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, 2020

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

For the transition period from to
Commission file number 001-39011

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.)**

2430 N. Halsted St.
Chicago, IL 60614
(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	**XCUR**	**The Nasdaq Stock Market LLC**
(Title of each class)	**(Trading symbol(s))**	**(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 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant as of June 30, 2020 was approximately $128.1 million, based on a closing price of $2.44 per share of the registrant's common stock as reported on The Nasdaq Capital Market. For purposes of this computation, all officers, directors, and 10% beneficial owners of the registrant are deemed to be affiliates. Such determination should not be deemed to be an admission that such officers, directors or 10% beneficial owners are, in fact, affiliates of the registrant.

As of March 5, 2021, the registrant had 87,960,327 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for the 2021 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.

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 titled "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 described in the "Risk Factor Summary" below and 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. These forward-looking statements include, but are not limited to, statements concerning the following:

- our expectations regarding the impact of the ongoing COVID-19 pandemic including the expected duration of disruption and immediate and long-term delays, interruptions or other adverse effects to clinical trials, patient enrollment and clinical activation, delays in regulatory review, preclinical research and development, or R&D, collaboration and partnership programs, manufacturing and supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy overall, and the overall impact of the COVID-19 pandemic on our business, financial condition and results of operations;
- our estimates of expenses, ongoing losses, future revenue and capital requirements, including our expectations relating to our needs for additional financing;
- the initiation, timing, progress and results of our current and future preclinical studies, clinical trials, collaboration and partnership programs, including our ongoing clinical trials and any planned clinical trials for cavrotolimod (AST-008) or any of our product candidates, and the research and development programs we pursue;
- our ability to advance our product candidates into, and successfully complete, clinical trials;
- the timing and likelihood of regulatory filings for our current and future product candidates including any 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 ability to obtain and maintain regulatory approval of our product candidates in the indications for which we plan to develop them, and any related restrictions, limitations or warnings in the label of an approved drug or therapy;
- the size and growth potential of the markets for our product candidates, if approved, and the rate and degree of market acceptance of our product candidates, including reimbursement that may be received from payors;
- the diversion of healthcare resources away from the conduct of clinical trials as a result of the ongoing COVID-19 pandemic, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;

- the interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel, quarantines or social distancing protocols imposed or recommended by federal or state governments, employers and others or voluntarily adopted in connection with the ongoing COVID-19 pandemic;
- our dependence on current and future collaborators for advancement of therapeutic candidates pursuant to the terms of such collaborations, including ability to obtain and maintain regulatory approval and commercialization, if approved;
- the status of clinical trials, development timelines and discussions with regulatory authorities related to product candidates under development by us and our collaborators;
- 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;
- the rate and degree of market acceptance of any approved therapeutic candidates;
- the commercialization of any approved therapeutic candidates;
- the implementation of our business model and strategic plans for our business, technologies and therapeutic candidates;
- 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 expectations regarding 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 JOBS Act;
- the impact of government laws and regulations as well as developments relating to our competitors or our industry; and
- other factors that may impact our financial and clinical results.

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.

SUMMARY RISK FACTORS

Investing in common stock involves numerous risks, including the risks described in "Item 1A. Risk Factors" of this Annual Report on Form 10-K. Below are some of these risks, any one of which could materially adversely affect our business, financial condition, results of operations and prospects.

- 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.
- Our approach to the discovery and development of innovative therapeutic treatments based on our technology is unproven and may not result in marketable products.
- 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.
- 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.
- 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.
- Our business could be adversely affected by the effects of health epidemics, including the global COVID-19 pandemic, in regions where we or third parties on which we rely have business operations and at our clinical trial sites, as well as the business or operations of our CROs or other third parties with whom we conduct business.
- If we continue to experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be further delayed or prevented.
- 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 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.
- 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.
- 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 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 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.
- Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.
- We will continue to increase the size of our organization, and we may experience difficulties in managing growth.
- 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.

- 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.

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.

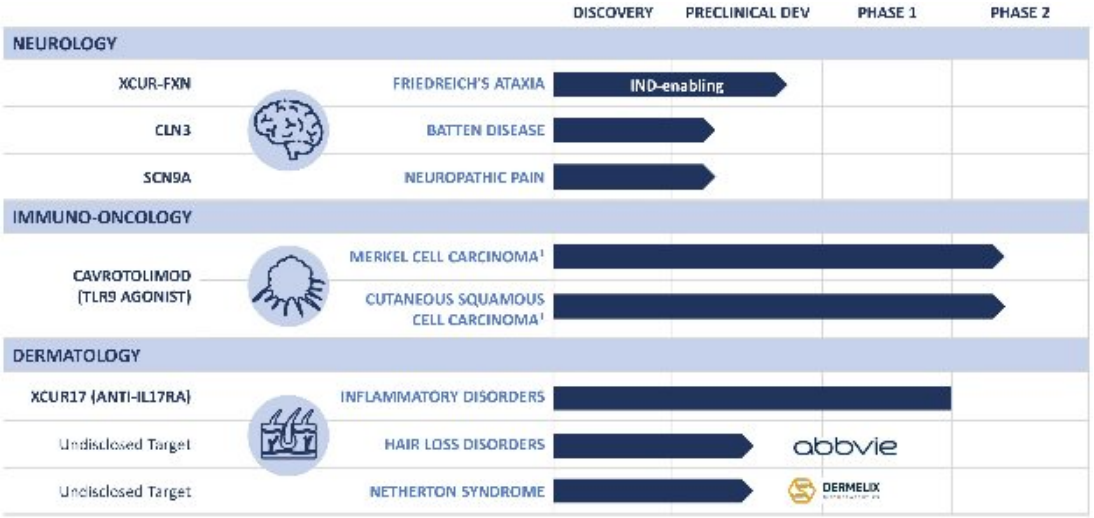
Overview

We are a clinical-stage biotechnology company developing therapeutics for immuno-oncology, genetic disorders and other indications 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. We are conducting IND-enabling studies for XCUR-FXN, an SNA–based therapeutic candidate, for the treatment of Friedreich's ataxia (FA) and expect to initiate a first-in-patient Phase 1b clinical trial in 2022. We are also working to advance our SNA–based therapeutic candidate cavrotolimod (AST-008) in an ongoing Phase 1b/2 clinical trial in cancer patients.

We believe that one of the key strengths of our proprietary SNAs is that they have the potential for increased cellular uptake compared to conventional linear oligonucleotides and as a result the potential to achieve higher efficacy at the same doses of oligonucleotide administered. We have shown in clinical and preclinical studies that SNAs may have therapeutic potential in neurology, immuno-oncology and dermatology. In addition, we have shown in preclinical studies that SNAs may have therapeutic potential in ophthalmology, pulmonology, and gastroenterology. As a consequence, we have expanded our pipeline into neurology, and are conducting early stage research activities in ophthalmology, pulmonology, and gastroenterology.

In June 2020, we reported that we dosed the first patient in the metastatic Merkel cell carcinoma (MCC) cohort of the Phase 2 portion of the clinical trial of cavrotolimod (AST-008). As of February 23, 2021, we had 16 clinical trial sites open for enrollment and 7 additional sites pending activation. We expect to open up to 30 sites for the Phase 2 stage of the clinical trial. We anticipate all sites will be activated by the end of 2021. As of February 23, 2021, we had dosed 16 patients with 32 mg of cavrotolimod (AST-008) in the Phase 2 portion of the clinical trial, including the primary and exploratory cohorts. Including the six patients dosed with 32 mg of cavrotolimod (AST-008) in the Phase 1b portion of the clinical trial, a total of 22 patients have been dosed with 32 mg of cavrotolimod (AST-008).

The table below sets forth the current status of development of our SNA therapeutic candidates. We are also conducting early stage research activities in ophthalmology, respiratory and gastrointestinal applications. These early stage research activities are described in more detail in the section titled "Our Therapeutic Development Programs–Preclinical research programs."



(1) In combination with checkpoint inhibitors.

Impact of Covid-19

With the global spread of the coronavirus disease 2019, or COVID-19, pandemic during 2020, we continue to monitor closely the developments and continue to take active measures to protect the health of our employees and their families, our communities, as well as our clinical trial investigators, patients, and caregivers. In response to the evolving COVID-19 pandemic and related public health directives, orders and guidance, and to ensure the safety and wellbeing of our employees and support community efforts to reduce transmission of COVID-19, we have implemented work-from-home policies in accordance with guidance from federal, state/provincial or municipal government and health authorities. We implemented a number of measures to ensure employee safety and business continuity. Under social distancing guidelines for COVID-19, we were typically operating with less than 50% of our R&D staff on-site at any one time through June 30, 2020. As of July 1, 2020, we took occupancy of approximately 30,000 square feet of laboratory and office space in our new headquarters in Chicago, Illinois. Since then, we have operated under COVID-19 social distancing guidelines and have generally operated with 100% of our R&D staff on-site. Our office and general and administrative team continues to work predominantly from home. We are managing laboratory staffing and taking other appropriate managerial actions to maintain progress on our preclinical and collaboration programs. Business travel has been suspended, and online and teleconference technology is used to meet virtually rather than in person. We have taken measures to secure our research and development project activities, while work in laboratories and facilities has been organized to reduce risk of COVID-19 transmission. For employees working in our laboratories and facilities, we have also taken additional

safety measures, including implementing social distancing, providing and requiring the use of personal protective equipment, temperature screening, restricting business travel, and under certain circumstances, requiring COVID-19 testing to access our workplace.

R&D operations

Our preclinical development program in FA is ongoing and we began IND-enabling studies for XCUR-FXN in late 2020. We also continue to progress our collaborations with AbbVie and Dermelix. However, if the COVID-19 pandemic or its impact or effects continues to persist for an extended period of time, we could experience additional delays in our enrollment of patients for the Phase 2 trial of cavrotolimod (AST-008) and significant disruptions to our preclinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects.

Supply chain

We are working closely with our third-party manufacturers and other partners to manage our supply chain activities and mitigate potential disruptions as a result of the COVID-19 pandemic. We have observed minor delays in receipt of key chemicals, reagents and materials as certain manufacturers have had supply disruptions, related to the COVID-19 pandemic. If the COVID-19 pandemic continues to persist for an extended period of time and impacts essential distribution systems such as FedEx and postal delivery, we could experience future disruptions to our supply chain and operations, and associated delays in the manufacturing and our clinical supply, which would adversely impact our preclinical and clinical development activities.

Clinical operations

We have one active clinical program, cavrotolimod (AST-008). We have completed enrollment for the Phase 1b stage of the clinical trial and have begun the Phase 2 dose expansion phase in patients with advanced or metastatic Merkel cell carcinoma, or cutaneous squamous cell carcinoma. During the third quarter of 2020 and through December 31, 2020, we observed delays in our enrollment plans and clinical trial site start-ups for the Phase 2 dose expansion phase of the trial. We believe the effects of the COVID-19 pandemic or its impact contributed to such delays. As a result, we have taken additional measures to increase the enrollment of patients, including frequent interaction with our clinical trial sites currently open as well as increasing the number of clinical trial sites that potentially are activated for this trial so that we may continue to enroll patients as initially planned, in accordance with related directives, orders and guidance from relevant health and safety authorities. However, these delays have caused us to lengthen our clinical development timeline for cavrotolimod (AST-008), and we now expect to report overall response rate, or ORR, results in the first half of 2022 rather than by year end 2021 as previously guided in September 2020.

We remain committed to maintaining our development plans for cavrotolimod (AST-008) and continue to monitor and manage the rapidly evolving situation. We have taken and continue to take measures to implement remote and virtual approaches, including remote patient monitoring where possible, to maintain patient safety and trial continuity and to preserve study integrity. Should the COVID-19 pandemic or its impact or effects continue, our ability to maintain patient enrollment and our clinical development timeline could continue to be negatively impacted. We could also see an impact on our ability to supply study drug, report trial results, or interact with regulators, ethics committees or other important agencies due to limitations in regulatory authority employee resources or otherwise. In addition, we rely on contract research organizations or other third parties to assist us with clinical trials, and we cannot guarantee that they will continue to perform their contractual duties in a timely and satisfactory manner as a result of the COVID-19 pandemic. As the COVID-19 pandemic persists for an extended period of time, we continue to be impacted and could experience additional delays in patient enrollment for our Phase 2 clinical trial of cavrotolimod (AST-008). Any significant disruptions to our clinical development timelines would further delay our anticipated timeline for results and adversely affect our business, financial condition, results of operations and growth prospects.

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 XCUR-FXN to clinical proof-of-concept and approval to offer meaningful benefit to Friedreich's ataxia (FA) patients.** We designed and optimized XCUR-FXN, our bi-specific FA therapeutic candidate, to increase frataxin protein levels via two distinct mechanisms and, in *in vitro* experiments, have observed synergistic upregulation of FXN mRNA in cells treated with XCUR-FXN compared to its mono-targeting components alone at the same total oligonucleotide dose. In FA patient-derived induced neurons, XCUR-FXN has shown potent, dose-dependent upregulation of frataxin protein. In isolated mitochondria from the same induced neurons, XCUR-FXN normalized frataxin protein levels at low concentrations, resulting in substantial improvements in mitochondrial respiration, as measured by succinate dehydrogenase (SDH) activity. We are working in collaboration with Friedreich's Ataxia Research Alliance (FARA), to develop XCUR-FXN. We commenced IND-enabling studies for XCUR-FXN in late 2020 and expect to initiate a first-in-patient Phase 1b clinical trial in 2022.

- **Expand our pipeline of therapeutic candidates for neurological disorders to fully exploit the potential of our SNA technology.** We have identified multiple SNA compounds that modulate SCN9A and CLN3 mRNA, for potential treatment of neuropathic pain and CLN3 Batten disease, respectively. We are also evaluating the application of our SNA technology in additional neurological conditions with unmet medical needs, including multiple forms of spinocerebellar ataxia, amyotrophic lateral sclerosis (ALS), Angelman syndrome, and Huntington's disease.

- **Rapidly advance cavrotolimod (AST-008) through clinical development for select cancer indications.** AST-008 is our most advanced therapeutic candidate. Using data from the completed Phase 1b stage of our Phase 1b/2 clinical trial, a recommended Phase 2 dose of 32 mg cavrotolimod (AST-008) was identified for the Phase 2 portion of the clinical trial which is currently underway, where cavrotolimod (AST-008) is being given in combination with pembrolizumab or cemiplimab for the treatment of locally advanced or metastatic Merkel cell carcinoma, or cutaneous squamous cell carcinoma, respectively, in patients with progression despite anti-PD-(L)1 therapy. We are enrolling two separate cohorts of patients with advanced or metastatic MCC or CSCC. Each cohort is expected to enroll up to 29 patients who have failed anti-PD-1/PD-L1, or programmed cell death protein 1/programmed death-ligand 1, therapy. In addition, we have added an exploratory cohort to include patients with melanoma who have progressed on PD-(L)-1 therapy and MCC patients who do not qualify for the primary MCC cohort. In June 2020, we reported that we dosed the first patient in the MCC cohort of the trial. As of February 23, 2021, we had 16 clinical trial sites open for enrollment and 7 additional sites pending activation. We expect to open up to 30 sites for the Phase 2 stage of the clinical trial. We anticipate all sites will be activated by the end of 2021. As of February 23, 2021, we had dosed 16 patients with 32 mg of cavrotolimod (AST-008) in the Phase 2 portion of the clinical trial, including the primary and exploratory cohorts. Including the six patients dosed with 32 mg of cavrotolimod (AST-008) in the Phase 1b portion of the clinical trial, a total of 22 patients have been dosed with 32 mg of cavrotolimod (AST-008). In January 2021, we announced that the U.S. Food and Drug Administration, or the FDA, has granted Fast Track designations for cavrotolimod (AST-008), for two development programs: (i) cavrotolimod in combination with anti-programmed death-1 (PD-1) therapy for the treatment of patients with locally advanced or metastatic MCC refractory to prior anti-PD-1/anti-PD-ligand 1 (anti-PD-(L)1) blockade and (ii) cavrotolimod in combination with anti-PD-1 therapy for the treatment of patients with locally advanced or metastatic cutaneous squamous cell carcinoma (CSCC) refractory to prior anti-PD-1 blockade. In March 2021, we announced that the FDA has granted Orphan Drug Designation for cavrotolimod (AST-008) for the treatment of patients with MCC.

- **Use our proprietary SNA technology to develop additional therapeutic candidates.** We have demonstrated in preclinical studies that in certain applications, 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 eye, gastrointestinal tract and lungs. We believe that we have the opportunity to enhance the therapeutic potential of known oligonucleotides of clinical utility by incorporating them in our SNA platform. In addition, we may be

able to develop novel therapeutic candidates targeting validated therapeutic targets. We are conducting early stage research activities in ophthalmology, pulmonology, and gastroenterology.

- **Advance SNA platform in dermatological indications with suitable partners.** In February 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. Additionally, in November 2019, we entered into the AbbVie Collaboration Agreement, pursuant to which we, in collaboration with AbbVie, are developing SNA-based treatments for hair loss disorders.

- **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.

- **Continue to expand our core capabilities in high throughput screening and automated analyses.** We believe there may be a number of therapeutic areas where our SNA technology can be applied to bring first-in-class or best-in-class medicines to patients. Our goal is to identify and advance to clinical development therapeutic candidates for multiple different genetically-defined disorders in parallel, either on our own or with strategic collaborators. We continue to invest in critical infrastructure and know-how to execute on this goal.

- **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 applications covering cavrotolimod (AST-008) would expire between 2034 and 2040. Our patent arising from an application covering XCUR-FXN would expire by 2041. Patents arising from applications covering XCUR17 and AST-005 would expire by 2037 and 2035, respectively.

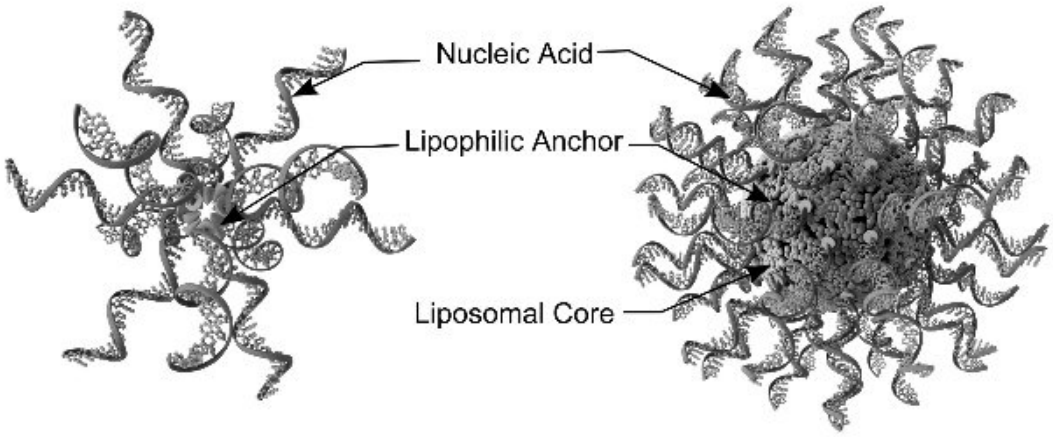
Our Proprietary Technology: Spherical Nucleic Acids

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 enhance the therapeutic potential of known oligonucleotides of clinical utility by incorporating them in our SNA platform. In addition, we may be able to develop novel therapeutic candidates using our SNA platform.

- **SNAs can potentially target multiple genes with a single therapeutic candidate.** Our development candidate for Friedreich's ataxia, XCUR-FXN, is employing a bi-specific approach to upregulate frataxin mRNA levels via two distinct mechanisms, employing an SNA carrying two distinct oligonucleotides. Furthermore, in collaboration with Dr. Amy Paller, one of our scientific advisors, at the 2019 meeting of the Society for Investigative Dermatology, we presented data demonstrating the application of our SNA technology for concurrently targeting two different genes in a single SNA compound. We believe we can concurrently target three or more genes with a single SNA compound. This feature potentially allows us to identify novel therapeutic candidates to treat multiple variants of a given genetic disorder or multiple genetic targets for a single disorder with one therapeutic candidate. We believe multi-targeting might be particularly beneficial for complex genetic diseases with more than one underlying genetic driver.

- **SNAs we have administered to date have been well-tolerated.** 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. 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. As of February 23, 2021, 1 of the 22 patients dosed with 32 mg of cavrotolimod (AST-008) has experienced a treatment-related SAE as determined by the clinical trial investigator. This patient, enrolled in the Phase 2 stage of the clinical trial, reported a treatment-related serious adverse event, or SAE, of hypotension, flu-like symptoms which subsequently resolved. None of the 14 patients dosed in the Phase 1b portion of the clinical trial with doses of cavrotolimod (AST-008) less than 32 mg experienced a treatment related SAE. Thus, as of February 23, 2021, in total, 1 of 36 patients treated with cavrotolimod (AST-008) have experienced a treatment related SAE.

- **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, cavrotolimod (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, cavrotolimod (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 current Good Manufacturing Practices, or cGMPs.

Our Therapeutic Development Programs

Neurology

We are investigating the utility of our SNA technology for the treatment of neurological conditions and have ongoing research programs underway. See below "Neurology–Proof-Of-Concept Work with Nusinersen" for more information on our initial studies and resulting data that indicate that the SNA platform may be well-suited for development of new therapeutics directed towards diseases of the central nervous system.

XCUR-FXN, Friedreich's ataxia

We are developing XCUR-FXN, an SNA-based therapeutic candidate for the treatment of Friedreich's ataxia, or FA. FA is an autosomal recessive, neurodegenerative disease characterized by progressively impaired muscle coordination caused by the degeneration of neurons in the cerebellum and dorsal root ganglia in the spinal cord. FA patients may also experience impairment of visual, auditory and speech functions. FA patients also commonly suffer from life-threatening heart conditions such as hypertrophic cardiomyopathy, myocardial fibrosis and heart failure. The typical age of onset for FA is between 5 and 15 years. We estimate that approximately 13,000 patients across the United States, Europe, Canada and Australia are affected by FA. There are currently no FDA-approved treatments for FA.

We have conducted extensive preclinical research evaluating the suitability of our SNA technology for genetically defined neurological diseases, including efficacy studies in animal models, and biodistribution in rodent and non-human primates. Based on the results, we believe we can target FA at the genetic source and meet an important unmet medical need for FA patients. FA is driven by expansion of guanine-adenine-adenine bases of the DNA sequence, or GAA, triplet repeats in the first intron of frataxin, or FXN, gene. The expanded repeat of FXN forms an intramolecular triple-helix, which impairs transcription and reduces levels of frataxin protein. Our strategy is to use a genetically-targeted SNA therapy to increase FXN protein.

We have designed XCUR-FXN to take advantage of a key attribute of our SNA technology, the ability to incorporate more than one active oligonucleotides in a single SNA molecule. We designed and optimized XCUR-FXN, our bi-specific FA therapeutic candidate, to increase frataxin protein levels via two distinct mechanisms and, in *in vitro* experiments, have observed synergistic upregulation of FXN mRNA in cells treated with XCUR-FXN compared to its mono-targeting components alone at the same total oligonucleotide dose. These two mechanisms are addressed by two different oligonucleotides, both of which are incorporated at a specific ratio in XCUR-FXN. As discussed during our R&D day presentation in January 2021, in preclinical experiments, we observed that XCUR-FXN increased frataxin protein levels in fibroblasts and neurons derived from FA patients to near normal levels. Importantly, we observed near normal levels of frataxin protein in mitochondrion, the target cellular compartment, and 70-80% of near normal mitochondrial activity in neurons derived from FA patients.

