CURIS INC
Form 10-K
March 26, 2019

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

FORM 10-K
(Mark One)
x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018
or
.. TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission File Number 000-30347
CURIS, INC.
(Exact Name of Registrant as Specified in Its Charter)

DELAWARE	04-3505116
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

4 Maguire Road
Lexington, Massachusetts 02421
(Address of principal executive offices) (Zip Code)
617-503-6500
(Registrant's telephone number, including area code)

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.01 par value per share	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None
Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x
Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. x 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). x Yes ¨ No
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company", and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨	Accelerated filer ¨	Non-accelerated filer x	Smaller reporting company x	Emerging growth company ¨

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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) based on the last reported sale price of the common stock on June 30, 2018 was approximately $38.7 million. As of March 19, 2019, there were 33,150,780 shares of the registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's proxy statement for the annual meeting of stockholders scheduled to be held on May 23, 2019, which are to be filed with the Commission not later than 120 days after the close of the Registrant's fiscal year ended December 31, 2018 pursuant to Regulation 14A, have been incorporated by reference in Items 10-14 of Part III of this Annual Report on Form 10-K.

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PART I

Cautionary Note Regarding Forward-Looking Statements

This annual report on Form 10-K contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. All statements other than statements of historical fact contained in this report are statements that could be deemed forward-looking statements, including without limitation any expectations of revenue, expenses, earnings or losses from operations, or other financial results; statements with respect to the plans, strategies and objectives of management for future operations; statements concerning product research, development and commercialization plans, timelines and anticipated results; statements of expectation or belief; statements with respect to clinical trials and studies; statements with respect to royalties and milestones; statements with respect to the therapeutic potential of drug candidates; and statements of assumptions underlying any of the foregoing. Without limiting the foregoing, the words “anticipates”, “believes”, “could”, “estimates”, “expects”, “intends”, “may”, “plans”, “seeks” , “will”, “strategy”, “potential”, “should”, “would and other similar language, wh negative or affirmative, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors. These statements 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 the forward-looking statements. We therefore caution you against relying on any of these forward-looking statements. Important factors that could cause actual results to differ materially from those in these forward-looking statements are discussed, among other places, in Item 1A., “Risk Factors” of Part I and Item 7, “Management’s Discussion and Analysis of Financial Condition and Results of Operations” of Part II of this report and in our Securities and Exchange Commission reports filed after this report.

The forward-looking statements included in this annual report represent our estimates as of the filing date of this annual report. We specifically disclaim any obligation to update these forward-looking statements in the future. These forward-looking statements should not be relied upon as representing our estimates or views as of any date subsequent to the date of this annual report.

Other Information

Unless otherwise indicated, all information in this annual report on Form 10-K gives effect to a 1-for-5 reverse stock split of Curis' common stock, that became effective on May 29, 2018. All common shares and per share amounts have been adjusted to reflect such reverse stock split.

Unless otherwise indicated, or unless the context of the discussion requires otherwise, we use the terms “we,” “us,” “our” and similar references to refer to Curis, Inc. and its subsidiaries, on a consolidated basis. We use the terms “Curis” to refer to Curis, Inc. on a stand-alone basis.

ITEM 1. BUSINESS

Overview

We are a biotechnology company focused on the development of first-in-class and innovative therapeutics for the treatment of cancer. Our clinical stage drug candidates are:

•Fimepinostat (“CUDC-907”), our internally-developed drug candidate for which our clinical studies in patients with relapsed refractory diffuse large B-cell lymphoma ("DLBCL")including those with MYC alterations are ongoing. Fimepinostat was granted Orphan Drug Designation in April 2015 and Fast Track Designation in May 2018 by the FDA for the treatment of DLBCL. We are planning a Phase 1 combination study with venetoclax in DLBCL patients with alterations in both MYC and the BCL2 gene, also referred to as double-hit lymphoma, with planned enrollment commencing in the first half of 2019. We expect to report initial clinical data from this combination study in the second half of 2019;

•CA-4948, for which, in January 2018 we initiated a dose escalating clinical trial in patients with non-Hodgkin lymphomas including those with MYD88 alterations. We expect to report initial Phase 1 clinical data from this study in mid-year 2019; and

•CA-170, for which we are currently conducting a clinical study in patients with advanced solid tumors and lymphomas. We have amended the protocol for the current study to include mesothelioma patients. We announced in January 2019 that we have begun enrollment of these patients and expect to report initial clinical data from this study with respect to mesothelioma in the second half of 2019.

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Our pipeline also includes CA-327, which is a pre-Investigational New Drug, or IND, stage oncology drug candidate. In March 2018, we exercised our option to license a fourth program, which is an immuno-oncology program, from our collaboration partner Aurigene.

