbursement practices or healthcare reform initiatives, thereby harming our business.***

The regulations that govern marketing approvals, pricing and reimbursement for new therapeutics vary widely from country to country. Some countries require approval of the sale price of a therapeutic before it can be marketed. In many countries, the pricing review period begins after marketing or therapeutic licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we intend to monitor these regulations, our programs are currently in the early stages of development and we will not be able to assess the impact of price regulations for a number of years. As a result, we might obtain regulatory approval for a therapeutic in a particular country, but then be subject to price regulations that delay our commercial launch of the therapeutic and negatively impact the revenues we are able to generate from the sale of the therapeutic in that country.

Our ability to commercialize any therapeutics successfully also will depend in part on the extent to which coverage and reimbursement for these therapeutics and related treatments will be available from government health administration authorities, private health insurers and other organizations. However, there may be significant delays in obtaining coverage for newly-approved therapeutics. Moreover, eligibility for coverage does not necessarily signify that a therapeutic will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution costs. Also, interim payments for new therapeutics, if applicable, may be insufficient to cover our costs and may not be made permanent. Thus, even if we succeed in bringing one or more therapeutics to the market, these therapeutics may not be considered cost-effective, and the amount reimbursed for any therapeutics may be insufficient to allow us to sell our therapeutics on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness or the likely level or method of reimbursement. Increasingly, the third party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are seeking greater upfront discounts, additional rebates and other concessions to reduce the prices for therapeutics. If the price we are able to charge for any therapeutics we develop, or the reimbursement provided for such therapeutics, is inadequate in light of our development and other costs, our return on investment could be adversely affected.

We currently expect that some therapeutics we develop may need to be administered under the supervision of a physician on an outpatient basis. Under currently applicable U.S. law, certain therapeutics that are not usually self-administered (including injectable therapeutics) may be eligible for coverage under Medicare through Medicare Part B. Medicare Part B is part of original Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain pharmaceutical products that are medically necessary to treat a beneficiary's health condition. Specifically, Medicare Part B coverage may be available for eligible beneficiaries when the following, among other requirements, have been satisfied:

- the product is reasonable and necessary for the diagnosis or treatment of the illness or injury for which the product is administered according to accepted standards of medical practice;
- the product is typically furnished incident to a physician's services;
- the product has been approved by the FDA.

Under the Medicaid Drug Rebate Statute, a manufacturer must participate in the Medicaid Drug Rebate Program in order to receive payment for its covered outpatient drugs under Medicare Part B (the Medicare program that generally covers physician-administered, outpatient drugs). 42 U.S.C. § 1396r-8(a)(1). In addition, manufacturers who participate in the Medicaid Drug Rebate Program are also required to (1) sign the Pharmaceutical Pricing Agreement and participate in the 340B Drug Pricing Program, and (2) sign the VA Master Agreement for inclusion of the manufacturer's drugs on the Federal Supply Schedule ("FSS"). *Id* . The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities eligible to

participate in the program. Average prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of therapeutics from countries where they may be sold at lower prices than in the U.S. Self-administered therapeutics are typically reimbursed under Medicare Part D, and therapeutics that are administered in an inpatient hospital setting are typically reimbursed under Medicare Part A under a bundled payment. It is difficult for us to predict how Medicare coverage and reimbursement policies will be applied to our therapeutics in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

Third-party payors often rely upon Medicare coverage policies and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage, and adequate reimbursement from both government-funded and private payors for new therapeutics we develop and for which we obtain regulatory approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our financial condition.

We believe that the efforts of governments and third party payors to contain or reduce the cost of healthcare, and specifically, therapeutics, and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of pharmaceutical and biotechnology companies. A number of legislative and regulatory changes in the healthcare system in the U.S. and other major healthcare markets have been proposed. These developments could, directly or indirectly, affect our ability to sell our therapeutics, if approved, at a favorable price.

For example, in the U.S., in 2010, the U.S. Congress passed the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of health 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 policy reforms.

Although the future of the ACA is uncertain, provisions of the ACA addressing coverage and reimbursement of pharmaceutical products that may be of importance to our potential therapeutic candidates include the following:

- Increases to pharmaceutical manufacturer rebate liability under the Medicaid Drug Rebate Program due to an increase in the minimum basic Medicaid rebate on most branded prescription drugs and the application of Medicaid rebate liability to drugs used in risk-based Medicaid managed care plans.
- The expansion of the 340B Drug Pricing Program to require discounts for “covered outpatient drugs” sold to certain children’s hospitals, critical access hospitals, freestanding cancer hospitals, rural referral centers, and sole community hospitals.
- Requirements imposed on pharmaceutical companies to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the “Donut Hole.” In February 2018, Congress passed the Bipartisan Budget Act of 2018, which, beginning in 2019, increased the discount to be paid by pharmaceutical companies from 50% to 70% of a brand-name drug’s negotiated price and added biosimilars to the coverage gap discount program.
- Requirements imposed on pharmaceutical companies to pay an annual non-tax-deductible fee to the federal government based on each company’s market share of prior year total sales of branded drugs to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs, and Department of Defense. Since we currently expect our branded pharmaceutical sales to constitute a small portion of the total federal healthcare program pharmaceutical market, we do not currently expect this annual assessment to have a material impact on our financial condition.
- For therapeutic candidates classified as biologics, marketing approval for a follow-on biologic therapeutic may not become effective until 12 years after the date on which the reference innovator biologic therapeutic was first licensed by the FDA, with a possible six-month extension for pediatric therapeutics. After this exclusivity ends, it may be possible for biosimilar manufacturers to enter the market, which is likely to reduce the pricing for such therapeutics and could affect our profitability if our therapeutics are classified as biologics.

Separately, pursuant to the health reform legislation and related initiatives, the Centers for Medicare and Medicaid Services, or CMS, is working with various healthcare providers to develop, refine, and implement Accountable Care Organizations, or ACOs, and other innovative models of care for Medicare and Medicaid beneficiaries, including the Bundled Payments for Care Improvement Initiative, the Financial Alignment Initiative Demonstration, and other models.

The continued development and expansion of ACOs and other innovative models of care will have an uncertain impact on any future reimbursement we may receive for approved therapeutics administered by such organizations.

From time to time, legislation is drafted, introduced and passed in the U.S. Congress that could significantly change the statutory provisions governing coverage, reimbursement, sales, and marketing of products regulated by CMS or other government agencies. In addition to new legislation, CMS, OIG, and other agency rules and policies addressing fraud and abuse, privacy, and coverage and reimbursement, among other things, are often revised or interpreted in ways that may significantly affect our business and our products. In particular, we expect that the Administration and the U.S. Congress may continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the U.S. healthcare reform legislation. Since taking office, President Trump has continued to support the repeal of all or portions of the ACA. President Trump has also issued an executive order in which he stated that it is his administration's policy to seek the prompt repeal of the ACA and in which he directed executive departments and federal agencies to waive, defer, grant exemptions from, or delay the implementation of the provisions of the ACA to the maximum extent permitted by law. Congress has also enacted legislation that repeals certain portions of the ACA, including the Tax Cuts and Jobs Act, passed in December 2017, which included a provision that eliminates the penalty under the ACA's individual mandate, effective January 1, 2019, as well as the Bipartisan Budget Act of 2018, passed in February 2018, which, among other things, repealed the Independent Payment Advisory Board that was established by the ACA and was intended to reduce the rate of growth in Medicare spending. However, attempts to completely repeal the ACA have been unsuccessful to date. There is still uncertainty with respect to the impact President Trump's Administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold. For example, in May 2018, the Trump Administration recently published in the Federal Register a request for information regarding its Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs (the "RFI"). In the RFI, the Administration sought feedback on actions it could take to restrict or reduce the use of rebates, including by prohibiting the use of rebates in contracts between Medicare Part D plan sponsors and drug manufactures and removing federal Anti-Kickback Statute safe harbor protection for such rebates. Subsequent to this, in July 2018, the Administration submitted to the White House Office of Management and Budget ("OMB") for regulatory review a proposed rule entitled "Removal of Safe Harbor Protection for Rebates to Plans or PBMs Involving Prescription Pharmaceuticals and Creation of New Safe Harbor Protection." The Administration has not specified the substantive changes it may make to the federal Anti-Kickback Statute safe harbors or subregulatory guidance and the rule is not yet publicly available. The Administration's Blueprint also suggests that the Administration is looking at options to require drug-pricing transparency, including requiring the inclusion of drug list prices in direct-to-consumer advertising. In August 2018, the Administration sent a proposed rule to OMB titled "Medicare and Medicaid Programs; Regulations to Require Drug Pricing Transparency." Like the federal Anti-Kickback Statute proposed rule, the substance of this rule is also not currently publicly available, but many speculate that the proposal seeks to implement direct-to-consumer advertising requirements regarding list price noted above. Separately, in a July 2018 speech outlining the Trump Administrations' healthcare regulatory reform efforts, the HHS Secretary announced that the Administration will soon begin considering changes to federal health privacy regulations. Such reforms, however, could have an adverse effect on anticipated revenues from therapeutic candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop therapeutic candidates. The financial impact of U.S. healthcare reform legislation over the next few years will depend on a number of factors, including the policies reflected in implementing regulations and guidance and changes in sales volumes for therapeutics affected by the legislation.

However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

***The healthcare industry is heavily regulated in the U.S. at the federal, state, and local levels, and our failure to comply with applicable requirements may subject us to penalties and negatively affect our financial condition.***

As a healthcare company, our operations, clinical trial activities and interactions with healthcare providers may be subject to extensive regulation in the U.S., particularly if the company receives FDA approval for any of its therapeutics in the future. For example, if we receive FDA approval for a therapeutic for which reimbursement is available under a federal healthcare program (e.g., Medicare, Medicaid), it would be subject to a variety of federal laws and regulations, including those that prohibit the filing of false or improper claims for payment by federal healthcare programs (e.g., the False Claims Act), prohibit unlawful inducements for the referral of business reimbursable by federal healthcare programs (e.g., the federal Anti-Kickback Statute), and require disclosure of certain payments or other transfers of value made to U.S.-licensed physicians and teaching hospitals, or Open Payments. We are not able to predict how third parties will interpret these laws and apply applicable governmental guidance and may challenge our practices and activities under one or more of these laws. If our past or present operations are found to be in violation of any of these laws, we could be subject to civil and criminal penalties, which could hurt our business, our operations and financial condition.

Similarly, HIPAA prohibits, among other offenses, knowingly and willfully executing a scheme to defraud any health care benefit program, including private payors, or falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for items or services under a health care benefit program. To the extent that we act as a business associate to a healthcare provider engaging in electronic transactions, we may also be subject to the privacy and security provisions of HIPAA, as amended by HITECH, which restricts the use and disclosure of patient-identifiable health information, mandates the adoption of standards relating to the privacy and security of patient-identifiable health information, and requires the reporting of certain security breaches to healthcare provider customers with respect to such information. Additionally, many states have enacted similar laws that may impose more stringent requirements on entities like ours. Failure to comply with applicable laws and regulations could result in substantial penalties and adversely affect our financial condition and results of operations.

***Our ability to obtain services, reimbursement or funding from the federal government may be impacted by possible reductions in federal spending.***

U.S. federal government agencies currently face potentially significant spending reductions. The Budget Control Act of 2011, or the BCA, established a Joint Select Committee on Deficit Reduction, which was tasked with achieving a reduction in the federal debt level of at least $1.2 trillion. That committee did not draft a proposal by the BCA's deadline. As a result, automatic cuts, referred to as sequestration, in various federal programs were scheduled to take place, beginning in January 2013, although the American Taxpayer Relief Act of 2012 delayed the BCA's automatic cuts until March 1, 2013. While the Medicare program's eligibility and scope of benefits are generally exempt from these cuts, Medicare payments to providers and Part D health plans are not exempt. The BCA did, however, provide that the Medicare cuts to providers and Part D health plans would not exceed two percent. President Obama issued the sequestration order on March 1, 2013, and cuts went into effect on April 1, 2013. Additionally, the Bipartisan Budget Act of 2018 extended sequestration for Medicare through fiscal year 2027.

The U.S. federal budget remains in flux, which could, among other things, cut Medicare payments to providers. Although the BBA passed in February 2018 enacts a two-year federal spending agreement and raises the federal spending cap on non-defense spending for fiscal years 2018 and 2019, the Medicare program is frequently identified as a target for spending cuts. The full impact on our business of any future cuts in Medicare or other programs is uncertain. In addition, we cannot predict any impact President Trump's administration and the U.S. Congress may have on the federal budget. If federal spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health, to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve therapeutic research and development, manufacturing, and marketing activities, which may delay our ability to develop, market, and sell any therapeutics we may develop.

***If any of our therapeutic candidates receives marketing approval and we or others later identify undesirable side effects caused by the therapeutic candidate, our ability to market and derive revenue from the therapeutic candidates could be compromised.***

In the event that any of our therapeutic candidates receive regulatory approval and we or others identify undesirable side effects, adverse events or other problems caused by one of our therapeutics, any of the following adverse events could occur, which could result in the loss of significant revenue to us and materially and adversely affect our results of operations and business:

- regulatory authorities may withdraw their approval of the therapeutic or seize the therapeutic;
- we may need to recall the therapeutic or change the way the therapeutic is administered to patients;
- additional restrictions may be imposed on the marketing of the particular therapeutic or the manufacturing processes for the therapeutic or any component thereof;
- we may be subject to fines, restitution or disgorgement of profits or revenues, injunctions, or the imposition of civil penalties or criminal prosecution;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- regulatory authorities may require us to implement a REMS, or to conduct post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the therapeutic;

- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the therapeutic may become less competitive; and
- our reputation may suffer.

***Significant developments stemming from the United Kingdom's recent referendum on membership in the European Union could have a material adverse effect on our business.***

On June 23, 2016, the United Kingdom held a referendum and voted in favor of leaving the European Union. This referendum has created political and economic uncertainty, particularly in the United Kingdom and the European Union, and this uncertainty may last for years. Any business we conduct, now and in the future, in the United Kingdom, the European Union, and worldwide could be affected during this period of uncertainty, and perhaps longer, by the impact of the United Kingdom's referendum. The referendum, and the likely withdrawal of the United Kingdom from the European Union it triggers, has caused and, along with events potentially occurring in the future as a consequence of the United Kingdom's withdrawal, including the possible breakup of the United Kingdom, may continue to cause significant volatility in global financial markets, including in global currency and debt markets. This volatility could cause a slowdown in economic activity in the United Kingdom, Europe, or globally, which could adversely affect our operating results and growth prospects. In addition, our business could be negatively affected by new trade agreements between the United Kingdom and other countries, including the U.S., and by the possible imposition of trade or other regulatory barriers in the United Kingdom.

It is currently unclear how regulations affecting clinical trials, the approval of our future therapeutic candidates, and the sale of these therapeutic candidates will be affected by this referendum either in the United Kingdom or elsewhere in Europe. These possible negative impacts, and others resulting from the United Kingdom's actual or threatened withdrawal from the European Union, may adversely affect our operating results and growth prospects.

**Risks Related to Our Common Stock**

***We are an "emerging growth company" and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.***

We are an "emerging growth company" as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (1) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, (2) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (3) exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements and two years of selected financial data. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have total annual gross revenue of $1.07 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, in which case we would no longer be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. 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 share price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

***Our stock price may be volatile and purchasers of our common stock could incur substantial losses.***

If a market for our common stock develops, its market price could fluctuate substantially due to a variety of factors, including the other risks described in this section titled "Risk Factors" and the following:

- the success of competitive therapeutics or technologies;
- results of our preclinical studies and clinical trials of our therapeutic candidates, or those of our competitors, or any current or future collaborators;
- regulatory or legal developments in the U.S. and other countries, especially changes in laws or regulations applicable to our therapeutics;
- introductions and announcements of new therapeutics by us, our future commercialization partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our therapeutics, clinical studies, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies, therapeutics or therapeutic candidates;
- developments concerning any current or future collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our therapeutics;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- trading volume of our common stock;
- sales of our common stock by us or our stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters and other calamities; and
- general economic, industry and market conditions.

In addition, the stock markets in general, and the markets for pharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that has been often unrelated to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance.

***The future issuance of equity or of debt securities that are convertible into equity may dilute your investment and reduce your equity interest.***

We may choose to raise additional capital in the future, depending on market conditions, strategic considerations and operational requirements. To the extent that we raise additional capital through the issuance of shares or other securities convertible into shares, our stockholders will be diluted. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the prevailing market price of our common stock and impair our ability to raise capital through future offerings of equity or equity-linked securities. For example, we have filed, and the SEC has declared effective, a registration statement to register the resale of up to 39,714,143 shares of our common stock issued in connection with the Merger and the 2017 Private Placement or held by pre-Merger stockholders of us. Additionally, we have filed, and the SEC has declared effective, a registration statement to register the resale of up to 5,034,683 shares of our common stock, consisting of (i) 4,889,217 shares that were privately issued through the August 2018 Private Placement and (ii) 145,466 shares that were privately issued in connection with consulting services on February 1, 2018. Such registration statements will permit the resale of these shares at any time while the registration statements remain effective. The resale of a substantial number of shares of our common stock in the public market could adversely affect the market price for our common stock and make it more difficult for you to sell shares of our common stock at times and prices that you feel are appropriate. Accordingly, the adverse market and price pressures resulting from an offering pursuant to this registration statement may continue for an extended period of time and continued negative pressure on the market price of our common stock could have a material adverse effect on our ability to raise additional equity capital.

***Our debt obligations expose us to risks that could adversely affect our business, operating results and financial condition and may result in further dilution to our stockholders.***

We have entered into a loan and security agreement with Hercules pursuant to which we may borrow in an aggregate principal amount of up to $10.0 million from Hercules at a floating per annum interest rate (based on a year consisting of 360 days) equal to the greater of either (i) 9.95% or (ii) the sum of (a) 9.95% plus (b) the prime rate (as reported in *The Wall Street Journal* ) minus 3.50%. We were required to make interest only payments on the amounts borrowed until June 2017. Commencing on July 1, 2017, the loan began amortizing in equal monthly installments of principal and interest in an amount sufficient to fully amortize the outstanding principal balance of the loan over the remaining scheduled monthly payments due prior to the maturity date on September 1, 2019. Pursuant to an amendment dated January 15, 2018, amortization payments due for the thirteen (13) consecutive months commencing on December 1, 2017 through and including December 1, 2018 were deferred. Commencing on January 1, 2019, and continuing on the first business day of each month thereafter, the loan, including the deferred payments, was to begin amortizing in equal monthly installments of principal and interest based upon an amortization schedule equal to eighteen (18) consecutive months. Any remaining obligations under the loan agreement and other loan documents (other than the warrant) were due and payable on the maturity date on September 1, 2019. On December 28, 2018, the Company and Hercules further amended its loan agreement so that interest amounts are payable on the first day of each business month and any remaining obligations under the loan agreement and other loan documents are due and payable on the maturity date on September 1, 2019. On the earliest to occur of the maturity date, the date we prepay the term loan in full or the date the loan otherwise becomes due and payable, we must pay the lender under the agreement an additional charge equal to 3.85% of the total amounts funded under the loan agreement. To the extent we desire to prepay the indebtedness prior to maturity, and after the date hereof, we would be obligated to pay a prepayment penalty to Hercules of 1% of the amounts being prepaid. Under the loan agreement, Hercules or its affiliates have a right to participate in a single subsequent unregistered financing by us in an amount of up $1.0 million on the same terms, conditions and pricing afforded to others participating in such financing. Hercules has not yet exercised this right to participate.

Our ability to make payments on this indebtedness depends on our ability to generate cash in the future. We expect to experience negative cash flow for the foreseeable future as we fund our operations and capital expenditures. There can be no assurance that we will be in a position to repay this indebtedness when due or obtain extensions of the maturity date. We anticipate that we will need to secure additional funding in order for us to be able to satisfy our obligations when due. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If that additional funding involves the sale of equity securities or convertible securities, it would result in the issuance of additional shares of our capital stock, which would result in dilution to our stockholders. The indebtedness is secured by

substantially all of our assets other than intellectual property, on which we have given Hercules a negative pledge. In addition, under the loan agreement, we are subject to certain customary covenants that limit or restrict our ability to, among other things, incur additional indebtedness, grant any security interests, pay cash dividends, repurchase our common stock, make loans, or enter into certain transactions without the prior consent of Hercules. The loan agreement was amended on October 10, 2016 to revise the language granting Hercules a contingent security interest in certain of our assets.

This level of debt could have important consequences to you as an investor in our securities. For example, it could:

- limit our flexibility in planning for the development, clinical testing, approval and marketing of our products;
- place us at a competitive disadvantage compared to any of our competitors that are less leveraged than we are;
- increase our vulnerability to both general and industry-specific adverse economic conditions; and
- limit our ability to obtain additional funds.

***The employment agreements with our executive officers may require us to pay severance benefits to officers in connection with termination of employment or upon a change of control of us, which could harm our financial condition.***

Each of David A. Giljohann, our Chief Executive Officer, David S. Snyder, our Chief Financial Officer, and Matthias G. Schroff, our Chief Operating Officer, is entitled to receive cash severance equal to twelve months, six months, and six months, respectively, of his base salary if his employment is terminated by us without cause (as such term is defined in his employment offer letter). In addition, our 2015 Plan, which was assumed by us in the Merger, generally provides for accelerated vesting of equity awards upon the involuntary termination of an employee within the twelve month period following a change in control (as defined under the plan) and accelerated vesting of equity awards upon a change of control (as defined under the plan) for each of our executive officers. This vesting acceleration is intended to provide each of our executive officers with the full benefit of their equity awards and reward them for a successful outcome for our stockholders. The accelerated vesting of equity awards could result in dilution to our existing stockholders and harm the market price of our common stock. The payment of these severance benefits could harm our financial condition. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

***Our common stock recently commenced trading on the OTCQB instead of a national exchange or quotation system, so you may be unable to sell your shares to raise money or otherwise desire to liquidate your shares.***

Our common stock is currently quoted on the OTC Market Group's OTCQB Market quotation system under the ticker symbol "XCUR." The OTCQB are regulated quotation services that display real-time quotes, last sale prices and volume limitations in over-the-counter securities. Trading in shares quoted on the OTCQB is often thin and characterized by volatility in trading prices. This volatility may be caused by a variety of factors, including the lack of readily available price quotations, the absence of consistent administrative supervision of bid and ask quotations, lower trading volume and market conditions. As a result, there may be wide fluctuations in the market price of the shares of our common stock for reasons unrelated to operating performance, and this volatility, when it occurs, may have a negative effect on the market price for our securities. Moreover, the OTCQB is not a stock exchange, and trading of securities on them is often more sporadic than the trading of securities listed on a national quotation system or stock exchange. Accordingly, our stockholders may not be able to realize a fair price from their shares when they determine to sell them or may have to hold them for a substantial period of time until the market for our common stock improves.