We initiated IND-enabling studies for XCUR-FXN in late 2020 and expect to initiate a first-in-patient Phase 1b clinical trial for XCUR-FXN in 2022. We are collaborating closely with the Friedreich's Ataxia Research Alliance (FARA), the non-profit, charitable organization dedicated to accelerating research leading to treatments and a cure for FA, in the design and site selection of the Phase 1b clinical trial. The Phase 1b clinical trial is designed to demonstrate safety and characterize pharmacokinetic properties of multiple ascending doses of XCUR-FXN in FA patients and inform Phase 2/3 dose selection. We are also planning to examine multiple biomarkers, including brain imaging and measurements of frataxin levels in patient cerebrospinal fluid (CSF), to provide rapid read-out for target engagement and pharmacodynamic (PD) effects. We may include one or more exploratory endpoints, such as modified Friedreich's Ataxia Rating Scale (mFARS), to prepare for a subsequent pivotal clinical trial.

Other neurological indications

We are building on our proof-of-concept work with nusinersen (see below) and our therapeutic candidate XCUR-FXN to further explore new therapeutic applications of our SNA technology in neurology. We aim to address indications with great unmet medical need and where we believe the attributes of our SNA technology would lead to therapeutic and commercial advantages. In order to select new therapeutic indications, we expect to analyze a variety of attributes including: (i) indications where there is a known genetic basis for the disorder, (ii) disorders where we can target multiple genes, (iii) the existence of a patient registry or a patient advocacy group that can work with us for easier trial enrollment, (iv) the competitive therapeutic landscape including disorders not easily addressable by small molecules or antibodies, (v) indications with no approved therapies, and (vi) indications amenable to localized therapeutic administration. Based on these and other criteria, we are currently exploring additional neurological conditions, including spinocerebellar ataxia, Batten disease, amyotrophic lateral sclerosis (ALS), and Huntington's disease. Preclinical development activities are underway for SCN9A for neuropathic pain and CLN3 for Batten disease.

Neurology–Proof-Of-Concept Work with Nusinersen

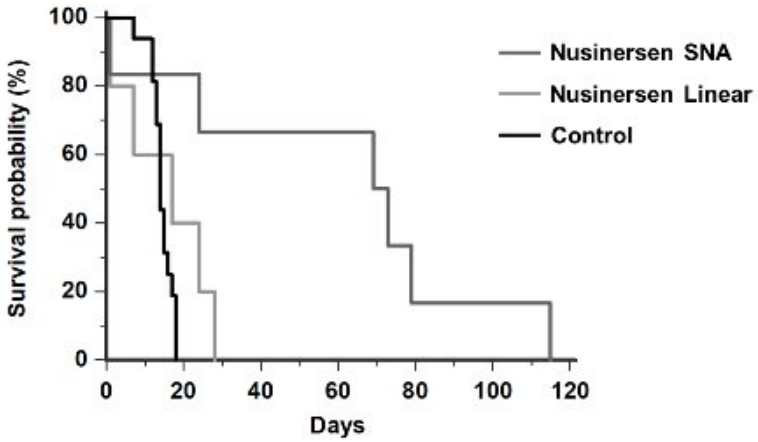
Despite delivery challenges, nucleic-acid based therapy has been successfully developed to treat a central nervous system, or CNS, disorder. Nusinersen, by Ionis Pharmaceuticals and Biogen Inc., was approved by the FDA in late 2016 for the treatment of spinal muscular atrophy, or SMA. SMA is a genetic 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 resulted 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. Newborn 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, we 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.

In June 2019, we announced data from a preclinical study evaluating the biodistribution of SNAs in the non-human primate central nervous system. In our study, 7 mg of radio-labeled SNAs were injected intrathecally into cynomolgus monkeys. The biodistribution of the SNAs was followed for 14 days by PET/CT scans. SNAs were observed throughout the entire brain and were found both in the brain stem as well as inside the brain. High content of SNA was observed in all 46 regions of the brain examined. These key data indicate that the SNA platform may be well-suited for development of new therapeutics directed towards diseases of the central nervous system.

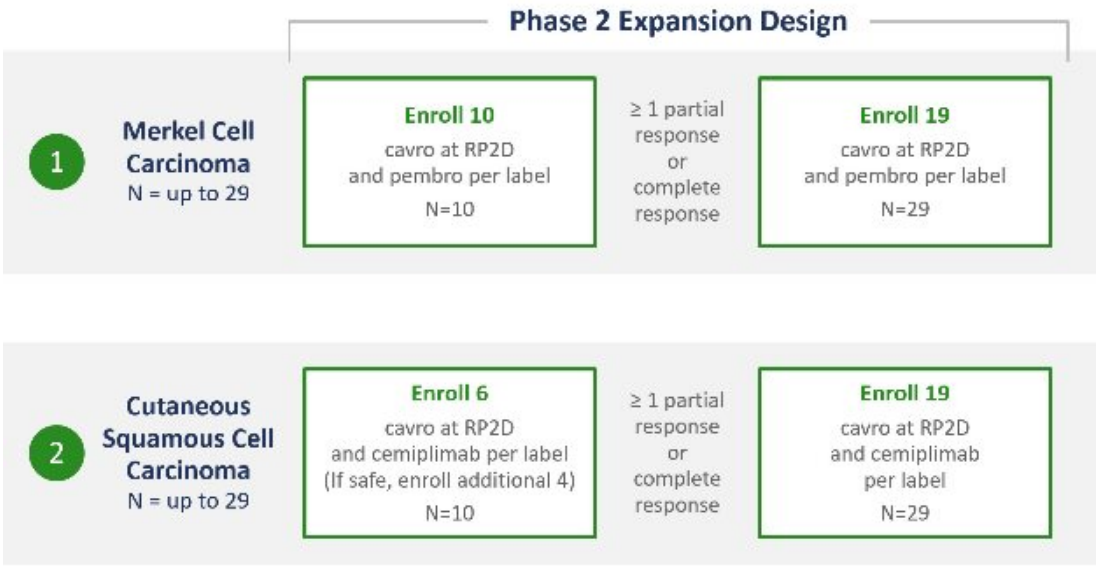
Immuno-oncology, *cavrotolimod (AST-008)*

Cavrotolimod (AST-008) is a toll-like receptor 9, or TLR9, agonist designed for immuno-oncology applications utilizing the key strengths of our SNA technology. TLR9 agonists bind to and activate TLR9. We believe cavrotolimod (AST-008) may be used for immuno-oncology applications in combination with checkpoint inhibitors. We have observed that, in preclinical studies in a variety of tumor models, cavrotolimod (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 cavrotolimod (AST-008) was active when administered subcutaneously, intratumorally or intravenously, in both prevention and established mouse tumor models. The administration of cavrotolimod (AST-008) also produced localized as well as abscopal anti-tumor activity in mouse cancer models. Additionally, the administration of cavrotolimod (AST-008) in combination with certain checkpoint inhibitors conferred adaptive immunity in breast and colon cancer mouse models. In mouse tumor models, administration of cavrotolimod (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 2 clinical development of cavrotolimod (AST-008)

Using data from the completed Phase 1b stage of our Phase 1b/2 clinical trial, a recommended Phase 2 dose of 32 mg cavrotolimod (AST-008) was identified for the Phase 2 portion of the clinical trial which is currently underway, whereby cavrotolimod (AST-008) is being given in combination with pembrolizumab or cemiplimab for the treatment of locally advanced or metastatic Merkel cell carcinoma, or cutaneous squamous cell carcinoma, respectively, in patients with progression despite approved anti-PD-(L)1 therapy. We are enrolling two separate cohorts of patients with advanced or metastatic MCC or CSCC. Each cohort is expected to enroll up to 29 patients who have failed anti-PD-1/PD-L1, or programmed cell death protein 1/programmed death-ligand 1, therapy. In addition, we have added an exploratory cohort to include patients with melanoma who have progressed on PD-(L)-1 therapy and MCC patients who do not qualify for the primary MCC cohort. In June 2020, we reported that we dosed the first patient in the MCC cohort of the trial.

The diagram below illustrates our planned design of the Phase 2 portion of the trial (not including the exploratory cohort):



Cavro: cavrotolimod (AST-008); RP2D: Recommended Phase 2 dose; Pembro: pembrolizumab

As of February 23, 2021, we had 16 clinical trial sites open for enrollment and 7 additional sites pending activation. We expect to open up to 30 sites for the Phase 2 stage of the clinical trial. We anticipate all sites will be activated by the end of 2021. As of February 23, 2021, we had dosed 16 patients with 32 mg of cavrotolimod (AST-008) in the Phase 2 portion of the clinical trial, including the primary and exploratory cohorts. Including the six patients dosed with 32 mg of cavrotolimod (AST-008) in the Phase 1b portion of the clinical trial, a total of 22 patients have been dosed with 32 mg of cavrotolimod (AST-008). As of February 23, 2021, 1 of the 22 patients dosed with 32 mg of cavrotolimod (AST-008) has experienced a treatment-related SAE as determined by the clinical trial investigator. This patient, enrolled in the Phase 2 stage of the clinical trial, reported a treatment-related SAE of hypotension, flu-like symptoms which subsequently resolved. None of the 14 patients dosed in the Phase 1b portion of the clinical trial with doses of cavrotolimod (AST-008) less than 32 mg experienced a treatment related SAE. Thus, as of February 23, 2021, in total, 1 of 36 patients treated with cavrotolimod (AST-008) have experienced a treatment related SAE.

In January 2021, we announced that the FDA has granted Fast Track designations for cavrotolimod (AST-008), for two development programs: (i) cavrotolimod in combination with anti-programmed death-1 (PD-1) therapy for the treatment of patients with locally advanced or metastatic Merkel cell carcinoma (MCC) refractory to prior anti-PD-1 blockade and (ii) cavrotolimod in combination with anti-PD-1 therapy for the treatment of patients with locally advanced or metastatic cutaneous squamous cell carcinoma (CSCC) refractory to prior anti-PD-(L)1 blockade.

In March 2021, we announced that the FDA has granted Orphan Drug Designation for cavrotolimod (AST-008) for the treatment of patients with MCC.

Phase 1b/2 clinical development of cavrotolimod (AST-008)

We commenced a Phase 1b/2 clinical trial of cavrotolimod (AST-008) in patients with advanced solid tumors in late 2018. The Phase 1b stage was an open-label, multi-center trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of intratumoral cavrotolimod (AST-008) injections alone and in combination with intravenous pembrolizumab in patients with advanced solid tumors. We have completed the enrollment of the Phase 1b stage of the clinical trial. The 20 patients from the Phase 1b stage included those with advanced or metastatic Merkel cell carcinoma, or MCC, head and neck squamous cell carcinoma,

cutaneous squamous cell carcinoma, or CSCC, melanoma and leiomyosarcoma. At the time of enrollment, 85% of patients were experiencing progressive disease despite treatment with PD-1 blockade and 65% of patients had been treated with 2 or more lines of systemic therapy. We have presented our findings from the Phase 1b stage in multiple public disclosures, including at numerous scientific meetings, in December 2019 when we reported preliminary results showing potential signs of anti-tumor activity in patients with MCC, and at a virtual meeting we hosted in September 2020. The key results from the Phase 1b stage include:

- No observed treatment-related SAEs or dose limiting toxicity, or DLT;
- Cavrotolimod (AST-008) was well tolerated with 98% of all treatment-emergent adverse events, or AEs, assessed as Grade 1 or 2 in severity; the most common adverse events were flu-like symptoms and injection site reactions, which we believe reflects local and systemic immune activation and are commonly expected effects from TLR9 activation;
- Confirmed overall response rate, or ORR, of 21% (4/19 evaluable patients) in the Phase 1b dose-escalation stage across all doses, with 1 complete response and 3 partial responses;
- Confirmed ORR 33% (2/6 patients) in the highest dose cohort (32 mg), which was selected as the Phase 2 recommended dose;
- Overall responses occurred in two patients with advanced MCC and two patients with melanoma;
- Three of four responders were progressing on anti-PD-1 therapy at the time of enrollment;
- Durable and ongoing responses, with progression-free survival exceeding six months in all four responders and 16 months in two responders;
- In addition to the four confirmed responses, target tumor shrinkage occurred in one CSCC patient and two melanoma patients, thus 37% of evaluable patients experienced target tumor shrinkage;
- Systemic or abscopal effects were observed, with regression in noninjected tumors distant from injected lesions;
- Increases in leukocytes in injected tumors after cavrotolimod (AST-008) alone and in combination with pembrolizumab versus baseline. Uninjected tumors also showed increased immune cell levels after patients received cavrotolimod (AST-008) plus pembrolizumab;
- Dose-dependent activation of key immune cells, including cytotoxic T cells and natural killer cells, as well as increases in cytokine/chemokine levels in patient blood after cavrotolimod (AST-008) treatment alone, and cavrotolimod (AST-008) plus pembrolizumab treatment; and
- The cavrotolimod pharmacodynamic profile corroborated the efficacy data, as increased serum cytokines/chemokines, activated immune cells, and tumor infiltration by immune cells were observed.

Phase 1 clinical development of cavrotolimod (AST-008)

The Phase 1 clinical trial was a first-in-human clinical trial of cavrotolimod (AST-008) evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of cavrotolimod (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, cavrotolimod (AST-008) was shown to be safe and tolerable in all subjects, with no serious adverse events and no dose limiting toxicity. Cavrotolimod (AST-008) was well tolerated and all cavrotolimod (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. Cavrotolimod (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 cavrotolimod (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, cavrotolimod (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, cavrotolimod (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 cavrotolimod (AST-008) of the key effectors cells of both the innate and adaptive immune system makes cavrotolimod (AST-008) suitable for combination with checkpoint inhibitors.

Dermatology

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 the fourth quarter of 2018, we reported results from our Phase 1 clinical trial of XCUR17. Of the 21 treated patients, we observed that the 11 patients treated with the highest strength of XCUR17 gel had a reduction in redness and improvement in healing as determined by blinded physician assessments. We also observed no adverse safety events and no relevant changes in mean psoriatic infiltrate thickness related to treatment with XCUR17.

In October 2019, at the 15th Annual Meeting of the Oligonucleotide Therapeutics Society, we disclosed biomarker results from the skin biopsies collected from the 21 patients treated in the Phase 1 clinical trial. Clinical observations in this Phase 1 trial correlated with psoriasis-related markers and histological changes from biopsies provided by the patients. In this trial, we observed clinically that XCUR17 had:

- Resulted in a decrease in the levels of psoriasis and inflammation markers downstream of its target, IL-17RA;
- Produced a statistically significant reduction in keratin 16 expression, a key marker of psoriasis (p=0.002);
- Resulted in reductions in the major inflammatory markers beta defensin 4A, interleukin 19, and interleukin 36A versus psoriatic skin at baseline; and
- Revealed clinical improvements that matched reductions in keratin 16 protein and epidermal thickness.

We believe these findings suggest that SNA-based drugs, such as XCUR17, may address clinical symptoms in patients with inflammatory diseases, such as psoriasis. We currently are not conducting additional clinical activities for XCUR17 and we seek to out-license the XCUR17 program.

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.

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.

We believe that the eye may be an attractive organ for locally-applied SNAs because (i) it is a small and immune-privileged organ, (ii) there are established and non-invasive clinical assessment procedures, and (iii) effective trials can be designed by using a contralateral control eye. We believe that our preclinical data using SNA technology may provide proof-of-concept for expansion of our research and development activities into ophthalmological genetic disorders. Our preclinical data indicated that SNAs distributed to both posterior (retinal) and anterior (cornea) ocular structures, exhibited higher distribution and persisted longer compared to linear oligonucleotides, and did not cause inflammation in the eye.

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 SNAs may possess key potential advantages over gene therapy in the eye. These key potential advantages include: (i) delivery via intravitreal injections which are safer and easier than subretinal injections, (ii) tunable and reversible control of target expression, and (iii) the ability to treat toxic gain-of-function diseases and target large genes. We believe, based on our internal analysis, that there are approximately 250 rare ophthalmological diseases with known genetic targets, such as CLN3 for Batten disease, BEST1 for vitelliform macular dystrophy, and USH2A for usher syndrome type 2A. As such, we intend to continue to evaluate expansion of our preclinical research and development activities in ophthalmology.

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.

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 cavrotolimod (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.

Our Collaboration Programs

AbbVie Collaboration Agreement

On November 13, 2019, we entered into a Collaboration, Option and License Agreement, or the "AbbVie Collaboration Agreement, with a wholly-owned subsidiary of Allergan plc, Allergan. On May 8, 2020, Allergan plc, including Allergan, was acquired by AbbVie. Pursuant to the AbbVie Collaboration Agreement, we granted to AbbVie exclusive access and options to license SNA based therapeutics arising from two collaboration programs related to the treatment of hair loss disorders. Under each such license, we grant to AbbVie exclusive, royalty-bearing, sublicenseable, nontransferable, worldwide rights to develop, manufacture, use and commercialize such SNA therapeutics.

Under the terms of the AbbVie Collaboration Agreement, we received an upfront payment of $25 million, and, if AbbVie exercises any of its option rights under the agreement, AbbVie will pay us an option exercise fee equal to $10 million for each exercised option, if such option is exercised during the initial option exercise period. AbbVie may extend an option exercise period beyond the applicable initial exercise period for a particular program for an additional fee.

If AbbVie exercises an option for a program, we are eligible to receive up to an aggregate of $55 million for development milestone payments and $132.5 million for product approval and launch milestones, per program. We are also eligible to receive up to $175 million in sales milestone payments, on a program by program basis, associated with aggregate worldwide sales. In the event a therapeutic candidate subject to the collaboration results in commercial sales, we are eligible to receive tiered royalties at percentages ranging from the mid-single digits to the mid-teens on future net product sales of such commercialized therapeutic candidates. A percentage of the aforementioned payments will be due to Northwestern University, or Northwestern, upon receipt, pursuant to our existing license agreements with Northwestern.

Dermelix Collaboration Agreement

On February 17, 2019, we 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, or NS, and, at Dermelix's option, up to five additional rare skin indications.

Dermelix will initially develop a targeted therapy for the treatment of 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 LEKTI involved in skin barrier function. NS affects approximately one 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 Dermelix License Agreement, Exicure received an upfront payment of $1 million at closing of the transaction and is eligible to receive up to 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 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 our expenses incurred in connection with development activities and in accordance with the development budget. 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 Agreement

AST-005

AST-005 is an SNA targeting TNF for the treatment of mild to moderate psoriasis. In a completed Phase 1 clinical trial, AST-005, when topically administered, 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.

In 2016, we entered into a research collaboration, option and license agreement with Purdue Pharma L.P., under which a Phase 1b clinical trial evaluated 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 previously studied, but did not result in a statistically significant decrease in echo lucent band thickness, one of the key indicators of efficacy. In 2018, Purdue declined to exercise its option to develop AST-005 at that time, but indicated its intent to retain rights relating to the TNF target and reserved its right to continue joint development, with Exicure, of new anti-TNF drug candidates and to retain its exclusivity and other rights in AST-005.

In 2019, Purdue, while re-asserting its right to develop new anti-TNF therapeutic candidates, indicated it will not select any collaboration targets. As a result, we will not receive any research, regulatory and commercial sales milestones contingent upon successful development of such collaboration targets. At this time, there are no active development activities underway for a new anti-TNF therapeutic candidate. As a consequence, we also believe that it is highly unlikely that we will receive any research, regulatory and commercial sales milestones from Purdue for any anti-TNF therapeutic candidates.

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 cavrotolimod (AST-008), XCUR-FXN, XCUR17, and AST-005 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, 2020, our patent portfolio consists of over 80 issued patents and allowed patent applications and over 110 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 29 from NU, we exclusively own 73, we jointly own 2 with Dermelix, 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 cavrotolimod (AST-008) patent portfolio includes 31 issued and 31 pending U.S. nonprovisional and foreign patent applications. Foreign jurisdictions where we are seeking patent protection for our cavrotolimod (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 between 2034 and 2040. 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 XCUR-FXN patent portfolio includes one pending U.S. provisional patent application. We intend to protect the composition of matter and methods of use of XCUR-FXN. Any patent that may issue from this application would expire by 2041. 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 XCUR17 patent portfolio includes four issued and eleven 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 three issued and seven pending U.S. nonprovisional and foreign patent applications. 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 cavrotolimod (AST-008), XCUR-FXN, 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, our former parent, 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, or 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, or Restated License Agreement. In February 2016, we obtained exclusive license as to Northwestern University's rights in certain SNA technology we jointly own with Northwestern University, or Co-owned Technology License. The Company's 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, or Wound Healing License. Our rights and obligations in the Co-owned Technology License and the Wound Healing License agreements are substantially the same as in the Restated License Agreement from August 2015, or collectively referred to as the Northwestern University License Agreements. As of December 31, 2019, all pending patent applications under the Wound Healing License have been abandoned. 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, a percentage of all sublicense payments we receive, and 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 the Northwestern University License Agreements 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 intellectual property strategy

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, patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country, assuming that all maintenance fees are paid and the patent has not been invalidated. In certain jurisdictions, and in certain circumstances, patent terms can be extended, for example, by patent term adjustment or extension, or shortened, for example, by terminal disclaimer. We are pursuing patent protection in jurisdictions that represent significant global pharmaceutical market 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 may 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., Stoke Therapeutics, Inc., Neubase Therapeutics, Inc., Idera Pharmaceuticals, Inc., Avidity Biosciences, Checkmate Pharmaceuticals, Inc., Dyne Therapeutics, Inc., Atalanta Therapeutics, Inc., and others. 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

In oncology, we face significant competition from pharmaceutical and biotechnology companies as well as universities and private and public research institutions. For application in conjunction with immune checkpoint inhibitors, there are several immuno-oncology competitors to cavrotolimod both in development and on the market. Cavroltolimod, a TLR9 agonist, is among several other agents in this class being studied in clinical trials for different tumor types, including melanoma and head and neck squamous cell carcinoma. Currently, the checkpoint inhibitors avelumab and pembrolizumab are approved by the FDA for patients with advanced MCC and cemiplimab is approve for the treatment of advanced CSCC. We are aware of many ongoing clinical trials where these and other checkpoint inhibitors are being tested in combination with experimental therapies to potentially treat MCC and CSCC, such as Replimune’s oncolytic virus-based RP1 which is in development for solid tumors, including melanoma and cutaneous squamous cell carcinoma, and experimental therapies by NantKWest, Kartos Therapeutics, 4SC, and others for potential treatment of MCC. Furthermore, adoptive cell therapies such as CAR-T cells, that demonstrate efficacy for the treatment of B-cell malignancies, are being evaluated for solid tumors.

Competition in Friedreich's ataxia

We consider the following therapeutics to be competitors and potential future competitors to XCUR-FXN for the treatment of Friedreich's ataxia:

Therapeutic	Company	Description of therapeutic	Development Phase
Omaveloxolone	Reata Pharmaceuticals	Synthetic triterpenoid that activates Nrf2 and restores mitochondial activity	Registrational phase 2
Vatiquinone	PTC Therapeutics	Small molecule antioxidant that protects against oxidative stress-mediated cell death	Registrational phase 3
CTI-1601	Larimar Therapeutics	Recombinant human frataxin fusion protein	Phase 1
Leriglitazone	Minoryx Therapeutics	Small molecule PPARγ that protects against mitochondrial dysfunction and oxidative stress	Phase 2
Syn-TEF	Design Therapeutics	Synthetic transcription elongation factor	Preclinical

In addition, there are ongoing programs and gene therapy approaches using adeno-associated virus (AAV) vectors that, if approved, may compete with XCUR-FXN for the treatment of FA.

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 United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, 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. 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. 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.

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.

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 program fee for approved products. Application 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. 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.

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. 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.

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 addition to the Fast Track, accelerated approval and priority review programs discussed above, 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.

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. Although physicians may in their independent medical judgment prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. Manufacturers may only share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including civil and criminal actions.

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 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, referred to as the national procedure; (ii) via mutual recognition of a national authorization in other EU Member States, referred to as 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 the applicant to choose the EU Member State in which they wish 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. Regulation (EC) No. 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the product in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must also demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the product has to be of significant benefit compared to products available for the condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance and the possibility to apply for a centralized European Union marketing authorization. The grant of a marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the EMA nor the European Commission or the Member States can accept an application or grant a marketing authorization for the same therapeutic indication in respect of a “similar medicinal product”. A “similar medicinal product” is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity. There are a number of derogations from the ten-year period of market exclusivity pursuant to which the European Commission may grant a marketing authorization for a similar medicinal product in the same therapeutic indication, including where the second applicant can establish that although their product is similar to the orphan medicinal product already authorized, the second product is safer, more effective or otherwise clinically superior.