In addition, we are party to a collaboration with F. Hoffmann-La Roche Ltd, or Roche, and Genentech Inc., or Genentech, a member of the Roche Group, under which Roche and Genentech are commercializing Erivedge, a first-in-class orally-administered small molecule Hedgehog signaling pathway inhibitor. Erivedge (vismodegib) is approved for the treatment of advanced basal cell carcinoma, or BCC.

Finally, on January 18, 2015 we entered into a collaboration agreement with Aurigene, a specialized, discovery-stage biotechnology company and wholly-owned subsidiary of Dr. Reddy's Laboratories for the discovery, development and commercialization of small molecule compounds in the areas of immuno-oncology and precision oncology, which we refer to as the Aurigene agreement, which was amended in September 2016. As of December 31, 2018, we have licensed four programs under the Aurigene collaboration.

1. IRAK4 Program - a precision oncology program of small molecule inhibitors of IRAK4. The development candidate is CA-4948, an orally available small molecule inhibitor of IRAK4.
2. PD1/VISTA Program - an immuno-oncology program of small molecule antagonists of PD1 and VISTA immune checkpoint pathways. The development candidate is CA-170, an orally available small molecule antagonist of VISTA and PDL1.
3. PD1/TIM3 Program - an immuno-oncology program of small molecule antagonists of PD1 and TIM3 immune checkpoint pathways. The development candidate is CA-327, an orally available small molecule antagonist of PDL1 and TIM3.
4. In March 2018, we exercised our option to license a fourth program, which is an immuno-oncology program.

Based on our clinical development plans for our pipeline, we intend to predominantly focus our available resources on the continued development of fimepinostat, as well as CA-4948 and CA-170 in collaboration with Aurigene in the near term.

Product Development Programs

We are seeking to develop and commercialize innovative drug candidates to treat cancer. Our product development initiatives, described in the table below, are being pursued using our internal resources or through our collaborations.

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Since our inception in 2000, substantially all of our revenues have been derived from collaborations and other agreements with third parties. For the years ended December 31, 2018 and 2017, milestone and royalty payments from Genentech accounted for $10.4 million, or 100% and $9.8 million, or 99%, respectively, of our revenue, all of which was related to the development and commercialization of Erivedge.

Fimepinostat

Fimepinostat was invented by Curis scientists and is an oral, dual inhibitor of HDAC and PI3K enzymes. Specifically, fimepinostat inhibits HDACs 1, 2, 3, 6 and 10 and PI3K-alpha, delta and beta isoforms. Inhibitors of HDAC enzymes can affect a number of cell functions and cancer cell viability by regulating the acetylation of both histone and non-histone substrates. Multiple inhibitors of HDACs have been approved by the FDA for treatment of hematologic malignancies. PI3 kinases are frequently activated through mutations or by receptor tyrosine kinases in many cancer types. Two PI3K inhibitors are currently approved by the FDA for treatment of patients with B cell malignancies. Fimepinostat has shown potent antitumor activity in a variety of hematologic tumor models such as non-Hodgkin's lymphoma, including some with alterations in MYC oncogene, and multiple myeloma.

Non-clinical results indicate that at the mechanistic level, fimepinostat effectively downregulates MYC protein levels in MYC-altered and MYC-dependent cells and tumor models, consistent with the roles of HDAC and PI3K in MYC regulation. These results provide a mechanistic rationale for the clinical development of fimepinostat in MYC-driven malignancies.

Clinical development of fimepinostat began in January 2013. Based on examination of multiple dose and schedules of administration in the Phase 1 trial, the recommended dose of fimepinostat was determined to be once daily oral administration of 60 mg dose using a 5 days "on"/2 days "off" schedule in 21-day cycles. The most common drug related adverse events, or AEs, reported in the Phase 1 trial were low grade, meaning Grade 1 and 2, diarrhea, fatigue and nausea. Dose limiting toxicities, or DLTs, have consisted of diarrhea and hyperglycemia, however no DLTs occurred at the recommended dose and schedule. Other drug-related Grade 3 or Grade 4 AEs reported in three or more patients included thrombocytopenia and neutrophil decrease, which are hematologic AEs, as well as diarrhea, hyperglycemia and fatigue, which are non-hematologic AEs. In the expansion stage of the Phase 1 trial, fimepinostat was tested as monotherapy or in combination with rituximab in patients with relapsed or refractory DLBCL, a type of non-Hodgkin's Lymphoma.

The Phase 2 study of monotherapy fimepinostat in patients with relapsed or refractory DLBCL, including those whose tumor harbors alterations of the MYC oncogene is ongoing, and is designed to enroll up to 100 patients with DLBCL with

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MYC alteration. Study objectives include measurement of objective response rate, progression-free survival, overall survival, duration of response, incidence and severity of adverse events and other safety parameters, and characterization of the pharmacokinetics of fimepinostat.