***Our common stock may not be eligible for listing or quotation on any securities exchange.***

We do not currently meet the initial quantitative listing standards of any national securities exchange. We cannot assure you that we will be able to meet the initial listing standards of any national securities exchange, or, if we do meet such initial listing standards, that we will be able to maintain any such listing. Until our common stock is listed on a national securities exchange, we expect that it will continue to be eligible and quoted on the OTCQB. In those venues, however, an investor may find it difficult to obtain accurate quotations as to the market value of our common stock. Further, the national securities exchanges are adopting so-called "seasoning" rules that will require that we meet certain requirements, including prescribed periods of time trading over-the-counter and minimum filings of periodic reports with the SEC, before we are eligible to apply for listing on such national securities exchanges. In addition, if we fail to meet the criteria set forth in SEC regulations, various requirements would be imposed by law on broker-dealers who sell our securities to persons other than established customers and accredited investors. Consequently, such regulations may deter

broker-dealers from recommending or selling our common stock, which may further affect its liquidity. This would also make it more difficult for us to raise additional capital

***The designation of our common stock as a "penny stock" would limit the liquidity of our common stock.***

Our common stock may be deemed a "penny stock" (as that term is defined under Rule 3a51-1 of the Exchange Act) in any market that may develop in the future. Generally, a "penny stock" is a common stock that is not listed on a securities exchange and trades for less than $5.00 a share. Prices often are not available to buyers and sellers and the market may be very limited. Penny stocks in start-up companies are among the riskiest equity investments. Broker-dealers who sell penny stocks must provide purchasers of these stocks with a standardized risk-disclosure document prepared by the SEC. The document provides information about penny stocks and the nature and level of risks involved in investing in the penny stock market. A broker must also provide purchasers with bid and offer quotations and information regarding broker and salesperson compensation and make a written determination that the penny stock is a suitable investment for the purchaser and obtain the purchaser's written agreement to the purchase. Many brokers choose not to participate in penny stock transactions. Because of the penny stock rules, there may be less trading activity in penny stocks in any market that develops for our common stock in the future and stockholders are likely to have difficulty selling their shares.

***FINRA sales practice requirements may limit a stockholder's ability to buy and sell our stock.***

The Financial Industry Regulatory Authority, or FINRA, has adopted rules requiring that, in recommending an investment to a customer, a broker-dealer must have reasonable grounds for believing that the investment is suitable for that customer. Prior to recommending speculative or low-priced securities to their non-institutional customers, broker-dealers must make reasonable efforts to obtain information about the customer's financial status, tax status, investment objectives and other information. Under interpretations of these rules, FINRA has indicated its belief that there is a high probability that speculative or low-priced securities will not be suitable for at least some customers. If these FINRA requirements are applicable to us or our securities, they may make it more difficult for broker-dealers to recommend that at least some of their customers buy our common stock, which may limit the ability of our stockholders to buy and sell our common stock and could have an adverse effect on the market for and price of our common stock.

***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 will be influenced by the research and reports that industry or securities analysts publish about us or our business. Our research coverage by securities and industry analysts is currently limited. In addition, because we did not become a reporting company by conducting an underwritten initial public offering of our common stock, and because we are not listed on a national securities exchange, security analysts of brokerage firms may not provide wider coverage of our Company. In addition, investment banks may be less likely to agree to underwrite secondary offerings on our behalf than they might if we became a public reporting company by means of an underwritten initial public offering, because they may be less familiar with our Company as a result of more limited coverage by analysts and the media, and because we became public at an early stage in our development. The failure to receive wider research coverage or support in the market for our shares will have an adverse effect on our ability to develop a liquid market for our common stock and the trading price for our stock would be negatively impacted.

In the event we obtain wider securities or industry analyst coverage, 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 target studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease 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.

***Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.***

Based on the beneficial ownership of our common stock as of December 31, 2018, our executive officers and directors, together with holders of five percent or more of our outstanding common stock and their respective affiliates, will beneficially own approximately 42.4 percent of our outstanding common stock. As a result, these stockholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our Company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an

opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

***Anti-takeover provisions in our charter documents and under the General Corporation Law of the State of Delaware could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our management.***

Provisions in our amended and restated certificate of incorporation and our bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders, and the ability of the board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which prohibits stockholders owning in excess of 15% of the outstanding combined organization voting stock from merging or combining with the combined organization. Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove then-current management by making it more difficult for stockholders to replace members of the board of directors, which is responsible for appointing the members of management.

***Anti-takeover provisions in our charter documents could discourage, delay or prevent a change in control of us and may affect the trading price of our common stock.***

Our corporate documents and the DGCL contain provisions that may enable our board of directors to resist a change in control of us even if a change in control were to be considered favorable by our stockholders. These provisions:

- stagger the terms of our board of directors and require 66 and 2/3% stockholder voting to remove directors, who may only be removed for cause;
- authorize our board of directors to issue "blank check" preferred stock and to determine the rights and preferences of those shares, which may be senior to our common stock, without prior stockholder approval;
- establish advance notice requirements for nominating directors and proposing matters to be voted on by stockholders at stockholders' meetings;
- prohibit our stockholders from calling a special meeting and prohibit stockholders from acting by written consent;
- require 66 and 2/3% stockholder voting to effect certain amendments to our certificate of incorporation and bylaws; and
- prohibit cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates.

These provisions could discourage, delay or prevent a transaction involving a change in control of us. These provisions could also discourage proxy contests and make it more difficult for stockholders to elect directors of their choosing and cause us to take other corporate actions our stockholders desire.

***The requirements of being a public company may strain our resources and divert management's attention.***

As a public company, we are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Act, and other applicable securities rules and regulations. In the future, we may also be subject to the listing requirements of the NASDAQ Stock Market. Despite recent reforms made possible by the JOBS Act, compliance with these rules and regulations nonetheless increases our legal and financial compliance costs, makes some activities more difficult, time-consuming or costly, and increases demand on our systems and resources, particularly after we will no longer be an "emerging growth company." The Exchange Act requires, among other things, that we file annual, quarterly, and current reports with respect to our business and operating results.

As a result of disclosure of information in this report and in other filings required of a public company, our business and financial condition are more visible, which we believe may result in threatened or actual litigation, including by competitors and other third parties. If such claims are successful, our business and operating results could be harmed, and even if the claims do not result in litigation or are resolved in our favor, these claims, and the time and resources

necessary to resolve them, could divert the resources of our management and adversely affect our business, brand and reputation and results of operations.

We also expect that being a public company and these new rules and regulations will make it more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

***Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your 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. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

***We may incur significant costs from class action litigation due to our expected stock volatility.***

Our stock price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts or the development efforts of current or future collaborators or competitors, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of pharmaceutical and biotechnology companies. This risk is especially relevant to us because pharmaceutical and biotechnology companies have experienced significant stock price volatility in recent years. When the market price of a stock has been volatile as our stock price may be, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

***Our amended and restated certificate of incorporation designates the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.***

Our amended and restated certificate of incorporation provides that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, any action asserting a claim arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws or any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein and the claim not being one which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery or for which the Court of Chancery does not have subject matter jurisdiction. Any person purchasing or otherwise acquiring any interest in any shares of our common stock shall be deemed to have notice of and to have consented to this provision of our amended and restated certificate of incorporation. This choice of forum provision may limit our stockholders' ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, employees or agents, which may discourage such lawsuits against us and our directors, officers, employees and agents even though an action, if successful, might benefit our stockholders. Stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near Delaware. The Court of Chancery may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. Alternatively, if a court were to find this provision of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have a material adverse effect on our business, financial condition or results of operations.

***Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.***

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the

Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. The Merger, our prior equity offerings and other changes in our stock ownership may have resulted in ownership changes. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may 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 NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

**Item 1B. Unresolved Staff Comments.**

None.

**Item 2. Properties.**

Our corporate headquarters are located in Skokie, Illinois, where we lease approximately 12,000 square feet of office and laboratory space. The lease term for our office and laboratory space in Skokie, Illinois commenced in March 2012 for a lease term of three years. In March 2014, we amended the lease agreement to extend the term for an additional six years, which expires in 2021. In May 2016, we amended the lease agreement to include additional space to be used primarily for administrative functions.

We believe that our existing facilities are adequate for our current needs and have sufficient laboratory space to house additional scientists as we grow. When our lease expires, we may exercise our renewal options or look for additional or alternate space for our operations. We believe that suitable additional or alternative space will be available in the future on commercially reasonable terms.

**Item 3. Legal Proceedings.**

From time to time, we may be subject to legal proceedings. We are not currently a party to or aware of any proceedings that we believe will have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations.

**Item 4. Mine Safety Disclosures.**

Not applicable.

## PART II

### Item 5. Market For Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases.

**Market Information for Common Stock**

Our common stock commenced trading on the OTC Market Group's OTCQB® Market quotation system under the ticker symbol "XCUR" effective at the market open on May 24, 2018. On March 5, 2019, the price of our common stock last reported on the OTC Markets was $2.80 per share. The following table sets forth, for each of the quarterly periods indicated, the high and low sales prices of our common stock, as reported on the OTCQB. These quotations reflect inter-dealer prices, without retail mark-up, mark-down or commission and may not represent actual transactions.

| 2018 | High | Low |
|---|---|---|
| Second Quarter (beginning May 22, 2018) | $ 6.25 | $ 3.02 |
| Third Quarter | 6.50 | 3.90 |
| Fourth Quarter | 4.78 | 2.78 |

**Holders of Record**

As of March 5, 2019, we have 44,358,000 shares of common stock outstanding held by 108 stockholders of record. Because many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of beneficial stockholders represented by these record holders.

**Dividend Policy**

We currently intend to retain future earnings, if any, for use in the operation of our business and to fund future growth. We have never declared or paid cash dividends on our common stock and we do not intend to pay any cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors in light of conditions then-existing, including factors such as our results of operations, financial condition and requirements, business conditions and covenants under any applicable contractual arrangements.

**Securities Authorized for Issuance under Equity Compensation Plans**

Information about our equity compensation plans is incorporated herein by reference to Part III, Item 12 of this Annual Report **.**

**Performance Graph**

Pursuant to the accompanying instructions, the information called for by Item 201(e) of Regulation S-K is not required.

**Unregistered Sales of Equity Securities and Use of Proceeds**

On August 22, 2018, in connection with the closing of the August 2018 Private Placement, we issued a total of 4,889,217 shares of the Company's common stock at a purchase price of $4.50 per share, resulting in approximately $22.0 million in gross proceeds to the Company. The aggregate net proceeds from the August 2018 Private Placement (after deducting placement agent fees and expenses of the offering of approximate $1.9 million) were $20.1 million.

The offer and sale of the shares in the August 2018 Private Placement were exempt from registration under Section 4(a)(2) of the Securities Act of 1933, as amended or Rule 506 of Regulation D promulgated by the SEC. The closing of the 2018 August Private Placement was conducted on a "reasonable best efforts" basis.

The Company also entered into a registration rights agreement with the investors in the August 2018 Private Placement, which required us to file a "resale" registration statement with the SEC covering the Shares issued in the August 2018 Private Placement within 30 calendar days from the final closing of the August 2018 Private Placement Offering. The Company filed such registration statement was filed with the SEC on October 5, 2018.

**Item 6. Selected Financial Data.**

*The following tables set forth selected financial data for us as of and for the years ended December 31, 2018, 2017, 2016 and 2015 and should be read together with the consolidated financial statements and the related notes and the sections of this Annual Report on Form 10-K entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing elsewhere in this Annual Report on Form 10-K. The selected financial data in this section is not intended to replace our financial statements and related notes. The selected financial data as of and for the years ended December 31, 2018, 2017, 2016 and 2015 are derived from our audited consolidated financial statements. Our audited consolidated financial statements as of and for the years ended December 31, 2018 and 2017 are included elsewhere in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of our future results.*

| | December 31, 2018 | December 31, 2017 | December 31, 2016 | December 31, 2015 |
|---|---|---|---|---|
| ***(in thousands)*** | | | | |
| **Balance Sheet Data** | | | | |
| Cash and cash equivalents | $ 26,268 | $ 25,764 | $ 19,623 | $ 18,731 |
| Current assets | 27,663 | 27,638 | 20,041 | 19,204 |
| Total assets | 28,756 | 28,987 | 20,576 | 19,621 |
| Current portion of long-term debt | — | — | 1,213 | — |
| Current liabilities | 2,043 | 3,356 | 12,158 | 1,343 |
| Long-term debt, net | 4,925 | 4,855 | 4,454 | — |
| Preferred stock warrant liability | — | — | 201 | — |
| Common stock warrant liability | 797 | 523 | — | — |
| Total liabilities | 7,804 | 9,012 | 18,128 | 1,391 |
| Non-redeemable preferred stock | | | | |
| Series C | — | — | 33,483 | 33,039 |
| Series B-2 | — | — | 3,641 | 3,641 |
| Series B-1 | — | — | 5,371 | 5,371 |
| Series A | — | — | 135 | 135 |
| Common stock | 4 | 4 | — | — |
| Additional paid-in capital | 75,942 | 53,586 | (17,578) | (18,293) |
| Accumulated deficit | (54,994) | (33,615) | (22,604) | (5,663) |
| Total stockholders' equity | 20,952 | 19,975 | 2,448 | 18,230 |

| *(in thousands except share and per share data)* | Year Ended December 31, | | | |
|---|---|---|---|---|
| | 2018 | 2017 | 2016 | 2015 |
| **Statement of Operations Data** | | | | |
| Revenue: | | | | |
| Collaboration revenue | $ 118 | $ 9,719 | $ 690 | $ — |
| Grant income | — | — | 346 | 2,388 |
| Total revenue | 118 | 9,719 | 1,036 | 2,388 |
| Operating expenses: | | | | |
| Research and development expense | 14,119 | 13,080 | 13,659 | 10,124 |
| General and administrative expense | 7,818 | 7,046 | 3,539 | 5,408 |
| Total operating expenses | 21,937 | 20,126 | 17,198 | 15,532 |
| Operating loss | (21,819) | (10,407) | (16,162) | (13,144) |
| Other income (expense), net: | | | | |
| Interest expense | (672) | (795) | (724) | — |
| Other income (loss), net | 78 | 191 | (55) | (7) |
| Total other income (loss), net | (594) | (604) | (779) | (7) |
| Net loss attributable to members of AuraSense Therapeutics, LLC | — | — | — | (7,488) |
| Net loss attributable to stockholders of Exicure, Inc. | (22,413) | (11,011) | (16,941) | (5,663) |
| Net loss attributable to members of AuraSense Therapeutics, LLC/stockholders of Exicure, Inc. | $ (22,413) | $ (11,011) | $ (16,941) | $ (13,151) |
| | | | | |
| Basic and diluted loss per common share | $ (0.54) | $ (1.09) | $ (149.37) | $ (244.13) |
| Basic and diluted weighted-average common shares outstanding | 41,189,177 | 10,119,569 | 113,418 | 53,870 |

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

*You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties as described under the heading "Cautionary Note Regarding Forward-Looking Statements" elsewhere in this Annual Report on Form 10-K. You should review the disclosure under the heading "Risk Factors" in this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

**Operating Overview**

We are a clinical-stage biotechnology company developing therapeutics for immuno-oncology, inflammatory diseases and genetic disorders based on our proprietary Spherical Nucleic Acid, or SNA, technology. SNAs are nanoscale constructs consisting of densely packed synthetic nucleic acid sequences that are radially arranged in three dimensions. We believe the design of our SNAs gives rise to distinct chemical and biological properties that may provide advantages over other nucleic acid therapeutics and enable therapeutic activity outside of the liver. Since our SNAs have shown in a Phase 1 clinical trial and in preclinical studies that they can cross certain biological barriers when administered locally, we believe that they have the therapeutic potential to target diseases not typically addressed with other nucleic acid therapeutics. We have demonstrated the ability to cross certain biological barriers in Phase 1 clinical trials of three therapeutic candidates, AST-008, XCUR17 and AST-005.

***Immuno-oncology***

AST-008 is an SNA consisting of toll-like receptor 9, or TLR9, agonists designed for immuno-oncology applications. TLR9 agonists bind to and activate TLR9 receptors. We believe AST-008 may be used for immuno-oncology applications as a monotherapy or in combination with checkpoint inhibitors. Checkpoint inhibitors are therapeutics that prevent tumors from evading destruction by the immune system. We have observed that administration of AST-008 as a monotherapy can have anti-tumor activity in mouse models of colon cancer, breast cancer, lymphoma and melanoma. We have also observed that, in preclinical studies in a variety of tumor models, AST-008, applied in combination with certain checkpoint inhibitors, exhibited anti-tumor responses and survival rates that were greater than those demonstrated by checkpoint inhibitors alone. We have also demonstrated that AST-008 was active when administered subcutaneously, intratumorally or intravenously, in both prevention and established mouse tumor models. The administration of AST-008 also produced localized as well as abscopal anti-tumor activity in mouse cancer models. Additionally, administration of AST-008 in combination with certain checkpoint inhibitors conferred adaptive immunity in breast and colon cancer mouse models.

During the fourth quarter of 2018 the FDA opened the IND for AST-008 and informed the Company that our proposed Phase1b/2 trial may proceed. Early in 2019, we opened four clinical sites and began dosing and recruiting patients in that trial. This is a Phase 1b/2, open-label, multi-center trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of intratumoral AST-008 injections alone and in combination with intravenous pembrolizumab in patients with advanced solid tumors. Conditions under study are planned to include advanced or metastatic: Merkel cell carcinoma, head and neck squamous cell carcinoma, cutaneous squamous cell carcinoma and melanoma. The primary outcome measure is the safety and tolerability of AST-008 alone and in combination with pembrolizumab. Secondary outcomes include the recommended Phase 2 dose and disease assessment with RECIST 1.1.

During the second quarter of 2017, we filed a CTA for a Phase 1 clinical trial of AST-008 in the United Kingdom. In the third quarter of 2017, we received an authorization from the MHRA, the competent health authority of the United Kingdom, to conduct a Phase 1 clinical trial with AST-008. We began subject dosing in our Phase 1 clinical trial for AST-008 in the fourth quarter of 2017. This trial was completed in the third quarter of 2018. Based on our initial analyses of the Phase 1 clinical trial results, AST-008 was shown to be safe and tolerable in all subjects, with no serious adverse events and no dose limiting toxicity. All AST-008-related adverse events were of short duration, reversible and consistent with TLR9 activation. In addition, AST-008 was shown to elicit high levels

of certain cytokines as well as to activate important effector cells of the immune system, including T cells and natural killer cells which are the main drivers of an anti-tumor response.

***Inflammatory diseases***

*XCUR17*

XCUR17, is an SNA that targets the mRNA that encodes interleukin 17 receptor alpha, or IL-17RA, a protein that is considered essential in the initiation and maintenance of psoriasis. Although the availability of inhibitors of TNF revolutionized the systemic treatment of severe psoriasis, studies of disease pathogenesis have shifted attention to the IL-17 pathway, in which IL-17RA is a key driver of psoriasis. Our strategy is to reduce the levels of IL-17RA in the skin by topically applying XCUR17. In preclinical studies, XCUR17 inhibited IL-17RA in the keratinocytes of the skin.

We filed a CTA for a Phase 1 clinical trial of XCUR17 in patients with psoriasis in Germany in the third quarter of 2017. Our CTA was approved in February 2018 and we began dosing patients in our Phase 1 clinical trial in April 2018. The Phase 1 clinical trial, which had final patient visits in the fourth quarter of 2018, was a randomized, double-blinded, placebo-controlled trial in twenty-one patients with mild to moderate chronic plaque psoriasis designed to assess the safety of XCUR17 formulated as a topical gel, and to evaluate early signs of efficacy. All patients received three strengths of XCUR17 gel, a vehicle gel, and a positive comparator (Daivonex® cream), which were all applied on different areas of psoriatic skin within each individual patient.

In the fourth quarter of 2018 we reported results from the Phase 1 trial of XCUR17. In the case of XCUR17, of the twenty-one treated patients, eleven treated with the highest strength XCUR17 gel were observed to have a reduction in redness and improvement in healing as determined by blinded physician assessments. Further, the highest strength XCUR17 gel showed a statistically significant improvement in psoriasis symptoms versus the vehicle gel. By comparison, seventeen of the twenty-one patients treated with the positive comparator showed a clinical response, while four patients treated with the placebo vehicle had a clinical response.

There were no adverse safety events related to treatment with XCUR17 observed. In addition to the safety, tolerability and clinical assessments, the trial measured psoriatic infiltrate thickness over the 26-day treatment period. No relevant changes in mean psoriatic infiltrate thickness were observed for the three XCUR17 gels or the active ingredient-free vehicle gel. At this time, assessments of IL-17RA mRNA levels from skin biopsies collected from the treated areas in patients have not yet been correlated with the clinical or infiltrate thickness assessments.

*Dermelix License Agreement*

On February 17, 2019 Exicure entered into a License and Development Agreement, or the Dermelix License Agreement, with DERMELIX, LLC, d/b/a Dermelix Biotherapeutics. Under the terms of agreement, Dermelix licensed worldwide rights to research, develop, and commercialize Exicure's technology for the treatment of Netherton Syndrome and, at Dermelix's option, up to five additional rare skin indications.

Dermelix will initially develop a targeted therapy for the treatment of Netherton Syndrome (NS). NS is a rare and severe autosomal recessive disorder caused by loss-of-function mutations in the *SPINK5* gene, which encodes the serine protease inhibitor LEKT1 involved in skin barrier function. NS affects approximately 1 in 200,000 children born each year, and is characterized by severely inflamed, red, scaled, itchy skin, and patients are at increased risk of mortality in the first year of life due to recurrent infections and dehydration as a result of the impaired skin barrier. Currently, there are no approved treatments for NS patients and off-label use of standard of care treatments are of limited utility.

Under the terms of the Dermerlix License Agreement, Exicure received an upfront payment of $1 million at closing of the transaction and will receive an additional $1 million upon the exercise of each of the five options granted to Dermelix. Exicure will be responsible for conducting the early stage development for each indication up to IND enabling toxicology studies. Dermelix will undertake subsequent development, commercial activities and financial responsibility. For each of NS as well as any additional licensed product for which Dermelix exercises one of its options, Exicure is eligible to receive potential payments totaling up to $13.5 million upon achievement of

certain development and regulatory milestones and up to $152.5 million upon achievement of certain sales milestones per indication in each of six indications. In addition, Exicure will receive low double-digit royalties on annual net sales for SNA therapeutics developed.

*Other Inflammatory Diseases*

We believe that one of the key strengths of our proprietary SNAs is that they have the potential to enter a number of different cells and organs. As a consequence, we are also conducting early stage research activities in ophthalmology, pulmonology, and gastroenterology.