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 manufacturers to participate in a coverage gap discount program, under which they must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.
- 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 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.

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.

Since its enactment, there have been judicial, administrative, executive and Congressional legislative challenges to certain aspects of the ACA. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate," or the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017, or the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unknown when a decision will be made. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the ACA.

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 for each item of false or omitted information and 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.

In the United States, no uniform policy exists for coverage and reimbursement for pharmaceutical products among third-party payors. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. 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. One third-party payor's decision to cover a particular product or service does not ensure that other payors will also provide coverage for the medical product or service, and the level of coverage and reimbursement can differ significantly from payor to payor. 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.

In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to

obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics. Additionally, if any companion diagnostic provider is unable to obtain reimbursement or is inadequately reimbursed, that may limit the availability of such companion diagnostic, which would negatively impact prescriptions for our product candidates, if approved.

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 2030 with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, 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. 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.

At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the Department of Health and Human Services finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the U.S. District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic.

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, Data Privacy and Security 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 as well as information security 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, per kickback plus three times the amount of remuneration and a 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 for each false claim and treble the amount of the government's damages. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. 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.

We may be subject to the federal Civil Monetary Penalties Law, which prohibits, among other things, the offering or transferring of remuneration to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of Medicare or Medicaid payable items or services. Federal government price reporting laws require manufacturers to calculate and report complex pricing metrics to government programs.

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, and their covered subcontractors. 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.

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 (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as physician ownership and investment interests held by physicians and their immediate family members in the manufacturer. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made in the previous year to certain non-physician providers, such as physician assistants and nurse practitioners. 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 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. There are also state and local laws that require the registration of pharmaceutical sales representatives. 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.

Human Capital Resources

As of December 31, 2020, we had 63 full time employees, of which 54 were engaged in research and development activities and 9 were 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.

To facilitate talent attraction and retention, we strive to make Exicure a safe and rewarding workplace, with opportunities for our employees to grow and develop in their careers, supported by strong compensation, benefits and health and wellness programs.

Our base pay program aims to compensate staff members relative to the value of the contributions of their role, which takes into account the skills, knowledge and abilities required to perform each position, as well as the experience brought to the job. In addition to salaries, our compensation program includes potential annual discretionary bonuses, equity awards under our equity incentive program, a 401(k) Plan with matching contributions, an employee stock purchase plan, healthcare and insurance benefits, health savings and flexible spending accounts, paid time off to include time for volunteer activities, family leave, flexible work schedules, among others. We also use targeted equity-based grants with vesting conditions to facilitate retention of personnel, particularly those with critical skills and experience. Potential annual discretionary bonuses are pursuant to our annual incentive programs to reward eligible staff in alignment with achievement of Company-wide goals that are established annually and designed to drive aspects of our strategic priorities that support and advance our strategy across our Company. All staff also participate in a regular performance measurement process that aligns pay to performance and through which staff receive performance and development feedback.

Our benefit programs are generally broad-based, promote health and overall well-being and emphasize saving for retirement. All full-time staff members are eligible to participate in the same core health and welfare and retirement savings plans.

Our Compensation Committee provides oversight over our compensation strategy including review of our plans, policies, and programs.

In response to the evolving COVID-19 pandemic and related public health directives, orders and guidance, and to ensure the safety and wellbeing of our employees, we have implemented work-from-home policies to support the community efforts to reduce the transmission of COVID-19 and protect employees, complying with guidance from federal, state/provincial or municipal government and health authorities. We implemented a number of measures to ensure employee safety and business continuity. Under social distancing guidelines for COVID-19, we were typically operating with less than 50% of our R&D staff on-site at any one time through June 30, 2020. As of July 1, 2020, we took occupancy of approximately 30,000 square feet of laboratory and office space in our new headquarters in Chicago, Illinois. Since then, we have operated under COVID-19 social distancing guidelines and have generally operated with 100% of our R&D staff on-site. Our office and general and administrative team continues to work predominantly from home. We are managing laboratory staffing and taking other appropriate managerial actions to maintain progress on our preclinical and collaboration programs. Business travel has been suspended, and online and teleconference technology is used to meet virtually rather than in person. We have taken measures to secure our research and development project activities, while work in laboratories and facilities has been organized to reduce risk of COVID-19 transmission. For employees working in our laboratories and facilities, we have also taken additional safety measures, including implementing social distancing, providing and requiring the use of personal protective equipment, temperature screening, restricting business travel, and under certain circumstances, requiring COVID-19 testing to access our workplace.

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 (as defined below), 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 Operating Company (Exicure OpCo) through a transaction on September 26, 2017, or the Merger. 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 a private placement transaction on September 26, 2017, the business of Exicure OpCo became our business.

Our corporate headquarters are located at 2430 N. Halsted St., Chicago, Illinois 60614, 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 are subject to the informational requirements of the Exchange Act, and, accordingly, file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, with the Securities and Exchange Commission, or SEC. In addition, the SEC maintains a web site (http://www.sec.gov) that contains material regarding issuers that file electronically, such as ourselves, with the SEC.

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 Annual Report on Form 10-K or our other filings with the SEC, and should not be relied upon.

Item 1A. Risk Factors.

In addition to other information contained in this Annual Report on Form 10-K, the following risks should be considered in evaluating our business and future prospects and an investment in our common stock. The risks and uncertainties described below are not the only ones we face. If any of the following risks and uncertainties develops into actual events, our business, financial condition, results of operations and cash flows could be materially adversely affected. In that case, the price of our common stock could decline and you may lose all or part of your investment.

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 therapeutics for immuno-oncology, genetic disorders and other indications based on our proprietary SNA technology. 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, 2020, we have generated an accumulated deficit of $124.8 million. For the years ended December 31, 2020 and 2019, our net loss was $24.7 million and $26.3 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 based on our proprietary SNA technology. We believe that therapeutic candidates identified with our therapeutic discovery technology may offer an improved therapeutic approach compared 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 SNA technology and the identification and optimization of SNA-based therapeutic candidates is relatively new. Further, the scientific evidence to support the feasibility of developing therapeutic treatments based on SNA technology 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 SNA-based therapeutic candidates 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 SNA-based therapeutic candidate. We may

spend substantial funds attempting to introduce these properties and may never succeed in doing so. In addition, therapeutic candidates based on SNA technology 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, or FDA, and equivalent foreign regulatory authorities have limited experience with SNA-based therapeutics. No regulatory authority has granted approval to any person or entity, including us, to market and commercialize SNA-based therapeutics, 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, or 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, the availability of effective treatments for the relevant disease, and COVID-19-related developments including the extent to which they may interact with any of the foregoing factors.

A therapeutic candidate can unexpectedly fail at any stage of preclinical and clinical development. 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 or ethics committees 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, or EMA, or European Union national competent authorities, regarding the scope or design of our clinical trials;
- further 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.

Additionally, some of the clinical trials we conduct may be open-label in study design and may be conducted at a limited number of clinical sites on a limited number of patients. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Given that our planned open-label Phase 1b/2 clinical trial of cavrotolimod (AST-008) includes an open-label dosing design, the results from this clinical trial may not be predictive of future clinical trial results with this or other product candidates for which we conduct an open-label clinical trial when studied in a controlled environment with a placebo or active control.

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, 2020, we had $34.5 million in cash, cash equivalents, and restricted cash and $48.8 million in short-term investments. Based on our current operating plans, we believe that existing working capital at December 31, 2020, including amounts borrowed and available under the MidCap Credit Facility, is sufficient to fund our operations for at least 12 months from the date of this report. 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 collaboration, option, and license agreement with AbbVie Inc., or AbbVie, our research collaboration, license, and option agreement with Purdue Pharma L.P., or Purdue, our license and development agreement with Dermelix LLC, or Dermelix, or as a primary contractor or as a subcontractor on government grants, proceeds from our credit and security agreement with MidCap Financial Trust, or MidCap, 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, and our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. If we raise additional funds by issuing equity securities or by sales pursuant to our "at the market" program, 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 business could be adversely affected by the effects of health epidemics, including the global COVID-19 pandemic, in regions where we or third parties on which we rely have business operations and at our clinical trial sites, as well as the business or operations of our CROs or other third parties with whom we conduct business.

The outbreak of the novel strain of coronavirus, SARS-CoV-2, which causes coronavirus disease 2019, or COVID-19, continues to negatively impact the global economy. Our business and operations could be adversely affected by the effects of health epidemics, including the ongoing COVID-19 pandemic, on our business activities performed by us or by third parties with whom we conduct business, including our third party manufacturers, contract research organizations, or CROs, shippers and others. Such effects could be more pronounced in regions where we have concentrations of clinical trial sites or other business operations. Our company headquarters is located in Chicago, Illinois, our CROs are located globally, and our substance and drug product manufacturers are located in the United States and Europe.

As of March 5, 2021, Illinois is under "Phase 4" of the Restore Illinois Plan, which is intended to permit the expansion of business and community operations based on their compliance with the safety guidelines described in the regulations, with new mitigation measures that may require additional restrictions or adaptations being applied on a regional basis within the State of Illinois based on risk levels depending on the health progress of each region to prevent the ongoing spread of COVID-19. Certain jurisdictions have begun re-opening only to return to restrictions in the face of increases in new COVID-19 cases. The extent of and timing for lifting of government restrictions remains uncertain as the COVID-19 pandemic continues to evolve. There is no guarantee that prior or new restrictions will not be reinstated in response to the continued spread of COVID-19.

In response to these public health directives and orders and to ensure the safety and wellbeing of our employees, we have implemented work-from-home policies to support the community efforts to reduce the transmission of COVID-19 and protect employees, complying with guidance from federal, state/provincial or municipal government and health authorities. We implemented a number of measures to ensure employee safety and business continuity. Under social distancing guidelines for COVID-19, we were typically operating with less than 50% of our R&D staff on-site at any one time through June 30, 2020. As of July 1, 2020, we took occupancy of approximately 30,000 square feet of laboratory and office space in our new headquarters in Chicago, Illinois. Since then, we have operated under COVID-19 social distancing guidelines and have generally operated with 100% of our R&D staff on-site. Our office and general and administrative team continues to work predominantly from home. We are managing laboratory staffing and taking other appropriate managerial actions to maintain progress on our preclinical and collaboration programs. Business travel has been suspended, and online and teleconference technology is used to meet virtually rather than in person. We have taken measures to secure our research and development project activities, while work in laboratories and facilities has been organized to reduce risk of COVID-19 transmission.

The regions in which we operate are currently being affected by COVID-19 and have become subject to additional government-imposed mitigation measures to prevent the ongoing spread of COVID-19. Further, timely enrollment in our clinical trials is dependent upon clinical trial sites which may be adversely affected by the COVID-19 pandemic or its impact or effects. During the third quarter of 2020 and through December 31, 2020, we have observed delays in our enrollment plans for the Phase 2 dose expansion phase of the trial. We believe the effects of the COVID-19 pandemic or its impact have contributed to such delays. As a result, we have lengthened our clinical development timeline for cavrotolimod (AST-008) and now expect to report ORR results in the first half of 2022 rather than by year end 2021 as previously guided in September 2020. Quarantines, shelter-in-place, safer-at-home, social distancing requirements and similar government orders, business shutdowns and closures, phased re-openings or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could continue to occur, related to COVID-19 or other infectious diseases could impact personnel at third-party manufacturing facilities and CROs in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain. Additionally, our clinical trials may involve immunocompromised patients who are at higher risk for COVID-19 and who are therefore more likely to avoid hospitals or other high risk areas.

The effects of the executive orders and our work-from-home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines (for example, our timelines for any of our product candidates), the magnitude of which will continue to depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course.

As a result of the COVID-19 outbreak, or similar pandemics, we may experience further disruptions that could severely impact our business, clinical trials and preclinical studies, including:

- further delays or difficulties in enrolling or maintaining patients in our clinical trials, including patients who may not be able to comply with clinical trial protocols if quarantines, shelter-in-place or safer-at-home restrictions, or social distancing practices or requirements, business shutdowns and closures, among other similar requirements or government orders, continue to impede patient movement or interrupt healthcare services;
- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19, being forced to quarantine, or being unable to visit clinical trial locations;

- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff who may have heightened exposure to COVID-19 or experience additional restrictions by their institutions, city, or state;
- delays or disruptions in non-clinical experiments and investigational new drug application-enabling good laboratory practice standard toxicology studies due to unforeseen circumstances in supply chain;
- diversion or prioritization of healthcare resources away from the conduct of clinical trials and towards the COVID-19 pandemic, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, and because, who, as healthcare providers, may have heightened exposure to COVID-19 and adversely impact our clinical trial operations;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- interruption of our key clinical trial activities , such as clinical assessments at pre-specified time points during the trial and clinical trial site data monitoring, due to limitations on travel imposed or recommended by governmental entities, employers and others or interruption of clinical trial subject visits and study procedures (particularly any procedures that may be deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA, European Medicines Agency and comparable foreign regulatory agencies or their refusal to accept data from clinical trials in affected geographies, which may impact approval timelines;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people.

For our clinical trials that we might conduct at sites outside the United States, in addition to the risks listed above, we may also experience the following adverse impacts, particularly in countries which are experiencing heightened impact from the COVID-19 pandemic:

- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global shipping that may affect the transport of clinical trial materials, such as investigational drug product and comparator drugs used in our clinical trials;
- changes in local regulations as part of a response to the COVID-19 outbreak which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and
- the refusal of the FDA to accept data from clinical trials in these affected geographies.

The spread of COVID-19, which continues to cause broad global impact, may materially affect us economically. The trading price for our shares as well as the trading prices of other biopharmaceutical companies, as well as the broader equity and debt markets overall, have been highly volatile as a result of the COVID-19 pandemic and the resulting impact on U.S. economic activities. Although the potential economic impact brought by, and the duration or subsequent reoccurrence of, the COVID-19 pandemic may be difficult to assess or predict, a widespread pandemic could continue to result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, even after the COVID-19 pandemic has

subsided, a recession or market correction that has occurred or may occur in the future because of the COVID-19 could materially affect our business and the value of our common stock.

The global outbreak of COVID-19 continues to rapidly evolve. The extent to which the COVID-19 pandemic or a similar pandemic will impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration and severity of the outbreak, the possibility of additional periods of increases or spikes in the number of COVID-19 cases, limitations on our ability to conduct our business in the ordinary course, any reopening plans and additional closures, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions for us, our third party contractors and the effectiveness of actions taken in the United States and other countries to contain and treat the disease, including, without limitation, the effectiveness and timing of vaccination initiatives in the United States and worldwide. The ultimate impact of the COVID-19 pandemic or a similar health pandemic is highly uncertain and subject to change; we continue to monitor the COVID-19 situation closely.

If we continue to experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be further delayed or prevented.

We may not be able to initiate or continue conducting clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. Some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is affected by other factors including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the eligibility criteria for, and design of, the trial in question;
- the perceived risks and benefits of the product candidate under study;
- competition in recruiting and enrolling patients in clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients; and
- delays or difficulties due to the COVID-19 pandemic or its impact or effects.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. We may encounter further difficulties and/or delays in completing our planned enrollments. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, or the inability to complete development of our product candidates, which would cause the value of our company to decline, limit our ability to obtain additional financing, and materially impair our ability to generate revenues.

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 economic, industry, political and market conditions, including, but not limited to, the ongoing impact of the COVID-19 pandemic.

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 AbbVie, which began in November 2019, and Dermelix, which began in February 2019, 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 therapeutic 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, 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 GLPs, and clinical trials to be conducted in accordance with applicable FDA regulations and 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.

In addition, the operations of our CROs may be constrained or disrupted by the COVID-19 pandemic. Clinical site closure and other activities that require visits to clinical sites, have been and may continue to be delayed due to prioritization of hospital resources toward the COVID-19 pandemic or concerns among patients about participating in clinical trials during a pandemic. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new

CRO commences work. As a result, delays could occur, which could compromise our ability to meet our desired development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition 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 limited number of suppliers 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 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 cGMPs 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.

If our relationships with our manufacturers, suppliers or other vendors are terminated or scaled back as a result of the COVID-19 pandemic or other health epidemics, we may not be able to enter into arrangements with alternative suppliers or vendors or do so on commercially reasonable terms or in a timely manner. Further, if the COVID-19 pandemic continues to persist for an extended period of time and impacts essential distribution systems such as FedEx and postal delivery, we could experience disruptions to our supply chain and operations, and associated delays in the manufacturing and supply of our product candidates. Switching or adding additional suppliers or vendors involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new supplier or vendor commences work. As a result, delays may occur, which could adversely impact our ability to meet our desired clinical development and any future commercialization timelines. Although we carefully manage our relationships with our suppliers and vendors, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not harm our business.

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., Arrowhead Pharmaceuticals, Inc., ProQR Therapeutics N.V., Stoke Therapeutics, Inc., Neubase Therapeutics, Inc., Idera Pharmaceuticals, Inc., Avidity Biosciences, Checkmate Pharmaceuticals, Inc., Dyne Therapeutics, Inc., and others. 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, pembrolizumab and others.

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 and interim Chief Financial Officer, Matthias G. Schroff, Ph.D., our Chief Operating Officer, and Douglas E. Feltner, M.D., our Chief Medical 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 or clinical trials 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.

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

As of December 31, 2020, we had 63 employees. As our development and commercialization plans and strategies develop, and as we further develop as a public company, we expect to need additional managerial, operational, financial and other personnel, including personnel to support our product development and planned future commercialization efforts. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical, FDA and EMA review processes for our product candidates; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a

disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

If we are not able to effectively expand our organization by hiring new employees, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

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. Although a physician may prescribe products for off-label use since the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. Companies may only share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. 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 & Medicaid Services, or CMS, the Department of Health and Human Services, or HHS, Office of Inspector General, or 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.

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 Chicago, 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 Chicago facilities comply with the relevant guidelines of Chicago, 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.

Increasing scrutiny and changing expectations from customers, regulators, investors, and other stakeholders with respect to our environmental, social and governance practices may impose additional costs on us or expose us to new or additional risks.

Companies are facing increasing scrutiny from customers, regulators, investors, and other stakeholders related to their environmental, social and governance practices. Investor advocacy groups, investment funds and influential investors are also increasingly focused on these practices, especially as they relate to the environment, health and safety, supply chain management, diversity and human rights. Failure to adapt to or comply with regulatory requirements or investor or stakeholder expectations and standards could negatively impact our reputation and the price of our ordinary shares.

Any of the factors mentioned above, or the perception that we or our suppliers, or contract manufacturers or collaborators have not responded appropriately to the growing concern for such issues, regardless of whether we are legally required to do so, may damage our reputation and have a material adverse effect on our business, financial condition, results of operations cash flows and/or ordinary share price.

Natural disasters or other unexpected events may disrupt our operations, adversely affect our results of operations and financial condition, and may not be covered by insurance.

The occurrence of one or more unexpected events, including fires, tornadoes, tsunamis, hurricanes, earthquakes, floods, and other forms of severe hazards in the United States or in other countries in which we or our suppliers or manufacturers operate or are located could adversely affect our operations and financial performance. These types of unexpected events could result in physical damage to and complete or partial closure of one or more of the manufacturing facilities operated by our contract manufacturers, or the temporary or long-term disruption in the supply of products, and/or disruption of our ability to deliver products to customers. Further, the long-term effects of climate change on general economic conditions and the pharmaceutical manufacturing and distribution industry in particular are unclear, and changes in the supply, demand or available sources of energy and the regulatory and other costs associated with energy production and delivery may affect the availability or cost of goods and services, including natural resources, necessary to run our businesses. Existing insurance arrangements may not provide protection for the costs that may arise from such events, particularly if such events are catastrophic in nature or occur in combination. Any long-term disruption in our ability to service our customers from one or more distribution centers or outsourcing facilities could have a material adverse effect on our operations, our business, results of operations and stock price.

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 Chicago, 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, 2020, we had $34.5 million in cash, cash equivalents, and restricted cash and $48.8 million in short-term investments. We historically have invested excess cash in certificates of deposit or money market

mutual funds that invest in securities issued or guaranteed by the U.S. government or U.S. government agencies, floating rate and variable rate demand notes of U.S. and foreign corporations, and commercial paper. During the fourth quarter of 2019, we have made direct purchases, and expect to continue to make direct purchases of, 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.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, the Sarbanes-Oxley Act of 2002 and the rules and regulations of The Nasdaq Capital Market. Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are now required to perform system and process evaluation and testing of our internal control over financial reporting to allow our management to report on the effectiveness of our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. Further, we may in the future discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Moreover, our internal controls over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. Moreover, we are aware that the remote working arrangements implemented in connection with the COVID-19 pandemic potentially present new areas of risk, and we continue to monitor carefully any impact to our internal controls and procedures.

If we are unable to assert that our internal control over financial reporting is effective, investors could lose confidence in the reliability of our financial statements, the market price of our stock could decline and we could be subject to sanctions or investigations by The Nasdaq Capital Market, the SEC or other regulatory authorities.

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, 2020, our patent portfolio consists of 80 issued patents and allowed patent applications and 110 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.

Patent term may be inadequate to protect our competitive position on our future therapeutics for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of new therapeutic candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the U.S. and, if available, in other countries where we have patents covering our product candidates. In the U.S., the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, the patent term extension or restoration cannot extend the remaining term of a patent beyond a total of 14 years from the approval date of the product candidate. Only one patent applicable to an approved product candidate is eligible for the extension and the application for extension must be made prior to expiration of the patent. The USPTO, 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 dates. However, the applicable authorities, including the FDA and the USPTO in the U.S., and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

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 or after grant by nonpayment of maintenance fees for the resulting patent. 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 protect the confidentiality 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 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. In addition, unfavorable changes in our industry or the global economy, including as a result of the COVID-19 pandemic, could contribute to some of the events listed above and further impact our ability to progress our clinical trials, submit for marketing approval or commercialize our product candidates, if approved, as planned.

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 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.

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, our current and future business operations may subject us 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, including 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 research, 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 (including any kickback, bribe, or certain rebate), 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. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers, among others, on the other. 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;
- 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. For example, pharmaceutical companies have been prosecuted under the False Claims Act in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. 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;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- HIPAA includes a fraud and abuse provision sometimes 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 the HITECH, and its implementing regulations, which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses and their business associates that perform certain services involving the use or disclosure of individually identifiable health information as well as their covered subcontractors, 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. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, 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 attorneys' fees and costs associated with pursuing federal civil actions;
- the federal Physician Payments 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, or collectively, the ACA, which require that certain manufacturers of pharmaceutical and biological drugs reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program report to CMS all consulting fees, travel reimbursements, research grants, and other

payments, transfers of value or gifts made to U.S.-licensed physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and U.S. teaching hospitals with limited exceptions, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made and ownership and investment interests held and payments made during the previous year to certain non-physician providers, such as physician assistants and nurse practitioners; 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, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of personal data (including personal 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 significant administrative, civil and/or criminal penalties, monetary damages, disgorgement, fines, imprisonment, additional integrity reporting requirements and regulatory oversight, 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.

Patients who are prescribed therapeutics for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved therapeutics. 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). 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, or FSS. 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.

Commercial 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.

In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics. Additionally, if any companion diagnostic provider is unable to obtain reimbursement or is inadequately reimbursed, that may limit the availability of such companion diagnostic, which would negatively impact prescriptions for our product candidates, if approved.

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, effective as of 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 certain health reform legislation and related initiatives, 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.

There have been judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate," or the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017, or the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unknown when a decision will be made. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the ACA and our business.

There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the U.S. District Court in Northern

California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives.