Data from the two clinical studies with fimepinostat have resulted in a number of patients with relapsed or refractory DLBCL (3rd line or later) achieving durable complete and partial responses. Overall, based on the combined results from a Phase 1 trial and interim analysis of the Phase 2 study, the objective response rate (ORR) in the MYC-altered patients was 14/60 (23%). These responses appear to be durable with a median duration of response of 13.6 months, with many of the patients currently continuing treatment. In comparison, based on the same combined results from the Phase 1 trial and Phase 2 interim analysis, the ORR was 3/22 (13.6%) with median duration of response of 8.8 months for MYC negative patients in these studies. An additional set of patients who had incomplete MYC testing, with only negative results if any, were considered MYC unknown had an ORR of 2/23 (8.7%) with response duration of 10.8 months.

The preponderance of data from historical non-Curis sponsored studies suggest that MYC-altered disease confers a negative prognosis in newly diagnosed patients with DLBCL as reflected by progression free survival and overall survival (OS). Patients with relapse and MYC-altered disease have an inferior outcome to any chemotherapy and to stem cell transplant. This poor prognosis conferred by MYC alteration is relevant in front-line, relapsed and relapsed/refractory stage of treatment and even after stem cell transplantation. Based on the most recent published and largest dataset for relapsed/refractory stage MYC-altered DLBCL patients, the two-year OS of this population is 0% as compared to 29.9% in their non-MYC-altered counterparts.

In light of the substantial unmet need for more effective therapies, in April 2015 and May 2018, respectively the FDA granted fimepinostat orphan drug and fast track designations for the treatment of DLBCL.

We are planning a Phase 1 combination study with venetoclax in DLBCL patients with alterations in both MYC and the BCL2 gene, also referred to as double-hit lymphoma, with planned enrollment commencing in the first half of 2019. We expect to report initial clinical data from this combination study in the second half of 2019.

We are party to an agreement with The Leukemia and Lymphoma Society, or LLS, dated November 2011, and as amended in August 2015. We agreed to make up to $1.7 million in future payments to LLS, which equals the aggregate payments previously received from LLS under the November 2011 agreement, pursuant to the achievement of certain objectives, including a licensing, sale, or other similar transaction, as well as regulatory and commercial objectives, in each case related to the fimepinostat program in hematological malignancies. However, if fimepinostat does not continue to meet its clinical safety endpoints in ongoing and future clinical trials in the defined field, or fails to obtain necessary regulatory approvals, all funding provided to us by LLS will be considered a non-refundable grant.

CA-4948

CA-4948 is an oral small molecule drug candidate that is designed to inhibit the IRAK4 kinase, which is an important transducer of toll-like receptor or certain interleukin receptor signaling pathways. These signaling pathways are shown to be involved in certain human cancers and inflammatory diseases.

CA-4948 is a potent inhibitor of IRAK4 in biochemical and cell-based assays, as well as in an in vivo tumor model of diffuse large B cell lymphoma that harbors mutation in the IRAK4 pathway. Lead compounds from this program were also shown to be effective in an in vivo preclinical model of acute inflammation, suggesting that CA-4948 and other program compounds have the potential for use in the treatment of cancer and inflammatory diseases. CA-4948 has been shown to be

active in in vivo xenograft models of human lymphoma, and demonstrates activity in ex-vivo models of acute myeloid leukemia ("AML") and myelodysplastic syndromes ("MDS"). In January 2018 we initiated a dose escalating clinical trial in patients with non-Hodgkin lymphomas including those with MYD88 alterations. We expect to report initial Phase 1 clinical data from this study in mid-year 2019.

CA-170

CA-170 is an oral small molecule drug candidate that is designed to selectively target VISTA and PDL1 immune checkpoint proteins, both of which independently function as negative regulators of immune activation. CA-170 is being developed by us under our collaboration with Aurigene.

CA-170 can potently rescue effector functions of T cells, such as cytokine secretion and proliferation, which are inhibited in the presence of VISTA and PDL1/L2 checkpoint proteins. CA-170 has demonstrated high selectivity, and is unable to rescue T cells functions in the presence of other checkpoint protein molecules such as TIM3, CTLA4, LAG-3 and BTLA. Additionally, in multiple syngeneic mouse tumor models (such as melanoma and colon cancer), oral administration of CA-170

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was demonstrated to result in anti-tumor activity but no such activity was observed in immune deficient mice, suggesting that the in vivo anti-cancer effects of CA-170 require an intact immune system.