We believe promising therapeutic targets for SNAs include antibody targets with confirmed therapeutic benefit. We envision inhibiting these targets with local application of SNAs in a variety of therapeutic areas. We believe that this approach combines the benefits of specifically inhibiting validated targets without the potential safety issues associated with systemic therapy.

***Genetic disorders***

We are investigating the utility of our SNA technology for the treatment of neurological conditions. In June 2018, the Company and researchers from The Ohio State University Wexner Medical Center presented a poster at the Cure SMA Annual Conference titled: "Nusinersen in spherical nucleic acid (SNA) format improves efficacy both in vitro in SMA patient fibroblasts and in Δ7 SMA mice and reduces toxicity in mice." It was observed in a preclinical study that nusinersen in SNA format prolonged survival by four-fold (maximal survival of 115 days compared to 28 days for nusinersen-treated mice) as well as doubled the levels of healthy full-length SMN2 mRNA and protein in SMA patient fibroblasts when compared to nusinersen.

Subsequently, in the fall of 2018, we completed a biodistribution study in rats comparing nusinersen to nusinersen in SNA format. We found that more nusinersen in SNA format was retained in the rats' brain and spinal cord compared to nusinersen retained in the rats' brain and spinal cord at 24, 72 and 168 hours.

We are now formulating our strategy for developing a pipeline of SNA therapeutics targeting neurological diseases. Preclinical research is underway in a number of indications including, spinal muscular atrophy, Huntington's Disease, spinocerebellar ataxia type 3 (SCA3), SCA2, SCA1, Friedreich's Ataxia, and Batten disease. We believe this preclinical research may lead to a therapeutic candidate for one of the above neurological indications.

***AST-005***

AST-005 is an SNA targeting TNF for the treatment of mild to moderate psoriasis. AST-005 is intended to be administered locally in a gel to psoriatic lesions. In a completed Phase 1 clinical trial, AST-005, when topically administered to the skin of patients with mild to moderate psoriasis, resulted in no drug associated adverse events, and demonstrated a reduction of TNF mRNA. The TNF mRNA reduction elicited by the highest strength of AST-005 gel was statistically significant when compared to the effects of the vehicle.

On December 2, 2016, we entered into a research collaboration, option and license agreement with Purdue Pharma L.P., referred to as the Purdue Collaboration. As part of our collaboration with Purdue, a Phase 1b clinical trial was conducted in Germany to evaluate the effect of AST-005 gel in patients with chronic plaque psoriasis. The trial demonstrated that AST-005 is safe and tolerable in patients at higher doses than were previously studied, however, the study did not result in a statistically significant decrease in echo lucent band thickness, one of the key indicators of efficacy in patients with psoriasis. In April 2018, Purdue notified the Company it had declined to exercise its option to develop AST-005 at that time, but that it also intended to retain rights relating to the TNF target, and Purdue reserved its right to continue joint development, with Exicure, of new anti-TNF drug candidates and to retain its exclusivity and other rights to AST-005. Purdue has not indicated that it has any plans to pursue AST-005 at this time and there no active therapeutic candidates in development.

***Other operating, financing, and cash flow considerations***

Since our inception in 2011, we have devoted substantial resources to the research and development of SNAs and the protection and enhancement of our intellectual property. We have no products approved for sale and all of our $15.6 million in revenue since inception through December 31, 2018 has been earned through our research collaboration, license, and option agreement with Purdue or as a primary contractor or as a subcontractor on government grants. In addition to our revenue, from inception through December 31, 2018, we have funded our operations through private placements of preferred stock with gross proceeds totaling $42.8 million, sales of common stock in the 2017 Private Placement with gross proceeds totaling $31.5 million, sales of common stock in the August 2018 Private Placement with gross proceeds totaling $22.0 million and debt financing totaling $6.0 million. As of December 31, 2018, our cash and cash equivalents were $26.3 million .

Since our inception, we have incurred significant operating losses. Our net loss was $22.4 million and $11.0 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, our accumulated deficit was $73.8 million . Substantially all of our operating losses resulted from expenses incurred in connection with our research programs and from general and administrative costs associated with our operations.

We expect to continue to incur significant and increasing losses in the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- advance AST-008 through clinical development for immuno-oncology applications;
- continue research and development in neurological applications;
- advance SNA platform in dermatological indications;
- increase research and development for the discovery and development of additional therapeutic candidates;
- advance other therapeutic candidates through preclinical and clinical development;
- increase our research and development to enhance our technology;
- procure clinical trial materials;
- seek regulatory approval for our therapeutic candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- operate as a public company.

We have not generated any commercial product revenue nor do we expect to generate substantial revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our therapeutic candidates. Successful therapeutic development and regulatory approval are subject to significant uncertainties and we expect such activities will take at least five years. If we obtain regulatory approval for any of our therapeutic candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Other sources of revenue could include a combination of research and development payments, license fees and other upfront payments, milestone payments, and royalties in connection with our current and any future collaborations and licenses. Until such time, if ever, that we generate revenue from whatever source, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings and research collaboration and license agreements. We may be unable to raise capital or enter into such other arrangements when needed or on favorable terms. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our therapeutic candidates.

**Basis of Presentation**

The audited financial statements of Exicure, Inc. for the fiscal years ended December 31, 2018 and 2017, contained herein, include a summary of our significant accounting policies and should be read in conjunction with the discussion below.

**Recent Developments**

***AST-008***

During the fourth quarter of 2018 the FDA opened the IND for AST-008 and informed the Company that our proposed Phase1b/2 trial may proceed. Early in 2019, we opened four clinical sites and began dosing and recruiting patients in that trial. This is a Phase 1b/2, open-label, multi-center trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of intratumoral AST-008 injections alone and in combination with intravenous pembrolizumab in patients with advanced solid tumors. Conditions under study are planned to include advanced or metastatic: Merkel cell carcinoma, head and neck squamous cell carcinoma, cutaneous squamous cell carcinoma and melanoma. The primary outcome measure is the safety and tolerability of AST-008 alone and in combination with pembrolizumab. Secondary outcomes include the recommended Phase 2 dose and disease assessment with RECIST 1.1.

***XCUR17***

In the fourth quarter of 2018 we reported results from the Phase 1 trial of XCUR17. In the case of XCUR17, of the twenty-one treated patients, eleven treated with the highest strength XCUR17 gel were observed to have a reduction in redness and improvement in healing as determined by blinded physician assessments. Further, the highest strength XCUR17 gel showed a statistically significant improvement in psoriasis symptoms versus the vehicle gel. By comparison, seventeen of the twenty-one patients treated with the positive comparator showed a clinical response, while four patients treated with the placebo vehicle had a clinical response.

There were no adverse safety events related to treatment with XCUR17 observed. In addition to the safety, tolerability and clinical assessments, the trial measured psoriatic infiltrate thickness over the 26-day treatment period. No relevant changes in mean psoriatic infiltrate thickness were observed for the three XCUR17 gels or the active ingredient-free vehicle gel. At this time, assessments of IL-17RA mRNA levels from skin biopsies collected from the treated areas in patients have not yet been correlated with the clinical or infiltrate thickness assessments.

***Dermelix License Agreement***

On February 17, 2019 Exicure entered into a License and Development Agreement, or the Dermelix License Agreement, with DERMELIX, LLC, d/b/a Dermelix Biotherapeutics. Under the terms of agreement, Dermelix licensed worldwide rights to research, develop, and commercialize Exicure's technology for the treatment of Netherton Syndrome and, at Dermelix's option, up to five additional rare skin indications.

Under the terms of the Dermerlix License Agreement, Exicure received an upfront payment of $1 million at closing of the transaction and will receive an additional $1 million upon the exercise of each of the five options granted to Dermelix. Exicure will be responsible for conducting the early stage development for each indication up to IND enabling toxicology studies. Dermelix will undertake subsequent development, commercial activities and financial responsibility. For each of NS as well as any additional licensed product for which Dermelix exercises one of its options, Exicure is eligible to receive potential payments totaling up to $13.5 million upon achievement of certain development and regulatory milestones and up to $152.5 million upon achievement of certain sales milestones per indication in each of six indications. In addition, Exicure will receive low double-digit royalties on annual net sales for SNA therapeutics developed.

***August 2018 Private Placement***

On August 22, 2018, we entered into subscription agreements with several accredited investors, pursuant to which we issued and sold a total of 4,889,217 shares of the Company's common stock, at a purchase price of $4.50 per share, resulting in approximately $22.0 million in gross proceeds to the Company (the "August 2018 Private Placement"). The aggregate net proceeds from the August 2018 Private Placement (after deducting accrued or paid placement agent fees and expenses of the offering of $1.9 million ) were $20.1 million .

We filed and caused to become effective a registration statement with the SEC on October 5, 2018 registering the resale of 5,034,683 shares of common stock of Exicure, Inc., par value $0.0001 per share, consisting of (i)

4,889,217 shares that were privately issued in the August 2018 Private Placement and (ii) 145,466 shares that were privately issued to certain selling stockholders in connection with consulting services on February 1, 2018.

***Trading of Common Stock***

The common stock of Exicure, Inc. commenced trading on the OTC Market Group's OTCQB® Market quotation system under the ticker symbol "XCUR" effective at the market open on May 24, 2018.

***Registration Statement - 2017 Private Placement***

We filed and caused to become effective a registration statement with the SEC on February 6, 2018 registering the resale of 39,714,143 shares of our common stock issued in connection with the 2017 Private Placement.

***Appointment of Chief Operating Officer***

On April 20, 2018, we announced that Matthias G. Schroff, Ph.D, was appointed to serve as Chief Operating Officer ("COO") of the Company, effective April 16, 2018. Dr. Schroff is a biotechnology industry veteran who brings more than 15 years of senior leadership experience within global biopharmaceutical companies where he gained deep scientific and clinical experience in immuno-oncology, TLR9 biology and broad clinical program management. For more information on the appointment of Dr. Schroff, please see the Current Report on Form 8-K filed with the SEC on April 20, 2018.

***Purdue Collaboration***

In April 2018, Purdue has notified the Company it has declined to exercise its option to develop AST-005 at this time and there are currently no active therapeutic candidates in development under the Purdue Collaboration .

**Segment Reporting**

We view our operations and manage our business as one segment, which is the discovery, research and development of treatments based on our SNA technology.

**Critical Accounting Policies and Significant Judgments and 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 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 revenue and expenses incurred during the reported periods. 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 apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in the notes to our financial statements appearing in this Annual Report on Form 10-K, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results.

***Revenue***

Effective January 1, 2018, the Company adopted the provisions of Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers* using the modified retrospective method for all contracts not completed as of the date of adoption. The reported results for 2018 reflect the application of ASC 606 guidance, while the reported results for 2017 were prepared under the guidance of ASC 605, *Revenue Recognition* (ASC 605). Under ASC 605, the Company's revenue recognition accounting policy was consistent with ASC 606 revenue recognition accounting policies, except the Company used to recognize upfront license fees on a straight line basis.

Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that are within the scope of ASC 606, the Company performs the following five steps:

1. *Identify the contract with the customer.* A contract with a customer exists when (i) the Company enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance, and (iii) the Company determines that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration. The Company applies judgment in determining the customer's intent and ability to pay, which is based on a variety of factors including the customer's historical payment experience, or in the case of a new customer, published credit and financial information pertaining to the customer.
2. *Identify the performance obligations in the contract.* Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, the Company must apply judgment to determine whether promised goods and services are both capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.
3. *Determine the transaction price.* The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method, depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in the Company's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes. Determining the transaction price requires significant judgment.
4. *Allocate the transaction price to performance obligations in the contract.* If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. However, if a series of distinct services that are substantially the same qualifies as a single performance obligation in a contract with variable consideration, the Company must determine if the variable consideration is attributable to the entire contract or to a specific part of the contract. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices.
5. *Recognize revenue when or as the Company satisfies a performance obligation.* The Company satisfies performance obligations either over time or at a point in time. Revenue is recognized over time if either (i) the customer simultaneously receives and consumes the benefits provided by the entity's performance, (ii) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or (iii) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer. Examples of control are using the asset to produce goods or services, enhance the value of other assets, or settle liabilities, and holding or selling the asset.

*Licenses of intellectual property* : If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from consideration allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the licenses. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

*Milestone payments:* At the inception of each arrangement that includes development milestone payments, the Company evaluates the probability of reaching the milestones and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur in the future, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore revenue recognized is constrained as management is unable to assert that a reversal of revenue would not be possible. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues and earnings in the period of adjustment.

*Royalties* : For arrangements that include sales-based royalties, including milestone payments based on levels of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its collaboration agreements.

As of December 31, 2018, the Company's only revenue recognized is related to the Purdue Collaboration (see Note 3).

***Equity-based compensation***

We measure the cost of common stock option awards at fair value and record the cost of the awards, net of estimated forfeitures, on a straight-line basis over the requisite service period. We measure fair value for all common stock options using the Black-Scholes option-pricing model. For all common stock option awards to employees, the fair value measurement date is the date of grant and the requisite service period is the period over which the employee is required to provide service in exchange for the common stock option awards, which is generally the vesting period. For all common stock option awards to nonemployees, we remeasure fair value at each financial statement reporting date and recognize compensation expense as services are rendered, generally on a straight-line basis.

The Black-Scholes option-pricing model requires the input of highly subjective assumptions, including: (1) the estimated grant date fair value of Exicure's or Exicure OpCo's (as the case may be) common stock; (2) the option exercise price; (3) the expected term of the option in years; (4) the annualized volatility of the stock; (5) the risk-free interest rate; and (6) the annual rate of quarterly dividends on the stock.

Prior to the commencement of trading of the common stock of Exicure, Inc. on the OTC Market Group's OTCQB® Market quotation system under the ticker symbol "XCUR" effective at the market open on May 24, 2018, the Company's common stock had not yet been publicly traded, therefore the Company estimated the fair value of its common stock underlying its common stock options. The grant date fair value of the Company's common stock had been determined by the Board exercising their judgment in the consideration of a variety of factors. For financial reporting purposes, the Company had periodically estimated the per share fair value of Exicure's common stock at various dates using valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation (Practice Aid). At December 31, 2017, for financial reporting purposes and principally to aid Exicure

in the revaluation of certain common stock option awards to non-employees and certain warrant liabilities, Exicure estimated the per share fair value of its common stock to be $3.00, which was the per share price paid by outside investors in the 2017 Private Placement on September 26, 2017, October 27, 2017, and November 2, 2017.

The expected term is based upon the "simplified method" as described in Staff Accounting Bulletin Topic 14.D.2. Currently, the Company does not have sufficient experience to provide a reasonable estimate of an expected term of its common stock options. The Company will continue to use the "simplified method" until there is sufficient experience to provide a more reasonable estimate in conformance with ASC 718-10-30-25 through 30-26. The risk-free interest rate assumptions were based on the U.S. Treasury bond rate appropriate for the expected term in effect at the time of grant. The expected volatility is based on calculated enterprise value volatilities for publicly traded companies in the same industry and general stage of development. The estimated forfeiture rates were based on historical experience for similar classes of employees. The dividend yield was based on expected dividends at the time of grant.

***Common stock warrant liability***

Freestanding warrants related to shares that are redeemable, contingently redeemable, or for purchases of common stock that are not indexed to the Company's own stock are classified as a liability on the Company's balance sheet. The common stock warrants are recorded at fair value, estimated using the Black-Scholes option-pricing model, and marked to market at each balance sheet date with changes in the fair value of the liability recorded in other income (expense), net in the statements of operations.

A 10% change in the estimate of expected volatility at December 31, 2018 would increase or decrease the fair value of the common stock warrant liability in the amount of $0.1 million . A 10% change in the estimate of fair value of the common stock at December 31, 2018 would increase or decrease the fair value of the common stock warrant liability in the amount of $0.1 million .

***Recently adopted accounting pronouncements***

Refer to Note 2 of the accompanying consolidated financial statements for a description of recently adopted accounting pronouncements.

***Recent accounting pronouncements not yet adopted***

Refer to Note 2 of the accompanying consolidated financial statements for a description of recent accounting pronouncements not yet adopted.

**Components of Statements of Operations**

***Revenue***

We have earned all of our revenue through December 31, 2018 through our research collaboration, license, and option agreement with Purdue or as a primary contractor or as a subcontractor on government grants. We do not intend for government grants to be a principal commercial or strategic focus, but will evaluate opportunities when consistent with our strategic priorities. We have not generated any commercial product revenue and do not expect to generate any product revenue for the foreseeable future.

In the future, we may generate revenue from partnership activities including a combination of research and development payments, license fees and other upfront payments, milestone payments, product sales and royalties, and reimbursement of certain research and development expenses, in connection with the Purdue Collaboration or any future collaborations and licenses. We expect that any such revenue we generate will fluctuate in future periods as a result of the timing of achievement, if at all, of preclinical, clinical, regulatory and commercialization milestones, the timing and amount of any payments to us relating to such milestones and the extent to which any of our therapeutic candidates are approved and successfully commercialized by us or potential development partners. If we, or any potential development partner fails to develop therapeutic candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially and adversely affected.

***Research and development expense***

Research and development expense consists of costs associated with our research activities, including basic research on our SNA platform, discovery and development of novel SNAs as prospective therapeutic candidates, preclinical and clinical development activities for SNAs we have nominated for clinical development as well as maintaining and protecting our intellectual property. Our research and development expenses include:

- employee-related expenses, including salaries, bonuses, benefits and equity-based compensation expense;
- early research and development expenses incurred under arrangements with third parties, such as contract research organizations, contract manufacturing organizations, and consultants;
- preclinical and clinical development expenses with third parties such as contract research organizations, contract manufacturing organizations, and consultants;
- costs of maintaining and protecting our intellectual property portfolio, including legal advisory fees, license fees, sublicense fees, patent maintenance and other similar fees;
- laboratory materials and supplies;
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment and laboratory and other supplies.

We expense research and development costs as they are incurred. A significant portion of our research and development costs are not tracked by project as they benefit multiple projects or our technology.

We expect our research and development expenses to increase for the foreseeable future as we advance our therapeutic candidates through preclinical studies and clinical trials. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time-consuming. We or future development partners may never succeed in obtaining marketing approval for any of our therapeutic candidates. The probability of success for each therapeutic candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability.

All of our research and development programs are at an early stage and successful development of future therapeutic candidates from these programs is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future therapeutic candidate and are difficult to predict. We anticipate we will make determinations as to which therapeutic candidates to pursue and how much funding to direct to each therapeutic candidate on an ongoing basis in response to the early scientific, preclinical and clinical success of each therapeutic candidate, our ability to maintain or enter into development partnerships with respect to a given therapeutic candidate, as well as ongoing assessments of the commercial potential of therapeutic candidates.

We will need to raise additional capital to fund our research and development activities. We have entered into, and may in the future seek, collaborations, licensing or other commercial relationships with other companies in order to advance our various therapeutic candidates. Such collaborations may provide near-term cash payments from the collaborators to us in exchange for license rights or for expense reimbursement, but may also materially reduce the long-term economic benefits that could otherwise be realized from a therapeutic candidate subject to a collaboration in the event that such therapeutic candidate becomes commercially viable. Additional private or public financings may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a material adverse effect on our financial condition and our ability to pursue our business strategy.

***General and administrative expense***

General and administrative expense consists primarily of salaries and related benefits, including equity-based compensation, related to our executive, finance, legal, business development and support functions. Other general and administrative expenses include travel expenses, professional fees for auditing, tax and legal services and allocated facility-related costs not otherwise included in research and development expenses.

We expect that general and administrative expenses will increase in the future as we expand our operating activities and incur additional costs associated with being a growing, publicly-traded company. These increases will likely include legal, accounting and filing fees, directors' and officers' liability insurance premiums and fees associated with investor relations.

***Interest expense***

Interest expense consists of interest expense pursuant to the loan and security agreement with Hercules Technology Growth Capital, or Hercules, that we closed on February 17, 2016 with an initial advance of $6.0 million.

***Other income (loss), net***

Other income (loss), net consists of interest income earned on our cash and cash equivalents, fair value adjustments of our preferred and common stock warrant liabilities, and gains and losses on foreign currency transactions.

**Results of Operations**

**Comparison of the Year Ended December 31, 2018 and 2017**

The following table summarizes the results of our operations for the years ended December 31, 2018 and 2017:

| | Year Ended December 31, | | | |
|---|---|---|---|---|
| *(dollars in thousands)* | **2018** | **2017** | **Change** | |
| Revenue: | | | | |
| Collaboration revenue | $ 118 | $ 9,719 | $ (9,601) | (99)% |
| Total revenue | 118 | 9,719 | (9,601) | (99)% |
| Operating expenses: | | | | |
| Research and development expense | 14,119 | 13,080 | 1,039 | 8 % |
| General and administrative expense | 7,818 | 7,046 | 772 | 11 % |
| Total operating expenses | 21,937 | 20,126 | 1,811 | 9 % |
| Operating loss | (21,819) | (10,407) | (11,412) | 110 % |
| Other income (expense), net: | | | | |
| Interest expense | (672) | (795) | 123 | (15)% |
| Other income (loss), net | 78 | 191 | (113) | n/m |
| Total other income (loss), net | (594) | (604) | 10 | (2)% |
| Net loss | $ (22,413) | $ (11,011) | $ (11,402) | 104 % |

*Revenue*

| | Year Ended December 31, | | | |
|---|---|---|---|---|
| *(dollars in thousands)* | **2018** | **2017** | **Change** | |
| Collaboration revenue | $ 118 | $ 9,719 | $ (9,601) | (99)% |
| Total revenue | $ 118 | $ 9,719 | $ (9,601) | (99)% |

Revenue in both the years ended December 31, 2018 and 2017 related to the Purdue Collaboration, and decreased from $9.7 million for the year ended December 31, 2017 to $0.1 million for the year ended December 31, 2018, or approximately 99% , mostly due to the absence of revenue recognized in the prior period related to the amortization of the upfront payment, and certain reimbursable research and development activities due to the completion of the AST-005 Phase 1b trial during 2018, under the Purdue Collaboration. In connection with the Purdue Collaboration, we received a non-refundable development fee of $10.0 million in December 2016. Prior to the adoption of ASC 606, the upfront payment of $10.0 million was accounted for pursuant to ASC 605 and was recorded as deferred revenue and recognized on a ratable basis over the estimated performance period of the relevant research and development activities. On January 1, 2018, in connection with the adoption of ASC 606, we recorded the unamortized deferred revenue of $1.0 million as an adjustment to the beginning balance of accumulated deficit at January 1, 2018.

The collaboration revenue of $0.1 million during the year ended December 31, 2018 related to research and development activities that is reimbursable by Purdue and is presented on a gross basis in the accompanying consolidated statement of operations. We recognized $9.7 million of collaboration revenue in the year ended December 31, 2017, which consisted of twelve months of amortization of deferred revenue mentioned above and $1.4 million related to research and development activities that was reimbursed by Purdue and is presented on a gross basis in the accompanying consolidated statement of operations.