In addition, individual states have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our therapeutic candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our therapeutic candidates, restrict or regulate post-approval activities and affect our ability to commercialize our therapeutic candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic. We cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our current or any future therapeutic candidates we may develop may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

We face potential liability related to the privacy and security of health information we obtain from clinical trials sponsored by us.

Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the HITECH. We are not currently classified as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial penalties if we receive or use individually identifiable health information from a HIPAA-covered healthcare provider or research institution or business associate that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information. In addition, we may maintain sensitive personally identifiable information, including health information, that we receive throughout the clinical trial process, in the course of our research collaborations, and directly from individuals (or their healthcare providers) who enroll in our patient assistance programs. As such, we may be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA.

Furthermore, certain health privacy laws, data security laws, data breach notification laws, consumer protection laws and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information. Patients about whom we or our collaborators obtain health information, as well as the providers who share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even

if we are not found liable, could be expensive and time- consuming to defend and could result in adverse publicity that could harm our business.

If we or third-party manufacturers, CROs or other contractors or consultants fail to comply with applicable federal, state or local regulatory requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our therapeutic candidates and could harm or prevent sales of any affected therapeutics that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing and marketing our therapeutics. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security or reputational damage.

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 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. This includes reductions to Medicare payments to providers of 2% per fiscal year, that began in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. COVID-19 relief legislation, including the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, which was signed into law in March 2020 , among other things, suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2021.

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.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has been, and is likely to continue to be, highly volatile, and you may not be able to resell your shares at or above the price you paid for them.

Since July 31, 2019, our stock price has been volatile and it is likely that the trading price of our common stock will continue to be volatile. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by 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 United States 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 and overall fluctuations in U.S. equity markets, including as a result of the COVID-19 pandemic;
- 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, political and market conditions, including, but not limited to, the ongoing impact of the COVID-19 pandemic.

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, such as those related to the COVID-19 pandemic, may seriously harm the market price of our common stock, regardless of our operating performance.

Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, grants and license and development agreements in connection with any collaborations. We do not have any committed external source of funds. 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, on December 23, 2019, we completed the sale of 10,000,000 shares of our common stock in the December 2019 Offering and on August 2, 2019 we completed the sale of 31,625,000 shares of our common stock in the August 2019 Offering. The issuance of shares in both the December 2019 Offering and August 2019 Offering were pursuant to a shelf registration statement on Form S-3 that was declared effective by the SEC on July 24, 2019. The shelf registration statement allows us to sell from time-to-time up to $125.0 million of common stock, preferred stock, debt securities, warrants, or units comprised of any combination of these securities, for our own account in one or more offerings; the remaining amount available under this shelf registration after the December 2019 Offering (inclusive of the exercise of the underwriters' option in January 2020 to purchase additional shares at the public offering price in connection with the December 2019 Offering) is approximately $31.3 million. Further, in December 2020 we entered into an equity distribution agreement with BMO Capital Markets Corp. providing for the sale of up to $50.0 million of our common stock from time to time in "at the market offerings" (as defined in Rule 415(a)(4) of the Securities Act of 1933, as amended) pursuant to a prospectus supplement and a shelf registration statement on Form S-3 that was declared effective by the SEC on January 7, 2021. The issuance of the shares pursuant to the December 2019 Offering and the August 2019 Offering and/or the resale of a substantial number of shares of our common stock in the public market or the sale of any shares of our common stock under the equity distribution agreement 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. Adverse market and price pressures that may result from the December 2019 Offering or the August 2019 Offering or an offering pursuant to the shelf registration statement or such 'at the market' offerings 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.

Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. Any debt financing that we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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 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 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, 2020, 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 39% 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 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 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, 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, 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 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 and require 66 and 2/3% stockholder voting to remove directors, who may only be removed for cause;
- authorize our Board 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.

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.

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 of the following types of actions or proceedings under Delaware statutory or common law: 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. This provision would not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, or any other claims for which a court or forum other than the Court of Chancery has exclusive jurisdiction or for which the Court of Chancery does not have subject matter jurisdiction. Furthermore, Section 22 of the Securities Act of 1933, as amended, or the Securities Act, creates concurrent jurisdiction for federal and state courts over all Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. Our amended and restated certificate of incorporation also provides that 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. If a court were to find this exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in any action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could have a material adverse effect on our business, financial condition or results of operations.

Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act, or the Tax Act, enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, the CARES Act modified certain provisions of the Tax Act. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the CARES Act, or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act or future reform legislation could

have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

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. Our net operating loss, or NOL, carryforwards generated in tax years beginning on or before December 31, 2017, are only permitted to be carried forward for 20 years under applicable U.S. tax law. Under the Tax Act, as modified by the CARES Act, our federal NOLs generated in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs in tax years beginning after December 31, 2020, is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to the Tax Act, or the CARES Act. In addition, 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 NOL carryforwards, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We have experienced ownership changes in the past. 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 NOL carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Risks Related to our Indebtedness

Our indebtedness could adversely affect our business, financial condition and competitive position.

As of December 31, 2020, after entering the MidCap Credit Agreement, we had $17.5 million of indebtedness outstanding, consisting of our borrowing under our MidCap Credit Facility.

In order to service this indebtedness and any additional indebtedness we may incur in the future, we need to generate cash. Our ability to generate cash is subject, to a certain extent, to our ability to successfully execute our business strategy, as well as general economic, financial, competitive, regulatory and other factors beyond our control. We cannot assure you that our business will be able to generate sufficient cash flow from operations or that future borrowings or other financing will be available to us in an amount sufficient to enable us to service our indebtedness and fund our other liquidity needs. To the extent we are required to use our cash flow from operations or the proceeds of any future financing to service our indebtedness instead of funding working capital, capital expenditures or other general corporate purposes, we will be less able to plan for, or react to, changes in our business, industry and in the economy generally. This will place us at a competitive disadvantage compared to our competitors that have less indebtedness.

In addition, the MidCap Credit Agreement contains, and any agreements evidencing or governing other future indebtedness may contain, certain restrictive covenants that limit our ability, among other things, to engage in certain activities that are in our long-term best interests, including our ability to:

- incur additional indebtedness;
- create or incur liens;
- engage in certain fundamental changes, including mergers or consolidations;
- make investments, loans, advances, guarantees and acquisitions;
- sell or transfer assets;
- pay dividends and distributions and repurchase capital stock;
- engage in certain transactions with affiliates;

- enter into negative pledge clauses and clauses restricting subsidiary distributions;
- modify the terms of material documents.

While we have not previously breached and are not in breach of any of these covenants, there can be no guarantee that we will not breach these covenants in the future.

Our ability to comply with these covenants and restrictions may be affected by events and factors beyond our control. Our failure to comply with any of these covenants or restrictions could result in an event of default under our MidCap Credit Facility. This would permit the lending banks under such facilities to take certain actions, including terminating all outstanding commitments and declaring all amounts due under our credit agreement, such as outstanding principal and accrued and unpaid interest thereon, to be immediately due and payable. In addition, the lenders would have the right to proceed against the collateral we have granted to them, which includes substantially all of our assets. The occurrence of any of these events could have a material adverse effect on our business, financial condition and results of operations.

We may not be able to secure additional financing on favorable terms, or at all, to meet our future capital needs.

In the future, we may require additional capital to respond to business opportunities, challenges, acquisitions or unforeseen circumstances, and may determine to engage in equity or debt financings or enter into credit facilities or refinance existing indebtedness for other reasons. We may not be able to timely secure additional debt or equity financing on favorable terms, or at all. As discussed above, the credit agreements governing the MidCap Credit Facility contain restrictive covenants that limit our ability to incur additional indebtedness and engage in other capital-raising activities. Any debt financing obtained by us in the future could involve covenants that further restrict our capital raising activities and other financial and operational matters, which may make it more difficult for us to operate our business, obtain additional capital and pursue business opportunities, including potential acquisitions. Furthermore, if we raise additional funds through the issuance of equity or convertible debt or other equity-linked securities or through the sale of our common stock pursuant to our "at the market" program, our existing stockholders could suffer significant dilution. If we are unable to obtain adequate financing or financing on terms satisfactory to us, when we require it, our ability to continue to grow or support our business and to respond to business challenges could be significantly limited.

General Risk Factors

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, 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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters are located in Chicago, Illinois, where we lease approximately 30,000 square feet of office and laboratory space (the "Chicago Lease"). The Chicago Lease commenced on July 1, 2020, and expires on July 1, 2030. Under the lease agreement, we are given an option to extend the lease term for two additional successive periods of five years each.

Our lease for our previous corporate headquarters in Skokie, Illinois expired on February 28, 2021.

We also lease office space at a multi-tenant facility in Cambridge, Massachusetts that commenced in March 2019 and is cancelable at any time.

We believe that this space is sufficient to meet our needs for the foreseeable future and that any additional or alternative space we may require 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 was approved for listing on the Nasdaq Capital Market under the symbol "XCUR" and began trading on July 31, 2019.

On March 5, 2021, the last reported sale price of our common stock on the Nasdaq Capital Market was $2.06 per share.

Holders of Record

As of March 5, 2021, we had 87,960,327 shares of common stock outstanding held by 90 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

None.

Item 6. Selected Financial Data.

We have elected to comply with Item 301 of Regulation S-K, as amended February 10, 2021 and are omitting this disclosure in reliance thereon.

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.

In addition, this section discusses 2020 and 2019 items and year-to-year comparisons between 2020 and 2019. Discussions of 2018 items and year-to-year comparisons between 2019 and 2018 are not included in this Annual Report and can be found in "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7 of our Annual Report on Form 10-K for year ended December 31, 2019, filed with the SEC on March 10, 2020.

Overview

We are a clinical-stage biotechnology company developing therapeutics for immuno-oncology, genetic disorders and other indications 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. We are conducting IND-enabling studies for XCUR-FXN, an SNA-based therapeutic candidate, for the treatment of Friedreich's ataxia (FA) and expect to initiate a first-in-patient Phase 1b clinical trial in 2022. We are also working to advance our SNA-based therapeutic candidate cavrotolimod (AST-008) in an ongoing Phase 1b/2 clinical trial in cancer patients.

We believe that one of the key strengths of our proprietary SNAs is that they have the potential for increased cellular uptake compared to conventional linear oligonucleotides and as a result the potential to achieve higher efficacy at the same doses of oligonucleotide administered. We have shown in clinical and preclinical studies that SNAs may have therapeutic potential in neurology, immuno-oncology and dermatology. In addition, we have shown in preclinical studies that SNAs may have therapeutic potential in ophthalmology, pulmonology, and gastroenterology. As a consequence, we have expanded our pipeline into neurology, and are conducting early stage research activities in ophthalmology, pulmonology, and gastroenterology.

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 have primarily funded our operations through sales of our securities and collaborations. Through December 31, 2020, we have raised gross proceeds of $190.1 million from the sale of common stock and preferred stock. We have also received $36.0 million in upfront payments under our current collaborations, including an upfront payment of $25.0 million we received in November 2019 in connection with the AbbVie Collaboration Agreement and an upfront payment of $1.0 million we received in February 2019 in connection with the Dermelix Collaboration Agreement. On September 25, 2020, we also borrowed $17.5 million under the terms of a credit and security agreement with MidCap Financial Trust (as described further below). As of December 31, 2020, our cash, cash equivalents, short-term investments, and restricted cash were $83.3 million.

Since our inception, we have incurred significant operating losses. As of December 31, 2020, we have generated an accumulated deficit of 124.8 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:

- continue to advance cavrotolimod (AST-008) through clinical development for immuno-oncology applications;
- continue research and development of XCUR-FXN and other neurological therapeutic candidates;
- advance our SNA platform in dermatological indications with suitable collaboration partners;
- initiate research and development, preclinical studies and clinical trials for any additional therapeutic candidates that we may pursue in the future;
- advance other therapeutic candidates through preclinical and clinical development;
- increase our research and development activities to enhance our technology;
- continue to manufacture increasing quantities of drug substance and drug product material for use in preclinical studies and clinical trials;
- seek regulatory approval for our therapeutic candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license other approved drugs, drug candidates or technologies;
- hire additional operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional costs associated with operating as a public company.

We have not generated any revenue from commercial drug sales nor do we expect to generate substantial revenue from product sales unless or until we successfully complete development and obtain regulatory approval of and commercialize one or more of our therapeutic candidates. We do not anticipate generating revenue from drug sales for the next several years, if ever. 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.

COVID-19 Business Update

With the global spread of the COVID-19 pandemic during 2020, we continue to monitor closely the developments and continue to take active measures to protect the health of our employees and their families, our communities, as well as our clinical trial investigators, patients, and caregivers. As of March 5, 2021, Illinois is under “Phase 4” of the Restore Illinois Plan, which is intended to permit the expansion of business and community operations based on their compliance with the safety guidelines described in the regulations, with new mitigation measures that may require additional restrictions or adaptations being applied on a regional basis within the State of Illinois based on risk levels depending on the health progress of each region to prevent the ongoing spread of COVID-19.

Business and R&D operations

Under social distancing guidelines for COVID-19, we were typically operating with less than 50% of our R&D staff on-site at any one time through June 30, 2020. As of July 1, 2020, we took occupancy of approximately 30,000 square feet of laboratory and office space in our new headquarters in Chicago, Illinois. Since then, we have operated under COVID-19 social distancing guidelines and have generally operated with 100% of our R&D staff on-site. Our office and general and administrative team continues to work predominantly from home. Our preclinical development program in FA is ongoing and we began IND-enabling studies for XCUR-FXN in late 2020. We also continue to progress our collaborations with AbbVie and Dermelix. If the COVID-19 pandemic or its impact or effects continues to persist for an extended period of time, we could experience additional delays in our enrollment of patients for the Phase 2 trial of cavrotolimod (AST-008) and significant disruptions to our preclinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects.

Our principal accounting systems are cloud-based and have been fully operational during the stay at home order. We believe that all of our fundamental internal control disciplines are being maintained despite work being conducted from our employees' homes.

Supply chain

We are working closely with our third-party manufacturers and other partners to manage our supply chain activities and mitigate potential disruptions as a result of the COVID-19 pandemic. We have observed minor delays in receipt of key chemicals, reagents and materials as certain manufacturers have had supply disruptions, related to the COVID-19 pandemic. If the COVID-19 pandemic continues to persist for an extended period of time and impacts essential distribution systems such as FedEx and postal delivery, we could experience future disruptions to our supply chain and operations, and associated delays in the manufacturing and our clinical supply, which would adversely impact our preclinical and clinical development activities.

Clinical operations

We have one active clinical program, cavrotolimod (AST-008). We have completed enrollment for the Phase 1b stage of the clinical trial and have begun the Phase 2 dose expansion phase in patients with advanced or metastatic Merkel cell carcinoma, or cutaneous squamous cell carcinoma. During the third quarter of 2020 and through December 31, 2020, we observed delays in our enrollment plans and clinical trial site start-ups for the Phase 2 dose expansion phase of the trial. We believe the effects of the COVID-19 pandemic or its impact contributed to such delays. As a result, we have taken additional measures to increase the enrollment of patients, including frequent interaction with our clinical trial sites currently open as well as increasing the number of clinical trial sites that potentially are activated for this trial so that we may continue to enroll patients as initially planned. However, these delays have caused us to lengthen our clinical development timeline for cavrotolimod (AST-008), and we now expect to report overall response rate, or ORR, results in the first half of 2022 rather than by year end 2021 as previously guided in September 2020.

We remain committed to maintaining our development plans for cavrotolimod (AST-008) and continue to monitor and manage the rapidly evolving situation. We have taken and continue to take measures to implement remote and virtual approaches, including remote patient monitoring where possible, to maintain patient safety and trial continuity and to preserve study integrity. Should the COVID-19 pandemic or its impact or effects continue, our ability to maintain patient enrollment and our clinical development timeline could continue to be negatively impacted. We could also see an impact on our ability to supply study drug, report trial results, or interact with regulators, ethics committees or other important agencies due to limitations in regulatory authority employee resources or otherwise. In addition, we rely on contract research organizations or other third parties to assist us with clinical trials, and we cannot guarantee that they will continue to perform their contractual duties in a timely and satisfactory manner as a result of the COVID-19 pandemic. As the COVID-19 pandemic continues to persist for an extended period of time, we continue to be impacted and could experience additional delays in patient enrollment for our Phase 2 clinical trial of cavrotolimod (AST-008). Any significant disruptions to our clinical development timelines would further delay our anticipated timeline for results and adversely affect our business, financial condition, results of operations and growth prospects.

Liquidity and capital resources

As of December 31, 2020, our cash, cash equivalents, short-term investments, and restricted cash were $83.3 million. Based on our current operating plans, we believe that existing working capital at December 31, 2020, including amounts borrowed and available under the MidCap Credit Facility (see below), is sufficient to fund our operations for at least 12 months from the date of this report. However, our operating plan may change as a result of many factors currently unknown to us including due to the effects of COVID-19, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. We have historically principally raised capital through the sale of our securities. However, the COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of global financial markets. We believe raising capital in the current market could be very difficult for early stage biotech companies like us. If the disruption continues to persist and deepens, we could experience an inability to access additional capital, which could in the future negatively affect our operations.

Recent Developments

Therapeutic Development Program Updates

Cavrotolimod (AST-008)

As of February 23, 2021, we had 16 clinical trial sites open for enrollment and 7 additional sites pending activation. We expect to open up to 30 sites for the Phase 2 stage of the clinical trial. We anticipate all sites will be activated by the end of 2021. As of February 23, 2021, we had dosed 16 patients with 32 mg of cavrotolimod (AST-008) in the Phase 2 portion of the clinical trial, including the primary and exploratory cohorts. Including the six patients dosed with 32 mg of cavrotolimod (AST-008) in the Phase 1b portion of the clinical trial, a total of 22 patients have been dosed with 32 mg of cavrotolimod (AST-008). As of February 23, 2021, 1 of the 22 patients dosed with 32 mg of cavrotolimod (AST-008) has experienced a treatment-related SAE as determined by the clinical trial investigator. This patient, enrolled in the Phase 2 stage of the clinical trial, reported a treatment-related SAE of hypotension, flu-like symptoms which subsequently resolved. None of the 14 patients dosed in the Phase 1b portion of the clinical trial with doses of cavrotolimod (AST-008) less than 32 mg experienced a treatment related SAE. Thus, as of February 23, 2021, in total, 1 of 36 patients treated with cavrotolimod (AST-008) have experienced a treatment related SAE.

Changes in Board of Directors

Effective March 5, 2021, Elizabeth Garofalo, M.D. and Andrew Sassine were appointed to our Board, each to serve as directors and as members of the Audit Committee. Effective January 2, 2021, James Sulat was appointed to our Board, to serve as a director and chairperson of the Audit Committee.

On March 8, 2021, David R. Walt, Ph.D. notified the Board of his intention not to stand for re-election as a director when his term expires at our upcoming 2021 Annual Meeting of Stockholders.

At-the-Market Offering Agreement

In December 2020, we entered into an equity distribution agreement with BMO Capital Markets Corp., or BMO, with respect to an “at the market offering” program under which we may offer and sell, from time to time at our sole discretion, shares of our common stock having an aggregate offering price of up to $50.0 million through BMO as our distribution agent. We are not obligated to sell any shares under the equity distribution agreement. As of December 31, 2020, no shares had been sold under the equity distribution agreement.

Basis of Presentation

The audited financial statements of Exicure, Inc. for the fiscal years ended December 31, 2020 and 2019, contained herein, include a summary of our significant accounting policies and should be read in conjunction with the discussion below.

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 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 recognition

Effective January 1, 2018, we adopted the provisions of Accounting Standards Codification, or ASC 606, *Revenue from Contracts with Customers* using the modified retrospective method for all contracts not completed as of the date of adoption.

Under ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that are within the scope of ASC 606, we perform the following five steps:

1. *Identify the contract with the customer.* A contract with a customer exists when (i) we enter into an enforceable contract with a customer that defines each party's rights and obligations regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance, and (iii) we determine 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. We apply 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, we 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 we will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, we estimate 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 our 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, we 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.* We satisfy 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 our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize 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, we utilize 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. We evaluate 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, we evaluate 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 our control 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 we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate 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. To date, we have not recognized any milestone payment revenue from any of its collaboration agreements.

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, we recognize 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, we have not recognized any royalty revenue resulting from any of its collaboration agreements.

During the years ended December 31, 2020 and 2019, we have primarily earned revenue under the collaboration agreements with AbbVie and Dermelix (see Note 3 to the accompanying consolidated financial statements).

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, the fair value measurement date is the date of grant and the requisite service period is the period over which the option recipient is required to provide service in exchange for the common stock option awards, which is generally the vesting period.

The Black-Scholes option-pricing model requires the input of highly subjective assumptions, including: (1) the estimated grant date fair value of our 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.

The expected term is based upon the "simplified method" as described in Staff Accounting Bulletin Topic 14.D.2. Currently, we do not have sufficient experience to provide a reasonable estimate of an expected term of its common stock options. We 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.

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, 2020 through our research collaboration license and option agreement with AbbVie, or the AbbVie Collaboration Agreement, our research collaboration, license, and option agreement with Purdue Pharma L.P., or the Purdue Collaboration Agreement, or through our research collaboration license and option agreement with Dermelix. We have also earned revenue 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 AbbVie Collaboration Agreement, the Dermelix Collaboration Agreement, 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 anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will incur significantly increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with operating as a public company.

Dividend income

Dividend income consists of income earned on our money market funds that are recorded as cash equivalents on our consolidated balance sheets.

Interest income

Interest income consists of income earned on our available for sale securities that are recorded as short-term investments on our consolidated balance sheets, as well as income earned on our cash balances.

Interest expense

Interest expense includes amounts pursuant to the loan and security agreement with Hercules Technology Growth Capital, or Hercules, for which we repaid all remaining outstanding obligations under the Hercules loan agreement at its maturity on March 1, 2020. Interest expense also includes amounts pursuant to the MidCap Credit Agreement. See "—MidCap Credit Agreement" below for additional information.

Other income (loss), net

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

Results of Operations

Comparison of the Year Ended December 31, 2020 and 2019

The following table summarizes the results of our operations for the years ended December 31, 2020 and 2019:

	Year Ended December 31,		Change	
(dollars in thousands)	2020	2019		
Revenue:				
Collaboration revenue	$ 16,613	$ 1,296	$ 15,317	1,182 %
Total revenue	16,613	1,296	15,317	1,182 %
Operating expenses:				
Research and development expense	32,094	19,340	12,754	66 %
General and administrative expense	9,955	8,573	1,382	16 %
Total operating expenses	42,049	27,913	14,136	51 %
Operating loss	(25,436)	(26,617)	1,181	(4) %
Other income, net:				
Dividend income	47	543	(496)	(91) %
Interest income	972	178	794	446 %
Interest expense	(573)	(786)	213	(27) %
Other income, net	322	379	(57)	(15) %
Total other income, net	768	314	454	145 %
Net loss before provision for income taxes	(24,668)	(26,303)	1,635	(6) %
Provision for income taxes	—	—	—	— %
Net loss	$ (24,668)	$ (26,303)	$ 1,635	(6) %

Revenue

The following table summarizes our revenue earned during the periods indicated:

	Year Ended December 31,		Change	
(dollars in thousands)	2020	2019		
Collaboration revenue:				
AbbVie Collaboration Agreement	$ 16,486	$ 171	$ 16,315	n/m
Dermelix Collaboration Agreement	127	1,125	(998)	n/m
Total collaboration revenue	$ 16,613	$ 1,296	$ 15,317	1,182 %
Total revenue	$ 16,613	$ 1,296	$ 15,317	1,182 %

We recognized collaboration revenue in the amount of $16.6 million during the year ended December 31, 2020, which is primarily related to activities performed under the AbbVie Collaboration Agreement. In November 2019, we received an upfront payment of $25.0 million in connection with the AbbVie Collaboration Agreement for which revenue has been deferred and will be recognized as revenue in future periods as we satisfy our obligations under the AbbVie Collaboration Agreement. At December 31, 2020, deferred revenue under the AbbVie Collaboration Agreement was $8.3 million and is expected to be recognized as revenue over the next twelve months as we satisfy our obligations under the AbbVie Collaboration Agreement. Refer to Note 3 of the accompanying consolidated financial statements for more information regarding revenue recognition for the AbbVie Collaboration Agreement.