In June 2016, we dosed the first patient in a Phase 1 trial of CA-170 being conducted in patients with solid tumors and lymphomas. In November 2018, we presented preliminary clinical data from the ongoing dose escalation stage of CA-170's Phase 1 trial at the Society for Immunotherapy of Cancer, or SITC, Meeting. The data demonstrated that CA-170 has a dose proportional and predictable PK profile in patients treated orally at various doses in the ongoing dose escalation stage of the study. Additionally, evaluation of patient blood samples demonstrated that CA-170 appears to be biologically active in modulating the immune system, with a several-fold increase in percentage of circulating CD8+ T cells expressing activation markers within 24 hours of oral dosing. As compared to pre-dosing, there was a marked increase in the population of CD8+ T cells detected in the post-treatment tumor biopsy samples in multiple patients. The data presented also demonstrated that multiple patients experienced tumor shrinkages, including two patients each with non-small cell lung cancer and melanoma, and one patient each with follicular lymphoma, esophageal, squamous carcinoma of the head and neck, and Hodgkin lymphoma. CA-170 was well tolerated up to the highest dose tested, 1200 mg twice daily oral administration, as of December 2018.

We have amended the protocol for the current study to include mesothelioma patients. We announced in January 2019 that we have begun enrollment of these patients and expect to report initial clinical data from this study with respect to mesothelioma in the second half of 2019.

Our collaboration partner, Aurigene, initiated a Phase 2 trial for CA-170 in India in the first quarter of 2018.

CA-327

In October 2016, we exercised our option within the collaboration with Aurigene to license the PDL1/TIM3 program. CA-327 is an oral small molecule drug candidate that is designed to selectively target PDL1 and TIM3 immune checkpoint proteins, both of which independently function as negative regulators of immune activation. CA-327 has demonstrated anti-tumor activity in multiple syngeneic mouse tumor models in an immune-dependent manner.

For a further discussion of our collaboration agreement with Aurigene, see “Business—Our Collaborations and License Agreements—Aurigene.”

Erivedge

Erivedge® is an orally bioavailable small molecule which is designed to selectively inhibit the Hedgehog signaling pathway by targeting a protein called Smoothened. The Hedgehog signaling pathway is normally active during embryonic development and unregulated activation of the pathway is believed to play a central role in allowing the proliferation and survival of cancer cells and leading to formation and maintenance of certain cancers. Genetic mutations that lead to unregulated activation of Hedgehog signaling are found in BCC and medulloblastoma. Aberrant signaling in the Hedgehog signaling pathway is implicated in over 90% of BCC cases.

Erivedge is FDA approved for treatment of adults with metastatic basal cell carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation and is being developed under a collaboration agreement with Genentech. Genentech and Roche are responsible for the clinical development and global commercialization of Erivedge. Erivedge is currently marketed and sold in the U.S. by Genentech and in the European Union, Australia and several other countries by Roche.

For a further discussion of our Hedgehog collaboration agreement with Genentech, see “Business—Our Collaborations and License Agreements —Genentech.”

Our Collaborations and License Agreements

Aurigene

In January 2015, we entered into an exclusive collaboration agreement with Aurigene for the discovery, development and commercialization of small molecule compounds in the areas of immuno-oncology and selected precision oncology targets. Under the collaboration agreement, Aurigene granted us an option to obtain exclusive, royalty-bearing licenses to relevant Aurigene technology to develop, manufacture and commercialize products containing certain of such compounds anywhere in the world, except for India and Russia, which are territories retained by Aurigene.

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In connection with the collaboration agreement, we issued to Aurigene 3,424,026 shares of our common stock valued at $24.3 million at the time of issuance in partial consideration for the rights granted to us under the collaboration agreement which we recognized as expense during the year ended December 31, 2015. The shares were issued pursuant to a stock purchase agreement with Aurigene dated January 18, 2015.

In September 2016, we and Aurigene entered into an amendment to the collaboration agreement. Under the terms of the amendment, in exchange for the issuance by us to Aurigene of 2,041,666 shares of our common stock, Aurigene waived payment of up to a total of $24.5 million in potential milestones and other payments associated with the first four programs in the collaboration that may have become due from us under the collaboration agreement. To the extent any of these waived milestones or other payments are not payable by us, for example in the event one or more of the milestone events do not occur, we will have the right to deduct the unused waived amount from any one or more of the milestone payment obligations tied to achievement of commercial milestone events. The amendment also provides that, in the event supplemental program activities are performed by Aurigene, we will provide up to $2.0 million of additional funding for each of the third and fourth licensed program. The shares were issued pursuant to a stock purchase agreement with Aurigene dated September 7, 2016.