We do not expect to generate any product revenue for the foreseeable future. However, future revenue may include amounts attributable to partnership activities including, a combination of research and development payments, license fees and other upfront payments, milestone payments, product sales and royalties, and reimbursement of certain research and development expenses, in connection with the Dermelix License Agreement or the Purdue Collaboration or any future collaboration and licenses.

*Research and development expense*

The following table summarizes our research and development expenses incurred during the periods indicated:

| | Year Ended December 31, | | | |
|---|---|---|---|---|
| *(dollars in thousands)* | 2018 | 2017 | Change | |
| Clinical development programs expense | $ 5,607 | $ 6,490 | $ (883) | (14)% |
| Platform and discovery-related expense | 3,764 | 3,146 | 618 | 20 % |
| Employee-related expense | 3,751 | 2,583 | 1,168 | 45 % |
| Facilities, depreciation, and other expenses | 997 | 861 | 136 | 16 % |
| Total research and development expense | $ 14,119 | $ 13,080 | $ 1,039 | 8 % |
| | | | | |
| Full time employees | 20 | 16 | 4 | |

Research and development expense was $14.1 million for the year ended December 31, 2018 and $13.1 million for the year ended December 31 2017, an increase of $1.0 million , or 8% . The increase in research and development expense of $1.0 million was primarily due to higher employee-related expenses of $1.2 million and higher platform and discovery-related expense of $0.6 million , partially offset by a net decrease in costs related to our clinical development programs of $0.9 million .

Higher employee-related expense of $1.2 million was due to higher compensation and related costs, non-cash stock-based compensation, and relocation costs all mostly in connection with the hire of our Chief Operating Officer as well as in connection with salary increases for existing employees. The increase in platform and discovery-related expense of $0.6 million is mostly due to higher costs to maintain our intellectual property portfolio.

The net decrease in clinical development programs expense of $0.9 million was mostly due to lower costs associated with AST-005 (for which the Phase 1b clinical trial, subject of the Purdue Collaboration, ended during the first quarter of 2018) and net lower costs associated with AST-008 (a decrease in costs related to the Phase 1 trial of AST-008 more than offset an increase in costs related to the preparation for the Phase 1b/2 trial of AST-008), partially offset by net higher costs associated with XCUR17 (an increase in costs to prepare for a Phase 2 clinical trial of XCUR17 was more than offset by a decrease in costs related to the Phase 1 clinical trial of XCUR17). Included in clinical development expense for the years ended December 31, 2018 and 2017 was approximately $0.1 million and $1.4 million , respectively, of expense that is reimbursed by Purdue (included in revenue) related to the Phase 1b trial of AST-005.

We expect our research and development expenses to increase in 2019 as we continue spending on our clinical development programs, further develop our SNA technology platform and broaden our pipeline of SNA-based therapeutic candidates.

*General and administrative expense*

| | Year Ended December 31, | | | |
|---|---|---|---|---|
| *(dollars in thousands)* | 2018 | 2017 | Change | |
| General and administrative expense | $ 7,818 | $ 7,046 | $ 772 | 11% |
| Full time employees | 7 | 7 | — | |

General and administrative expense was $7.8 million for the year ended December 31, 2018 and $7.0 million for the year ended December 31, 2017, an increase of $0.8 million , or 11% . This increase is due to higher costs associated with being a public company of $0.9 million, including higher expense for investor and public relations and director and officer insurance, as well as higher compensation and related expense of $0.5 million associated with salary increases and the addition of an executive during 2018, partially offset by lower legal and accounting costs of $0.7 million resulting in a change in mix of transaction support in 2018 as compared to 2017.

*Interest expense*

Interest expense consists of interest expense pursuant to the loan and security agreement with Hercules that we closed on February 17, 2016 with an initial advance of $6.0 million.

*Other income (loss), net*

Other income (loss), net consists of interest income earned on our cash and cash equivalents, fair value adjustments of our common stock warrant liabilities, and gains and losses on foreign currency transactions.

**Inflation**

We do not believe that inflation has had a material adverse impact on our revenues or operations in any of the past three years.

**Liquidity and Capital Resources**

***Overview***

To date we have primarily funded our operations through private placements of equity securities, the Purdue Collaboration, a debt financing, and grants from governmental agencies. Since inception and through December 31, 2018, we have received approximately $117.3 million in aggregate gross proceeds from these transactions, including: $42.8 million in aggregate gross proceeds from private placement offerings of preferred stock; $31.5 million in gross proceeds from sales of common stock in the 2017 Private Placement; $22.0 million in gross proceeds from the sales of common stock in the August 2018 Private Placement; an upfront payment of $10.0 million in connection with the Purdue Collaboration; $6.0 million in debt financing; and an aggregate of $5.0 million from grants awarded by governmental agencies.

Since our inception, we have not generated any product revenue and have incurred recurring net losses. Our Company is not profitable, and we cannot provide any assurance that we will ever be profitable. As of December 31, 2018, we have an accumulated deficit of $73.8 million . Based on the Company's current operating plans, it believes that existing working capital at December 31, 2018 is sufficient to fund its current operating plans into January 2020. Management believes that it will be able to obtain additional working capital through equity financings, partnerships and licensing, or other arrangements, to fund operations. However, there can be no assurance that such additional financing will be available and, if available, can be obtained on terms acceptable to us. If we are unable to obtain such additional financing, we will need to reevaluate future operating plans. Accordingly, there is substantial doubt regarding the Company's ability to continue as a going concern.

See "—Funding Requirements" below for additional information on our future capital needs.

***Cash Flows***

The following table shows a summary of our cash flows for the years ended December 31, 2018 and 2017:

| | Years Ended December 31, | |
|---|---|---|
| *(in thousands)* | **2018** | **2017** |
| Net cash used in operating activities | $ (19,487) | $ (19,789) |
| Net cash used in investing activities | (94) | (926) |
| Net cash provided by financing activities | 20,085 | 26,856 |
| Net increase in cash and cash equivalents | $ 504 | $ 6,141 |

*Operating activities*

Net cash used in operating activities was $19.5 million and $19.8 million for the years ended December 31, 2018 and 2017, respectively. The decrease in cash used in operating activities of $0.3 million was primarily due to lower prepaid research and development contract costs in the 2018 period and the absence of the first quarter 2017 payment of $1.5 million in connection with the Northwestern University License Agreements, partially offset by higher cash used for working capital.

*Investing activities*

Net cash used in investing activities was $0.1 million and $0.9 million for the years ended December 31, 2018 and 2017, respectively. Cash used in investing activities for each of the years ended December 31, 2018 and 2017 was primarily due to the purchase of scientific equipment.

*Financing activities*

Net cash provided by financing activities of $20.1 million for the year ended December 31, 2018 is primarily due to the sale of common stock in the August 2018 Private Placement. On August 22, 2018, we sold 4,889,217 shares of the Company's common stock at a purchase price of $4.50 per share, resulting in approximately $22.0 million in gross proceeds to the Company. The aggregate net proceeds from the August 2018 Private Placement (after deducting placement agent fees and expenses of the offering of $1.9 million ) were $20.1 million .

Net cash provided by financing activities of $26.9 million for the year ended December 31, 2017 is primarily due to the sale of common stock in the 2017 Private Placement. On September 26, 2017, October 27, 2017, and November 2, 2017, we sold 10,504,196 shares of the Company's common stock at a purchase price of $3.00 per share, resulting in approximately $31.5 million of gross proceeds to the Company. The aggregate net proceeds from the 2017 Private Placement (after deducting placement agent fees and expenses of the offering paid in 2017 of $3.7 million ) were $27.8 million . This was partially offset by the repayment of debt of $1.0 million .

***Hercules Loan and Security Agreement***

On February 17, 2016, we entered into a loan and security agreement with Hercules. The loan agreement provided for funding in an aggregate principal amount of up to $10.0 million in two separate tranches. The first tranche was funded on February 17, 2016 in the amount of $6.0 million. A second tranche of $4.0 million was available provided that we met certain milestones on or before December 31, 2016. We did not meet these milestones and, therefore, we did not draw the second tranche, the availability of which expired on December 31, 2016. The principal balance of the term loan under the Hercules loan facility bears interest at a floating per annum interest rate (based on a year consisting of 360 days) equal to the greater of either (i) 9.95% or (ii) the sum of (a) 9.95% plus (b) the prime rate (as reported in The Wall Street Journal) minus 3.50%. We were required to make interest-only payments through June 2017. Commencing on July 1, 2017, the loan began amortizing in equal monthly installments of principal and interest in an amount sufficient to fully amortize the outstanding principal balance of the loan over the remaining scheduled monthly payments due prior to the maturity date on September 1, 2019. Pursuant to an amendment dated January 15, 2018, amortization payments due for the thirteen (13) consecutive months commencing on December 1, 2017 through and including December 1, 2018 were deferred. Commencing on January 1, 2019, and continuing on the first business day of each month thereafter, the loan, including the deferred payments, was to begin amortizing in equal monthly installments of principal and interest based upon an amortization schedule equal to eighteen (18) consecutive months. Any remaining obligations under the loan agreement and other loan documents were due and payable on the maturity date. On December 28, 2018, the Company and Hercules further amended its loan agreement so that interest amounts are payable on the first day of each business month and any remaining obligations under the loan agreement and other loan documents are due and payable on the maturity date on September 1, 2019. On the earliest to occur of the maturity date, the date we prepay the term loan in full or the date the loan otherwise becomes due and payable, we must pay the lender under the agreement an additional charge equal to 3.85% of the total amounts funded under the loan agreement. In addition, if we prepaid the term loan on or prior to February 1, 2017, we would have been required to pay a prepayment charge equal to 3% of the amount being prepaid, if we prepaid the term loan after February 1, 2017 but on or prior to February 1, 2018, we would have been required to pay a prepayment charge equal to 2% of the

amount being prepaid, and if we prepay the term loan after February 1, 2018, we must pay a prepayment charge of 1% of the amount being prepaid. As of the date of this Annual Report on Form 10-K, we have not prepaid the Hercules term loan.

The term loan under the Hercules loan facility is secured by substantially all of our assets, other than intellectual property, which is the subject of a negative pledge. Under the loan agreement, we are subject to certain customary covenants that limit or restrict our ability to, among other things, incur additional indebtedness, grant any security interests, pay cash dividends, repurchase our common stock, make loans, or enter into certain transactions without Hercules' prior consent. The loan agreement was amended on October 10, 2016 to revise the language granting Hercules a contingent security interest in certain of our assets.

Under the loan agreement, Hercules or its affiliates have a right to participate in a single subsequent unregistered financing by us in an amount of up $1.0 million on the same terms, conditions and pricing afforded to others participating in such financing. Hercules has not yet exercised this right to participate which expires on the earliest to occur of the maturity date, the date we prepay the term loan in full or the date the loan otherwise becomes due and payable.

Refer to Note 15, *Subsequent Events* , in the accompanying Notes to Consolidated Financial Statements included elsewhere in this report for more information.

***Funding Requirements***

We expect that our primary uses of capital will continue to be third-party clinical and research and development services, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses and general overhead costs. Based on the Company's current operating plans, we believe that existing working capital at December 31, 2018 is sufficient to fund our current operating plans into January 2020. However, we may require additional capital for the further development of our existing therapeutic candidates and may also need to raise additional funds sooner to pursue other development activities related to additional therapeutic candidates. We believe that we will be able to obtain additional working capital through equity financings, partnerships and licensing, or other arrangements to fund our current operating plans, which we believe will allow us to execute on the strategy and pipeline development as described in this Annual Report on Form 10-K. To the extent that we raise additional capital through future equity financings, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. We cannot assure you that such additional financing, if available, can be obtained on terms acceptable to us. If we are unable to obtain such additional financing, we would need to reevaluate our future operating plans.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially as a result of a number of factors. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the terms and timing of any other collaboration, licensing and other arrangements that we may establish;
- the initiation, progress, timing and completion of preclinical studies and clinical trials for our potential therapeutic candidates;
- the number and characteristics of therapeutic candidates that we pursue;
- the progress, costs and results of our preclinical studies and clinical trials;
- the outcome, timing and cost of regulatory approvals;
- delays that may be caused by changing regulatory requirements;

- the cost and timing of hiring new employees to support our continued growth;
- unknown legal, administrative, regulatory, accounting, and information technology costs as well as additional costs associated with operating as a public company;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the costs of filing and prosecuting intellectual property rights and enforcing and defending any intellectual property-related claims;
- the costs and timing of procuring clinical and commercial supplies of our therapeutic candidates;
- the extent to which we acquire or in-license other therapeutic candidates and technologies; and
- the extent to which we acquire or invest in other businesses, therapeutic candidates or technologies.

Please see the section titled "Risk Factors" elsewhere in this Annual Report on Form 10-K for additional risks associated with our substantial capital requirements.

Until such time, if ever, we generate product revenue, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings and research collaboration and license agreements. We may be unable to raise capital or enter into such other arrangements when needed or on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our therapeutic candidates.

**Contractual Obligations and Commitments**

The following is a summary of our significant contractual obligations as of December 31, 2018 (in thousands):

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| **Contractual Obligations** | **Total** | **Less than 1 Year** | **1-3 Years** | **3-5 Years** | **After 5 Years** |
| Long-term debt (1) | $ 4,999 | $ — | $ 4,999 | $ — | $ — |
| Operating lease obligations (2) | 759 | 347 | 412 | — | — |
| Interest payments on long-term debt | 454 | 454 | — | — | — |
| Total | $ 6,212 | $ 801 | $ 5,411 | $ — | $ — |

(1) Includes principal only. Refer to Note 15, *Subsequent Events* , in the accompanying Notes to Consolidated Financial Statements included elsewhere in this report for more information.
(2) Future minimum lease payments under our non-cancelable operating lease for our current office and lab space in Skokie, Illinois that expires in February 2021.

We enter into agreements in the normal course of business with contract research organizations and vendors for clinical trials, preclinical studies, and other services and products for operating purposes which are cancelable at any time by us, generally upon 30 days prior written notice. We also have obligations to make future payments to Northwestern University that become due and payable on the achievement of certain commercial milestones. These payments are not included in this table of contractual obligations.

**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 in the rules and regulations of the SEC.

**JOBS Act**

In April 2012, the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act") was enacted by the federal government. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

In addition, as an emerging growth company, we will not be required to provide an auditor's attestation report on our internal control over financial reporting in future annual reports on Form 10-K as otherwise required by Section 404(b) of the Sarbanes-Oxley Act.

**Item 7A. Quantitative and Qualitative Disclosures about Market Risk.**

The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our marketable securities without significantly increasing risk. Some of the securities that we invest in may have market risk related to changes in interest rates. As of December 31, 2018 and 2017, we had cash and cash equivalents of $26.3 million and $25.8 million , respectively, consisting of interest-bearing money market accounts. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term maturities of our cash equivalents and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents. To minimize the risk in the future, we intend to maintain our portfolio of cash equivalents and short-term investments in a variety of securities, including commercial paper, money market funds, government and non-government debt securities and corporate obligations.

We are subject to interest rate risk in connection with our borrowings under the $6.0 million term loan with Hercules. The principal balance of the term loan under the Hercules loan facility bears interest at a floating per annum interest rate (based on a year consisting of 360 days) equal to the greater of (i) 9.95% or (ii) the sum of (a) 9.95% plus (b) the prime rate (as reported in The Wall Street Journal) minus 3.50% which bears interest at a variable per annum rate calculated for any day as the greater of (i) the prime rate plus 6.80%, and (ii) 10.55%. We currently do not engage in any interest rate hedging activity and we have no intention to do so in the foreseeable future. Based on the current interest rate of the term loan with Hercules and the scheduled payments thereunder, we believe a 100 basis point increase in interest rates would not have a material impact on our financial condition or results of operations.

**Item 8. Financial Statements and Supplementary Data.**

**EXICURE, INC.**
**INDEX TO FINANCIAL STATEMENTS**

## Report of Independent Registered Public Accounting Firm

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

*Opinion on the Consolidated Financial Statements*

We have audited the accompanying consolidated balance sheets of Exicure, Inc. and subsidiary (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations, changes in stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2018, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

*Change in Accounting Principle*

As discussed in Note 2 to the consolidated financial statements, the Company has changed its method of accounting for revenue recognition in 2018 due to the adoption of the Financial Accounting Standards Board Accounting Standards Codification (ASC) Topic 606, *Revenue from Contracts with Customers* .

*Going Concern*

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring losses from operations and will be required to raise additional capital or alternative means of financial support to fund operations. These factors 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 consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

*Basis for Opinion*

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

(signed) KPMG LLP

We have served as the Company's auditor since 2014.

Chicago, Illinois
March 8, 2019

**EXICURE, INC.**

**CONSOLIDATED BALANCE SHEETS**
**(in thousands, except share and per share data)**

| | December 31, 2018 | December 31, 2017 |
|---|---|---|
| **ASSETS** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 26,268 | $ 25,764 |
| Unbilled revenue receivable | 3 | 13 |
| Receivable from related party | 10 | 17 |
| Prepaid expenses and other assets | 1,382 | 1,844 |
| Total current assets | 27,663 | 27,638 |
| Property and equipment, net | 1,061 | 1,317 |
| Other noncurrent assets | 32 | 32 |
| Total assets | $ 28,756 | $ 28,987 |
| **LIABILITIES AND STOCKHOLDERS' EQUITY** | | |
| Current liabilities: | | |
| Accounts payable | $ 500 | $ 1,049 |
| Accrued expenses and other current liabilities | 1,543 | 1,273 |
| Current portion of deferred revenue | — | 1,034 |
| Total current liabilities | 2,043 | 3,356 |
| Long-term debt, net | 4,925 | 4,855 |
| Common stock warrant liability | 797 | 523 |
| Other noncurrent liabilities | 39 | 278 |
| Total liabilities | $ 7,804 | $ 9,012 |
| | | |
| Stockholders' equity: | | |
| Common stock, $0.0001 par value per share; 200,000,000 shares authorized, 44,358,000 issued and outstanding, December 31, 2018; 39,300,823 shares issued and outstanding, December 31, 2017 | 4 | 4 |
| Additional paid-in capital | 75,942 | 53,586 |
| Accumulated deficit | (54,994) | (33,615) |
| Total stockholders' equity | 20,952 | 19,975 |
| Total liabilities and stockholders' equity | $ 28,756 | $ 28,987 |

See Accompanying Notes to Consolidated Financial Statements.

**EXICURE, INC.**

**CONSOLIDATED STATEMENTS OF OPERATIONS**
**(in thousands, except share and per share data)**

| | Year Ended December 31, | |
|---|---|---|
| | **2018** | **2017** |
| Revenue: | | |
| Collaboration revenue | $ 118 | $ 9,719 |
| Total revenue | 118 | 9,719 |
| Operating expenses: | | |
| Research and development expense | 14,119 | 13,080 |
| General and administrative expense | 7,818 | 7,046 |
| Total operating expenses | 21,937 | 20,126 |
| Operating loss | (21,819) | (10,407) |
| Other income (expense), net: | | |
| Interest expense | (672) | (795) |
| Other income (loss), net | 78 | 191 |
| Total other income (loss), net | (594) | (604) |
| Net loss | $ (22,413) | $ (11,011) |
| | | |
| Basic and diluted loss per common share | $ (0.54) | $ (1.09) |
| Basic and diluted weighted-average common shares outstanding | 41,189,177 | 10,119,569 |

See Accompanying Notes to Consolidated Financial Statements.

**EXICURE, INC.**

**CONSOLIDATED STATEMENT OF CHANGES IN STOCKHOLDERS' EQUITY**
**(in thousands, except shares)**

| | Non-Redeemable Preferred Stock | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Series C | | Series B-2 | | Series B-1 | | Series A | | Common Stock | | | | |
| | Shares | $ | Shares | $ | Shares | $ | Shares | $ | Shares | $ | Additional Paid-in-Capital | Accumulated Deficit | Total Stockholders' Equity |
| **Balance at December 31, 2016** | **11,239,359** | **$33,483** | **1,403,984** | **$3,641** | **2,451,560** | **$5,371** | **11,381,640** | **$135** | **131,644** | **$—** | **$(17,578)** | **$ (22,604)** | **$ 2,448** |
| Exercise of options | — | — | — | — | — | — | — | — | 58,440 | — | 43 | — | 43 |
| Equity-based compensation | — | — | — | — | — | — | — | — | — | — | 1,462 | — | 1,462 |
| Share conversion in connection with the Merger | (11,239,359) | (33,483) | (1,403,984) | (3,641) | (2,451,560) | (5,371) | (11,381,640) | (135) | 28,556,543 | 3 | 42,596 | — | (31) |
| Issuance of common stock, net | — | — | — | — | — | — | — | — | 10,554,196 | 1 | 27,063 | — | 27,064 |
| Net loss | — | — | — | — | — | — | — | — | — | — | — | (11,011) | (11,011) |
| **Balance at December 31, 2017** | **—** | **$ —** | **—** | **$ —** | **—** | **$ —** | **—** | **$ —** | **39,300,823** | **$ 4** | **$ 53,586** | **$ (33,615)** | **$ 19,975** |
| Adoption of new accounting standard - ASC 606 | — | — | — | — | — | — | — | — | — | — | — | 1,034 | 1,034 |
| **Balance at January 1, 2018** | **—** | **$ —** | **—** | **$ —** | **—** | **$ —** | **—** | **$ —** | **39,300,823** | **$ 4** | **$ 53,586** | **$ (32,581)** | **$ 21,009** |
| Exercise of options | — | — | — | — | — | — | — | — | 22,494 | — | 41 | — | 41 |
| Equity-based compensation | — | — | — | — | — | — | — | — | — | — | 1,809 | — | 1,809 |
| Issuance of common stock to consultants, net | — | — | — | — | — | — | — | — | 145,466 | — | 436 | — | 436 |
| Issuance of common stock in private placement, net | — | — | — | — | — | — | — | — | 4,889,217 | — | 20,070 | — | 20,070 |
| Net loss | — | — | — | — | — | — | — | — | — | — | — | (22,413) | (22,413) |
| **Balance at December 31, 2018** | **—** | **$ —** | **—** | **$ —** | **—** | **$ —** | **—** | **$ —** | **44,358,000** | **$ 4** | **$ 75,942** | **$ (54,994)** | **$ 20,952** |

See Accompanying Notes to Consolidated Financial Statements.