The collaboration revenue of $1.3 million during the year ended December 31, 2019 related to the reimbursable research and development activities performed under the Dermelix Collaboration Agreement, for which related costs are 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 AbbVie Collaboration Agreement or the Dermelix License Agreement 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)	2020	2019	Change	
Platform and discovery-related expense	$ 13,361	$ 8,442	$ 4,919	58 %
Clinical development programs expense	8,259	5,025	3,234	64 %
Employee-related expense	7,725	4,677	3,048	65 %
Facilities, depreciation, and other expenses	2,749	1,196	1,553	130 %
Total research and development expense	$ 32,094	$ 19,340	$ 12,754	66 %
Full time employees	54	29	25	

Research and development expense was $32.1 million for the year ended December 31, 2020, reflecting an increase of $12.8 million, or 66%, from research and development expense of $19.3 million for the year ended December 31, 2019. Since December 31, 2019, we have increased our headcount in research and development from 29 to 54 at December 31, 2020. The increase in research and development expense for the year ended December 31, 2020 of $12.8 million reflects this increased staffing level and the related increase in research and development activities, in addition to the growth in clinical trial activities. More specifically, the increase in research and development expense for the year ended December 31, 2020 of $12.8 million was primarily due to higher platform and discovery-related expense of $4.9 million, a net increase in costs related to our clinical development programs of $3.2 million, higher employee-related expenses of $3.0 million, and higher facilities, depreciation, and other expenses in the amount of $1.6 million.

The increase in platform and discovery-related expense of $4.9 million is mostly due to higher costs for materials, reagents, lab supplies, and contract research organizations, all in connection with increased research and development activities related to the AbbVie Collaboration Agreement, our FA program, XCUR-FXN, and our discovery efforts for other therapeutic candidates for neurology and ophthalmology, partially offset by the absence of a license fee of $3.8 million paid in 2019 to Northwestern University in connection with the receipt of the $25.0 million upfront payment from AbbVie.

The net increase in clinical development programs expense for the year ended December 31, 2020 of $3.2 million was primarily due to manufacturing costs in connection with the initiation of the upcoming Phase 2 phase of our Phase 1b/2 clinical trial for cavrotolimod (AST-008) and other higher clinical trial expenses, as well as manufacturing costs in connection with the preparation of IND-enabling and Phase 1 clinical trial activities for XCUR-FXN, partially offset by lower clinical trial expenses for XCUR17.

The increase in employee-related expense for the year ended December 31, 2020 of $3.0 million was due to higher compensation and related costs in connection with the net increase in headcount during the period presented as well as certain salary increases in 2020 for existing employees and higher recruiting costs. The increase in facilities, depreciation, and other expenses for the year ended December 31, 2020 of $1.6 million was mostly due to the acceleration of amortization expense for our right-of-use asset related to our Skokie lease which we no longer

use effective July 1, 2020 due to our move to our Chicago headquarters, higher lease costs related to our Chicago Lease that commenced on July 1, 2020 as well as higher depreciation expense in connection with the acquisition of additional scientific equipment that were placed in service since the prior-year period.

We expect our research and development expenses to increase during 2021 as we broaden our pipeline of SNA-based therapeutic candidates, continue spending on our clinical development programs, and further develop our SNA technology platform.

General and administrative expense

	Year Ended December 31,			
(dollars in thousands)	2020	2019	Change	
General and administrative expense	$ 9,955	$ 8,573	$ 1,382	16 %
Full time employees	9	7	2	

General and administrative expense was $10.0 million for the year ended December 31, 2020, representing an increase of $1.4 million, or 16%, from $8.6 million for the year ended December 31, 2019. The increase for the year ended December 31, 2020 is mostly due to higher legal and accounting costs associated with operating as a public company, higher franchise tax costs, higher D&O insurance premium costs, partially offset by lower travel and related costs.

Dividend income

The decrease in dividend income of $0.5 million for the year ended December 31, 2020 was the result of lower average balances invested in money market funds during 2020 as compared to 2019.

Interest income

The increase in interest income of $0.8 million for the year ended December 31, 2020 was the result of higher average balances invested in available for sale securities during 2020 as compared to 2019.

Interest expense

The decrease in interest expense of $0.2 million for the year ended December 31, 2020 was mostly due to lower interest expense resulting from the repayment of outstanding obligations under the Hercules Loan Agreement upon maturity on March 2, 2020, partially offset by incremental interest expense resulting from $17.5 million borrowed on September 25, 2020 under the MidCap Credit Agreement.

Liquidity and Capital Resources

Overview

As of December 31, 2020, our cash, cash equivalents, short-term investments, and restricted cash were $83.3 million. Based on our current operating plans, we believe that existing working capital at December 31, 2020, including amounts borrowed and available under the MidCap Credit Facility (see below), is sufficient to fund our operations for at least 12 months from the date of this report. However, our operating plan may change as a result of many factors currently unknown to us including due to the effects of COVID-19, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. We have historically principally raised capital through the sale of our securities. However, the COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of global financial markets. We believe raising capital in the current market could be very difficult for early stage biotech companies like us. If the disruption continues to persist and deepens, we could experience an inability to access additional capital, which could in the future negatively affect our operations.

On September 25, 2020, we borrowed the first advance of $17.5 million (Tranche 1) under the terms of the MidCap Credit Agreement (as discussed further below). The second advance of $7.5 million (Tranche 2) will be available to us from April 1, 2021 to September 30, 2021, subject to our satisfaction of certain conditions described in the MidCap Credit Agreement. See "—MidCap Credit Agreement" below for additional information.

In December 2020, we entered into an equity distribution agreement with BMO under which we may offer and sell in "at the market offerings" (as defined in Rule 415(a)(4) of the Securities Act of 1933, as amended) from time to time at our sole discretion, shares of our common stock having an aggregate offering price of up to $50.0 million through BMO acting as our distribution agent, or the ATM Offering. During the year ended December 31, 2020, we did not sell any shares under the equity distribution agreement.

In March 2019, we filed a shelf registration statement on Form S-3 with the SEC, which was declared effective by the SEC on July 24, 2019. The shelf registration statement allows us to sell from time-to-time up to $125.0 million of common stock, preferred stock, debt securities, warrants, or units comprised of any combination of these securities, for our own account in one or more offerings; the remaining amount available under this shelf registration is approximately $31.3 million.

On January 6, 2020, we sold 1,081,184 shares of our common stock at a price of $2.75 per share pursuant to the exercise of the underwriters' option to purchase additional shares at the public offering price in connection with the December 2019 Offering. We received gross proceeds of $3.0 million before deducting underwriting discounts and commissions and offering expenses of $0.2 million in January 2020 in connection with the December 2019 offering.

Similar to other development stage biotechnology companies, we have not generated any revenue since inception. We have incurred losses and experienced negative operating cash flows since our inception and anticipate that we will continue to incur losses for at least the next several years. As of December 31, 2020, we have generated an accumulated deficit of 124.8 million.

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, 2020 and 2019:

	Years Ended December 31,	
(in thousands)	**2020**	**2019**
Net cash (used in) provided by operating activities	$ (39,270)	$ 1,317
Net cash provided by (used in) investing activities	10,142	(63,432)
Net cash provided by financing activities	15,130	84,307
Net (decrease) increase in cash, cash equivalents, and restricted cash	$ (13,998)	$ 22,192

Operating activities

Net cash (used in) provided by operating activities was $(39.3) million and $1.3 million for the years ended December 31, 2020 and 2019, respectively. The increase in cash used in operating activities of $40.6 million was primarily due to higher cash used for working capital and the absence of a $25.0 million upfront payment received in 2019 in connection with the AbbVie Collaboration Agreement.

Investing activities

Net cash provided by (used in) investing activities was $10.1 million and $(63.4) million for the years ended December 31, 2020 and 2019, respectively. The increase in cash provided by investing activities of $73.6 million was primarily due to lower purchases, net of maturities, of available-for-sale securities.

Financing activities

Net cash provided by financing activities of $15.1 million for the year ended December 31, 2020 is primarily due to the net proceeds we received of $17.3 million during the period in connection with the MidCap Credit Agreement, as well as the net proceeds received from the sale of shares of our common stock in the amount of $2.8 million pursuant to the partial exercise of the option to purchase additional shares by the underwriters from our December 2019 financing, partially offset by the repayment of the Hercules loan in the amount of $5.0 million upon the loan's maturity.

Net cash provided by financing activities of $84.3 million for the year ended December 31, 2019 is primarily due to the sale of common stock in our December 2019 and August 2019 offerings. In December 2019 , we completed the offering and sale of 10,000,000 shares of our common stock at a public offering price of $2.75 per share, resulting in net proceeds of approximately $25.3 million. In August 2019 , we completed the offering and sale of 31,625,000 shares of our common stock at a public offering price of $2.00 per share, resulting in net proceeds of approximately $58.9 million.

MidCap Credit and Security Agreement

On September 25, 2020, the Company and its wholly owned subsidiary, Exicure Operating Company, entered into the MidCap Credit Agreement, with MidCap , as agent, and the lenders party thereto from time to time.

The MidCap Credit Agreement provides for a secured term loan facility in an aggregate principal amount of up to $25.0 million, or the MidCap Credit Facility. We borrowed the first advance of $17.5 million, or Tranche 1, on September 25, 2020, or the Closing Date. Under the terms of the MidCap Credit Agreement, the second advance of $7.5 million, or Tranche 2, will be available to us from April 1, 2021 to September 30, 2021, subject to our satisfaction of certain conditions described in the MidCap Credit Agreement. The proceeds from the MidCap Credit Facility are expected to be used for working capital and general corporate purposes.

Tranche 1, and if borrowed Tranche 2, each bear interest at a floating rate equal to 6.25% per annum, plus the greater of (i) 1.50% or (ii) one-month LIBOR. Interest on each loan advance is due and payable monthly in arrears. Principal on each loan advance is payable in 36 equal monthly installments beginning October 1, 2022 until paid in full on October 1, 2025, or Maturity Date. Prepayments of the loans under the MidCap Credit Agreement, in whole or in part, will be subject to early termination fees in an amount equal to 3.0% of principal prepaid if prepayment occurs on or prior to the first anniversary of the Closing Date and 1.0% of principal prepaid if prepayment occurs after the first anniversary of the Closing Date and prior to the maturity date. In connection with execution of the MidCap Credit Agreement, we paid MidCap a $125,000 origination fee.

At the Maturity Date or on any earlier date on which all amounts advanced to us become due and payable in full, or are otherwise paid in full, we are required to pay an exit fee equal to 3.75% of the principal amount of all loans advanced to us under the MidCap Credit Agreement.

Our obligations under the MidCap Credit Agreement are secured by a security interest in substantially all of our assets, excluding intellectual property (which is subject to a negative pledge). Additionally, our future subsidiaries, if any, may be required to become co-borrowers or guarantors under the MidCap Credit Agreement.

The MidCap Credit Agreement contains customary affirmative covenants and customary negative covenants limiting our ability and the ability of our subsidiaries, if any, to, among other things, dispose of assets, undergo a change in control, merge or consolidate, make acquisitions, incur debt, incur liens, pay dividends, repurchase stock and make investments, in each case subject to certain exceptions.

The MidCap Credit Agreement also contains customary events of default relating to, among other things, payment defaults, breaches of covenants, a material adverse change, delisting of our common stock, bankruptcy and insolvency, cross defaults with certain material indebtedness and certain material contracts, judgments, and inaccuracies of representations and warranties. Upon an event of default, the agent and the lenders may declare all or a portion of our outstanding obligations to be immediately due and payable and exercise other rights and remedies

provided for under the agreement. During the existence of an event of default, interest on the obligations could be increased by 2.0%.

Hercules Loan and Security Agreement

On March 2, 2020, pursuant to the terms of the loan agreement with Hercules Technology Growth Capital, or Hercules, and subsequent amendments thereto, or Hercules Loan Agreement, we repaid all remaining outstanding obligations under the Hercules Loan Agreement, to include the outstanding principal balance of $5.0 million and a deferred end of term fee of $0.1 million. As a result, Hercules no longer has a security interest in any of our assets.

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. Because of the numerous risks and uncertainties associated with research, development and commercialization of therapeutic candidates, we are unable to estimate the exact amount of our working capital requirements. 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 effects of health epidemics, including the ongoing COVID-19 pandemic, on our operations or the business or operations of our CROs or other third parties with whom we conduct business;
- 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.

Based on our current operating plans, we believe that our existing working capital at December 31, 2020, including amounts borrowed and available under the MidCap Credit Facility is sufficient to fund our operations for at least 12 months from the date of this report. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our capital resources sooner than we expect.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and marketing, distribution or licensing arrangements with third parties. The COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of global financial markets. If the disruption continues to persist and deepens, we could experience an inability to access additional capital, which could in the future negatively affect our operations.

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. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, reduce or eliminate our product development efforts or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

Chicago Lease

In February 2020, we entered into a new lease signed in February 2020 to secure approximately 30,000 square feet of office and laboratory space at 2430 N. Halsted St., Chicago, Illinois, or the Chicago Lease. The Chicago Lease commenced on July 1, 2020, which is when the premises leased thereunder were ready for occupancy, and expires 10 years from July 1, 2020 with an option to renew for two additional successive periods of five years each.

The initial annual base rent during the original term of the Chicago Lease is approximately $1.1 million for the first 12-month period of the original term, payable in monthly installments beginning on the lease commencement. Base rent thereafter is subject to annual increases of 3%, for an aggregate amount of $12.8 million over the initial term. We must also pay our proportionate share of certain operating expenses and taxes for each calendar year during the term. During the first 12 months, the base rent and our proportionate share of operating expenses and taxes are subject to certain abatements.

In connection with the Chicago Lease, we will maintain a letter of credit for the benefit of the landlord in an initial amount of $1.2 million, which amount is subject to reduction over time.

MidCap Credit and Security Agreement

On September 25, 2020, we borrowed the first advance of $17.5 million (Tranche 1) under the terms of the MidCap Credit Agreement (as discussed further above). Tranche 1 bears interest at a floating rate equal to 6.25% per annum, plus the greater of (i) 1.50% or (ii) one-month LIBOR. Interest on each loan advance is due and payable monthly in arrears. Principal on the Tranche 1 loan advance is payable in 36 equal monthly installments beginning October 1, 2022 until paid in full on October 1, 2025. Upon termination of the MidCap Credit Agreement, we are required to pay an exit fee equal to 3.75% of the principal amount of all loans advanced to us under the MidCap Credit Agreement.

Other

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

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, an emerging growth company can take advantage of an 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, 2020, we had cash and cash equivalents of $33.3 million, primarily held in money market funds, consisting of U.S. government-backed securities, and interest-bearing money market accounts. As of December 31, 2020, we had short-term investments of $48.8 million consisting of debt instruments of corporations, the U.S. Treasury, financial institutions, and U.S. government agencies with strong credit ratings and an investment grade rating at or above a long-term rating of Aa3/AA- and a short-term rating of P1/A1. 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 MidCap Credit Agreement. The principal balance outstanding of $17.5 million under the MidCap Credit Agreement bears interest at a floating rate equal to 6.25% per annum, plus the greater of (i) 1.50% or (ii) one-month LIBOR. 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.

While we contract with certain vendors internationally, substantially all of our total liabilities as of December 31, 2020 were denominated in U.S dollars and we believe that we do not have any material exposure to foreign currency exchange rate risk.

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, 2020 and 2019, the related consolidated statements of operations, comprehensive loss, changes in stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

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. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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 11, 2021

EXICURE, INC.

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

	December 31,	
	2020	2019
ASSETS		
Current assets:		
Cash and cash equivalents	$ 33,262	$ 48,460
Short-term investments	48,818	62,326
Accounts receivable	11	16
Unbilled revenue receivable	—	19
Prepaid expenses and other assets	4,231	1,955
Total current assets	86,322	112,776
Property and equipment, net	4,123	2,099
Right-of-use asset	8,606	356
Other noncurrent assets	1,393	32
Total assets	$ 100,444	$ 115,263
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Current portion of long-term debt	$ —	$ 4,965
Accounts payable	1,866	1,814
Accrued expenses and other current liabilities	3,525	2,435
Deferred revenue, current	8,343	21,873
Total current liabilities	13,734	31,087
Long-term debt, net	16,589	—
Common stock warrant liability, noncurrent	—	414
Deferred revenue, noncurrent	—	2,956
Lease liability, noncurrent	7,959	59
Other noncurrent liabilities	656	—
Total liabilities	$ 38,938	$ 34,516
Stockholders' equity:		
Preferred stock, $0.0001 par value per share; 10,000,000 shares authorized, no shares issued and outstanding, December 31, 2020 and December 31, 2019	—	—
Common stock, $0.0001 par value per share; 200,000,000 shares authorized, 87,651,352 issued and outstanding, December 31, 2020; 86,069,263 issued and outstanding, December 31, 2019	9	9
Additional paid-in capital	167,379	162,062
Accumulated other comprehensive income (loss)	83	(27)
Accumulated deficit	(105,965)	(81,297)
Total stockholders' equity	61,506	80,747
Total liabilities and stockholders' equity	$ 100,444	$ 115,263

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,	
	2020	**2019**
Revenue:		
Collaboration revenue	$ 16,613	$ 1,296
Total revenue	16,613	1,296
Operating expenses:		
Research and development expense	32,094	19,340
General and administrative expense	9,955	8,573
Total operating expenses	42,049	27,913
Operating loss	(25,436)	(26,617)
Other income, net:		
Dividend income	47	543
Interest income	972	178
Interest expense	(573)	(786)
Other income, net	322	379
Total other income, net	768	314
Net loss before provision for income taxes	(24,668)	(26,303)
Provision for income taxes	—	—
Net loss	$ (24,668)	$ (26,303)
Basic and diluted loss per common share	$ (0.28)	$ (0.46)
Weighted-average basic and diluted common shares outstanding	87,203,588	57,671,734

See Accompanying Notes to Consolidated Financial Statements.

EXICURE, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands, except share and per share data)

	Year Ended December 31,	
	2020	2019
Net loss	$ (24,668)	$ (26,3(
Other comprehensive income (loss), net of taxes		
Unrealized gains (losses) on available for sale securities, net of tax	110	(
Other comprehensive income (loss)	110	(
Comprehensive loss	$ (24,558)	$ (26,3

See Accompanying Notes to Consolidated Financial Statements.

EXICURE, INC.

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

	Common Stock					
	Shares	$	Additional Paid-in-Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
Balance at December 31, 2018	**44,358,000**	**$ 4**	**$ 75,942**	**$ (54,994)**	**$ —**	**$ 20,952**
Exercise of options	86,263	—	75	—	—	75
Equity-based compensation	—	—	1,840	—	—	1,840
Issuance of common stock in August 2019 Offering, net	31,625,000	4	58,862	—	—	58,866
Issuance of common stock in December 2019 Offering, net	10,000,000	1	25,343	—	—	25,344
Other comprehensive loss, net	—	—	—	—	(27)	(27)
Net loss	—	—	—	(26,303)	—	(26,303)
Balance at December 31, 2019	**86,069,263**	**$ 9**	**$ 162,062**	**$ (81,297)**	**$ (27)**	**$ 80,747**
Exercise of options	500,905	—	367	—	—	367
Equity-based compensation	—	—	2,184	—	—	2,184
Issuance of common stock	1,081,184	—	2,766	—	—	2,766
Other comprehensive income, net	—	—	—	—	110	110
Net loss	—	—	—	(24,668)	—	(24,668)
Balance at December 31, 2020	**87,651,352**	**$ 9**	**$ 167,379**	**$ (105,965)**	**$ 83**	**$ 61,506**

See Accompanying Notes to Consolidated Financial Statements.

EXICURE, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (24,668)	$ (26,303)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation and amortization	766	392
Amortization of right-of-use asset	681	332
Equity-based compensation	2,184	1,840
Amortization of long-term debt issuance costs and fees	111	192
Amortization (accretion) of investments	319	(3)
Other	68	36
Change in fair value of warrant liabilities	(399)	(383)
Changes in operating assets and liabilities:		
Unbilled revenue receivable and accounts receivable	24	(32)
Prepaid expenses and other current assets	(3,000)	(628)
Other noncurrent assets	(161)	—
Accounts payable	364	789
Accrued expenses	1,174	578
Deferred revenue	(16,486)	24,829
Other liabilities	(247)	(322)
Net cash (used in) provided by operating activities	(39,270)	1,317
Cash flows from investing activities:		
Purchase of available for sale securities	(56,640)	(62,350)
Proceeds from sale or maturity of available for sale securities	69,953	—
Capital expenditures	(3,171)	(1,082)
Net cash provided by (used in) investing activities	10,142	(63,432)
Cash flows from financing activities:		
Proceeds from common stock offering	2,973	90,750
Payment of common stock financing costs	(207)	(6,235)
Proceeds from long-term borrowing	17,500	—
Payment of long-term debt fees and issuance costs	(504)	(283)
Repayment of long-term debt	(4,999)	—
Proceeds from exercise of common stock options	367	75
Net cash provided by financing activities	15,130	84,307
Net (decrease) increase in cash, cash equivalents, and restricted cash	(13,998)	22,192
Cash, cash equivalents, and restricted cash - beginning of period	48,460	26,268
Cash, cash equivalents, and restricted cash - end of period	$ 34,462	$ 48,460

EXICURE, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2020	2019
Supplemental disclosure of cash flow information		
Non-cash operating activities:		
Right-of-use asset acquired through operating leases	$ 8,147	$ —
Non-cash investing activities:		
Capital expenditures (accounts payable and accrued expenses)	43	348
Non-cash financing activities:		
Debt fees (accrued expense and other noncurrent liabilities)	656	100
Common stock issuance costs (accounts payable and accrued expenses)	—	305

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheets that sum to the total of the amounts shown in the consolidated statements of cash flows:

	Year Ended December 31,	
	2020	2019
Cash and cash equivalents	$ 33,262	$ 48,460
Restricted cash included in other noncurrent assets	1,200	—
Total cash, cash equivalents, and restricted cash shown in the consolidated statements of cash flows	$ 34,462	$ 48,460

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, Inc. (the "Company") is a clinical-stage biotechnology company developing therapeutics for immuno-oncology, genetic disorders and other indications based on its proprietary Spherical Nucleic Acid ("SNA"), technology. SNAs are nanoscale constructs consisting of densely packed synthetic nucleic acid sequences that are radially arranged in three dimensions. The Company believes the design of its 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 is in IND-enabling development of XCUR-FXN, an SNA–based therapeutic candidate, for the treatment of Friedreich's ataxia (FA) and expect to initiate a first-in-patient Phase 1b clinical trial in 2022. The Company is also working to advance its SNA–based therapeutic candidate cavrotolimod (AST-008) in an ongoing Phase 1b/2 clinical trial in cancer patients.

The Company believes that one of the key strengths of its proprietary SNAs is that they have the potential for increased cellular uptake compared to conventional linear oligonucleotides and as a result the potential to achieve higher efficacy at the same doses of oligonucleotide administered. The Company has shown in clinical and preclinical studies that SNAs may have therapeutic potential in immuno-oncology and dermatology. In addition, the Company has shown in preclinical studies that SNAs may have therapeutic potential in neurology, ophthalmology, pulmonology, and gastroenterology. Accordingly, the Company has expanded its pipeline into neurology, and is conducting early stage research activities in ophthalmology, pulmonology, and gastroenterology.

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

Basis of Presentation

The accompanying consolidated financial statements as of December 31, 2020 and 2019, and for the years then ended, have been presented in conformity with generally accepted accounting principles in the United States ("GAAP"). Certain amounts from the prior period have been reclassified to conform to the current year presentation. Specifically, in the accompanying consolidated balance sheet, right-of-use assets and non-current lease liabilities are presented separately and, in the accompanying consolidated statement of cash flows, amortization of investments is presented separately.