As of December 31, 2018, we have exercised our option to license the following four programs under the collaboration:

1. IRAK4 Program - a precision oncology program of small molecule inhibitors of IRAK4. The development candidate is CA-4948, an orally available small molecule inhibitor of IRAK4.
2. PD1/VISTA Program - an immuno-oncology program of small molecule antagonists of PD1 and VISTA immune checkpoint pathways. The development candidate is CA-170, an orally available small molecule antagonist of VISTA and PDL1.
3. PD1/TIM3 Program - an immuno-oncology program of small molecule antagonists of PD1 and TIM3 immune checkpoint pathways. The development candidate is CA-327, an orally available small molecule antagonist of PDL1 and TIM3.
4. In March 2018, we exercised our option to license a fourth program, which is an immuno-oncology program.

For each of our licensed programs (as described above) we are obligated to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize at least one product in each of the U.S., specified countries in the European Union and Japan, and Aurigene is obligated to use commercially reasonable efforts to perform its obligations under the development plan for such licensed program in an expeditious manner.

Subject to specified exceptions, we and Aurigene agreed to collaborate exclusively with each other on the discovery, research, development and commercialization of programs and compounds within immuno-oncology for an initial period of approximately two years from the effective date of the collaboration agreement. At our option, and subject to specified conditions, we may extend such exclusivity for up to three additional one-year periods by paying to Aurigene additional exclusivity option fees on an annual basis. We exercised the first one-year exclusivity option in the first quarter of 2017. The fee for this exclusivity option exercise was $7.5 million, which we paid in two equal installments in the first and third quarters of 2017. We have elected not to further exercise our exclusivity option and thus did not make the $10.0 million payment required for this additional exclusivity in 2018. As a result of our election to not further exercise our exclusivity option, we are no longer operating under the broad immuno-oncology exclusivity with Aurigene. We elected to exercise our option to extend exclusivity on a program-by-program, year-by-year, basis for the IRAK4 Program and the PD1/VISTA Program in 2018. In 2019, we elected not to further extend, on a program-by-program, year-by-year basis, exclusivity for the IRAK4 Program and the PD1/VISTA Program.

Since January 2015, we have paid $14.5 million in research payments, and have waived $19.5 million in milestones under the terms of the 2016 amendment.

For each of the IRAK4, PD1/VISTA,PD1/TIM3 programs, and the fourth immuno-oncology program: we have remaining unpaid or unwaived payment obligations of $42.5 million per program, related to regulatory approval and commercial sales milestones, plus specified additional payments for approvals for additional indications, if any.

We have agreed to pay Aurigene tiered royalties on our and our affiliates' annual net sales of products at percentage rates ranging from the high single digits up to 10%, subject to specified reductions.

We have agreed to make certain payments to Aurigene upon our entry into sublicense agreements on any program(s), including:

- with respect to amounts that we and our affiliates receive from sublicensees under a licensed program in the U.S. or the European Union, a declining percentage of non-royalty sublicense revenues that is dependent on the stage of the most advanced product for such licensed program at the time the sublicense is granted, including, for example 25% of such amounts following our initiation of a Phase 2 clinical study and 15% of such amounts after initiation of the

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first pivotal study. This sharing will also extend to royalties that we receive from sublicensees, subject to minimum royalty percentage rates that we are obligated to pay to Aurigene, which generally range from mid-to-high single-digit royalty percentage rates up to 10%;

- with respect to sublicensing revenues we and our affiliates receive from sublicensees under a licensed program in Asia, 50% of such sublicensing revenues, including both non-royalty sublicensee revenues and royalties that we receive from sublicensees; and
- with respect to non-royalty sublicensing revenues we and our affiliates receive from sublicensees under a licensed program outside of the U.S., the European Union and Asia, a percentage of such non-royalty sublicense revenues ranging from 30% to 50%. We are also obligated to share 50% of royalties that we receive from sublicensees that we receive in these territories.

Our royalty payment obligations (including those on sales by sublicensees) under the collaboration agreement with respect to a product in a country will expire on a product-by-product and country-by-country basis on the later of: (i) expiration of the last-to-expire valid claim of the Aurigene patents covering the manufacture, use or sale of such product in such country; and (ii) 10 years from the first commercial sale of such product in such country.

The term of the collaboration agreement begins upon signing and, unless earlier terminated, will expire upon either: (i) 90 days after the completion by Aurigene of its obligations under all research plans if we have not exercised the option with respect to at least one program by such time; or (ii) expiration of the last-to-expire royalty term for any and all products. Upon expiration (but not on earlier termination) of the collaboration agreement, all licenses granted by Aurigene to us that were in effect immediately prior to such expiration shall survive on a non-exclusive, royalty-free, fully paid, irrevocable, perpetual basis.