**EXICURE, INC.**

**CONSOLIDATED STATEMENTS OF CASH FLOWS**
**(in thousands)**

| | Year Ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Cash flows from operating activities: | | |
| Net loss | $ (22,413) | $ (11,011) |
| Adjustments to reconcile net loss to cash used in operating activities: | | |
| Depreciation and amortization | 358 | 232 |
| Equity-based compensation | 1,809 | 1,462 |
| Amortization of long-term debt issuance costs and fees | 96 | 189 |
| Other | 400 | — |
| Change in fair value of warrant liabilities | 274 | (214) |
| Changes in operating assets and liabilities: | | |
| Unbilled revenue receivable and accounts receivable | 10 | (13) |
| Receivable from related party | 7 | (2) |
| Prepaid expenses and other current assets | 498 | (1,442) |
| Accounts payable | (557) | 195 |
| Accrued expenses and other current liabilities | 270 | (906) |
| Deferred revenue | — | (8,276) |
| Other noncurrent liabilities | (239) | (3) |
| Net cash used in operating activities | (19,487) | (19,789) |
| Cash flows from investing activities: | | |
| Capital expenditures | (94) | (926) |
| Net cash used in investing activities | (94) | (926) |
| Cash flows from financing activities: | | |
| Proceeds from common stock offering | 22,001 | 31,513 |
| Proceeds from exercise of common stock options | 41 | 43 |
| Repayment of long-term debt | — | (1,001) |
| Payment of long-term debt fees and issuance costs | (26) | — |
| Payment of common stock financing costs | (1,931) | (3,699) |
| Net cash provided by financing activities | 20,085 | 26,856 |
| Net increase in cash and cash equivalents | 504 | 6,141 |
| Cash and cash equivalents - beginning of period | 25,764 | 19,623 |
| Cash and cash equivalents - end of period | $ 26,268 | $ 25,764 |
| | | |
| Supplemental disclosure of cash flow information | | |
| Non-cash financing activities: | | |
| Issuance of common stock for professional services | $ 436 | $ — |
| Issuance of common stock warrants | — | 536 |
| Common stock issuance costs (accounts payable and accrued expenses) | — | 214 |
| Non-cash investing activities: | | |
| Capital expenditures (accounts payable and accrued expenses) | 8 | 120 |

See Accompanying Notes to Consolidated Financial Statements.

**EXICURE, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**
**(in thousands, except share and per share data)**

## 1. Description of Business and Basis of Presentation

***Description of Business***

Exicure is a clinical-stage biotechnology company developing therapeutics for immuno-oncology, inflammatory diseases and genetic disorders based on the Company's proprietary Spherical Nucleic Acid ("SNA") technology. We believe the design of the Company's SNAs gives rise to distinct chemical and biological properties that may provide advantages over other nucleic acid therapeutics and enable therapeutic activity outside of the liver. The Company intends to build a leading nucleic acid therapeutics company focused on the discovery and development of therapeutics based on the Company's proprietary SNA technology, either on its own or in collaboration with pharmaceutical partners.

Throughout these consolidated financial statements, the terms "the Company" and "Exicure" refer to Exicure, Inc. and its 100% owned subsidiary, Exicure Operating Company. Exicure Operating Company holds all material assets, and conducts all business activities and operations, of the Company.

*The Merger*

On September 26, 2017, pursuant to the merger agreement, Max-1 Acquisition Sub, Inc., a wholly-owned subsidiary of Max-1 Acquisition Corporation ("Max-1"), merged with and into Exicure Operating Company (f/k/a Exicure, Inc.), a privately-held Delaware corporation referred to herein as Exicure OpCo, with Exicure OpCo remaining as the surviving entity and a wholly-owned operating subsidiary of Max-1 (the "Merger"). The Merger was effective as of September 26, 2017 (the "Effective Time"), upon the filing of a Certificate of Merger with the Secretary of State of the State of Delaware.

At the Effective Time, the legal existence of Max-1 Acquisition Sub, Inc. ceased. At the Effective Time, each share of Exicure OpCo common and preferred stock (other than shares of Exicure OpCo's Series C preferred stock) issued and outstanding immediately prior to the closing of the Merger was converted into 0.49649 shares of Max-1's common stock, and each share of Exicure OpCo's Series C preferred stock issued and outstanding immediately prior to the closing of the Merger was converted into 0.7666652 shares of Max-1's common stock. As a result, an aggregate of 26,666,627 shares of Max-1's common stock were issued to the holders of Exicure OpCo's capital stock, which is incremental to the 2,080,000 shares of Max-1 common stock that were outstanding immediately prior to the Merger. In addition, pursuant to the Merger Agreement, options to purchase 7,414,115 shares of Exicure OpCo common stock issued and outstanding immediately prior to the closing of the Merger were assumed by Max-1 and converted into options to purchase 3,680,997 shares of Max-1's common stock. After the filing of the Certificate of Merger with the Secretary of State of the State of Delaware, Max-1 changed its name to Exicure, Inc.

The Merger is considered a "reverse merger," whereby Exicure OpCo is considered the accounting acquirer in the Merger. Exicure OpCo was determined to be the accounting acquirer based on the terms of the Merger and other factors including: (i) legacy Exicure OpCo shareholders own approximately 94% of the combined company on a fully diluted basis immediately following the closing of the Merger, (ii) legacy Exicure OpCo directors will hold all six board seats of the combined company, and (iii) legacy Exicure OpCo management will hold all positions in management of the combined company. The transaction is accounted for as an asset acquisition rather than a business combination because as of the acquisition date, Max-1 does not meet the definition of a business as defined by accounting principles generally accepted in the United States of America ("GAAP"). Consequently, the assets, liabilities and operations that are reflected in Exicure's historical financial statements prior to the Merger will be those of Exicure OpCo, and the consolidated financial statements after completion of the Merger will include the assets, liabilities and results of operations of Exicure OpCo up to the day prior to the closing of the Merger and the assets, liabilities and results of operations of the combined company from and after the closing date of the Merger. The assets and liabilities of Max-1 included in the accompanying consolidated financial statements are recorded at the historical cost basis of Max-1.

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In these consolidated financial statements, unless otherwise indicated, all share and per share figures are retrospectively adjusted to reflect the conversion of each share of Exicure OpCo common and preferred stock (other than shares of Exicure OpCo's Series C preferred stock), preferred stock warrant liability, and common stock options issued and outstanding immediately prior to the closing of the Merger into 0.49649 shares of the Company's common stock, and each share of Exicure OpCo's Series C preferred stock issued and outstanding immediately prior to the closing of the Merger into 0.7666652 shares of the Company's common stock.

*Capitalization Prior to the Merger*

AuraSense Therapeutics, LLC was formed on June 13, 2011 as a wholly owned subsidiary of AuraSense, LLC, but did not conduct substantive business until December 12, 2011, which is considered the inception date. On December 12, 2011, AuraSense, LLC contributed the assets and liabilities comprising the business of the Company to the Company through a Bill of Sale and Assumption Agreement. Pursuant to this agreement AuraSense, LLC received 11,381,611 Class A Units of the Company.

The assets and liabilities contributed by AuraSense, LLC were transferred at their historical cost and consisted of an unbilled revenue receivable of $143 , scientific equipment of $309 and a liability of $317 for accrued legal expenses related to patent protection. The net book value of AuraSense, LLC's contribution at inception was $135 .

Also on December 12, 2011, the Company and AuraSense, LLC entered into a Partial Assignment of License Agreement whereby certain license rights held by AuraSense, LLC pursuant to a License Agreement with Northwestern University were assigned to the Company. Under the terms of the License Agreement and the Partial Assignment of License Agreement, Northwestern University received 1.0% of the Class A units received by AuraSense, LLC in the formation transaction, which amounted to 113,816 units.

On July 9, 2015, AuraSense Therapeutics, LLC was converted into AuraSense Therapeutics, Inc., a Delaware corporation, and on the same date changed its name to Exicure, Inc., which actions together are referred to in these Notes to Consolidated Financial Statements as the corporate conversion. In connection with the corporate conversion, each common unit, Class A unit, Class B-1 unit, Class B-2 unit and Class C unit of AuraSense Therapeutics, LLC issued and outstanding immediately prior to the effectiveness of the corporate conversion was converted into one share of common stock, Series A preferred stock, Series B-1 preferred stock, Series B-2 preferred stock and Series C preferred stock of Exicure OpCo, respectively. No preferred stock was provided in consideration for fractional membership units. Each outstanding option to purchase one common unit of AuraSense Therapeutics, LLC was converted into an option to purchase one share of common stock of Exicure OpCo. In connection with the corporate conversion, the accumulated deficit of AuraSense Therapeutics, LLC of $18,837 was reclassified to Additional paid in capital.

Refer to Note 6, *Stockholders' Equity,* for more information on capital stock transactions.

***Basis of Presentation***

The accompanying consolidated financial statements as of December 31, 2018 and 2017, and for the years then ended, have been presented in conformity with generally accepted accounting principles in the United States ("GAAP").

*Principles of Consolidation*

The accompanying consolidated financial statements include the accounts of Exicure, Inc. and its 100% owned subsidiary, Exicure Operating Company. All intercompany transactions and accounts are eliminated in consolidation.

*Going Concern*

As of December 31, 2018, the Company has generated an accumulated deficit of $73,831 since inception and expects to incur significant expenses and negative cash flows for the foreseeable future. Based on the Company's current operating plans, it believes that existing working capital at December 31, 2018 is sufficient to fund its

current operating plans into January 2020. Management believes that it will be able to obtain additional working capital through equity financings, partnerships and licensing, or other arrangements, to fund operations. However, there can be no assurance that such additional financing will be available and, if available, can be obtained on terms acceptable to the Company. If the Company is unable to obtain such additional financing, the Company will need to reevaluate future operating plans. Accordingly, there is substantial doubt regarding the Company's ability to continue as a going concern.

The accompanying consolidated financial statements have been prepared as though the Company will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might be necessary should the Company be unable to continue as a going concern.

*Use of Estimates*

The preparation of the financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Management bases its estimates on certain assumptions which it believes are reasonable in the circumstance and while actual results could differ from those estimates, management does not believe that any change in those assumptions in the near term would have a significant effect on the Company's financial position, results of operations or cash flows. Actual results in future periods could differ from those estimates.

*Revision of Prior Period Financial Statements*

In connection with preparing our condensed consolidated interim financial information for the three months ended March 31, 2018, we identified errors that affected prior interim and annual periods related to the timing of recognition of research and development expense related to a contract for the clinical trial of one of our therapeutic candidates. We evaluated whether our previously issued consolidated financial statements were materially misstated and concluded that the errors individually and in the aggregate were not material to any of our previously issued financial statements. We revised the financial statements to correct the immaterial errors, and the accompanying comparative financial statements reflect these corrections. The correction of the errors increased prepaid expense and other current assets by $933 , decreased accrued expenses by $95 , and decreased accumulated deficit by $1,028 at December 31, 2017; and decreased research and development expense, operating loss, and net loss by $1,028 and loss per share by $0.10 for the year ended December 31, 2017.

**2. Significant Accounting Policies**

***Cash and cash equivalents***

The Company considers all highly liquid investments with original maturities of three months or less to be cash equivalents.

***Accounts receivable and unbilled revenue receivable***

Accounts receivable and unbilled revenue receivable consist of reimbursement for research and development activities in connection with the research collaboration, license, and option agreement with Purdue Pharma L.P. ("Purdue"). The Company's management believes these receivables are fully collectible.

***Fair value of financial instruments***

The carrying amounts of financial instruments, which include cash and cash equivalents and accounts payable, approximate their respective fair values due to the relatively short-term nature of these instruments. Management believes that the Company's long-term debt bears interest at the prevailing market rate for instruments with similar characteristics and, accordingly, the carrying value of long-term debt also approximates their fair value.

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***Concentrations of credit risk and other risks and uncertainties***

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. As of December 31, 2018 and 2017, the Company had cash and cash equivalents of $26,268 and $25,764 , respectively. The cash balances at each respective period were maintained at two institutions. These deposits exceed federally insured limits.

During the years ended December 31, 2018 and 2017, one counterparty accounted for all of the Company's revenue.

The Company is currently not profitable and no assurance can be provided that it will ever be profitable. The Company's research and development activities have required significant investment since inception and operations are expected to continue to require cash investment in excess of its revenues. See also Note 1, *Description of Business and Basis of Presentation—Going Concern* , for more information.

The Company is subject to risks common in therapeutic development including, but not limited to, therapeutic candidates that appear promising in the early phases of development often fail because they prove to be inefficacious or unsafe, clinical trial results are unsuccessful, regulatory bodies may not approve the therapeutic or the therapeutic may not be economical in production or distribution. The Company is also subject to risks common to biotechnology firms including, but not limited to new and disruptive technological innovations, dependence on key personnel, protection of proprietary technology, the validity of and continued access to its owned and licensed intellectual property, limitations on the supply of critical materials, compliance with governmental regulations and market acceptance.

***Property and equipment***

Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the various classes of property and equipment, which range from three to seven years. Leasehold improvements are amortized using the straight-line method over the shorter of the remaining terms of the respective leases or the estimated lives of the assets. Depreciation begins at the time the asset is placed in service.

Property and equipment are reviewed for impairment at least annually or whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. No impairment losses were recorded from inception in December 2011 through December 31, 2018.

***Common stock warrant liability***

Freestanding warrants related to shares that are redeemable, contingently redeemable, or for purchases of common stock that are not indexed to the Company's own stock are classified as a liability on the Company's balance sheet. The common stock warrants are recorded at fair value, estimated using the Black-Scholes option-pricing model, and marked to market at each balance sheet date with changes in the fair value of the liability recorded in other income (expense), net in the statements of operations.

***Revenue recognition***

Effective January 1, 2018, the Company adopted the provisions of Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers* using the modified retrospective method for all contracts not completed as of the date of adoption. The reported results for 2018 reflect the application of ASC 606 guidance, while the reported results for 2017 were prepared under the guidance of ASC 605, *Revenue Recognition* (ASC 605). Under ASC 605, the Company's revenue recognition accounting policy was consistent with ASC 606 revenue recognition accounting policies, except the Company used to recognize upfront license fees on a straight line basis.

Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those

goods or services. To determine revenue recognition for arrangements that are within the scope of ASC 606, the Company performs the following five steps:

1. *Identify the contract with the customer.* A contract with a customer exists when (i) the Company enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance, and (iii) the Company determines that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration. The Company applies judgment in determining the customer's intent and ability to pay, which is based on a variety of factors including the customer's historical payment experience, or in the case of a new customer, published credit and financial information pertaining to the customer.
2. *Identify the performance obligations in the contract.* Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, the Company must apply judgment to determine whether promised goods and services are both capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.
3. *Determine the transaction price.* The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method, depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in the Company's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes. Determining the transaction price requires significant judgment.
4. *Allocate the transaction price to performance obligations in the contract.* If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. However, if a series of distinct services that are substantially the same qualifies as a single performance obligation in a contract with variable consideration, the Company must determine if the variable consideration is attributable to the entire contract or to a specific part of the contract. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices.
5. *Recognize revenue when or as the Company satisfies a performance obligation.* The Company satisfies performance obligations either over time or at a point in time. Revenue is recognized over time if either (i) the customer simultaneously receives and consumes the benefits provided by the entity's performance, (ii) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or (iii) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer. Examples of control are using the asset to produce goods or services, enhance the value of other assets, or settle liabilities, and holding or selling the asset.

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*Licenses of intellectual property* : If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from consideration allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the licenses. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

*Milestone payments:* At the inception of each arrangement that includes development milestone payments, the Company evaluates the probability of reaching the milestones and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur in the future, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore revenue recognized is constrained as management is unable to assert that a reversal of revenue would not be possible. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues and earnings in the period of adjustment.

*Royalties* : For arrangements that include sales-based royalties, including milestone payments based on levels of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its collaboration agreements.

For the years ended December 31, 2018 and 2017, the Company's only revenue recognized is related to the Purdue Collaboration (see Note 3).

***Equity-based compensation***

The Company measures the cost of common stock option awards at fair value and records the cost of the awards, net of estimated forfeitures, on a straight-line basis over the requisite service period. The Company measures fair value for all common stock options using the Black-Scholes option-pricing model. For all common stock option awards to employees, the fair value measurement date is the date of grant and the requisite service period is the period over which the employee is required to provide service in exchange for the common stock option awards, which is generally the vesting period. For all common stock option awards to nonemployees, the Company remeasures fair value at each financial statement reporting date and recognizes compensation expense as services are rendered, generally on a straight-line basis.

***Segments and geographic information***

The Company has determined it has one reporting segment. Disaggregating the Company's operations is impracticable because the Company's research and development activities and its assets overlap and management reviews its business as a single operating segment. Thus, discrete financial information is not available by more than one operating segment. All long-lived assets of the Company are located in the United States.

***Deferred rent***

Deferred rent consists of rent escalation payment terms, tenant improvement allowances and other incentives received from the landlord related to the Company's operating lease and is presented in "Other noncurrent assets" in the accompanying balance sheet. Rent escalation represents the difference between actual operating lease payments

due and straight-line rent expense, which is recorded by the Company over the term of the lease. Tenant improvement allowances and other incentives are recorded as deferred rent and amortized as a reduction of periodic rent expense, over the term of the applicable lease.

***Research and development expense***

Research and development expense includes wages, benefits, research materials, external services, legal fees related to patent protection, overhead and other expenses directly related to research and development operations. Research and development costs are expensed as incurred in accordance with ASC 730, Research and Development. Research and development costs that are paid in advance of performance are deferred as a prepaid expense and recognized as expense as the services are provided.

***Income taxes***

From inception through July 9, 2015, the Company was a Delaware LLC for federal and state tax purposes and, therefore, all items of income or loss through July 9, 2015 flowed through to the members of AuraSense Therapeutics, LLC. Effective July 9, 2015, the Company converted from an LLC to a C corporation for federal and state income tax purposes. Accordingly, prior to the conversion to a C corporation, the Company did not record deferred tax assets or liabilities or have any net operating loss carryforwards. The Company recognizes deferred tax assets and liabilities for temporary differences between the financial reporting basis and the tax basis of its assets and liabilities and the expected benefits of net operating loss carryforwards. The impact of changes in tax rates and laws on deferred taxes, if any, is applied during the years in which temporary differences are expected to be settled and is reflected in the financial statements in the period of enactment. The measurement of deferred tax assets is reduced, if necessary, if, based on weight of the evidence, it is more likely than not that some, or all, of the deferred tax assets will not be realized. At December 31, 2018 and 2017, the Company established a full valuation allowance against its deferred tax assets to an amount that is more likely than not to be realized.

***Recently Adopted Accounting Pronouncements***

*Revenue Recognition*

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2014-09 (ASC 606), *Revenue from Contracts with Customers* . This ASU, as amended by ASU 2015-14, affects any entity that either enters into contracts with customers to transfer goods and services or enters into contracts for the transfer of nonfinancial assets. ASU 2014-09 replaces most existing revenue recognition guidance in GAAP when it becomes effective. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. In doing so, companies will need to use more judgment and make more estimates than under the currently effective guidance. These may include identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each separate performance obligation. ASU 2014-09 is effective for Exicure in the first quarter of 2018 and early adoption is permitted beginning in the first quarter of 2017. The Company adopted ASC 606 on a modified retrospective basis. See above "Revenue Recognition" for a discussion of the Company's updated policies related to revenue recognition effective January 1, 2018.

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*Impact of adoption of ASC 606*

The Company adopted ASC 606 using the modified retrospective method. The cumulative effect of applying the new guidance to all contracts with customers that were not completed as of January 1, 2018 was recorded as an adjustment to accumulated deficit as of the adoption date. As a result of applying the modified retrospective method to adopt the new guidance, the Company recorded reductions to both accumulated deficit and deferred revenue, current of $1,034 as of the date of adoption.

As a result of the adoption of ASC 606: (i) there were no impacts to the totals of our cash flows from operating activities, cash flows from investing activities, or cash flows from financing activities in the accompanying consolidated statement of cash flows for the year ended December 31, 2018; (ii) there were no impacts to the balances of the accompanying consolidated balance sheet as of December 31, 2018, and (iii) total revenue, operating loss, and net loss were lower by $1,034 each in the accompanying consolidated statement of operations for the year ended December 31, 2018.

*Cash Flows*

In August 2016, the FASB issued ASU 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments* . ASU 2016-15 addresses the classification of certain specific cash flow issues including debt prepayment or extinguishment costs, settlement of certain debt instruments, contingent consideration payments made after a business combination, proceeds from the settlement of certain insurance claims and distributions received from equity method investees. ASU 2016-15 is effective for the Company in the first quarter of 2018 and early adoption is permitted. An entity that elects early adoption must adopt all of the amendments in the same period. The Company adopted this guidance on January 1, 2018. The adoption of ASU 2016-15 did not have a material impact to the Company's statement of cash flows.

*Stock-Based Compensation*

In May 2017, the FASB issued ASU 2017-09, *Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting* . ASU 2017-09 clarifies when changes to the terms or conditions of a share-based payment award must be accounted for as modifications. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award changes as a result of the change in terms or conditions. ASU 2017-09 will be applied prospectively to awards modified on or after the adoption date. ASU 2017-09 is effective for the Company for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Early adoption is permitted. The Company adopted this guidance on January 1, 2018. The adoption of ASU 2017-09 did not have a material impact to the Company's financial statements.

***Recent Accounting Pronouncements Not Yet Adopted***

*Leases*

In February 2016, FASB issued ASU 2016-02, *Leases (Topic 842)* , which requires lessees to recognize right-of-use assets and lease liabilities on the balance sheet. ASU 2016-02 is to be applied using a modified retrospective approach at the beginning of the earliest comparative period in the financial statements. ASU 2016-02 will be effective for the Company beginning in the first quarter of 2019. ASU 2016-02 requires a modified retrospective transition approach for all leases existing at, or entered into after, the date of initial application, with an option to use certain transition relief. In July 2018, the FASB issued ASU 2018-11, *Leases (Topic 842): Targeted Improvements* ("ASU 2018-11"), which allows entities to initially apply the new lease guidance at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. We expect to adopt the new standard on January 1, 2019 and use the effective date as our date of initial application. Consequently, financial information will not be updated and the disclosures required under the new standard will not be provided for dates and periods before January 1, 2019. The Company is in the process of gathering a complete inventory of its lease contracts and evaluating the impact of the new guidance on its consolidated financial statements and related disclosures; however, management expects that the adoption of ASU 2016-02 will result in

(in thousands, except share and per share data)

the recognition of a right-of-use asset and related liability associated with the Company's non-cancelable operating lease arrangement for office and laboratory space that was executed in 2012 (see Note 12, *Commitments and Contingencies* ).