Principles of Consolidation

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

EXICURE, INC.

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

Significant Risks and Uncertainties

In response to the ongoing COVID-19 pandemic, the Company has taken and continues to take active measures designed to address and mitigate the impact of the COVID-19 pandemic on its business, such as remote working policies, facilitating management's routine communication to address employee and business concerns and providing frequent updates to the Company's board of directors (the "Board"). As of July 1, 2020, the Company took occupancy of approximately 30,000 square feet of laboratory and office space in its new headquarters in Chicago, Illinois. Since then, the Company has operated under COVID-19 social distancing guidelines and has generally operated with 100% of its R&D staff on-site. The Company's office and general and administrative team continues to work predominantly from home. The Company's preclinical development program in Friedreich's ataxia ("FA") is ongoing and it began IND-enabling studies for XCUR-FXN in late 2020. The Company also continues to progress its collaborations with AbbVie Inc. ("AbbVie") and DERMELIX, LLC, d/b/a Dermelix Biotherapeutics ("Dermelix"). However, if the COVID-19 pandemic continues to persist for an extended period of time, the Company could experience further significant disruptions to its preclinical development timelines, which would adversely affect its business, financial condition, results of operations and growth prospects.

The Company believes that the effects of the COVID-19 pandemic or its impact contributed to delays in its enrollment plans and clinical trial site start-ups for the Phase 2 dose expansion phase of the trial for its cavrotolimod (AST-008) clinical program. The Company now anticipates to report overall response rate ("ORR") results for cavrotolimod (AST-008) in the first half of 2022 rather than by year end 2021 as previously guided in September 2020. The extent to which the COVID-19 pandemic or its impact or effects may continue to impact the Company's business, its clinical development and regulatory efforts, its corporate development objectives and the value of and market for its common stock, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration or spread of the pandemic, its impact and effects, the possibility of additional periods of increases or spikes in the number of COVID-19 cases, travel restrictions, quarantines, social distancing, phased re-openings and business closure requirements in the United States and other countries, and the effectiveness of actions taken globally to contain and treat the disease, including, without limitation, the effectiveness and timing of vaccination initiatives in the United States and worldwide. The global economic slowdown, the overall disruption of global healthcare systems and the other risks and uncertainties associated with the pandemic could have a material adverse effect on the Company's business, financial condition, results of operations and growth prospects.

In addition, the Company is subject to other challenges and risks specific to its business and its ability to execute on its business plan and strategy, as well as risks and uncertainties common to companies in the biotechnology industry with research and development operations, including, without limitation, risks and uncertainties associated with: obtaining regulatory approval of its product candidates; delays or problems in obtaining clinical supply, loss of single source suppliers or failure to comply with manufacturing regulations; identifying, acquiring or in-licensing additional products or product candidates; product development and the inherent uncertainty of clinical success; and the challenges of protecting and enhancing its intellectual property rights; and the challenges of complying with applicable regulatory requirements. In addition, to the extent the ongoing COVID-19 pandemic adversely affects the Company's business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties.

Liquidity Risk

As of December 31, 2020, the Company has generated an accumulated deficit of $124,802 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, 2020, including amounts borrowed and available under the MidCap Credit Facility (see Note 6), is sufficient to fund the Company's current plans for at least the next 12 months from the date of this report. Management believes that it will be able to obtain additional working capital through equity financings, partnerships and licensing, or other arrangements, such as its "at the market offering" program pursuant to its equity distribution agreement with BMO Capital Markets Corp., 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. The Company has historically principally raised capital through the sale of its securities. However, the COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of global financial markets. If the disruption continues to persist and deepens, the Company could experience an inability to access additional capital, which could in the future negatively affect its operations.

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 circumstances 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.

2. Significant Accounting Policies

Cash, cash equivalents, and short-term investments

The Company considers all highly liquid investments with original maturities of three months or less to be cash equivalents. The Company's short-term investments have initial maturities of greater than three months from date of purchase. The Company classifies its marketable debt security investments as "available-for-sale" and carries them at fair market value based upon prices on the last day of the fiscal period for identical or similar items. The Company records unrealized gains and losses on marketable debt securities in other comprehensive income (loss) as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or interest expense over the life of the of the underlying security. Realized gains and losses are included in other income, net. The Company uses the specific identification method to determine the cost of securities sold.

The Company secures a standby letter of credit with a restricted certificate of deposit account as part of its Chicago lease agreement. The Company considers the restricted certificate of deposit account to be restricted cash because its use to the Company is contractually limited and presents the balance within other noncurrent assets on the Company's consolidated balance sheet at December 31, 2020.

Accounts receivable and unbilled revenue receivable

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. The Company's receivables as of December 31, 2020 and December 31, 2019 relate to amounts reimbursed under its collaboration agreement with Dermelix. The Company believes that credit risks associated with its collaboration partner are not significant and that these receivables are fully collectible. To date, the Company has not had any write-offs of uncollectible receivables, and the Company did not have an allowance for doubtful accounts as of December 31, 2020 and 2019.

Fair value of financial instruments

The Company has estimated the fair value of its financial instruments. The carrying amounts for cash, cash equivalents, accounts receivable, and accounts payable approximate their fair value due to the relatively short-term nature of these instruments. The Company records short-term investments at their estimated fair value based on quoted market prices for identical or similar instruments. The Company believes that the its 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 its fair value.

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, cash equivalents, short-term investments, and accounts receivable. The Company places its cash, cash equivalents, and short-term investments with reputable financial institutions. The Company primarily invests its excess cash in debt instruments of corporations, the U.S. Treasury, financial institutions, and U.S. government agencies with strong credit ratings and an investment grade rating at or above a long-term rating of Aa3/AA- and a short-term rating of P1/A1. The Company has established guidelines relative to diversification and maturities that maintain safety and liquidity. The Company periodically reviews and modifies these guidelines to maximize trends in yields and interest rates without compromising safety and liquidity. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no financial instruments with off-balance sheet risk of loss.

As of December 31, 2020, the Company's receivables primarily relate to amounts reimbursed under its collaboration agreement with Dermelix. For the year ended December 31, 2020, the Company's revenue was generated from its collaborations with AbbVie and Dermelix.

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, *Liquidity Risk*, 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, 2020.

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 consolidated statements of operations.

Revenue recognition

The Company recognizes revenue when the Company's 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 Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers* ("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 and obligations 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. To date, the Company has not recognized any milestone payment revenue from any of its collaboration agreements.

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.

During the years ended December 31, 2020 and 2019, the Company has primarily earned revenue under the collaboration agreements with AbbVie and Dermelix (see Note 3 for more information).

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, the fair value measurement date is the date of grant and the requisite service period is the period over which the option recipient is required to provide service in exchange for the common stock option awards, which is generally the vesting period.

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.

Leases

The Company determines if an arrangement is a lease at contract inception. Operating lease assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease assets and liabilities are recognized on the balance sheet at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, the Company includes options to extend or to terminate the lease when it is reasonably certain that the Company will exercise that option. The Company uses the implicit interest rate when readily determinable and uses the Company's incremental borrowing rate when the implicit rate is not readily determinable based upon the information available at the commencement date in determining the present value of the lease payments.

The lease payments used to determine the Company's operating lease assets may include lease incentives, stated rent increases and escalation clauses linked to rates of inflation when determinable. In addition, the Company's lease arrangements may contain lease and non-lease components. The Company combines lease and non-lease components, which are accounted for together as a single lease component. Variable lease payments, such as real estate taxes and facility maintenance costs that are allocated by the lessor to the lessee and are not based on an index or a rate, are excluded from the measurement of the lease liability.

Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term. Short-term leases, defined as leases that have a lease term of twelve months or less at the commencement date, are

excluded from this treatment and are recognized on a straight-line basis over the term of the lease. Costs for variable lease payments that are not included in the lease liability are recognized as expense as incurred.

Research and development expense

Research and development expenses are charged to expense as incurred in performing research and development activities in accordance with ASC 730, *Research and Development*. The costs include employee-related expenses including salaries, benefits, and stock-based compensation expense, costs of funding research performed by third parties that conduct research and development and preclinical and clinical activities on the Company's behalf, the cost of purchasing lab supplies and non-capital equipment used in preclinical and clinical activities and in manufacturing preclinical and clinical study materials, consultant fees, facility costs including rent, depreciation and maintenance expenses, fees for acquiring and maintaining licenses under third party licensing agreements, including any sublicensing or success payments made to the Company's licensors, and overhead and other expenses directly related to research and development operations. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the Company's estimate, the accrual or prepaid is adjusted accordingly. The Company defers and capitalizes non-refundable advance payments made by the Company for research and development activities until the related goods are received or the related services are performed. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense.

Income taxes

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, 2020 and 2019, 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

Equity-based compensation

In June 2018, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2018-07, *Compensation-Stock Compensation: Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"), which aligns the measurement and classification guidance for share-based payment to non-employees with the guidance for share-based payments to employees. Under the new guidance, the measurement period for equity-classified non-employee awards will be fixed at the grant date. Prior to the adoption of ASU 2018-07, the Company remeasured fair value of stock option awards to nonemployees at each financial statement reporting date. The Company adopted the guidance of ASU 2018-07 in the first quarter of 2019 on a modified retrospective basis. The adoption of ASU 2018-07 did not have a material impact on the Company's financial statements.

Leases

In February 2016, FASB issued ASU 2016-02, *Leases (Topic 842)* (or "ASC 842), which replaces the guidance in ASC 840, *Leases* ("ASC 840") and requires lessees to recognize right-of-use assets and lease liabilities on the balance sheet. The Company adopted ASC 842 on the required effective date of January 1, 2019 utilizing the modified retrospective transition method with no restatement of prior periods or cumulative adjustment to accumulated deficit. The Company has elected the package of practical expedients, which allows the Company not to reassess (1) whether any expired or existing contracts as of the adoption date are or contain a lease, (2) lease

(in thousands, except share and per share data)

classification for any expired or existing leases as of the adoption date and (3) initial direct costs for any existing leases as of the adoption date. The Company elected to combine lease and non-lease components, elected not to record leases with an initial term of twelve months or less on the balance sheet and will recognize the associated lease payments in the consolidated statements of operations on a straight-line basis over the lease term. The Company did not elect to apply the hindsight practical expedient when determining lease term and assessing impairment of right-of-use assets.

The adoption of ASC 842 on January 1, 2019 resulted in the recognition of an operating lease asset of approximately $613 and operating lease liabilities of approximately $623, with no impact to operating expense, net loss, or basic and diluted loss per common share for the year ended December 31, 2019. The impact to the consolidated balance sheet upon adoption of ASC 842 is as follows:

	As Previously Reported December 31, 2018	ASC 842 Adoption Adjustment	As Reported Under ASC 842 January 1, 2019
Prepaid expenses and other current assets	$ 1,392	$ (28)	$ 1,364
Right-of-use asset	—	613	613
Accrued expenses and other current liabilities	1,543	243	1,786
Lease liability, noncurrent	—	342	342

See Note 7, *Leases*, for more information on leases.

Recent Accounting Pronouncements Not Yet Adopted

Financial Instruments - Credit Losses

In June 2016, the FASB issued ASU 2016-13, *Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13). ASU 2016-13 is a new standard intended to improve reporting requirements specific to loans, receivables and other financial instruments. ASU 2016-13 requires that credit losses on financial assets measured at amortized cost be determined using an expected loss model, instead of the current incurred loss model, and requires that credit losses related to available-for-sale debt securities be recorded through an allowance for credit losses and limited to the amount by which carrying value exceeds fair value. ASU 2016-13 also requires enhanced disclosure of credit risk associated with financial assets. The effective date of ASU 2016-13 was deferred by ASU 2019-10, *Financial Instruments—Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842)—Effective Dates* to the annual period beginning after December 15, 2022 for companies that (i) meet the definition of an SEC filer and (ii) are eligible as "smaller reporting companies" as such term is defined by the SEC, with early adoption permitted. The Company is currently assessing the impact of adoption of ASU 2016-13 to its consolidated financial statements.

3. Collaborative Research and License Agreements

AbbVie Collaboration Agreement

Summary of Agreement

On November 13, 2019 (the "Effective Date"), the Company entered into a Collaboration, Option and License Agreement (the "AbbVie Collaboration Agreement"), with a wholly-owned subsidiary of Allergan plc, Allergan. On May 8, 2020, Allergan plc, including Allergan was acquired by AbbVie. Pursuant to the AbbVie Collaboration Agreement, the Company granted to AbbVie exclusive access and options to license SNA based therapeutics arising from two collaboration programs related to the treatment of hair loss disorders (each, a "Collaboration Program"). Under each such license (obtained in connection with the exercise of an Option, as defined and discussed further below), the Company would grant to AbbVie exclusive, royalty-bearing, sublicenseable, nontransferable, worldwide rights to develop, manufacture, use and commercialize such SNA therapeutics. Under the AbbVie Collaboration Agreement, the Company will use commercially reasonable efforts to conduct two Collaboration Programs, each focused on one or more hair loss disorders to discover one or more SNA products that are directed to, bind to or inhibit one or more specific Collaboration Program targets (each, a "Program Target").

As of the Effective Date, the Company and AbbVie have agreed upon a development plan for each Collaboration Program that describes the development activities and timelines required to advance such Collaboration Program through first IND filing (each, a "Development Plan"). The activities described in the Development Plan are conducted under the supervision of the Joint Development Committee (the "JDC") consisting of three members from each of the Company and AbbVie. The Company is primarily responsible for performing early stage discovery and preclinical activities (the "Initial Development Activities") set forth in the Development Plan for each Collaboration Program and will be solely responsible for all costs and expenses related to the Initial Development Activities. AbbVie may elect, in its sole discretion and at its sole cost and expense, to conduct formulation assessment and *in vivo* testing as set forth in a Development Plan.

Following the completion of all Initial Development Activities, the Company is required to deliver to AbbVie a report that describes the results of the Initial Development Activities and identifies at least one SNA-based compound that satisfies certain criteria for such Collaboration Program as determined by the JDC (the "Initial Development Report"). Following the delivery of the Initial Development Report for a Collaboration Program, AbbVie will have the ability for a defined period of time (the "Initial Option Exercise Period") to exercise an option (each an "Option") to obtain worldwide rights and license to the Company's SNA technology and the Company's interest in joint collaboration technology to make, have made, import, use, sell or offer for sale any product (each a "Licensed Product") that results from such Collaboration Program during the term of the AbbVie Collaboration Agreement.

At AbbVie's sole option, AbbVie may extend the Initial Option Exercise Period (the "Option Extension") and require the Company to perform IND-enabling activities described in the Development Plan (the "IND-Enabling Activities"), subject to the payment of additional consideration ("Extension Exercise"). If AbbVie exercises the Option Extension, the Company would be responsible for conducting the IND-Enabling Activities and would be solely responsible for all costs and expenses associated with such activities. Upon completion of the IND-Enabling Activities, the Company is required to deliver a report that describes the results of the IND-Enabling Activities (the "IND-Enabling Activities Data Package") to AbbVie. Following the delivery of IND-Enabling Activities Data Package, AbbVie will have the ability for a defined period of time (the "Extended Option Exercise Period") to exercise an Option with respect to such Collaboration Program. After the exercise of an Option with respect to a Collaboration Program, AbbVie will be responsible for all development, manufacturing, and commercialization activities, and costs and expense associated with such activities in connection with Licensed Products arising from such Collaboration Program.

The Company's obligation to conduct the activities defined in the Development Plan under the AbbVie Collaboration Agreement commenced on November 13, 2019 and continues until the earlier of (i) the date AbbVie

exercises an Option, (ii) the date AbbVie abandons a Collaboration Program and foregoes its Option to that Collaboration Program, or (iii) the fifth anniversary of the Effective Date (the "Research Term"). If the Initial Option Exercise Period or Extended Option Exercise Period is still in effect for a Collaboration Program or if the Company has not delivered a complete Initial Development Report or, if AbbVie made an Extension Exercise for a Collaboration Program, a complete IND-Enabling Activities Data Package for such Collaboration Program, as determined by the JDC, then the Research Term will automatically extend by one-year increments until such obligation is satisfied, but in no event past the seventh anniversary of the Effective Date.

Under the terms of the AbbVie Collaboration Agreement, the Company received a $25,000 upfront, non-refundable, non-creditable cash payment (the "AbbVie Upfront Payment") related to the Company's research and development costs for conducting the Development Plan for two Collaboration Programs, each focused on one or more targets, and certain options to obtain exclusive, worldwide licenses under certain intellectual property rights owned or controlled by the Company to develop, manufacture and commercialize certain products resulting from each such Collaboration Programs. The option exercise fee during the Initial Option Exercise Period is $10,000 per Collaboration Program. If AbbVie elects to extend the Initial Option Exercise Period, AbbVie is required to pay an additional fee of $10,000. If AbbVie elects to exercise its option during the Extended Option Exercise Period, AbbVie must pay the Company the option exercise fee of $15,000.

Following the exercise by AbbVie of an Option with respect to a Collaboration Program, AbbVie would be required to make certain milestone payments to the Company upon the achievement of specified development, product approval and launch, and commercial events, on a Licensed Product by Licensed Product basis. On a Licensed Product by Licensed Product basis, for the first Licensed Product to achieve the associated milestone event, the Company is eligible to receive up to an aggregate of $55,000 for development milestone payments and $132,500 for product approval and launch milestone payments. The Company is also eligible for up to $175,000 in sales milestone payments on a Collaboration Program by Collaboration Program basis, associated with aggregate worldwide sales. Certain product approval milestones are subject to certain reductions under specified circumstances, including for payments required to be made by AbbVie to obtain certain third party intellectual property rights.

In addition, to the extent there is any Licensed Product, the Company would be entitled to receive tiered royalty payments of mid-single digits to the mid-teens percentage on future net worldwide product sales of such Licensed Products, subject to certain reductions under specified circumstances. Royalties are due on a Licensed Product by Licensed Product and country by country basis from the date of the first commercial sale of each Licensed Product in a country until the latest to occur of: (i) the expiration date in such country of the last to expire valid claim within the licensed intellectual property covering the manufacture, use or sale of such Licensed Product in such country, (ii) the tenth anniversary of the first commercial sale of such Licensed Product in such country, and (iii) the expiration of regulatory exclusivity for such Licensed Product in such country.

AbbVie may terminate the AbbVie Collaboration Agreement for any reason or no reason, either in its entirety or on a Collaboration Program by Collaboration Program basis, at any time on 90 days' prior written notice to the Company. Unless earlier terminated, the term of the AbbVie Collaboration Agreement shall continue until (i) if both Option Exercise Periods expire without AbbVie exercising either Option, the expiration of the later to expire Option Exercise Period, and (ii) if either or both Options are exercised on a Licensed Product-by-Licensed Product and country-by-country basis, the expiration of the royalty term for such Licensed Product in such country. Either party may terminate the AbbVie Collaboration Agreement if the other party has materially breached or defaulted in the performance of any of its material obligations and such breach or default continues after the specified cure period.

Termination of the AbbVie Collaboration Agreement for any reason will not release either party from any liability which, at the time of such termination, has already accrued to the other party or which is attributable to a period prior to such termination. In addition, termination of the AbbVie Collaboration Agreement will not preclude either party from pursuing any rights and remedies it may have under the agreement or at law or in equity with respect to any breach of the AbbVie Collaboration Agreement. If either party terminates the AbbVie Collaboration

Agreement, the license and rights granted to AbbVie with respect to the terminated Collaboration Program or License Product shall terminate.

Accounting Analysis

The Company concluded that AbbVie is a customer in this arrangement, and as such the arrangement falls within the scope of the revenue recognition guidance. Under the AbbVie Collaboration Agreement, the Company has identified a single performance obligation that includes (i) the research and development activities during the Research Term (the "AbbVie R&D Services"), and (ii) Joint Development Committee services during the Research Term (the "AbbVie JDC Services"). The Company has concluded that the AbbVie R&D Services is not distinct from the AbbVie JDC Services during the Research Term. The JDC provides oversight and management of the overall AbbVie Collaboration Agreement, and the members of the JDC from the Company have specialized industry knowledge, particularly as it relates to SNA technology. The JDC is meant to facilitate the early stage research being performed and coordinate the activities of both the Company and AbbVie. Further, the JDC services are critical to the ongoing evaluation of a Collaboration Program and the drafting and evaluation of the Initial Development Report and the IND-Enabling Data Package. Accordingly, the Company's participation on the JDC is essential to AbbVie receiving value from the AbbVie R&D Services and as such, the AbbVie JDC Services along with the AbbVie R&D Services are considered one performance obligation (the "Collaboration Program Services"). In addition, the Company has concluded that the option to purchase two development and commercialization licenses is considered a marketing offer as the options did not provide any discounts or other rights that would be considered a material right in the arrangement, and thus, not a performance obligation at the onset of the agreement. The consideration for these options will be accounted for when they are exercised.

As of the Effective Date of the AbbVie Collaboration Agreement, the total transaction price was determined to be $25,000, consisting solely of the AbbVie Upfront Payment. The Company also utilized the most likely amount method to estimate any development and regulatory milestone payments to be received. As of the Effective Date of the AbbVie Collaboration Agreement, there were no milestones included in the transaction price. The milestones were fully constrained due to the significant uncertainties surrounding such payments. The Company considered the stage of development and the risks associated with the remaining development required to achieve the milestone, as well as whether the achievement of the milestone is outside the control of the Company or AbbVie. The Company has determined that any commercial milestones and sales-based royalties will be recognized when the related sales occur and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur. As of December 31, 2020, the Company determined that any development, regulatory, or commercial milestones continue to be constrained and therefore the related milestone payments continue to be excluded from the transaction price at December 31, 2020.

The Company will recognize revenue related to the Collaboration Program Services as the performance obligation is satisfied using an input method to measure progress. The Company believes the input method that most accurately depicts the measure of progress is the actual hours incurred to date relative to projected hours to complete the research service.

During the years ended December 31, 2020 and December 31, 2019, the Company recognized revenue under the AbbVie Collaboration Agreement of approximately $16,486 and $171, respectively. As of December 31, 2020, there was $8,343 of deferred revenue related to the AbbVie Collaboration Agreement, which is classified as current on the consolidated balance sheet. As of December 31, 2019, there was $24,829 of deferred revenue related to the AbbVie Collaboration Agreement, of which $21,873 is classified as current and $2,956 is classified as noncurrent on the consolidated balance sheet.

During the three months ended December 31, 2019, the Company incurred $3,750 in license fees owed to Northwestern University in connection with the receipt of the AbbVie Upfront Payment, which the Company recorded as research and development expenses during such period.

Dermelix Collaboration Agreement

Summary of Agreement

On February 17, 2019, Exicure entered into a License and Development Agreement with Dermelix (the "Dermelix Collaboration Agreement.") Pursuant to the Dermelix Collaboration Agreement, the Company granted to Dermelix exclusive, worldwide royalty-bearing license rights to, develop, manufacture, have manufactured, use and commercialize the Company's 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 Collaboration 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 Collaboration 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 Collaboration Agreement, including the Company's expenses incurred in connection with development activities and in accordance with the development budget. Under the terms of the Dermelix Collaboration 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 Collaboration 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 is 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. 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. The commercial sales milestones are payable upon achievement of specified aggregate annual product sales thresholds. In the event a therapeutic candidate subject to the collaboration results in commercial sales, the Company will receive low double-digit royalties on annual net sales for such licensed products.

Accounting Analysis

The Company concluded that Dermelix is a customer in this arrangement, and as such the arrangement falls within the scope of the revenue recognition guidance. The Company identified performance obligations under the Dermelix Collaboration Agreement for the license of intellectual property for the NS therapeutic candidate and associated research and development services for the NS therapeutic candidate. The Company determined that the performance obligations were not separately identifiable and were not distinct or distinct within the context of the contract due to the specialized nature of the services to be provided by Exicure, specifically with respect to the

(in thousands, except share and per share data)

Company's expertise related to SNA technology, and the interdependent relationship between the performance obligations. As such, the Company concluded that there is a single identified performance obligation.