The collaboration agreement may be terminated, either in its entirety or with respect to a particular program, by either Aurigene or us for uncured material breach by the other party, other than an uncured material breach by the other party of its diligence obligations with respect to a program or licensed program. If an uncured material breach other than a diligence breach relates to a particular program or licensed program, the non-breaching party may terminate the collaboration agreement only with respect to that program or licensed program. However, after initiation of the first pivotal clinical trial of a product for a licensed program, Aurigene may not terminate the collaboration agreement with respect to such licensed program for an uncured non-diligence breach by us, except in the case of our uncured material breach of our payment obligations with respect to such licensed program, but Aurigene may pursue any and all remedies that may be available to it at law or in equity as a result of such breach. Similarly, after initiation of the first pivotal clinical trial of a product for a licensed program, we may not terminate the collaboration agreement with respect to the license we have granted Aurigene for its territory of India and Russia for such licensed program for an uncured non-diligence breach by Aurigene, but we may pursue any and all remedies that may be available to us at law or in equity as a result of such breach.

On a program-by-program basis, we may terminate the collaboration agreement as it relates to a program or licensed program for an uncured breach by Aurigene with respect to such program or licensed program, and Aurigene may terminate the collaboration agreement as it relates to a licensed program for an uncured breach by us with respect to such licensed program.

In addition, we may terminate the collaboration agreement in its entirety or as it relates to a particular program or licensed program or on a country-by-country basis, for any reason or for no reason at any time upon 60 days' prior written notice to Aurigene.

In the event of termination of the collaboration agreement in its entirety before we have exercised the option for any program, or termination of the collaboration agreement as it relates to any program prior to exercise of the option for such program, all rights and licenses granted by either Aurigene or us to the other party with respect to such program under the collaboration agreement (including the option for such program) will automatically terminate.

If the royalty term with respect to a product for any licensed program in any country has expired on or before any termination of the collaboration agreement in its entirety or as to such licensed program, the license granted by Aurigene to us with respect to such product in such country, as well as the corresponding license granted to Aurigene in its territory, shall survive such termination of the collaboration agreement.

Solely in the event of termination of the collaboration agreement by Aurigene for our uncured breach, or our termination of the collaboration agreement for convenience, the following will apply to any program that was a licensed program immediately prior to such termination:

- our license with respect to any licensed program that is not a terminated program (defined below), either in our entire territory or in countries within our territory outside of the terminated region (defined below), as applicable, shall

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continue in full force and effect, subject to all terms and conditions of the collaboration agreement, including our payment obligations;

- our license with respect to any terminated program, either in our entire territory or in the terminated region, as applicable, shall terminate and revert to Aurigene;
- we will grant Aurigene a perpetual, royalty-free (except for pass-through royalties and milestone payments payable by us under licenses to third party patent rights with respect to products developed or commercialized by or on behalf of Aurigene) license, with the right to sublicense, under our relevant patent rights and other technology solely to develop, manufacture and commercialize compounds and products for any terminated program, either in our entire territory or in the terminated region, as applicable. The foregoing license will be non-exclusive with respect to our patent rights and exclusive with respect to our other technology;
- we will grant to Aurigene a right of first negotiation, exercisable within 90 days after termination, to obtain an exclusive, royalty-bearing license, with the right to sublicense, under our relevant patent rights solely to develop, manufacture and commercialize compounds and products for any terminated program, either in our entire territory or in the terminated region, as applicable, upon commercially reasonable terms and conditions to be negotiated in good faith by the parties;
- we will perform other specified activities and actions reasonably necessary for Aurigene to develop, manufacture and commercialize compounds and products for any terminated program, either in our entire territory or in the terminated region, as applicable; and
- the applicable license to Aurigene will survive termination.

For purposes of the foregoing, “terminated program” means: (i) in the case of termination of the collaboration agreement in its entirety by Aurigene for our uncured non diligence breach, any program that was a licensed program immediately prior to such termination, but excluding, except in the case of our uncured material breach of our payment obligations with respect to such licensed program, any such licensed program for which initiation of the first pivotal clinical trial of a product has occurred prior to such termination; (ii) in the case of any termination of the collaboration agreement as to a particular licensed program by Aurigene either for our uncured non diligence breach (to the extent termination as to such licensed program is permitted) or our uncured diligence breach, such licensed program; (iii) in the case of our termination of the collaboration agreement in its entirety for convenience, any program that was a licensed program immediately prior to such termination; or (iv) in the case of our termination of the collaboration agreement as to a particular licensed program for convenience, such licensed program; provided, however, that, in the case of the preceding clauses (iii) and (iv), if our termination of the collaboration agreement in its entirety or as to a particular licensed program for convenience was with respect only to a particular country or subset of countries within the entire territory (as applicable, a “terminated region”), the applicable licensed program(s) shall be considered “terminated program(s)” only in the terminated region but shall remain licensed program(s) in the rest of our territory.