**3. Purdue Collaboration**

On December 2, 2016, the Company entered into a research collaboration, option and license agreement with Purdue and referred to herein as the "Purdue Collaboration." Purdue has the option to obtain from us the full worldwide development and commercial rights to AST-005 (the Company's therapeutic candidate that targets tumor necrosis factor), an option to obtain three additional collaboration targets and a further option to obtain from us the full worldwide development and commercial rights to any therapeutic candidates developed targeting the three additional collaboration targets. In connection with the Purdue Collaboration, the Company received a non-refundable development fee of $10,000 . The Company is eligible to receive up to $776,500 upon successful completion of certain research, regulatory and commercial sales milestones. The research milestones are payable upon target identification and IND-enabling pre-clinical development, per program, with an aggregate total of up to $16,500 . The regulatory milestones are payable upon the initiation or completion of clinical trials, and regulatory approval in the United States and outside the United States, per program, with an aggregate total of up to $410,000 . The commercial sales milestones are payable upon achievement of specified aggregate product sales thresholds and total up to $350,000 . In the event a therapeutic candidate subject to the collaboration results in commercial sales, the Company is eligible to receive royalties ranging from the low single digits to a maximum of 10% on future net sales of such commercialized therapeutic candidates.

In April 2018, Purdue notified the Company it had declined to exercise its option to develop AST-005 at that time and there are currently no active therapeutic candidates in development under the Purdue Collaboration. There can be no assurance that any research, regulatory and commercial sales milestones or royalties will be achieved as they are subject to highly significant risks and uncertainties, many of which are outside of our control.

Prior to the adoption of ASC 606, the upfront payment of $10,000 was accounted for pursuant to ASC 605 and was recorded as deferred revenue and recognized on a ratable basis over the estimated performance period of the relevant research and development activities. On January 1, 2018, in connection with the adoption of ASC 606, the Company recorded the unamortized deferred revenue of $1,034 as an adjustment to the beginning balance of retained deficit at January 1, 2018. See Note 2, *Significant Accounting Policies* , for more information related to the adoption of ASC 606.

The Company identified multiple performance obligations as part of the Purdue Collaboration agreement, including the upfront payment of $10,000 , discussed above, and the research and development services. The Company determined that the performance obligations should not be combined, the license should be recognized at the time the license is granted, and the research and development services should be recognized at the time the service is performed. The Purdue Collaboration agreement includes contingent promises related to specified research, development and regulatory milestones and sale-based milestones. Each contingent promise related to contingent and milestone payment is evaluated to determine whether it represents a material right. The Company recognizes any payment that is contingent upon the achievement of a substantive milestone entirely in the period in which it is determined that the revenue is not subject to a significant reversal. To date, the Company has not recognized any contingent payments in connection with the Purdue Collaboration agreement as revenue.

During the year ended December 31, 2018, the Company recognized collaboration revenue of $118 which consisted entirely of research and development activities that will be reimbursed by Purdue and is presented on a gross basis in the accompanying statement of operations. During the year ended December 31, 2017, the Company recognized collaboration revenue of $9,719 which included $1,443 of research and development activities that was reimbursed by Purdue and is presented on a gross basis in the accompanying statement of operations.

**4. Supplemental Balance Sheet Information**

***Property and equipment, net***

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Scientific equipment | $ 1,979 | $ 1,797 |
| Leasehold improvements | 192 | 192 |
| Furniture and fixtures | 41 | 31 |
| Computers and software | 26 | 26 |
| Construction in process | 12 | 120 |
| Property and equipment, gross | 2,250 | 2,166 |
| Less: accumulated depreciation | (1,189) | (849) |
| Property and equipment, net | $ 1,061 | $ 1,317 |

Depreciation and amortization expense was $358 and $232 , for the years ended December 31, 2018 and 2017, respectively.

***Accrued expenses and other current liabilities***

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Accrued legal expenses | $ 189 | $ 251 |
| Accrued payroll-related expenses | 899 | 718 |
| Accrued clinical, contract research and manufacturing costs | 102 | 205 |

| | | |
|---|---|---|
| Other accrued expenses | 353 | 99 |
| Accrued expenses and other current liabilities | $ 1,543 | $ 1,273 |

**5. Debt**

On February 17, 2016, the Company closed a $10,000 loan facility, with an initial advance against this loan facility of $6,000 , with Hercules Technology Growth Capital (“Hercules”). The loan bears a floating interest rate equal to the greater of either (i) 9.95% or (ii) the sum of 9.95% plus the United States prime rate minus 3.50% . Total proceeds net of fees and issuance costs were $5,839 . Fees and issuance costs of $161 , as well as fees of $231 that are payable to the lender at maturity, are recorded as a reduction in the carrying amount of long-term debt on our balance sheet and will be amortized to interest expense through the maturity date of September 1, 2019 using the effective interest method. Interest amounts were payable monthly beginning on March 1, 2016 through the maturity date of September 1, 2019 . Initially, principal amounts were payable monthly beginning on April 1, 2017 through the maturity date. In 2016, the Company met certain terms in the loan agreement so that principal amounts became payable monthly beginning on July 1, 2017.

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On January 15, 2018, the Company and Hercules amended its loan agreement so that amortization payments due for the thirteen (13) consecutive months commencing on December 1, 2017 through and including December 1, 2018 were deferred. Commencing on January 1, 2019, and continuing on the first business day of each month thereafter, the loan, including the deferred payments, was to begin amortizing in equal monthly installments of principal and interest based upon an amortization schedule equal to eighteen (18) consecutive months. Any remaining obligations under the loan agreement and other loan documents were due and payable on the maturity date on September 1, 2019.

On December 28, 2018, the Company and Hercules further amended its loan agreement so that interest amounts are payable on the first day of each business month and any remaining obligations under the loan agreement and other loan documents are due and payable on the maturity date on September 1, 2019.

The loan is collateralized by a security interest in all tangible assets. In addition, the Company is subject to certain financial reporting requirements and certain negative covenants requiring lender consent.

In connection with the February 2016 Hercules loan, Hercules also had the right to purchase 80,000 shares of Series C preferred stock at $3.00 per share under the terms of a warrant agreement with the Company. The preferred stock warrant liability was recorded at fair value at the date of issuance of February 17, 2016 in the amount of $134 and recorded as a reduction in the carrying amount of long-term debt on our balance sheet. This discount of $134 will be amortized to interest expense through the loan maturity date of September 1, 2019 using the effective interest method. The Company estimated the fair value of the preferred stock warrant liability at the end of each reporting period using the Black-Scholes model and recorded any changes in fair value to other income (expense), net on its statement of operations. See Note 10, *Fair Value Measurements* , for more information on the fair value of the preferred stock warrant liability. The warrant agreement to purchase shares of preferred stock was terminated on September 26, 2017 in connection with the Merger.

At December 31, 2018 and 2017, the aggregate carrying value of the current and noncurrent portion of long-term debt is $4,925 and $4,855 , respectively.

At December 31, 2018, the principal maturities of the long-term debt were as follows:

| | December 31, 2018 |
|---|---|
| 2019 | $ — |
| 2020 | 4,999 |
| Principal balance outstanding | 4,999 |
| less: unamortized discount | (69) |
| less: unamortized debt issuance costs | (5) |
| Long-term debt | 4,925 |
| Current portion | — |
| Noncurrent portion | $ 4,925 |

The Company paid interest on debt of $572 and $611 during the years ended December 31, 2018 and 2017, respectively.

Refer to Note 15, *Subsequent Events* , for more information on our loan agreement with Hercules.

**EXICURE, INC.**

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**6. Stockholders' Equity**

***Preferred Stock***

As of December 31, 2018 and 2017, the Company had 10,000,000 shares of preferred stock, par value $0.0001 authorized and no shares issued and outstanding.

***Common Stock***

As of December 31, 2018 and 2017, the Company had authorized 200,000,000 shares of common stock, par value $0.0001 . As of December 31, 2018, the Company had 44,358,000 shares issued and outstanding. As of December 31, 2017, the Company had 39,300,823 shares issued and outstanding.

The holders of shares of the Company's common stock are entitled to one vote per share on all matters to be voted upon by Exicure stockholders and there are no cumulative rights. Subject to preferences that may be applicable to any outstanding preferred stock, the holders of shares of the Company's common stock are entitled to receive ratably any dividends that may be declared from time to time by Exicure's board of directors (the "Board") out of funds legally available for that purpose. In the event of the Company's liquidation, dissolution or winding up, the holders of shares of Exicure common stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock then outstanding. Exicure common stock has no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to Exicure common stock. The outstanding shares of Exicure common stock are fully paid and non-assessable.

*August 2018 Private Placement*

On August 22, 2018, the Company entered into subscription agreements with several accredited investors, pursuant to which it agreed to issue and sell a total of 4,889,217 shares of the Company's common stock, at a purchase price of $4.50 per share, resulting in approximately $22,001 in gross proceeds to the Company (the "August 2018 Private Placement"). The aggregate net proceeds from the August 2018 Private Placement (after deducting placement agent fees and expenses of the offering of $1,931 ) were $20,070 .

The Company also entered into a registration rights agreement with the investors in the August 2018 Private Placement, which required it to file a "resale" registration statement with the SEC covering the shares issued in the August 2018 Private Placement within 30 calendar days from the final closing of the August 2018 Private Placement Offering. The Company filed and caused to become effective a registration statement with the SEC on October 5, 2018 registering the resale of 5,034,683 shares of our common stock, consisting of (i) 4,889,217 shares that were privately issued through the August 2018 Private Placement and (ii) 145,466 shares that were privately issued on February 1, 2018 in connection with consulting services.

In connection with the closing of the August 2018 Private Placement, the placement agents received an aggregate of $1,680 in cash placement fees, and the Company reimbursed up to $87 of expenses incurred by the placement agents in connection with this closing of the August 2018 Private Placement.

*2017 Private Placement*

On September 26, 2017, following the Effective Time of the Merger, the Company sold 6,767,360 shares of Exicure, Inc. common stock pursuant to an initial closing of a private placement offering (the "Offering") for up to 13,333,333 shares of Exicure, Inc. common stock at a purchase price of $3.00 per share (the "Offering Price"). The aggregate net proceeds from the initial closing of the Offering (after deducting placement agent fees and expenses of the initial offering of $3,037 ) were $17,235 .

On October 27, 2017 and November 2, 2017, Exicure entered into subscription agreements (the "Subscription Agreements") with several accredited investors (the "Investors") pursuant to which the Company agreed to issue and sell a total of 3,736,836 shares of the Company's common stock, par value $0.0001 per share (the "Shares")

resulting in approximately $11,211 in gross proceeds to the Company. These shares were issued in Subsequent Closings of the Offering for up to 13,333,333 shares of common stock (the "Maximum Amount") at a purchase price of $3.00 per share (the "Sale Price").

The Company has sold a total of 10,504,196 shares of common stock for a total of approximately $31,513 in connection with all closings of the Offering (before deducting placement agent fees and expenses which are estimated at $3,966 ) (the "2017 Private Placement"). Placement Agents have received an aggregate of $1,968 in cash placement fees and have received warrants to purchase an aggregate of 413,320 shares of Exicure common stock (the "Warrants") in connection with the 2017 Private Placement. The Warrants expire on March 27, 2021, have an exercise price of $3.00 per share, and have been issued on the same terms in all closings of the Offering. The warrants to purchase common stock are classified as a liability and presented as a dividend that offsets the gross proceeds of the 2017 Private Placement within the accompanying consolidated statement of changes in stockholders' equity. The common stock warrant liability will be remeasured each period at fair value. See Note 10, *Fair Value Measurements* for more information on the common stock warrant liability. The Placement Agents also received 50,000 shares of Exicure common stock in connection with all closings of the Offering.

Subject to certain customary exceptions, investors in the 2017 Private Placement have anti-dilution protection with respect to the shares of common stock sold in the Offering such that if within eighteen (18) months after the initial closing of the Offering the Company issues certain additional shares of common stock or common stock equivalents for a consideration per share less than the Offering Price (the "Lower Price"), each such investor will be entitled to receive from the Company additional shares of common stock in an amount such that, when added to the number of shares of common stock initially purchased by such investor in the Offering and still held of record and beneficially owned by such investor at the time of the dilutive issuance (the "Held Shares"), will equal the number of shares of common stock that such investor's aggregate purchase price for the Held Shares would have purchased at the Lower Price. Either (i) holders of a majority of the then Held Shares or (ii) a representative of the holders of the then Held Shares, which representative shall be appointed by the three investors who then hold the largest number of Held Shares, may waive the anti-dilution rights of all Offering investors with respect to a particular issuance by the Company.

This price-based anti-dilution protection automatically terminated on August 22, 2018 in connection with the August 2018 Private Placement.

The 2017 Private Placement was exempt from registration under Section 4(a)(2) of the Securities Act of 1933, as amended (the "Securities Act"), and Rule 506 of Regulation D promulgated by the SEC. The common stock in the Offering was sold to "accredited investors," as defined in Regulation D, and was conducted on a "reasonable best efforts" basis.

In connection with the Merger and the 2017 Private Placement, the Company entered into a Registration Rights Agreement, pursuant to which the Company has agreed that promptly, but no later than 60 calendar days from the final closing of the Offering, the Company will file a registration statement with the SEC, or the Registration Statement. Each Investor in the Subsequent Closing also entered into the same registration rights agreement signed by investors in the initial closing of the Offering, which requires that the Company file a "resale" registration statement with the SEC covering the shares of common stock and warrants issued in the 2017 Private Placement, certain other shares of common stock issued in connection with the Company's recently closed reverse merger, and shares held by the Company's pre-merger stockholders, within 60 calendar days from the final closing of the Offering. The Company filed and caused to become effective a registration statement with the SEC on February 6, 2018 registering the resale of 39,714,143 shares of our common stock issued in connection with the Reverse Merger and the 2017 Private Placement.

***Common Stock Warrants***

As discussed above, in connection with the 2017 Private Placement, placement agents received warrants to purchase an aggregate of 413,320 shares of Exicure common stock in connection with all closings of the 2017

**EXICURE, INC.**

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Private Placement. The Warrants expire on March 27, 2021, have an exercise price of $3.00 per share, and have been issued on the same terms in all closings of the 2017 Private Placement. The Warrants are classified as a liability. The common stock warrant liability is remeasured each period at fair value. As of December 31, 2018, Warrants to purchase 413,320 shares of common stock remain outstanding. See Note 10, *Fair Value Measurements* for more information on the fair value of the common stock warrant liability.

***The Merger***

On September 26, 2017, in connection with the Merger, each share of Exicure OpCo common and preferred stock (other than shares of Exicure OpCo's Series C preferred stock) issued and outstanding immediately prior to the closing of the Merger was converted into 0.49649 shares of Max-1's common stock, and each share of Exicure OpCo's Series C preferred stock issued and outstanding immediately prior to the closing of the Merger was converted into 0.7666652 shares of Max-1's common stock. As a result, an aggregate of 26,666,627 shares of the Max-1's common stock were issued to the holders of Exicure OpCo's capital stock, which is incremental to the 2,080,000 shares of Max-1's common stock that were outstanding immediately prior to the Merger. In addition, pursuant to the Merger Agreement options to purchase 7,414,115 shares of Exicure OpCo common stock issued and outstanding immediately prior to the closing of the Merger were assumed by Max-1 and converted into options to purchase 3,680,997 shares of the Max-1's common stock.

***Other - Prior to the Merger***

*Series C Preferred Stock*

On January 11, 2016, the Company sold 149,999 shares of its Series C preferred stock at a price of $3.00 per share. Total gross proceeds raised thereby were $450 . Net proceeds after associated costs and expenses of $6 were $444 .

*Liquidation preference* . The Series C preferred stock were senior to the Class A and Class B preferred stock and common stock in rights and privileges as established in the Exicure OpCo Operating Agreement. Principal among the rights of Class C preferred stock was the creation of the Class C liquidation preference whereby, in the event of a liquidation event (i.e., a liquidation, dissolution or winding up of the Company or a sale of the Company), the Class C preferred stock holders were entitled to receive 1.5 times the aggregate cash contribution of all holders of Class C preferred units/stock.

**7. Equity-Based Compensation**

On September 22, 2017, the Board adopted and Exicure's stockholders approved the Exicure, Inc. 2017 Equity Incentive Plan (the "2017 Plan"), which became effective on November 15, 2017. The 2017 Plan provides for the issuance of incentive awards of up to 5,842,525 shares of Exicure common stock, which includes 2,169,905 shares of Exicure common stock to be issued to officers, employees, consultants and directors, plus a number of shares not to exceed 3,683,817 that are subject to issued and outstanding awards under the Exicure OpCo 2015 Equity Incentive Plan (the "2015 Plan") and were assumed in the Merger. Awards that may be awarded under the 2017 Plan include non-qualified and incentive stock options, stock appreciation rights, bonus shares, restricted stock, restricted stock units, performance units and cash-based awards. The 2017 Plan also provides that the number of shares reserved for issuance thereunder will be increased annually on the first day of each year beginning in 2020 by the least of 4,600,000 shares, five percent ( 5% ) of the shares of Exicure common stock outstanding on the last day of the immediately preceding year, or a lesser number of shares as determined by the Company's compensation committee. No future awards will be made under the 2015 Plan upon the effectiveness of the 2017 Plan. As of December 31, 2018, the aggregate number of common stock options available for grant under the 2017 Equity Incentive Plan was 928,443 .

The common stock options are contingent on the participants' continued employment or provision of non-employee services and are subject to forfeiture if employment or continued service terminates for any reason. The initial stock option grant to an employee, director or consultant vests 25% on the first 12-month anniversary of the

(in thousands, except share and per share data)

grant date and vests 1/48th monthly thereafter until fully vested at the end of 48 months . Subsequent stock option grants vest 1/48th monthly until fully vested at the end of 48 months . The term of common stock option grants is ten years unless terminated earlier as described above.

Equity-based compensation expense is classified in the statements of operations as follows:

| | Year Ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Research and development expense | $ 485 | $ 172 |
| General and administrative expense | 1,324 | 1,290 |
| | $ 1,809 | $ 1,462 |

Unamortized equity-based compensation expense at December 31, 2018 was $3,172 , which is expected to be amortized over a weighted-average period of 2.5 years .

The Company utilizes the Black-Scholes option-pricing model to determine the fair value of common stock option grants. The Black-Scholes option-pricing model was developed for use in estimating the fair value of traded options that have no vesting restrictions and are fully transferable. The model also requires the input of highly subjective assumptions. In addition to an assumption on the expected term of the option grants as discussed below, application of the Black-Scholes model requires additional inputs for which we have assumed the values described in the table below:

| | Year Ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Expected term | 5.3 to 6.0 years | 5.3 to 6.5 years |
| Risk-free interest rate | 2.72% to 2.87%; weighted avg. 2.78% | 1.97% to 2.17%; weighted avg. 2.07% |
| Expected volatility | 78.1% to 82.4%; weighted avg. 80.6% | 80.8% to 83.1%; weighted avg. 81.0% |
| Forfeiture rate | 5% | 5% |
| Expected dividend yield | —% | —% |

The expected term is based upon the “simplified method” as described in Staff Accounting Bulletin Topic 14.D.2. Currently, the Company does not have sufficient experience to provide a reasonable estimate of an expected term of its common stock options. The Company will continue to use the “simplified method” until there is sufficient experience to provide a more reasonable estimate in conformance with ASC 718-10-30-25 through 30-26. The risk-free interest rate assumptions were based on the U.S. Treasury bond rate appropriate for the expected term in effect at the time of grant. The expected volatility is based on calculated enterprise value volatilities for publicly traded companies in the same industry and general stage of development. The estimated forfeiture rates were based on historical experience for similar classes of employees. The dividend yield was based on expected dividends at the time of grant.

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The fair value of the underlying common stock and the exercise price for the common stock options granted during the years ended December 31, 2018 and 2017 are summarized in the table below:

| Common Stock Options Granted During Period Ended: | Fair Value of Underlying Common Stock | Exercise Price of Common Stock Option |
|---|---|---|
| | $3.00 to $5.82; weighted avg. | $3.00 to $5.82; weighted avg. |
| Year ended December 31, 2018 | $3.45 | $3.45 |
| Year ended December 31, 2017 | $4.21 | $4.21 |

The weighted-average grant date fair value of common stock options granted in the years ended December 31, 2018 and 2017 was $2.40 and $2.92 per common stock option, respectively.

A summary of common stock option activity as of the periods indicated is as follows:

| | Options | Weighted-Average Exercise Price | Weighted-Average Remaining Contractual Term (years) | Aggregate Intrinsic Value (thousands) |
|---|---|---|---|---|
| Outstanding - December 31, 2017 | 3,672,620 | $ 1.79 | 7.5 | $ 5,221 |
| Granted | 1,277,744 | 3.45 | | |
| Exercised | (22,494) | 1.81 | | |
| Forfeited | (36,282) | 2.29 | | |
| Outstanding - December 31, 2018 | 4,891,588 | $ 2.22 | 7.3 | $ 7,330 |
| Exercisable - December 31, 2018 | 3,238,798 | $ 1.70 | 6.7 | $ 6,352 |
| Vested and Expected to Vest - December 31, 2018 | 4,799,984 | $ 2.20 | 7.3 | $ 7,287 |

The aggregate intrinsic value of common stock options exercised during the years ended December 31, 2018 and 2017 was $44 and $202 , respectively.

**8. Income Taxes**

Pretax loss before income taxes was $22,413 and $11,011 for the years ended December 31, 2018 and 2017, respectively, which consists entirely of losses in the U.S. and resulted in no provision for income tax expense during the years then ended.

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The differences between income taxes computed using the U.S. federal income tax rate and the provision for income taxes are as follows:

| | Year Ended December 31, | | | |
|---|---|---|---|---|
| | 2018 | | 2017 | |
| Federal income tax expense at statutory rate | $ (4,707) | 21.0 % | $ (4,093) | 34.0 % |
| State income tax expense at statutory rate | (1,595) | 7.1 | (610) | 5.1 |
| Permanent differences | 243 | (1.1) | (125) | 1.0 |
| Impact of Tax Reform Act | — | — | 3,760 | (31.2) |
| Other | — | — | (10) | 0.1 |
| Change in valuation allowance | 6,059 | (27.0) | 1,078 | (9.0) |
| | $ — | — % | $ — | — % |

The Company's effective income tax rate for the years ended December 31, 2018 and 2017 is 0% because the Company has generated tax losses and has provided a full valuation allowance against its deferred tax assets to an amount that is more likely than not to be realized.

The significant components of the Company's net deferred tax assets are as follows:

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| ***Deferred Tax Assets*** | | |
| Net operating losses | $ 14,827 | $ 8,748 |
| Intangibles | 187 | 205 |
| Accrued expenses | 271 | 198 |
| Equity-based compensation | 796 | 728 |
| Deferred revenue | — | 295 |
| Other | 204 | — |
| Less: Valuation allowance | (16,225) | (10,166) |
| Total deferred tax assets | 60 | 8 |
| ***Deferred Tax Liabilities*** | | |
| Fixed assets and other | (60) | (8) |
| Total deferred tax liabilities | (60) | (8) |
| Deferred taxes, net | $ — | $ — |

The Company has recorded a full valuation allowance against its deferred tax assets to an amount that is more likely than not to be realized at December 31, 2018 and 2017. This determination is based on significant negative evidence, including:

- *Cumulative losses:* The Company has been in a significant cumulative loss position since its inception in 2011.
- *Projected realization of net operating loss carry forward amounts:* Projections of future pre-tax book loss and taxable losses based on the Company's recent actual performance and current industry data indicate it is more likely than not that the benefits will not be recognized.