The Company used the most likely amount method to estimate variable consideration and estimated that the most likely amount for each potential development and regulatory milestone, which is considered variable consideration, was zero, as the achievement of those milestones is uncertain and highly susceptible to factors outside of the Company's control. Accordingly, all such milestones were excluded from the transaction price. Management will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur and adjust the transaction price as necessary. Sales-based royalties, including commercial sales milestone payments based on the level of sales, were also excluded from the transaction price, as the license is deemed to be the predominant item to which the royalties relate. The Company will recognize such 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).

Revenue associated with the performance obligation will be recognized as services are provided using a cost-to-cost measure of progress method. The transfer of control occurs over time and, in management's judgment, this input method is the best measure of progress towards satisfying the performance obligation under the Dermelix Collaboration Agreement and reflects a faithful depiction of the transfer of goods and services.

The Company initially recorded the upfront payment of $1,000 as deferred revenue related to its wholly unsatisfied performance obligation and reduced this balance to zero during 2019 by recognizing revenue as services were provided. The Company recognized $127 and $1,125 of revenue under the Dermelix Collaboration Agreement during the years ended December 31, 2020 and December 31, 2019, respectively, which reflects full recognition of the upfront payment as revenue as well as reimbursement by Dermelix for additional costs incurred by Exicure for early stage development costs beyond the initial $1,000 upfront payment.

4. Supplemental Balance Sheet Information

Property and equipment, net

	December 31,	
	2020	2019
Scientific equipment	$ 5,476	$ 2,7
Leasehold improvements	192	
Computers and software	46	
Furniture and fixtures	30	
Construction in process	119	
Property and equipment, gross	5,863	3,4
Less: accumulated depreciation	(1,740)	(1,3
Property and equipment, net	$ 4,123	$ 2,0

Depreciation and amortization expense was $766 and $392, for the years ended December 31, 2020 and 2019, respectively.

(in thousands, except share and per share data)

Accrued expenses and other current liabilities

	December 31,	
	2020	2019
Accrued clinical, contract research and manufacturing costs	$ 1,372	$ 515
Accrued payroll-related expenses	1,158	920
Lease liability, current	223	292
Accrued other expenses	772	708
Accrued expenses and other current liabilities	$ 3,525	$ 2,435

5. Investments

As of December 31, 2020 and 2019, the Company primarily invested its excess cash in debt instruments of corporations, the U.S. Treasury, financial institutions, and U.S. government agencies with strong credit ratings and an investment grade rating at or above a long-term rating of Aa3/AA- and a short-term rating of P1/A1. The Company has established guidelines relative to diversification and maturities that maintain safety and liquidity. The Company periodically reviews and modifies these guidelines to maximize trends in yields and interest rates without compromising safety and liquidity.

The following table summarizes the contract maturity of the available-for-sale securities the Company held as of December 31, 2020:

One year or less	100	%
After one year but within two years	—	%
Total	100	%

(in thousands, except share and per share data)

The amortized cost, gross unrealized holding gains, gross unrealized holding losses and fair value of cash equivalents and available-for-sale securities by type of security at December 31,2020 and December 31, 2019 were as follows:

	December 31, 2020			
	Amortized Costs	Gross Unrealized Holding Gains	Gross Unrealized Holding Losses	Fair Value
Commercial paper	$ 15,992	$ 2	$ (3)	$ 15,991
Corporate notes/bonds	29,227	72	(3)	29,296
U.S. Treasuries	2,251	2	—	2,253
U.S. Government agency securities	1,265	13	—	1,278
	$ 48,735	$ 89	$ (6)	$ 48,818

	December 31, 2019			
	Amortized Costs	Gross Unrealized Holding Gains	Gross Unrealized Holding Losses	Fair Value
Commercial paper	$ 13,932	$ 1	$ (2)	$ 13,931
Corporate notes/bonds	36,620	1	(24)	36,597
U.S. Treasuries	4,513	—	(1)	4,512
U.S. Government agency securities	9,786	—	(2)	9,784
	$ 64,851	$ 2	$ (29)	$ 64,824

6. Debt

MidCap Credit Agreement

On September 25, 2020, the Company entered into a Credit and Security Agreement, as amended on October 21, 2020, (the "MidCap Credit Agreement"), with MidCap Financial Trust ("MidCap"), as agent, and the lenders party thereto from time to time.

The MidCap Credit Agreement provides for a secured term loan facility in an aggregate principal amount of up to $25,000 (the "MidCap Credit Facility"). The Company borrowed the first advance of $17,500 ("Tranche 1") on September 25, 2020 (the "Closing Date"). Under the terms of the MidCap Credit Agreement, the second advance of $7,500 ("Tranche 2") will be available to the Company from April 1, 2021 to September 30, 2021, subject to the Company's satisfaction of certain conditions described in the MidCap Credit Agreement. The proceeds from the MidCap Credit Facility are expected to be used for working capital and general corporate purposes.

Tranche 1, and if borrowed Tranche 2, each bear interest at a floating rate equal to 6.25% per annum, plus the greater of (i) 1.50% or (ii) one-month LIBOR. Interest on each loan advance is due and payable monthly in arrears. Principal on each loan advance is payable in 36 equal monthly installments beginning October 1, 2022 until paid in full on October 1, 2025 (the "Maturity Date"). Prepayments of the loans under the MidCap Credit Agreement, in whole or in part, will be subject to early termination fees in an amount equal to 3.0% of principal prepaid if prepayment occurs on or prior to the first anniversary of the Closing Date and 1.0% of principal prepaid if prepayment occurs after the first anniversary of the Closing Date and prior to the maturity date. In connection with execution of the Midcap Credit Agreement, the Company paid MidCap a $125 origination fee.

At the Maturity Date or on any earlier date on which all amounts advanced to the Company become due and payable in full, or are otherwise paid in full, the Company is required to pay an exit fee equal to 3.75% of the principal amount of all loans advanced to the Company under the MidCap Credit Agreement. Upon the advance of Tranche 1, the Company accrued $656 for the related exit fee.

The Company's obligations under the MidCap Credit Agreement are secured by a security interest in substantially all of its assets, excluding intellectual property (which is subject to a negative pledge). Additionally, the Company's future subsidiaries, if any, may be required to become co-borrowers or guarantors under the MidCap Credit Agreement.

The MidCap Credit Agreement contains customary affirmative covenants and customary negative covenants limiting the Company's ability and the ability of the Company's subsidiaries, if any, to, among other things, dispose of assets, undergo a change in control, merge or consolidate, make acquisitions, incur debt, incur liens, pay dividends, repurchase stock and make investments, in each case subject to certain exceptions.

The MidCap Credit Agreement also contains customary events of default relating to, among other things, payment defaults, breaches of covenants, a material adverse change, delisting of the Company's common stock, bankruptcy and insolvency, cross defaults with certain material indebtedness and certain material contracts, judgments, and inaccuracies of representations and warranties. Upon an event of default, the agent and the lenders may declare all or a portion of the Company's outstanding obligations to be immediately due and payable and exercise other rights and remedies provided for under the agreement. During the existence of an event of default, interest on the obligations could be increased by 2.0%.

Total proceeds, net of fees and issuance costs, borrowed under Tranche 1 were $16,512. Fees and issuance costs of $332, as well as fees of $656 that are payable to MidCap at maturity of Tranche 1, are recorded as a reduction to the carrying amount of long-term debt on the Company's balance sheet and will be amortized to interest expense through the maturity date of October 1, 2025 using the effective interest method. Fees and issuance costs of $73 attributed to the amount available to be borrowed under Tranche 2 were paid or accrued and recorded as deferred financing costs (other assets) and will be recorded as a reduction in the carrying amount of long-term debt in future periods if amounts are borrowed under Tranche 2.

Hercules Loan Agreement

On March 2, 2020, pursuant to the terms of the loan agreement with Hercules Technology Growth Capital ("Hercules") and subsequent amendments thereto (the "Hercules Loan Agreement"), the Company repaid all remaining outstanding obligations under the Hercules Loan Agreement as of the maturity date, including the outstanding principal balance of $4,999 and the end of term fee of $100.

(in thousands, except share and per share data)

As of December 31, 2020, the aggregate carrying value of the Company's long-term debt is $16,589.

As of December 31, 2020, the principal maturities of the Company's long-term debt were as follows:

	December 31, 2020
2021	$ —
2022	1,459
2023	5,833
2024	5,833
2025	4,375
Principal balance outstanding	17,500
less: unamortized discount and debt issuance costs	(911)
Long-term debt	16,589
Current portion	—
Noncurrent portion	$ 16,589

The Company paid interest on debt of $394 and $597 during the years ended December 31, 2020 and 2019, respectively.

7. Leases

The Company's lease arrangements consist of (i) a lease for office and laboratory space at its headquarters in Chicago, Illinois that commenced in July 2021 (the "Chicago Lease"), (ii) a lease for office and laboratory space at its former headquarters in Skokie, Illinois that commenced in March 2012 and is scheduled to end in February 2021 (the "Skokie Lease"), (iii) a lease for office space at a multi-tenant facility in Cambridge, MA that commenced in March 2019 and is cancelable at any time (the "Cambridge Lease"), and (iv) leases for office equipment (the "Office Equipment Leases"). Each of these leases are classified as operating leases.

The Skokie Lease includes a renewal option which the Company concluded is not reasonably certain to be exercised. Lease payments for the Skokie Lease include a fixed payment amount as well as variable payments related to a proportionate share of operating and real estate expenses.

Due to the nature of the Cambridge Lease, the Company determined that this lease represented a short-term lease with an initial term of less than twelve months and, as such, the Cambridge Lease is not recorded on the balance sheet and related lease costs are recognized in the statement of operations as they are incurred. The Company has also elected to not record the Office Equipment Leases on the balance sheet since related payment amounts and lease costs are insignificant. Lease costs for the Office Equipment Leases are recognized in the statement of operations on a straight-line basis over the lease term.

Chicago Lease

The Company has approximately thirty thousand square feet of office and laboratory space in Chicago, Illinois (the "Chicago Lease"). The original term (the "Original Term") of the Chicago Lease is 10 years, commencing on July 1, 2020 (the "Commencement Date"), which is the date the premises were ready for occupancy under the terms of the Chicago Lease. The Company has options to extend the term of the Chicago Lease for two additional successive periods of five years each (the "Extension Periods") at the then prevailing effective market rental rate.

The initial annual base rent during the Original Term is approximately $1,113 for the first 12-month period of the Original Term, payable in monthly installments beginning on the Commencement Date. Base rent thereafter is subject to annual increases of 3%, for an aggregate amount of $12,761 over the Original Term. The Company must

(in thousands, except share and per share data)

also pay its proportionate share of certain operating expenses and taxes for each calendar year during the term. During the first 12-month period of the Original Term, the base rent and the Company's proportionate share of operating expenses and taxes are subject to certain abatements.

Upon execution of the Chicago Lease, the Company paid to the landlord the first installment of base rent and the estimated monthly amount of its pro rata share of taxes and its pro rata share of operating expenses in the aggregate amount of $87 which amount had been adjusted for the abatement as set forth in the lease agreement. The Company also paid the landlord a net amount of $697 toward tenant improvements.

As part of the agreement for the Chicago Lease, the Company is required to maintain a standby letter of credit during the term of the lease, currently in the amount of $1,200 and subject to reduction over time, which is secured by a restricted certificate of deposit account and presented within other noncurrent assets on the Company's consolidated balance sheet at December 31, 2020.

The Company recognized a right of use asset of $8,931 and a lease liability of $8,147 on the Commencement Date. Because the rate implicit in the Chicago Lease is not readily determinable, the Company used its incremental borrowing rate of 8.3% on the Commencement Date to determine the present value of the lease payments over the Original Term. The incremental borrowing rate represents an estimate of the interest rate the Company would incur at lease commencement to borrow an amount equal to the lease payments on a collateralized basis over the term of a lease. As of December 31, 2020, the Company determined it is not reasonably certain that the renewal option would be exercised.

Skokie Lease

In connection with the Company's relocation of its headquarters from Skokie, Illinois to its new facility in Chicago, Illinois on July 1, 2020, the Company determined that the remaining useful life of the right of use asset underlying the Skokie Lease at June 30, 2020 was zero and therefore recognized remaining amortization expense related to the Skokie Lease of $211 during the three month period then ended.

Information related to the Company's operating lease asset and related operating lease liabilities were as follows:

	December 31, 2020	December 31, 2019
Weighted-average remaining lease term	9.5 years	1.2 years
Weighted-average discount rate	8.3 %	16.1 %

The following table summarizes lease costs in the Company's consolidated statement of operations:

	December 31,	
	2020	2019
Operating lease costs	$ 1,042	$ 336
Short term lease costs	127	100
Variable lease costs	521	344
Total lease costs	$ 1,690	$ 780

The Company made cash payments for operating leases of $2,244 and $847 during the years ended December 31, 2020 and 2019, respectively.

(in thousands, except share and per share data)

Maturities of the Company's lease liability as of December 31, 2020 were as follows:

Years Ending December 31,		Operating Leases
2021		870
2022		1,163
2023		1,198
2024		1,235
2025		1,272
Thereafter		6,207
Total	$	11,945
Less: imputed interest		(3,763)
Total lease liability	$	8,182
Current operating lease liability	$	223
Noncurrent operating lease liability		7,959
Total lease liability	$	8,182

8. Stockholders' Equity

Preferred Stock

The Company has 10,000,000 shares of preferred stock, par value $0.0001 authorized and no shares issued and outstanding.

Common Stock

The Company has 200,000,000 shares of common stock, par value $0.0001, authorized. As of December 31, 2020 and December 31, 2019, the Company had 87,651,352 and 86,069,263 shares issued and outstanding, respectively.

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 the Company's 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 the Company's 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 the Company's 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. The Company's common stock has no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the Company's common stock. The outstanding shares of the Company's common stock are fully paid and non-assessable.

December 2019 Offering

On December 23, 2019, the Company sold 10,000,000 shares of its common stock at the public offering price of $2.75 per share in an underwritten public offering for gross proceeds of $27,500 and estimated net proceeds of $25,344 after deducting underwriting discounts and commission and other offering expenses payable by the Company (the "December 2019 Offering"). In addition, the Company granted the underwriters a 30-day option to purchase an additional 1,500,000 shares of common stock. On January 6, 2020, the underwriters exercised such option with respect to 1,081,184 shares of common stock at the public offering price of $2.75 per share for

(in thousands, except share and per share data)

additional gross proceeds of $2,973 and net proceeds of $2,766 after deducting underwriting discounts and commission and other offering expenses.

The shares sold in the December 2019 Offering were sold pursuant to a registration statement on Form S-3 that was declared effective by the SEC on July 24, 2019.

August 2019 Offering

On August 2, 2019, the Company completed the sale of 31,625,000 shares of its common stock at a public offering price of $2.00 per share in an underwritten public offering, which included the exercise in full of the underwriters' option to purchase an additional 4,125,000 shares at the public offering price (the "August 2019 Offering"). The Company received gross proceeds of $63,250 in the August 2019 Offering before deducting underwriting discounts and commissions and offering expenses of $4,384.

The shares sold in the August 2019 Offering were sold pursuant to a shelf-registration the Company filed on Form S-3 with the SEC which was declared effective by the SEC on July 24, 2019.

Common Stock Warrants

As of December 31, 2020, warrants to purchase 413,320 shares of common stock at a price of $3.00 per share remain outstanding. The warrants expire as follows: 163,174 warrants expire on March 27, 2021; 132,884 expire on April 28, 2021; and 117,262 expire on May 3, 2021. The warrants are classified as a liability which is remeasured each period at fair value. See Note 12, *Fair Value Measurements,* for more information on the fair value of the common stock warrant liability.

Accumulated Other Comprehensive Loss

The following table summarizes the changes in each component of accumulated other comprehensive loss, net of tax, for 2020:

	Unrealized gains (losses) on short-term investments	Total
Balance at December 31, 2019	$ (27)	$ (27)
Other comprehensive income (loss) before reclassifications	107	107
Net losses reclassified from accumulated other comprehensive loss	3	3
Net current period other comprehensive income	110	110
Balance at December 31, 2020	$ 83	$ 83

The net loss reclassified from accumulated other comprehensive loss during the year ended December 31, 2020 resulted from sales of available-for-sale securities prior to maturity. The gross realized gains and gross realized losses of these sales for the year ended December 31, 2020 were $23 and $6, respectively. The basis on which the cost of the securities was determined was specific identification. Proceeds related to these sales were $9,404.

9. Equity-Based Compensation

On September 22, 2017, the Company'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 transaction on September 26, 2017. 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

(in thousands, except share and per share data)

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, 2020, the aggregate number of common stock options available for grant under the 2017 Plan was 2,309,030. On January 1, 2021, pursuant to the terms of the 2017 Plan, the number of awards that are reserved and may be awarded under the 2017 Plan was automatically increased by 4,382,567 awards.

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 or consultant generally vests 25% on the first 12-month anniversary of the grant date and vests 1/48th monthly thereafter until fully vested at the end of 48 months. Subsequent stock option grants to employees or consultants generally vest 1/48th monthly until fully vested at the end of 48 months. The initial stock option grant to a non-employee director vests 1/36th monthly until fully vested at the end of 36 months. Subsequent stock option grants to a non-employee director vests 1/12th monthly until fully vested at the end of 12 months. The term of common stock option grants is 10 years unless terminated earlier as described above.

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

	Year Ended December 31,	
	2020	2019
Research and development expense	$ 878	$ 535
General and administrative expense	1,306	1,305
	$ 2,184	$ 1,840

Unamortized equity-based compensation expense at December 31, 2020 was $3,933, which is expected to be amortized over a weighted-average period of 2.6 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,	
	2020	2019
Expected term	5.2 to 6.1 years	5.3 to 6.1 y
Risk-free interest rate	0.31% to 1.68%; weighted avg. 0.61%	1.55% to 2.56%; weighted 1.9
Expected volatility	81.0% to 85.8%; weighted avg. 83.8%	80.2% to 86.7%; weighted 82
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

(in thousands, except share and per share data)

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.

The fair value of the underlying common stock and the exercise price for the common stock options granted during the years ended December 31, 2020 and 2019 are summarized in the table below:

Common Stock Options Granted During Period Ended:	Fair Value of Underlying Common Stock	Exercise Price of Common Stoc Option
Year ended December 31, 2020	$1.19 to $2.80; weighted avg. $1.89	$1.19 to $2.80; weighted av $1.93
Year ended December 31, 2019	$2.32 to $3.05; weighted avg. $2.86	$2.32 to $3.05; weighted av $2.86

The weighted-average grant date fair value of common stock options granted in the years ended December 31, 2020 and 2019 was $1.32 and $2.01 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 Intri Value (thousands)
Outstanding - December 31, 2019	5,697,714	$ 2.34	6.7	$ 4,(
Granted	2,755,248	1.93		
Exercised	(500,905)	0.73		
Forfeited	(724,761)	2.90		
Outstanding - December 31, 2020	7,227,296	$ 2.24	6.8	$ 1,7
Exercisable - December 31, 2020	4,216,647	$ 2.23	5.1	$ 1,2
Vested and Expected to Vest - December 31, 2020	7,013,117	$ 2.24	6.7	$ 1,(

The aggregate intrinsic value of common stock options exercised during the years ended December 31, 2020 and 2019 was $526 and $172, respectively.

10. Income Taxes

Pretax loss before income taxes was $24,668 and $26,303 for the years ended December 31, 2020 and 2019, respectively, which consists entirely of losses in the U.S. and resulted in no provision for income tax expense during the years then ended.

(in thousands, except share and per share data)

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,					
	2020			2019		
Federal income tax expense at statutory rate	$ (5,180)	21.0	%	$ (5,524)	21.0	%
State income tax expense at statutory rate	(1,801)	7.3		(1,934)	7.3	
Permanent differences	142	(0.6)		113	(0.4)	
Change in valuation allowance	6,839	(27.7)		7,345	(27.9)	
	$ —	—	%	$ —	—	%

The Company's effective income tax rate for the years ended December 31, 2020 and 2019 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,	
	2020	2019
Deferred Tax Assets		
Net operating losses	$ 26,346	$ 22,340
Intangibles	152	169
Accrued expenses	810	80
Operating lease liability	2,333	108
Equity-based compensation	1,206	1,023
Deferred revenue	2,378	—
Other	54	5
Less: Valuation allowance	(30,406)	(23,567)
Total deferred tax assets	2,873	158
Deferred Tax Liabilities		
Prepaid Expenses	(335)	—
Fixed assets and other	(85)	(57)
Right-of-use asset	(2,453)	(101)
Total deferred tax liabilities	(2,873)	(158)
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, 2020 and 2019. 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.

At December 31, 2020, the Company had a federal net operating loss carryforward of $93,040, of which $31,809 will begin to expire in 2035 and $61,231 which do not expire and may be carried forward indefinitely. At December 31, 2020, the Company had $90,705 of state net operating loss carryforwards which will begin to expire in 2027.

As provided by Section 382 of the Internal Revenue Code of 1986 ("Section 382"), and similar state provisions, utilization of net operating losses and tax credit carryforwards may be subject to substantial annual limitations due to ownership change limitations that have previously occurred or that could occur in the future. Ownership changes may limit the amount of net operating losses and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions that increase the ownership of five percent stockholders in the stock of a corporation by more than 50 percent in the aggregate over a three-year period. For the year ended December 31, 2019, the Company completed a review of its changes in ownership and determined that the August 2019 Offering resulted in an ownership change during the year then ended, as defined by Section 382. However, the Company does not expect that the Section 382 limitation resulting from the August 2019 ownership change will place a material restriction on the Company's ability to utilize its net operating losses and tax credit carryforwards. For the year ended December 31, 2020, the Company completed a review of its changes in ownership and determined that no additional ownership changes have occurred. There could be additional ownership changes after December 31, 2020 that could limit the amount of net operating losses and tax credit carryforwards that the Company can utilize in the future.

At December 31, 2020 and 2019, the Company had no unrecognized tax benefits. The Company's estimate of the potential outcome of any uncertain tax positions 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 2020. There are no pending examinations in any jurisdiction.

On March 27, 2020 and December 27, 2020, the President of the United States signed and enacted into law the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) and the Consolidated Appropriations Act, 2021 (CAA). Among other provisions, the CARES Act and the CAA provide relief to U.S. federal corporate taxpayers through temporary adjustments to net operating loss rules, changes to limitations on interest expense deductibility, and the acceleration of available refunds for minimum tax credit carryforwards. The CARES Act and the CAA did not have a material effect on the Company's consolidated financial statements.

11. 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 for the periods presented 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, 2020 and 2019.

(in thousands, except share and per share data)

The following is the computation of loss per common share for the years ended December 31, 2020 and 2019:

	Year Ended December 31,	
	2020	2019
Net loss	$ (24,668)	$ (26,303)
Weighted-average basic and diluted common shares outstanding	87,203,588	57,671,734
Loss per share - basic and diluted	$ (0.28)	$ (0.46)

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

	December 31,	
	2020	2019
Options to purchase common stock	7,227,296	5,697,7
Warrants to purchase common stock	413,320	413,3

12. 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.