Genentech

In 2003, we entered into a collaborative research, development and license agreement with Genentech, which we refer to as the collaboration agreement.

Under the terms of our collaboration agreement with Genentech, we granted Genentech an exclusive, global, royalty-bearing license, with the right to sublicense, to make, use, sell and import molecules capable of inhibiting the Hedgehog signaling pathway (including small molecules, proteins and antibodies) for human therapeutic applications, including cancer therapy. Genentech subsequently granted a sublicense to Roche for non-U.S. rights to Erivedge other than in Japan where such rights are held by Chugai. Genentech and Roche are responsible for worldwide clinical development, regulatory affairs, manufacturing and supply, formulation, and sales and marketing.

We are eligible to receive up to an aggregate of $115.0 million in contingent cash milestone payments, exclusive of royalty payments, in connection with the development of Erivedge or another small molecule hedgehog pathway inhibitor, assuming the successful achievement by Genentech and Roche of specified clinical development and regulatory objectives. Of this amount, we have received $59.0 million to date.

In addition to the contingent cash milestone payments, our wholly-owned subsidiary, Curis Royalty, is entitled to a royalty on net sales of Erivedge that ranges from 5% to 7.5% based upon global Erivedge sales by Roche and

Genentech. The royalty rate applicable to Erivedge may be decreased by 2% on a country-by-country basis in certain specified circumstances, including when a competing product that binds to the same molecular target as Erivedge is approved by the applicable country's regulatory authority in another country and is being sold in such country by a third party for use in the same indication as Erivedge, or, when there is no issued intellectual property covering Erivedge in a territory in which sales are recorded. During

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the third quarter of 2015, the FDA and the European Medicine Agency's Committee for Medicinal Products for Human Use, or CHMP, approved another Hedgehog signaling pathway inhibitor, Odomzo® (sonidegib), which is marketed by Sun Pharmaceutical Industries Ltd., for use in locally advanced BCC. Accordingly, Genentech reduced royalties to Curis Royalty on its net sales in the United States of Erivedge by 2% since the fourth quarter of 2015, and we anticipate that Genentech will reduce by 2% royalties on net sales of Erivedge outside of the United States on a country-by-country basis to the extent that sonidegib is approved by the applicable country's regulatory authority and is being sold in such country. However, pursuant to the Oberland Purchase Agreement described below, Curis has retained its rights with respect to the 2% of royalties that are subject to such reduction in countries where such reduction has not occurred, subject to the terms and conditions of the Oberland Purchase Agreement, which we refer to as the "Retained Royalty Amounts".

As a result of our licensing agreements with various universities, we are also obligated to make payments to university licensors on royalties that Curis Royalty earns in all territories (other than Australia) in an amount that is equal to 5% of the royalty payments received from Genentech. This obligation endures on a country-by-country basis for a period of 10 years from the first commercial sale of Erivedge, which occurred in February 2012 in the U.S. For royalties that we earn from Roche's sales of Erivedge in Australia, we will be obligated to make payments to university licensors of 2% of Roche's direct net sales in Australia until the expiration of the Australian patent in April 2019, after which the amount will decrease to 5% of the royalty payments that we receive from Genentech for the remainder of the period ending 10 years from the first commercial sale of Erivedge.

Unless terminated earlier, the collaboration agreement will expire six months after the later of the expiration of Genentech's obligation to pay royalties to us under the agreement or such time as no activities have occurred under the agreement for a period of twelve months. The collaboration agreement may be terminated earlier by either party for cause upon sixty days prior written notice. In addition, Genentech may terminate the agreement, either in whole or in part, without cause, upon six months prior written notice. In the event of any termination where specific license grants survive, we will continue to have the right to receive clinical development and regulatory approval milestones and royalties on product sales for such licensed compound, if any. If we terminate the agreement for cause or Genentech terminates the agreement without cause, all licenses granted to Genentech automatically terminate and revert to us. In addition, Genentech has agreed that it will no longer conduct any development or commercialization activities on any compounds identified in the course of conducting activities under the research plan for the agreement for so long as such compounds continue to be covered by valid patent claims.

In November 2012, we formed a wholly-owned subsidiary, Curis Royalty, which received a $30.0 million loan at an annual interest rate of 12.25% pursuant to a credit agreement between Curis Royalty and BioPharma Secured Debt Fund II Sub, S. à r. l., a Luxembourg limited liability company managed by Pharmakon Advisors, or BioPharma-II. In connection with the loan, we transferred to Curis Royalty our rights to receive royalty and royalty related payments on the commercial sales of Erivedge that we receive from Genentech, and any payment made by Genentech to us pursuant to Genentech's indemnification obligations under the collaboration agreement. The loan and accrued interest was being repaid by Curis Royalty using such royalty and royalty related payments. The loan constituted an obligation of Curis Royalty and was non-recourse to Curis.