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On December 22, 2017, the President of the United States signed into law the Tax Reform Act. The legislation significantly changes U.S. tax law by, among other things, lowering corporate income tax rates, implementing a modified territorial tax system and imposing a repatriation tax on deemed repatriated earnings of foreign subsidiaries. The Tax Reform Act permanently reduces the U.S. corporate income tax rate from a maximum of 35% to a flat 21% rate, effective January 1, 2018. The Company's U.S. deferred tax assets, net of deferred tax liabilities, were remeasured at December 31, 2017 and reduced by $3,760 , entirely offset by a valuation allowance reduction. As a result, the remeasurement of the Company's deferred tax assets, net of deferred tax liabilities, including the valuation allowance, did not impact the Company's income tax expense or net loss.

At December 31, 2018, the Company had a federal net operating loss carryforward of $52,629 which will begin to expire in 2035. The Company has $50,294 of state net operating loss carryforwards which will begin to expire in 2027.

At December 31, 2018 and 2017, the Company had no unrecognized tax benefits. The Company's estimate of the potential outcome of any uncertain tax position is subject to management's assessment of relevant risks, facts and circumstances existing at that time. The Company evaluates uncertain tax positions to determine if it is more-likely-than-not that they would be sustained upon examination. The Company recognizes interest and penalties related to unrecognized tax benefits in the provision for income taxes.

The Company is subject to taxation in the U.S. and various state jurisdictions. The Company remains subject to examination by U.S. federal and state tax authorities for the years 2015 through 2018. There are no pending examinations in any jurisdiction.

**9. Loss Per Common Share**

Basic loss per common share is calculated by dividing net loss by the weighted-average number of shares of common stock outstanding during the period. Diluted loss per common share is calculated using the treasury share method by giving effect to all potentially dilutive securities that were outstanding. Potentially dilutive options and warrants to purchase common stock that were outstanding during the periods presented were excluded from the diluted loss per share calculation because such shares had an anti-dilutive effect due to the net loss reported in those periods. Therefore, basic and diluted loss per common share is the same for each of the years ended December 31, 2018 and 2017.

The following is the computation of loss per common share for the years ended December 31, 2018 and 2017:

| | Year Ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Net loss | $ (22,413) | $ (11,011) |
| Weighted-average basic and diluted common shares outstanding | 41,189,177 | 10,119,569 |
| Loss per share - basic and diluted | $ (0.54) | $ (1.09) |

The outstanding securities presented below were excluded from the calculation of net loss per common share, because such securities would have been anti-dilutive due to the Company's net loss per share during the periods ending on the dates presented:

(in thousands, except share and per share data)

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Options to purchase common stock | 4,891,588 | 3,672,620 |
| Warrants to purchase common stock | 413,320 | 413,320 |

**10. Fair Value Measurements**

ASC Topic 820, Fair Value Measurement, establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value, as follows: Level 1 Inputs - unadjusted quoted prices in active markets for identical assets or liabilities accessible to the reporting entity at the measurement date; Level 2 Inputs - other than quoted prices included in Level 1 inputs that are observable for the asset or liability, either directly or indirectly, for substantially the full term of the asset or liability; and Level 3 Inputs - unobservable inputs for the asset or liability used to measure fair value to the extent that observable inputs are not available, thereby allowing for situations in which there is little, if any, market activity for the asset or liability at measurement date.

The Company uses the market approach and Level 1 inputs to value its cash equivalents.

The Company's long-term debt bore interest at the prevailing market rates for instruments with similar characteristics and, accordingly, the carrying value for this instrument also approximates its fair value and the financial measurement is also classified within Level 2 of the fair value hierarchy.

The Company's common stock warrant liability (refer to Note 6, *Stockholders' Equity* , for more information) and preferred stock warrant liability (terminated on September 26, 2017 in connection with the Merger; see Note 5, *Debt* , for more information) are classified within Level 3 of the fair value hierarchy. The fair values of the common stock warrant liability and preferred stock warrant liability were determined using the Black-Scholes option-pricing model.

The fair value of the common stock warrant liability is based significantly on the fair value of the Company's common stock. At the date of issuance, the common stock warrant liability was determined using the following weighted-average assumptions: expected term of 2.0 years , risk-free interest rate of 1.53% , expected volatility of 78.97% , and no expected dividends.

The fair value of the preferred stock warrant liability was based significantly on the fair value of the Series C preferred stock, which was developed using unobservable inputs, which are classified within Level 3. At the date of issuance, the preferred stock warrant liability was determined using the following assumptions: expected term of 5.0 years , risk-free interest rate of 1.26% , expected volatility of 62.99% , and no expected dividends. In connection with the Merger, the warrants to purchase preferred stock were terminated and therefore the related liability was reduced to zero during 2017.

The following weighted-average assumptions were used to estimate the fair value of the common stock warrant liability at December 31, 2018:

| | December 31, 2018 |
|---|---|
| Expected term | 2.3 |
| Risk-free interest rate | 2.46% |
| Expected volatility | 86.74% |
| Expected dividend yield | —% |

A 10% change in the estimate of expected volatility at December 31, 2018 would increase or decrease the fair value of the common stock warrant liability in the amount of $53 . A 10% change in the estimate of fair value of the

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common stock at December 31, 2018 would increase or decrease the fair value of the common stock warrant liability in the amount of $118 .

The following is a reconciliation of the Company's liabilities measured at fair value on a recurring basis using unobservable inputs (Level 3) for the years ended December 31, 2018 and 2017:

| | Fair Value Measurements Using Significant Unobservable Inputs (Level 3) | | |
|---|---|---|---|
| | Preferred Stock Warrant Liability | Common Stock Warrant Liability | Total |
| Balance at January 1, 2017 | $ 201 | $ — | $ 201 |
| Additions | — | 536 | 536 |
| Gain included in other income (expense), net | (201) | (13) | (214) |
| Balance at December 31, 2017 | $ — | $ 523 | $ 523 |
| Loss included in other income (expense), net | — | 274 | 274 |
| Balance at December 31, 2018 | $ — | $ 797 | $ 797 |

**11. Defined Contribution Plan**

Exicure maintains a defined contribution savings plan for the benefit of its employees. During 2018, Exicure began contributing to the defined contribution plan. Company contributions are determined under various formulas. The expense recognized for this plan was $107 for the year ended December 31, 2018.

**12. Commitments and Contingencies**

***Leases***

The Company conducts all operations in a facility under an operating lease which commenced in March 2012 and was originally scheduled to end in February 2015. The lease was extended for an additional six years through February 2021 during the first quarter of 2014 and includes a renewal option. During the second quarter of 2016, the Company amended the lease agreement to include additional space to be used primarily for administrative functions effective in May 2016. Lease payments include a fixed payment amount as well as contingent payments related to a proportionate share of operating and real estate expenses. At the inception of the lease, the lessor paid for leasehold improvements totaling $52 which has been capitalized and is being amortized over the lease term. The fixed payment amounts, including those in connection with the amended lease agreement in the second quarter of 2016, increase over the term of the lease but rent expense is recognized on a straight-line basis resulting in the recognition of deferred rent liability of $39 and $48 as of December 31, 2018 and December 31, 2017, respectively, calculated on the basis of the extended lease agreement.

Rent expense consisted of the following:

| | Years Ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Straight-line rent expense | $ 332 | $ 332 |
| Contingent rent expense | 298 | 281 |
| Total rent expense | $ 630 | $ 613 |

(in thousands, except share and per share data)

Future minimum lease payments as of December 31, 2018 are as follows:

| Years Ending December 31, | Operating Leases |
|---|---|
| 2019 | 347 |
| 2020 | 353 |
| 2021 | 59 |
| Thereafter | — |
| Total | $ 759 |

***Northwestern University License Agreements***

On December 12, 2011, (1) AuraSense, LLC assigned to the Company all of its worldwide rights and interests under AuraSense, LLC's 2009 license agreement with Northwestern University ("NU") in the field of the use of nanoparticles, nanotechnology, microtechnology or nanomaterial-based constructs as therapeutics or accompanying therapeutics as a means of delivery, but expressly excluding diagnostics (the "assigned field"); (2) in accordance with the terms and conditions of this assignment, the Company assumed all liabilities and obligations of AuraSense, LLC as set forth in its license agreement in the assigned field; and (3) in order to secure this assignment and the patent rights from NU, the Company agreed (i) to pay NU an annual license fee, which may be credited against any royalties due to NU in the same year, (ii) to reimburse NU for expenses associated with the prosecution and maintenance of the license patent rights, (iii) to pay NU royalties based on any net revenue generated by the Company's sale or transfer of any licensed product, and (iv) to pay NU, in the event the Company grants a sublicense under the licensed patent rights, the greater of a percentage of all sublicensee royalties or a percentage of any net revenue generated by a sublicensee's sale or transfer of any licensed product. In August 2015, we entered into a restated license agreement with NU (the "restated license agreement"). In February 2016, we obtained exclusive license as to NU's rights in certain SNA technology we jointly own with NU. Our license to NU's rights is limited to the assigned field, however we have no such limitation as to our own rights in this jointly owned technology. In June 2016, we entered into an exclusive license with NU to obtain worldwide rights to certain inhibitors of glucosylceramide synthase and their use in wound healing in diabetes. Our rights and obligations in these 2016 agreements are substantially the same as in the restated license agreement from August 2015 (collectively referred to as "the Northwestern University License Agreements"). As of December 31, 2018, the Company has paid to NU an aggregate of $3,864 in consideration of each of the obligations described above.

**13. Related-Party Transactions**

Since its inception in 2011, the Company has shared facilities, certain staff members and certain operating expenses with AuraSense, LLC, our former parent and largest stockholder. On an infrequent basis, the Company also pays certain expenses directly on behalf of AuraSense, LLC which are related to AuraSense, LLC's grants, and AuraSense, LLC sometimes pays expenses directly on behalf of the Company. These costs are summarized and directly billed between the Company and AuraSense, LLC on a quarterly basis. In addition, certain expense and administrative activities are shared between the Company and AuraSense, LLC. Effective January 1, 2016, the Company and AuraSense, LLC amended its shared services agreement to simplify the billing arrangement. Under the amended shared services agreement, the Company bills AuraSense, LLC $8 per quarter for indirect costs incurred by the Company plus a specified rate for hours worked by Company scientists on projects directly related to AuraSense, LLC. The amended shared services arrangement continues to require direct non-labor expenses incurred by the Company to be billed to AuraSense, LLC. Effective January 1, 2017, the Company and AuraSense, LLC further amended its shared services agreement so that the quarterly fee related to administrative activities billed by the Company to AuraSense, LLC be reduced to $3 per quarter. This decrease was to reflect the current and expected future reduction in administrative activities to be provided by the Company to AuraSense, LLC.

The amounts due from AuraSense, LLC in connection with the above mentioned activities were $10 and $17 at December 31, 2018 and 2017, respectively.

EXICURE, INC.

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

The following is a summary of amounts billed to AuraSense, LLC and recognized in the accompanying consolidated statement of operations in connection with the above mentioned activities:

| | For the Years Ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Quarterly fee for indirect costs | $ 12 | $ 12 |
| Direct costs of AuraSense LLC paid by the Company | 26 | 5 |
| | $ 38 | $ 17 |

The Company received consulting services from, and paid fees to, one of its co-founders who is not an employee but serves as a member of the Board. The Company paid $100 in each of the years ended December 31, 2018 and 2017 in connection with these consulting services and these amounts are recognized as an expense in the accompanying consolidated statement of operations.

**14. Quarterly Financial Data (Unaudited)**

Selected quarterly financial data for the years ended December 31, 2018 and 2017 are as follows:

| | 2018 | | | |
|---|---|---|---|---|
| | First Quarter | Second Quarter | Third Quarter | Fourth Quarter |
| Revenue (1) | 36 | 19 | 57 | 6 |
| Net loss (1)(2) | (5,509) | (6,825) | (5,324) | (4,755) |
| Basic and diluted loss per common share (3) | $ (0.14) | $ (0.17) | $ (0.13) | $ (0.11) |

| | 2017 | | | |
|---|---|---|---|---|
| | First Quarter | Second Quarter | Third Quarter | Fourth Quarter |
| Revenue | 2,432 | 2,695 | 2,497 | 2,095 |
| Net loss | (2,652) | (2,984) | (1,932) | (3,443) |
| Basic and diluted loss per common share (3) | $ (15.62) | $ (15.70) | $ (1.12) | $ (0.09) |

(1) - As discussed in Note 2, *Significant Accounting Policies - Recently Adopted Accounting Pronouncements* , the Company adopted ASC 606 on a modified retrospective basis effective January 1, 2018. As a result of the adoption of ASC 606, total revenue and net loss were lower by $1,034 each in the three months ended March 31, 2018.

(2) - Net loss includes a non-cash unrealized (loss) gain related to the fair value adjustment of the common stock warrant liability of ($128) , ($915) , $581 , and $186 in the three months ended March 31, 2018, June 30, 2018, September 30, 2018, and December 31, 2018, respectively.

(3) - As discussed in Note 1, *Description of Business and Basis of Presentation - The Merger* , shares of preferred stock issued and outstanding immediately prior to the closing of the Merger were converted into an aggregate of 26,476,543 shares of common stock. As such, these shares of common stock are included in the computation of basic and diluted loss per common share beginning with September 26, 2017 and

excluded from the computation of basic and diluted loss per common share for dates prior to September 26, 2017.

## 15. Subsequent Events

The Company has evaluated subsequent events which may require adjustment to or disclosure in the accompanying consolidated financial statements and has concluded that, other than the Hercules loan amendment and license agreement with Dermelix disclosed below, there are no subsequent events or transactions that occurred subsequent to the balance sheet date that would require recognition or disclosure in the accompanying consolidated financial statements.

***Hercules loan amendment***

On March 8, 2019, the Company and Hercules amended its loan agreement so that the maturity date of its loan agreement is extended to March 1, 2020 and amortization payments are deferred to, and payable at, the new maturity date of March 1, 2020.

***Dermelix license agreement***

On February 17, 2019, Exicure entered into a License and Development Agreement (the "Dermelix License Agreement") with Dermelix, LLC d/b/a Dermelix Biotherapeutics ("Dermelix"). Pursuant to the Dermelix License Agreement, the Company granted to Dermelix exclusive, worldwide royalty-bearing license rights to, develop, manufacture, have manufactured, use and commercialize the Company's spherical nucleic acid ("SNA") technology for the treatment of Netherton Syndrome ("NS") and, at Dermelix's option, up to five additional specified orphan diseases that are within the dermatology field. Upon written notice to the Company, Dermelix may exercise its option at any time following the effective date of the Dermelix License Agreement until the date that is six (6) years from the date that the first collaboration SNA therapeutic achieves first dosing in humans in a Phase 1 clinical trial for NS.

Dermelix will initially seek to develop a targeted therapy for the treatment of NS. Under the terms of the Dermelix License Agreement, the Company will be responsible for conducting the early stage development for each indication up to IND enabling toxicology studies. Dermelix will assume subsequent development, commercial activities and financial responsibility for such indications. Dermelix will pay the costs and expenses of development and commercialization of any licensed products under the Dermelix License Agreement, including the Company's expenses incurred in connection with development activities and in accordance with the development budget. Under the terms of the Dermerlix License Agreement, Exicure received an upfront payment of $1,000 , to be applied against the initial $1,000 of the Company's development expenses. If Dermelix exercises any of its option rights for additional indications, Dermelix will pay an option exercise fee equal to $1,000 for each exercised option (each, an "Option Exercise Fee"). Any Option Exercise Fee will be applied against the Company's development expenses with respect to the particular indication for which the option was exercised.

Pursuant to the Dermelix License Agreement, the Company shall have the right to pursue the development and commercialization of SNA technology for the treatment of orphan diseases which are neither NS nor one of the additional specified orphan diseases selected by Dermelix pursuant to its option rights. If the Company commences development activities of SNA technology for the treatment of such an orphan disease, the Company will notify Dermelix in writing of such development and Dermelix will have thirty (30) days following receipt of such notice to use one of its remaining option rights on such orphan disease. If Dermelix does not use one of its remaining option rights on such orphan disease, or has no option rights remaining, then the Company will have no further obligations to Dermelix with respect to the development of SNA therapeutics for such orphan disease and shall be free to continue commercialization and development activities with respect thereto.

For each of NS as well as any additional licensed product for which Dermelix exercises one of its options, the Company shall be eligible to receive additional cash payments totaling up to $13,500 upon achievement of certain development and regulatory milestones and up to $152,500 upon achievement of certain sales milestones. In addition, the Company will receive low double-digit royalties on annual net sales for such licensed products.

The Dermelix License Agreement will remain in effect, unless terminated earlier, until the last-to-expire royalty term under the Dermelix License Agreement. Each party has the right to terminate the Dermelix License Agreement for the other party's material breach of its obligations or representations and warranties under the Dermelix License Agreement, subject to cure rights. Additionally, Dermelix may terminate the Dermelix License Agreement in its sole discretion and in its entirety with specified prior written notice. The Company may also terminate the Dermelix License Agreement in part with respect to a particular indication if Dermelix fails to pay a development milestone payment following non-achievement of a development milestone. Upon termination of the term with respect to a particular licensed product, the license for such product will convert to a fully-paid, royalty-free, irrevocable, perpetual, exclusive and sublicensable license. Upon termination of the Dermelix License Agreement by Dermelix for convenience, by the Company following non-achievement of a development milestone, or by either party for the other's breach or bankruptcy, all licenses granted by the Company to Dermelix will terminate.

The Dermelix License Agreement includes customary representations and warranties on behalf of both the Company and Dermelix, including representations and operative provisions as to the licensed intellectual property. The Dermelix License Agreement also provides for certain mutual indemnities for breaches of representations, warranties and covenants.

Upon a change of control of the Company, Dermelix will have 90 days to exercise any of its remaining options for additional indications, and any options that are not exercised within such 90 -day period will lapse. Either party may assign the Dermelix License Agreement or delegate its obligations to an affiliate or to a successor without the consent of the other party.

**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***

As we are an emerging growth company and a newly public company, we have not engaged an independent registered public accounting firm to perform an audit of our internal control over financial reporting as of any balance sheet date in our condensed consolidated interim financial statements. Our compliance with Section 404 of the Sarbanes-Oxley Act first became subject to management's assessment regarding internal control over financial reporting in connection with the filing of our Annual Report on Form 10-K for the fiscal year ending December 31, 2018, and we will not be required to have an independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting until the filing of our first Annual Report on Form 10-K after we lose emerging growth company status, which may not be until the 2022 Annual Report on Form 10-K.

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2018. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to its management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. 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. Based on the evaluation of our disclosure controls and procedures as of December 31, 2018, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were effective.

***Changes in Internal Control over Financial Reporting***

During the preparation of our financial statements for the period ended March 31, 2018, we concluded that our disclosure controls and procedures were not effective to provide reasonable assurance that all information required to be disclosed in reports filed or submitted under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, due to a material weakness in internal control over financial reporting. The material weakness related to a deficiency in the Company's information and communication controls, which led to ineffectively designed controls over management's review of certain research and development contracts to ensure expenses were recognized as incurred by third-party contract research organizations. Specifically these ineffectively designed controls, which arose in a prior period and were identified in the quarter ended March 31, 2018, resulted in an immaterial error, which we corrected in previously issued financial statements beginning with those included in our Quarterly Reports on Form 10-Q for the period ended March 31, 2018 and as further discussed in Note 1 to the accompanying consolidated financial statements.

During the periods subsequent to March 31, 2018, we worked towards remediation of the deficiencies that led to the material weakness by enhancing the information used for periodic assessment of contract progress and increasing the frequency of communication in the process for accounting for certain research and development contracts with contract research organization s to ensure expenses are recognized as incurred. As of December 31, 2018, we believe that the applicable remedial controls have operated for a sufficient period of time and therefore management has concluded that the material weakness discussed above is remediated at December 31, 2018.

Other than the remedial controls discussed above, no changes occurred in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange

Act during the fiscal quarter ended December 31, 2018 that have materially affected, or are reasonably likely to materially affect, our 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 and not set forth below will be set forth in the definitive proxy statement for our 2019 Annual Meeting of Stockholders to be filed with the SEC pursuant to Regulation 14A , or the Proxy Statement, not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics applicable to all employees, including the principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions. The Code of Business Conduct and Ethics is posted on our website at *www.exicuretx.com* . Amendments to, and waivers from, the Code of Business Conduct and Ethics that apply to any of these officers, or persons performing similar functions, and that relate to any element of the code of ethics definition enumerated in Item 406(b) of Regulation S-K will be disclosed at the website address provided above and, to the extent required by applicable regulations, on a current report on Form 8-K.