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2020 are as follows:

	Total	Level 1	Level 2	Level 3
Assets				
Cash equivalents:				
Money market funds	$ 24,586	$ 24,586	$ —	$ —
Short-term investments:				
Commercial paper	15,991	—	15,991	—
Corporate notes/bonds	29,296	—	29,296	—
U.S. Treasuries	2,253	—	2,253	—
U.S. Government agency securities	1,278	—	1,278	—
Total financial assets	$ 73,404	$ 24,586	$ 48,818	$ —
Liabilities				
Common stock warrant liability	$ 15	$ —	$ —	$ 15
Total financial liabilities	$ 15	$ —	$ —	$ 15

(in thousands, except share and per share data)

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2019 are as follows:

	Total	Level 1	Level 2	Level 3
Assets				
Cash equivalents:				
Money market funds	$ 31,078	$ 31,078	$ —	$ —
Commercial paper	2,498	—	2,498	—
Short-term investments:				
Commercial paper	11,433	—	11,433	—
Corporate notes/bonds	36,597	—	36,597	—
U.S. Treasuries	4,512	—	4,512	—
U.S. Government agency securities	9,784	—	9,784	—
Total financial assets	$ 95,902	$ 31,078	$ 64,824	$ —
Liabilities				
Common stock warrant liability	$ 414	$ —	$ —	$ 414
Total financial liabilities	$ 414	$ —	$ —	$ 414

The Company uses the market approach and Level 1 and Level 2 inputs to value its cash equivalents and Level 2 inputs to value its short-term investments. 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 8, *Stockholders' Equity*, for more information) is classified within Level 3 of the fair value hierarchy. The fair value of the common stock warrant liability was 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 following weighted-average assumptions were used to estimate the fair value of the common stock warrant liability at December 31, 2020:

	December 31, 2020
Expected term	0.3
Risk-free interest rate	0.10 %
Expected volatility	68.91 %
Expected dividend yield	— %

A 10% change in the estimate of expected volatility at December 31, 2020 would increase or decrease the fair value of the common stock warrant liability in the amount of $6. A 10% change in the estimate of fair value of the common stock at December 31, 2020 would increase or decrease the fair value of the common stock warrant liability in the amount of $10.

(in thousands, except share and per share data)

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, 2020 and 2019:

	Fair Value Measurements Using Significant Unobservable Inputs (Level 3)	
		Common Stock Warrant Liability
Balance at December 31, 2018	$	797
Gain included in other income (expense), net		(383)
Balance at December 31, 2019	$	414
Gain included in other income (expense), net		(399)
Balance at December 31, 2020	$	15

13. Defined Contribution Plan

Exicure maintains a defined contribution savings plan for the benefit of its employees. Company contributions are determined under various formulas. The expense recognized for this plan was $257 and $185 for the years ended December 31, 2020 and 2019, respectively.

14. Commitments and Contingencies

Leases

Refer to Note 7, *Leases*, for a discussion of the commitments associated with the Company's lease agreements.

Northwestern University License Agreements

On December 12, 2011, (1) AuraSense, LLC, the Company's former parent, 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, (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, and (v) to pay NU a percentage of all other sublicense payments received by the Company. In August 2015, the Company entered into a restated license agreement with NU (the "Restated License Agreement"). In February 2016, the Company obtained exclusive license as to NU's rights in certain SNA technology it jointly owns with NU (the "Co-owned Technology License"). The Company's license to NU's rights is limited to the assigned field, however the Company has no such limitation as to its own rights in this jointly owned technology. In June 2016, the Company 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 (the "Wound Healing License"). The Company's rights and obligations in the Co-owned Technology License and the Wound Healing License 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, 2019, all pending patent applications under the Wound Healing License have been abandoned. As of December 31, 2020, the Company has paid to NU an aggregate of $8,317 in consideration of each of the obligations described above.

(in thousands, except share and per share data)

15. Related-Party Transactions

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, 2020 and 2019 in connection with these consulting services and these amounts are recognized as an expense in the accompanying consolidated statement of operations.

16. Quarterly Financial Data (Unaudited)

Selected quarterly financial data for the years ended December 31, 2020 and 2019 are as follows:

	2020			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter [3]
Revenue	$ 9,183	$ 4,847	$ 2,443	$ 140
Net income (loss) [1]	1,150	(4,311)	(8,822)	(12,685)
Basic earnings (loss) per common share	$ 0.01	$ (0.05)	$ (0.10)	$ (0.15)
Diluted earnings (loss) per common share	$ 0.01	$ (0.05)	$ (0.10)	$ (0.15)

	2019			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ 25	$ 434	$ 527	$ 310
Net loss [1] [2]	(5,286)	(5,220)	(5,816)	(9,981)
Basic and diluted loss per common share	$ (0.12)	$ (0.12)	$ (0.09)	$ (0.13)

(1) - Net income (loss) includes a non-cash unrealized gain (loss) related to the fair value adjustment of the common stock warrant liability of $346, $(189), $186, $56 in the three months ended March 31, 2020, June 30, 2020, September 30, 2020, and December 31, 2020 and $370, $(113), $103, and $24 in the three months ended March 31, 2019, June 30, 2019, September 30, 2019, and December 31, 2019, respectively.

(2) - Net loss in the three months ended December 31, 2019 includes $3,750 of research and development expense related to license fees owed to Northwestern University in connection with the receipt of the AbbVie Upfront Payment during that period. Refer to Note 3, *Collaborative Research and License Agreements* for more information on the AbbVie Upfront Payment and Note 14, *Commitments and Contingencies* for more information on the Northwestern University License Agreements.

(3) - Revenue for the three months ended December 31, 2020 reflects events and conditions that occurred during the period that increased the estimated hours to complete the services under the AbbVie Collaboration Agreement. These increased estimated efforts resulted in less progress occurring relative to the increased estimate of total projected hours to complete the research services (and thus limited revenue recognized) during the three months ended December 31, 2020.

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

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, 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.

As of the end of the period covered by this Annual Report on Form 10-K, we carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer/interim principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-15. Based upon, and as of the date of, this evaluation, our principal executive officer/interim principal financial officer concluded that our disclosure controls and procedures were effective. Accordingly, management believes that the financial statements included in this report fairly present in all material respects our financial condition, results of operations and cash flows for the periods presented.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act). Under the supervision and with the participation of our management, including our principal executive officer/interim principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2020 based on the guidelines established in Internal Control-Integrated Framework 2013 issued by the Committee of Sponsoring Organizations of the Treadway Commission. Our internal control over financial reporting includes policies and procedures that provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles.

Based on that evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2020.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm as we are a smaller reporting company and an "emerging growth company" as of December 31, 2020, as defined in the Jumpstart Our Business Startups Act of 2012.

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 2023 Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

We continuously seek to improve the efficiency and effectiveness of our internal controls. There was no change 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, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None

PART III

We will file a definitive proxy statement for our 2021 Annual Meeting of Stockholders, or the Proxy Statement, with the SEC, pursuant to Regulation 14A, not later than 120 days after the end of our fiscal year. Accordingly, certain information required by Part III has been omitted under General Instruction G(3) to Form 10-K. Only those sections of the Proxy Statement that specifically address the items set forth herein are incorporated by reference.

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

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 and Financial Statement Schedules.

(a) The following documents are filed as part of this report:

1. Financial Statements

See Index to Financial Statements on page 108 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, the following exhibits are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

hibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
	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
	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
	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
	Amended and Restated Certificate of Incorporation, as filed with the Secretary of State of the State of Delaware on November 15, 2017.	X			
	Amended and Restated Bylaws, as currently in effect.		8-K (Exhibit 3.4)	10/2/2017	000-55764
	Form of Warrant to Purchase Shares of Common Stock issued to Placement Agent.		8-K (Exhibit 4.1)	10/2/2017	000-55764
	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
	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
	Description of Securities		10-K (Exhibit 4.4)	3/10/2020	001-39011
	Form of Indenture, between the Registrant and one or more trustees to be named.		S-3 (Exhibit 4.2)	12/21/2020	333-251555
	Form of Common Stock Warrant Agreement and Warrant Certificate.		S-3 (Exhibit 4.4)	12/21/2020	333-251555
	Form of Preferred Stock Warrant Agreement and Warrant Certificate.		S-3 (Exhibit 4.5)	12/21/2020	333-251555
	Form of Debt Securities Warrant Agreement and Warrant Certificate.		S-3 (Exhibit 4.6)	12/21/2020	333-251555
†	2015 Equity Incentive Plan and forms of awards thereunder, assumed in the Merger.		8-K (Exhibit 10.1)	10/2/2017	000-55764

+	2017 Equity Incentive Plan and forms of award agreements thereunder.	8-K (Exhibit 10.2)	10/2/2017	000-55764
+	2017 Employee Stock Purchase Plan.	8-K (Exhibit 10.3)	10/2/2017	000-55764
+	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
+	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
+	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
+	Amended and Restated Employment Agreement as of December 10, 2019 by and between Exicure, Inc. and Matthias G. Schroff, Ph.D.	10-K (Exhibit 10.9)	3/10/2020	001-39011
+	Amended and Restated Employment Agreement dated as of June 30, 2020 by and between Douglas E. Feltner, M.D. and Exicure, Inc.	10-Q (Exhibit 10.2)	8/12/2020	001-39011
+	Form of Executive Employment Side Letter Agreement	8-K (Exhibit 10.1)	6/9/2020	001-39011
)+	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
l	Lease Agreement dated as of February 28, 2020 by and between 2430 N. Halsted, LLC and Exicure, Inc.	10-Q (Exhibit 10.1)	5/14/2020	001-39011
2	Credit and Security Agreement, dated as of September 25, 2020, by and among Exicure, Inc., Exicure Operating Company, the lenders party thereto from time to time and MidCap Financial Trust, as agent.	8-K (Exhibit 10.1)	10/1/2020	001-39011
3	Amendment No. 1 dated as of October 21, 2020 to Credit and Security Agreement, dated as of September 25, 2020 by and among Exicure, Inc., Exicure Operating Company, the lenders party thereto from time to time and MidCap Financial Trust, as agent.	10-Q (Exhibit 10.2)	11/12/2020	001-39011
4	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
5	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
5.1	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
5.2	Amendment No. 3 to Loan and Security Agreement dated as of December 28, 2018 by and between Exicure OpCo and Hercules.	10-K (Exhibit 10.18.2)	3/8/2019	000-55764
5.3	Amendment No. 4 to Loan and Security Agreement dated as of March 8, 2019 by and between Exicure OpCo and Hercules.	8-K (Exhibit 10.1)	3/14/2019	000-55764
6*	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
7*	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
7.1*	Amendment Two to the Amended Restated License Agreement between Exicure OpCo and Northwestern University dated as of November 30, 2017.	10-K (Exhibit 10.22)	3/10/2020	001-39011
7.2*	Amendment Three to the Amended Restated License Agreement between Exicure OpCo and Northwestern University dated as of January 1, 2019.	10-K (Exhibit 10.23)	3/10/2020	001-39011
7.3	Amendment Four to the Amended Restated License Agreement between Exicure OpCo and Northwestern University dated as of November 13, 2019.	10-K (Exhibit 10.24)	3/10/2020	001-39011

3*	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
9*	Amendment One dated and effective as of June 11, 2018 to the License Agreement between Exicure OpCo and Northwestern University dated as of February 10, 2016 and effective as of May 27, 2014.		10-K (Exhibit 10.26)	3/10/2020	001-39011
9.1	Amendment Two dated and effective as of November 13, 2019 to the License Agreement between Exicure OpCo and Northwestern University dated as of February 10, 2016 and effective as of May 27, 2014.		10-K (Exhibit 10.27)	3/10/2020	001-39011
0*	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
1*	Amendment One dated and effective June 11, 2018 to the License Agreement between Exicure OpCo and Northwestern University dated as of June 17, 2016.		10-K (Exhibit 10.27)	3/10/2020	001-39011
2*	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
3*	License and Development Agreement between Exicure, Inc. and DERMELIX LLC dated February 17, 2019.		10-Q (Exhibit 10.2)	5/8/2019	000-55764
4	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
5*	Collaboration, Option and License Agreement between Exicure, Inc. and Allergan Pharmaceuticals International Limited dated as of November 13, 2019		10-K (Exhibit 10.33)	3/10/2020	001-39011
5	Side Agreement to Northwestern Agreements by and among Exicure Inc., Northwestern University and Allergan Pharmaceuticals International Limited dated as of November 13, 2019.		10-K (Exhibit 10.34)	3/10/2020	001-39011
7	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
8	Equity Distribution Agreement, dated as of December 21, 2020, between the Registrant and BMO Capital Markets Corp.		S-3 (Exhibit 1.2)	12/21/2020	333-251555
	Subsidiaries of Exicure, Inc.	X			
	Consent of KPMG LLP, independent registered public accounting firm.	X			
	Power of Attorney (included on the signature page hereto).	X			
	Certification of Principal Executive Officer/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			
**	Certifications of Principal Executive Officer/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			
NS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document	X			
SCH	Inline XBRL Taxonomy Extension Schema Document	X			
CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X			
DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X			
LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X			

?RE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X
	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)	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.

* Indicates that portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

** This certification is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Exicure, Inc. 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 such Form 10-K), irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary.

None.

SIGNATURES

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 Chicago, State of Illinois, on March 11, 2021.

EXICURE, INC.

By: /s/ David A. Giljohann
David A. Giljohann, Ph.D.
President, Chief Executive Officer, Interim Chief Financial Officer and Director

POWER OF ATTORNEY

We, the undersigned directors and officers of Exicure, Inc., hereby severally constitute and appoint David A. Giljohann and Timothy P. Walbert, 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 David A. Giljohann, Ph.D.	President, Chief Executive Officer, Interim Chief Financial Officer and Director (*Principal Executive Officer, Interim Principal Financial Officer and Interim Principal Accounting Officer)*	March 11, 2021
/s/ Timothy P. Walbert Timothy P. Walbert	Director and Chairman of the Board of Directors	March 11, 2021
/s/ Jeffrey L. Cleland Jeffrey L. Cleland, Ph.D.	Director	March 11, 2021
Elizabeth Garofalo, M.D.	Director	
/s/ Bosun Hau Bosun Hau	Director	March 11, 2021
/s/ Chad A. Mirkin Chad A. Mirkin, Ph.D.	Director	March 11, 2021
/s/ Bali Muralidhar Bali Muralidhar, M.D., Ph.D.	Director	March 11, 2021
Andrew Sassine	Director	
/s/ James R. Sulat James R. Sulat	Director	March 11, 2021
/s/ David R. Walt David R. Walt, Ph.D.	Director	March 11, 2021

Exhibit 3.3

AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
EXICURE, INC.

Pursuant to Sections 242 and 245 of the General Corporation Law of the State of Delaware, Exicure, Inc. (the ***"Corporation'),*** a corporation organized and existing under the General Corporation Law of the State of Delaware, as amended (the ***"DGCL"),***

DOES HEREBY CERTIFY:

1. The name of the Corporation is Exicure, Inc.

2. The original name of this corporation is Max-1 Acquisition Corporation and this Amended and Restated Certificate of Incorporation (the ***"Amended and Restated Certificate of Incorporation")*** amends and restates the Corporation's original Certificate of Incorporation filed with the Secretary of State of the State of Delaware on February 6, 2017, as amended (the ***"Prior Certificate'),*** and has been duly adopted in accordance with the provisions of Sections 242,245 and 228 of the DGCL.

3. The text of the Prior Certificate is hereby amended and restated in its entirety to read as set forth in Exhibit A attached hereto.

IN WITNESS WHEREOF, this Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this Corporation on this 15th day of November, 2017.

By:

/s/ David Giljohann Name: David Giljohann, Ph.D.
Title: Chief Executive Officer

Exhibit A

ARTICLE I

The name of this Corporation is Exicure, Inc.

ARTICLE II

The address of the registered office of the Corporation in the State of Delaware is 251 Little Falls Drive, Wilmington, DE 19808, County of New Castle. The name of its registered agent at such address is Corporation Service Company.

ARTICLE III

The nature of the business or purposes to be conducted or promoted is to engage in any lawful act or activity for which corporations may be organized under the DGCL.

ARTICLE IV

A. The total number of shares of all classes of stock which the Corporation shall have authority to issue is (i) 200,000,000 shares of Common Stock, $0.0001 par value per share **("Common Stock"),** and (ii) 10,000,000 shares of Preferred Stock, $0.0001 par value per share **("Preferred Stock").**

B. The Preferred Stock may be issued from time to time in one or more series. The Board of Directors of the Company (the **"Board")** is hereby expressly authorized, by filing a certificate **("Certificate of Designation")** pursuant to the DGCL, to provide for the issue of any or all of the unissued and undesignated shares of the Preferred Stock in one or more series, and to fix the number of shares and to determine or alter for each such series, such voting powers, full or limited, or no voting powers, and such designation, preferences and relative, participating, optional, or other rights and such qualifications, limitations or restrictions thereof as shall be stated and expressed in the resolution or resolutions adopted by the Board providing for the issuance of such shares and as may be permitted by the DGCL. The Board of Directors is also expressly authorized to increase or decrease the number of shares of any series subsequent to the issuance of shares of that series, but not below the number of shares of such series then outstanding. In case the number of shares of any series shall be decreased in accordance with the foregoing sentence, the shares constituting such decrease shall resume the status that they had prior to the adoption of the resolution originally fixing the number of shares of such series. The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the voting power of the stock of the Company entitled to vote thereon, without a separate vote of the holders of the Preferred Stock, or of any series thereof, unless a vote of any such holders is required pursuant to the terms of any certificate of designation filed with respect to any series of Preferred Stock.

Each outstanding share of Common Stock shall entitle the holder thereof to one vote on each matter properly submitted to the stockholders of the Company for their vote; *provided, however,* that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Amended and Restated Certificate of Incorporation (this **"Certificate of Incorporation")** (including any Certificate of Designation filed with respect to any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series of Preferred Stock are entitled, either separately or together as a class with the holders of one or more other series of Preferred Stock, to vote thereon by law or pursuant to this Certificate of Incorporation (including any Certificate of Designation filed with respect to any series of Preferred Stock).

ARTICLE V

In furtherance and not in limitation of the powers conferred by the DGCL, subject to the rights of the holders of any series of Preferred Stock that may be designated from time to time, the Board is expressly authorized to adopt, amend or repeal the bylaws of the Corporation (the **"Bylaws"),** subject to the power of the stockholders of the Corporation to alter or repeal any Bylaws whether adopted by them or otherwise; *provided, however,* that, in addition to any vote of the holders of any class or series of stock of the Corporation required by law or by this Certificate of Incorporation (including any Certificate of Designation that may be filed from time to time), the affirmative vote of holders of not less than sixty-six and two-thirds percent (66 2/3%) of the votes of all outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors, considered for purposes hereof as a single class, shall be required for the stockholders to adopt new Bylaws or to alter, amend or repeal the Bylaws.

ARTICLE VI

A. The management of the business and the conduct of the affairs of the Corporation shall be vested in the Board. The number of directors which shall constitute the whole Board shall be fixed exclusively by one or more resolutions adopted from time to time by the Board.

B. The directors shall be divided into three classes, designated as Class I, Class II and Class III, as nearly equal in number as possible. Directors shall be assigned to each class in accordance with a resolution or resolutions adopted by the Board. At the first annual meeting of stockholders following the effectiveness of this Certificate of Incorporation (the **"Qualifying Record Date"),** the term of office of the Class I directors shall expire and Class I directors shall be elected for a full term of three years. At the second annual meeting of stockholders following the Qualifying Record Date, the term of office of the Class II directors shall expire and Class II directors shall be elected for a full term of three years. At the third annual meeting of stockholders following the Qualifying Record Date, the term of office of the Class III directors shall expire and Class III directors shall be elected for a full term of three years. At each succeeding annual meeting of stockholders, directors shall be elected for a full term of three years to succeed the directors of the class whose terms expire at such annual meeting. Notwithstanding the foregoing provisions of this Article VI.B., each director shall serve until his or her successor is duly elected and qualified, or until his or her earlier death, resignation or removal. No decrease in the number of directors constituting the Board shall shorten the term of any incumbent director.

C. The Board or any individual director may be removed from office only for cause at a meeting of stockholders called for that purpose, by the affirmative vote of the holders of at least at least sixty-six and two-thirds percent (66 2/3%) of the voting power of all the then outstanding shares of voting stock of the Corporation entitled to vote at an election of directors, voting together as a single class.

D. Any vacancies on the Board resulting from death, resignation, disqualification, removal or other causes and any newly created directorships resulting from any increase in the number of directors shall, unless the Board determines by resolution that any such vacancies or newly created directorships shall be filled by the stockholders, except as otherwise provided by law and or by this Certificate of Incorporation or any Certificate of Designation that may be filed with respect to a series of Preferred Stock, be filled only by the affirmative vote of a majority of the directors then in office, even though less than a quorum of the Board, and not by the stockholders. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified.

E. The directors of the Corporation need not be elected by written ballot unless the Bylaws so provide.

F. There shall be no cumulative voting in the election of directors.

ARTICLE VII

A. Subject to the rights of the holders of any series of Preferred Stock or any other class of stock or series thereof having a preference over the Common Stock as to dividends or upon liquidation, any action required or permitted to be taken by the stockholders of the Corporation must be effected at a duly called annual or special meeting of the stockholders of the Corporation. The taking of any action by written consent of the stockholders in lieu of a meeting of the stockholders is specifically denied.

B. Special meetings of the stockholders of the Corporation may be called, for any purpose or purposes, by the Secretary of the Corporation at the direction of the Board, pursuant to a resolution adopted by a majority of the entire Board, but such special meetings may not be called by any other person or persons.

C. Advance notice of stockholder nominations for the election of directors and of business to be brought by stockholders before any meeting of the stockholders of the Corporation shall be given in the manner provided in the Bylaws of the Corporation.

ARTICLE VIII

A. To the fullest extent permitted by the DGCL, a director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director. If the DGCL is amended after approval by the stockholders of this Article VIII to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the DGCL as so amended.

B. Any repeal or modification of the foregoing provisions of this Article VIII shall not adversely affect any right or protection of a director of the Corporation existing at the time of, or increase the liability of any director of the Corporation with respect to any acts or omissions of such director occurring prior to, such repeal or modification.

ARTICLE IX

Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall, to the fullest extent permitted by law, be the sole and exclusive forum for (a) any derivative action or proceeding brought on behalf of the Corporation, (b) any action asserting a claim of breach of a fiduciary duty owed by any director, officer, employee or agent of the Corporation to the Corporation or the Corporation's stockholders, (c) any action asserting a claim arising pursuant to any provision of the DGCL, this Certificate of Incorporation or the Bylaws, or (d) any action asserting a claim that is governed by the internal affairs doctrine, in each such 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 the Corporation's capital stock shall be deemed to have notice of, and to have consented to the provisions of this Article IX.

ARTICLE X

Notwithstanding any other provisions of this Certificate of Incorporation or any provision of law which might otherwise permit a lesser vote or no vote, but in addition to any affirmative vote of the holders of any particular class or series of the Corporation required by law or by this Certificate of Incorporation or any Certificate of Designation that may be filed with respect to a series of Preferred Stock, the affirmative vote of the holders of at least sixty-six and two-thirds percent (66 2/3%) of the voting power of all of the then-outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to alter, amend or repeal Articles VI, VII, VIII, IX and this Article X.

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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 statements (Nos. 333-237043 and 333-222999) on Form S-8 and registration statements (No. 333-251555, 333-227475, 333-221791 and 333-230175) on Form S-3 of Exicure, Inc. of our report dated March 11, 2021, with respect to the consolidated balance sheets of Exicure, Inc. as of December 31, 2020 and 2019, the related consolidated statements of operations, comprehensive loss, changes in stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2020, and the related notes, which report appears in the December 31, 2020 annual report on Form 10-K of Exicure, Inc.

/s/ KPMG LLP

Chicago, Illinois
March 11, 2021

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 11, 2021

/s/ David A. Giljohann

David A. Giljohann, Ph.D.

President, Chief Executive Officer and Interim Chief Financial Officer
(Principal Executive Officer, Interim Principal Financial Officer, and Interim Principal Accounting 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., Chief Executive Officer and Interim Chief Financial Officer of Exicure, Inc. (the "Company") 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, 2020, 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 11, 2021

/s/ David A. Giljohann

David A. Giljohann, Ph.D.

President, Chief Executive Officer, and Interim Chief Financial Officer
(Principal Executive Officer, Interim Principal Financial Officer and Interim Principal Accounting Officer)

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* 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.