**Item 11. Executive Compensation.**

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

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

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

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

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

**Item 14. Principal Accounting Fees and Services.**

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

## PART IV

**Item 15. Exhibits, Financial Statement Schedules.**

(a) The following documents are filed as part of this report:

1. Financial Statements

See Index to Financial Statements on page 100 of this Annual Report on Form 10-K.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

Except as so indicated in Exhibit 32.1, the following exhibits are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

| Exhibit Number | Exhibit Description | Filed with this Report | Incorporated by Reference herein from Form or Schedule | Filing Date | SEC File/Reg. Number |
|---|---|---|---|---|---|
| 2.1† | Agreement and Plan of Merger and Reorganization, dated September 26, 2017, by and among Max-1 Acquisition Corporation, Max-1 Acquisition Sub, Inc., a Delaware corporation and wholly-owned subsidiary of the Company, and Exicure OpCo, a Delaware corporation. | | 8-K (Exhibit 2.1) | 10/2/2017 | 000-55764 |
| 3.1 | Certificate of Merger relating to the merger of Max-1 Acquisition Sub., Inc. with and into Exicure OpCo, filed with the Secretary of State of the State of Delaware on September 26, 2017. | | 8-K (Exhibit 3.1) | 10/2/2017 | 000-55764 |
| 3.2 | Certificate of Amendment to Certificate of Incorporation, filed with the Secretary of State of the State of Delaware on September 26, 2017. | | 8-K (Exhibit 3.2) | 10/2/2017 | 000-55764 |
| 3.3 | Form of Amended and Restated Certificate of Incorporation, as filed with the Secretary of State of the State of Delaware on November 15, 2017. | | 8-K (Exhibit 3.3) | 10/2/2017 | 000-55764 |
| 3.4 | Amended and Restated Bylaws, as currently in effect. | | 8-K (Exhibit 3.4) | 10/2/2017 | 000-55764 |
| 4.1 | Form of Warrant to Purchase Shares of Common Stock issued to Placement Agent. | | 8-K (Exhibit 4.1) | 10/2/2017 | 000-55764 |
| 4.2 | Form of Registration Rights Agreement by and among the Company and the persons named therein. | | 8-K (Exhibit 4.2) | 10/2/2017 | 000-55764 |
| 4.3 | Form of Registration Rights Agreement by and among the Company and the persons named therein. | | 8-K (Exhibit 4.1) | 8/28/2018 | 000-55764 |
| 10.1+ | 2015 Equity Incentive Plan and forms of awards thereunder, assumed in the Merger. | | 8-K (Exhibit 10.1) | 10/2/2017 | 000-55764 |
| 10.2+ | 2017 Equity Incentive Plan and forms of award agreements thereunder. | | 8-K (Exhibit 10.2) | 10/2/2017 | 000-55764 |
| 10.3+ | 2017 Employee Stock Purchase Plan. | | 8-K (Exhibit 10.3) | 10/2/2017 | 000-55764 |
| 10.4+ | Form of Indemnification Agreement by and between the Company and each of its directors and executive officers. | | 8-K (Exhibit 10.4) | 10/2/2017 | 000-55764 |
| 10.5 | Form of Subscription Agreement by and between the Company and each investor in the initial closing of the 2017 Private Placement. | | 8-K (Exhibit 10.5) | 10/2/2017 | 000-55764 |
| 10.6+ | Form of Amended and Restated Board Member Service Agreement by and between Exicure OpCo and each of its non-executive directors. | | 8-K (Exhibit 10.6) | 10/2/2017 | 000-55764 |

| | | | | | |
|---|---|---|---|---|---|
| 10.7+ | Employment Agreement dated as of February 2, 2016 by and between Exicure OpCo and David A. Giljohann, Ph.D. | | 8-K (Exhibit 10.7) | 10/2/2017 | 000-55764 |
| 10.8+ | Amended and Restated Employment Agreement dated as of February 2, 2016 by and between Exicure OpCo and David S. Snyder. | | 8-K (Exhibit 10.8) | 10/2/2017 | 000-55764 |
| 10.9+ | Employment Offer Letter dated as of September 16, 2015 by and between Exicure OpCo and Ekambar Kandimalla, Ph.D. | | 8-K (Exhibit 10.9) | 10/2/2017 | 000-55764 |
| 10.10+ | First Amendment to Offer Letter dated as of January 8, 2016 by and between Exicure OpCo and Ekambar Kandimalla, Ph.D. | | 8-K (Exhibit 10.10) | 10/2/2017 | 000-55764 |
| 10.11+ | Offer Letter dated as of January 18, 2018 by and between Exicure, Inc. and Matthias G. Schroff, Ph.D. | | 10-Q (Exhibit 10.1) | 5/15/18 | 000-55764 |
| 10.12+ | Consulting Agreement dated as of October 1, 2011 by and between AuraSense Therapeutics, LLC and Chad A. Mirkin, Ph.D. | | 8-K (Exhibit 10.11) | 10/2/2017 | 000-55764 |
| 10.13 | Lease Agreement dated as of February 13, 2012 by and between AuraSense Therapeutics, LLC and FC Skokie SPE, LLC. | | 8-K (Exhibit 10.12) | 10/2/2017 | 000-55764 |
| 10.14 | Letter dated as of March 12, 2012 regarding the Lease Agreement by and between AuraSense Therapeutics, LLC and FC Skokie SPE, LLC. | | 8-K (Exhibit 10.13) | 10/2/2017 | 000-55764 |
| 10.15 | First Amendment to Lease dated as of March 31, 2014 by and between AuraSense Therapeutics, LLC and FC Skokie PQ, LLC, as successor in interest to FC Skokie SPE, LLC. | | 8-K (Exhibit 10.14) | 10/2/2017 | 000-55764 |
| 10.16 | Second Amendment to Lease dated as of May 26, 2016 by and between Exicure OpCo and FC Skokie PQ, LLC, as successor in interest to FC Skokie SPE, LLC. | | 8-K (Exhibit 10.15) | 10/2/2017 | 000-55764 |
| 10.17 | Loan and Security Agreement dated as of February 17, 2016 by and between Exicure OpCo and Hercules. | | 8-K (Exhibit 10.16) | 10/2/2017 | 000-55764 |
| 10.18 | Amendment No. 1 to Loan and Security Agreement dated as of October 10, 2016 by and between Exicure OpCo and Hercules. | | 8-K (Exhibit 10.17) | 10/2/2017 | 000-55764 |
| 10.18.1 | Amendment No. 2 to Loan and Security Agreement dated as of January 15, 2018 by and between Exicure OpCo and Hercules. | | S-1/A (Exhibit 10.17.1) | 1/26/2018 | 333-221791 |
| 10.18.2 | Amendment No. 3 to Loan and Security Agreement dated as of December 28, 2018 by and between Exicure OpCo and Hercules. | X | | | |
| 10.19+ | Form of Pre-Merger Indemnity Agreement. | | 8-K (Exhibit 10.18) | 10/2/2017 | 000-55764 |
| 10.20 | Form of Common Stock Purchase Agreement. | | 8-K (Exhibit 10.1) | 6/19/2017 | 000-55764 |
| 10.21* | Restated License Agreement between Exicure OpCo and Northwestern University dated as of August 15, 2015. | | 8-K/A (Exhibit 10.20) | 11/7/2017 | 000-55764 |
| 10.22* | License Agreement between Exicure OpCo and Northwestern University dated as of February 10, 2016 and effective as of May 27, 2014. | | 8-K/A (Exhibit 10.21) | 11/7/2017 | 000-55764 |
| 10.23* | License Agreement between Exicure OpCo and Northwestern University dated as of June 17, 2016. | | 8-K/A (Exhibit 10.22) | 11/7/2017 | 000-55764 |
| 10.24* | Amendment One to the Amended Restated License Agreement between Exicure OpCo and Northwestern University dated as of September 27, 2016. | | 8-K/A (Exhibit 10.23) | 11/7/2017 | 000-55764 |
| 10.25* | Research Collaboration, Option and License Agreement between Exicure OpCo and Purdue Pharma L.P. dated as of December 2, 2016. | | 8-K/A (Exhibit 10.24) | 11/7/2017 | 000-55764 |
| 10.26 | Side Agreement to Northwestern Agreements by and among Exicure OpCo, Northwestern University and Purdue Pharma L.P. dated as of October 11, 2016. | | 8-K/A (Exhibit 10.25) | 11/7/2017 | 000-55764 |
| 10.27 | Form of Subscription Agreement by and between the Company and each investor in connection with the subsequent closings of the 2017 Private Placement. | | 8-K (Exhibit 10.1 ) | 11/2/2017 | 000-55764 |

| | | | | | |
|---|---|---|---|---|---|
| 10.28 | Form of Purchaser Rights Letter to be delivered by the Company to each investor in the initial closing of the 2017 Private Placement. | | 8-K (Exhibit 10.2 ) | 11/2/2017 | 000-55764 |
| 10.29 | Form of Subscription Agreement by and between the Company and each investor in connection with the initial closing of the August 2018 Private Placement. | | 8-K (Exhibit 10.1 ) | 8/28/18 | 000-55764 |
| 21.1 | Subsidiaries of Exicure, Inc. | X | | | |
| 23.1 | Consent of KPMG LLP, independent registered public accounting firm. | X | | | |
| 24.1 | Power of Attorney (included on the signature page hereto). | X | | | |
| 31.1 | Certification of Principal Executive Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, As Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | X | | | |
| 31.2 | Certification of Principal Financial Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, As Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | X | | | |
| 32** | Certifications of Principal Executive Officer and Principal 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. | X | | | |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document. | X | | | |
| 101.PRE | XBRL Taxonomy Presentation Linkbase Document. | X | | | |

† Annexes, schedules and/or exhibits have been omitted pursuant to Item 601(b)(2) of Regulation S-K. We hereby undertake to furnish supplementally a copy of any of the omitted schedules and exhibits to the SEC on a confidential basis upon request.

+ Indicates a management contract or compensatory plan.

* Portions of this exhibit have been omitted pursuant to a request for confidential treatment granted by the SEC, and omitted portions have been filed separately with the SEC.

** Furnished herewith.

**Item 16. Form 10-K Summary.**

None.

**SIGNAT URES**

Pursuant to the requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Skokie, State of Illinois, on March 8, 2019.

**EXICURE, INC.**

By: /s/ David A. Giljohann

David A. Giljohann, Ph.D.

Chief Executive Officer ( *principal executive officer)*

By: /s/ David S. Snyder

David S. Snyder

Chief Financial Officer

( *principal financial officer and principal accounting officer* )

**POWER OF ATTORNEY**

We, the undersigned directors and officers of Exicure, Inc., hereby severally constitute and appoint David A. Giljohann and David S. Snyder, and each of them singly, our true and lawful attorneys-in-fact, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of them might or could do in person, and hereby ratifying and confirming all that said attorneys-in-fact, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney. This Power of Attorney does not revoke any power of attorney previously granted by the undersigned, or any of them.

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 and in the capacities and on the dates indicated:

| SIGNATURE | TITLE | DATE |
|---|---|---|
| /s/ David A. Giljohann<br>David A. Giljohann, Ph.D. | Chief Executive Officer and Director<br>( *principal executive officer)* | March 8, 2019 |
| /s/ David S. Snyder<br>David S. Snyder | Chief Financial Officer<br>( *principal financial officer and principal accounting officer* ) | March 8, 2019 |
| /s/ Chad A. Mirkin<br>Chad A. Mirkin, Ph.D. | Director and Chairman of the Board of Directors | March 8, 2019 |
| /s/ C. Shad Thaxton<br>C. Shad Thaxton, M.D., Ph.D. | Director | March 8, 2019 |
| /s/ David R. Walt<br>David R. Walt, Ph.D. | Director | March 8, 2019 |
| /s/ Jay R. Venkatesan<br>Jay R. Venkatesan, M.D. | Director | March 8, 2019 |
| /s/ Helen S. Kim<br>Helen S. Kim | Director | March 8, 2019 |

# AMENDMENT NO. 3 TO LOAN AND SECURITY AGREEMENT

This Amendment No. 3 to Loan and Security Agreement (this " **Amendment** ") is entered into this 28th day of December, 2018 by and among (a) **HERCULES CAPITAL, INC.** (f/k/a Hercules Technology Growth Capital, Inc.), a Maryland corporation, in its capacity as administrative agent for itself and the Lender (as defined herein) (in such capacity, the " **Agent** "); (b) the several banks and other financial institutions or entities from time to time parties to the Loan Agreement (as defined below) (collectively, referred to as the " **Lender** "); and (c) **EXICURE OPERATING COMPANY** (f/k/a Exicure, Inc.), a Delaware corporation (" **Borrower** ").

**WHEREAS** , Lender and Borrower are parties to that certain Loan and Security Agreement dated as of February 17, 2016, as amended by that certain Amendment No. 1 to Loan and Security Agreement dated as of October 10, 2016 among Lender and Borrower, and as further amended by that certain Amendment No. 2 to Loan and Security Agreement dated as of January 15, 2018, among Lender and Borrower (as the same has been and may from time to time be further amended, modified, supplemented or restated, the " **Loan Agreement** "); and

**WHEREAS** , in accordance with Section 11.3 of the Loan Agreement, Borrower and Lender desire to amend the Loan Agreement as more fully set forth herein.

**NOW, THEREFORE,** in consideration of the foregoing recitals and other good and valuable consideration, the receipt and adequacy of which is hereby acknowledged, and intending to be legally bound, the parties hereto agree as follows:

**1. Definitions.** Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.

**2. Amendment to Loan Agreement-** Subject to the satisfaction of the conditions set forth in Section 3 of this Amendment, the Loan Agreement is hereby amended as follows:

(a) The Loan Agreement shall be amended by inserting the following new definitions to appear alphabetically in Section 1.1 thereof:

" " **Amendment No. 3 Commitment Fee** " means a fully earned, non-refundable commitment fee of Twenty-Five Thousand Dollars, ($25,000.00), which is due to Agent on or prior to the Amendment No. 3 Effective Date."

" " **Amendment No. 3 Effective Date** " is December 28, 2018."

(b) Section 2.1(d) of the Loan Agreement is deleted in its entirety and replaced with the following:

"(d) Payment. Borrower will pay interest on each Term Loan Advance on the first (1 st ) Business Day of each month, beginning the month after the Advance Date. On the Term Loan Maturity Date, Borrower shall repay the

aggregate principal balance of Term Loan Advances that are outstanding on the Term Loan Maturity Date and any accrued but unpaid interest hereunder and all other Secured Obligations with respect to the Term Loan Advances (Lender acknowledges receipt of principal payments from Borrower in the amount of $1,001,007.75 as of the Amendment No. 3 Effective Date). Borrower shall make all payments under this Agreement without setoff, recoupment or deduction and regardless of any counterclaim or defense. Lender will initiate debit entries to Borrower's account as authorized on the ACH Authorization (i) on each payment date of all periodic obligations payable to Lender under each Term Advance and (ii) out-of-pocket legal fees and costs incurred by Agent or Lender in connection with Section 11.11 of this Agreement. Once repaid, a Term Loan Advance or any portion thereof may not be reborrowed."

**3. Conditions to Effectiveness.** Agent, Lender and Borrower agree that this Amendment shall become effective upon the satisfaction of the following conditions precedent, each in form and substance satisfactory to Lender:

(a) Agent and Lender shall have received a fully-executed counterpart of this Amendment signed by Borrower;

(b) Borrower shall have paid to Agent the Amendment No. 3 Commitment Fee on or prior to the Amendment No. 3 Effective Date;

(c) Agent shall have received payment for all reasonable and documented out-of-pocket fees and expenses incurred by Lender and Agent in connection with this Amendment, including, but not limited to, all legal fees and expenses, payable pursuant to Section 11.11 of the Loan Agreement.

**4. Representations and Warranties.** The Borrower hereby represents and warrants to Lender as follows:

(a) Representations and Warranties in the Agreement . The representations and warranties of Borrower set forth in Section 5 of the Loan Agreement (after giving effect to this Amendment) are true and correct in all material respects on and as of the date hereof with the same effect as though made on and as of such date, except to the extent such representations and warranties expressly relate to an earlier date, in which case they are true and correct as of such date.

(b) Authority, Etc . The execution and delivery by Borrower of this Amendment and the performance by Borrower of all of its agreements and obligations under the Loan Agreement and the other Loan Documents, as amended hereby, are within the corporate authority of Borrower and have been duly authorized by all necessary corporate action on the part of Borrower. With respect to Borrower, the execution and delivery by Borrower of this Amendment does not and will not require any registration with, consent or approval of, or notice to any Person (including any governmental authority).

(c) Enforceability of Obligations . This Amendment, the Loan Agreement and the other Loan Documents, as amended hereby, constitute the legal, valid and binding obligations of Borrower enforceable against Borrower in accordance with their terms, except as enforceability is limited by bankruptcy, insolvency, reorganization, moratorium, general equitable principles or other laws relating to or affecting generally the enforcement of, creditors' rights and except to the extent that availability of the remedy of specific performance or injunctive relief is subject to the discretion of the court before which any proceeding therefor may be brought.

(d) No Default . Before and after giving effect to this Amendment (i) no fact or condition exists that would (or would, with the passage of time, the giving of notice, or both) constitute an Event of Default, and (ii) no event that has had or could reasonably be expected to have a Material Adverse Effect has occurred and is continuing.

(e) Event of Default . By its signature below, Borrower hereby agrees that it shall constitute an Event of Default if any representation or warranty made herein should be false or misleading in any material respect when made.

**5. Reaffirmations.** Except as expressly provided in this Amendment, all of the terms and conditions of the Loan Agreement and the other Loan Documents remain in full force and effect. Nothing contained in this Amendment shall in any way prejudice, impair or effect any rights or remedies of Agent or Lender under the Loan Agreement and the other Loan Documents. Except as specifically amended hereby, Borrower hereby ratifies, confirms, and reaffirms all covenants contained in the Loan Agreement and the other Loan Documents. The Loan Agreement, together with this Amendment, shall be read and construed as a single agreement. All references in the Loan Documents to the Loan Agreement or any other Loan Document shall hereafter refer to the Loan Agreement or any other Loan Document as amended hereby.

**6. Execution in Counterparts.** This Amendment may be signed in any number of counterparts, and by different parties hereto in separate counterparts, with the same effect as if the signatures to each such counterpart were upon a single instrument. All counterparts shall be deemed an original of this Amendment. This Amendment may be executed by facsimile, portable document format (.pdf) or similar technology signature, and such signature shall constitute an original for all purposes.

**7. Release** . In consideration of the agreements of Agent and each Lender contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Borrower, on behalf of itself and its successors, assigns, and other legal representatives, hereby fully, absolutely, unconditionally and irrevocably releases, remises and forever discharges Agent and each Lender, and its successors and assigns, and its present and former shareholders, affiliates, subsidiaries, divisions, predecessors, directors, officers, attorneys, employees, agents and other representatives (Agent, each Lender and all such other persons being hereinafter referred to collectively as the "Releasees" and individually as a "Releasee"), of and from all demands, actions, causes of action, suits, covenants, contracts, controversies, agreements, promises, sums of money, accounts, bills, reckonings, damages and any and all other claims, counterclaims, defenses, rights of set-off, demands and liabilities whatsoever of every name and nature, known or unknown, suspected or unsuspected, both at law and in equity, which Borrower,

or any of its successors, assigns, or other legal representatives may now or hereafter own, hold, have or claim to have against the Releasees or any of them for, upon, or by reason of any circumstance, action, cause or thing whatsoever which arises at any time on or prior to the day and date of this Amendment, for or on account of, or in relation to, or in any way in connection with the Loan Agreement, or any of the other Loan Documents or transactions thereunder or related thereto. Borrower understands, acknowledges and agrees that the release set forth above may be pleaded as a full and complete defense and may be used as a basis for an injunction against any action, suit or other proceeding which may be instituted, prosecuted or attempted in breach of the provisions of such release. Borrower agrees that no fact, event, circumstance, evidence or transaction which could now be asserted or which may hereafter be discovered shall affect in any manner the final, absolute and unconditional nature of the release set forth above.

**8. Miscellaneous.**

(a) THIS AMENDMENT SHALL BE GOVERNED BY, AND CONSTRUED AND ENFORCED IN ACCORDANCE WITH, THE LAWS OF THE STATE OF CALIFORNIA, EXCLUDING CONFLICT OF LAWS PRINCIPLES THAT WOULD CAUSE THE APPLICATION OF LAWS OF ANY OTHER JURISDICTION.

(b) The captions in this Amendment are for convenience of reference only and shall not define or limit the provisions hereof.

(c) This Amendment expresses the entire understanding of the parties with respect to the transactions contemplated hereby. No prior negotiations or discussions shall limit, modify, or otherwise affect the provisions hereof.

(d) Any determination that any provision of this Amendment or any application hereof is invalid, illegal or unenforceable in any respect and in any instance shall not affect the validity, legality, or enforceability of such provision in any other instance, or the validity, legality or enforceability of any other provisions of this Amendment.

[Signature page follows.]

**IN WITNESS WHEREOF,** the parties hereto have caused this Amendment to be duly executed and delivered as of the date first written above.

**LENDER**

HERCULES CAPITAL FUNDING TRUST 2018-1

By: ___/s/ Jennifer Choe_____
Name: ___Jennifer Choe _____
Title: ___Assistant General Counsel___

**BORROWER**

EXICURE OPERATING COMPANY (f/k/a Exicure, Inc.)

By: ___/s/ David S. Snyder_____
Name: ___ David S. Snyder_____
Title: ____CFO _____

**AGENT**

HERCULES CAPITAL, INC.

By: ___/s/ Jennifer Choe_____
Name: ___Jennifer Choe _____
Title: ___Assistant General Counsel___

**Exhibit 21.1**

**Subsidiaries of Exicure, Inc.**

| **Name:** | **Jurisdiction of Organization:** |
| --- | --- |
| Exicure Operating Company | Delaware |

**Exhibit 23.1**

**Consent of Independent Registered Public Accounting Firm**

The Board of Directors

Exicure, Inc.:

We consent to the incorporation by reference in the registration statement (No. 333-222999) on Form S-8 of Exicure, Inc. of our report dated March 8, 2019, with respect to the consolidated balance sheets of Exicure, Inc. as of December 31, 2018 and 2017, and the related consolidated statements of operations, changes in stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2018, and the related notes (collectively, the consolidated financial statements), which report appears in the December 31, 2018 annual report on Form 10-K of Exicure, Inc. Our report dated March 8, 2019, on the consolidated financial statements refers to the adoption of Financial Accounting Standards Board Accounting Standards Codification (ASC) Topic 606, *Revenue from Contracts with Customers* . Our report dated March 8, 2019 contains an explanatory paragraph that states that the Company has suffered recurring losses from operations and will be required to raise additional capital or alternative means of financial support to fund operations, which raise substantial doubt about its ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of that uncertainty.

Chicago, Illinois
March 8, 2019

**Exhibit 31.1**

**CERTIFICATIONS**

I, David A. Giljohann, Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Exicure, Inc.;

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(s) 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)) and internal control over financial reporting (as defined in Exchange Act rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) 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

d) 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; and

5. The registrant's other certifying officer(s) 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.

Date: March 8, 2019

/s/ David A. Giljohann, Ph.D.

**David A. Giljohann, Ph.D.**

**President and Chief Executive Officer**

**Exhibit 31.2**

**CERTIFICATIONS**

I, David S. Snyder, certify that:

1. I have reviewed this Annual Report on Form 10-K of Exicure, Inc.;

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(s) 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)) and internal control over financial reporting (as defined in Exchange Act rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under my supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) 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

d) 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; and

5. The registrant's other certifying officer(s) 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.

Date: March 8, 2019

/s/ David S. Snyder

**David S. Snyder**

**Chief Financial Officer**

**Exhibit 32.1**

**SECTION 1350 CERTIFICATIONS***

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350), David A. Giljohann, Ph. D., President and Chief Executive Officer of Exicure, Inc. (the "Company"), and David S. Snyder, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the year ended December 31, 2018, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act; and

2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 8, 2019

| | |
|---|---|
| /s/ David A. Giljohann, Ph.D. | /s/ David S. Snyder |
| **David A. Giljohann, Ph.D.** | **David S. Snyder** |
| **President and Chief Executive Officer** | **Chief Financial Officer** |

* This certification accompanies the Annual Report on Form 10-K, to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to 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 the Annual Report on Form 10-K), irrespective of any general incorporation language contained in such filing.