Under the terms of the credit agreement, with BioPharma-II, quarterly royalty and royalty-related payments from Genentech were first applied to pay interest and second, principal on the loan from BioPharma-II. As a result of the loan received from BioPharma-II, we continued to record royalty revenue from Genentech but expect such revenues would have been used to pay down such loan until it is repaid in full. Curis Royalty retained the right to royalty payments related to sales of Erivedge following repayment of the loan.

In March 2017, we and Curis Royalty entered into a new credit agreement with HealthCare Royalty Partners III, L.P., or HealthCare Royalty, for the purpose of refinancing and terminating the loan from BioPharma-II. HealthCare Royalty made a $45.0 million loan at an interest rate of 9.95% to Curis Royalty, which was used, in part, to pay off $18.4 million in remaining loan obligations to BioPharma-II under the prior loan, with the residual proceeds of $26.6 million distributed to us as sole equity member of Curis Royalty. As of December 31, 2018, Curis Royalty owed HealthCare Royalty a total of $35.8 million , which was comprised of principal and accrued interest. The final maturity date of the loan was the earlier of such date that the principal is paid in full, or Curis Royalty's right to

receive royalties under the collaboration agreement with Genentech is terminated. On March 22, 2019 we terminated the loan with HealthCare Royalty, and repaid in full all amounts outstanding under the credit agreement. For further discussion please refer to “Part II, Item 9B. Other Information - Royalty Interest Purchase Agreement.”

In connection with our repayment and termination of the credit agreement with HealthCare Royalty, on March 22, 2019, we and Curis Royalty entered into a royalty interest purchase agreement, referred to as the Oberland Purchase Agreement, with TPC Investments I LP and TPC Investments II LP, referred to as the Purchasers, each of which is a Delaware limited partnership managed by Oberland Capital Management, LLC, and Lind SA LLC, referred to as the Agent, a Delaware limited liability company managed by Oberland Capital Management, LLC, as collateral agent for the Purchasers, for the purpose of

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providing operating cash flow and extinguishing the credit agreement with HealthCare Royalty. In connection with entering in the Oberland Purchase Agreement, Curis Royalty and the Agent also entered into a security agreement, we and the Agent entered into a pledge agreement and we and Curis Royalty entered into a consent and payment direction letter agreement with Genentech.

Pursuant to the Oberland Purchase Agreement, the Purchasers acquired the rights to a portion of certain royalty and royalty-related payments excluding a portion of non-US royalties retained by Curis Royalty, referred to as the Purchased Receivables, owed by Genentech under our collaboration agreement with Genentech. Upon closing of the Oberland Purchase Agreement, Curis Royalty received an upfront purchase price of $65.0 million from the Purchasers, approximately $33.8 million of which was used to pay off the remaining loan principal under the credit agreement with HealthCare Royalty, and $3.7 million of which was used to pay transaction costs, including $3.4 million to HealthCare Royalty in accrued and unpaid interest and prepayment fees under the credit agreement, resulting in net proceeds of $27.5 million. Curis Royalty will also be entitled to receive milestone payments of (i) $17.2 million if the Purchasers and Curis Royalty receive aggregate royalty payments as described in clauses (4) and (5) of the following paragraph pursuant to the Oberland Purchase Agreement in excess of $18.0 million during the calendar year 2021 and (ii) $53.5 million if the Purchasers receive payments pursuant to the Oberland Purchase Agreement in excess of $117.0 million on or prior to December 31, 2026, which milestone payments may each be paid, at the option of the Purchasers, in a lump sum in cash or out of the Purchaser's portion of future payments under the Oberland Purchase Agreement.

Pursuant to the terms of the Oberland Purchase Agreement, so long as an event of default by Curis Royalty has not occurred under the security agreement, royalty and royalty-related payments owed by Genentech under the Genentech collaboration agreement in each calendar year shall be allocated in the following order: (1) Curis Royalty shall receive payments reflecting the Retained Royalty Amounts (as defined above) to the extent actually paid by Genentech under the Genentech collaboration agreement, (2) Curis Royalty shall receive payments to satisfy Curis' royalty obligations to certain academic institutions subject to a specified percentage cap and/or a specified period of time, (3) Curis Royalty shall receive a fixed amount of payments to reimburse intellectual property and other enforcement costs, whether or not actually incurred by us, (4) the Purchasers shall receive 100.0% of all payments up to $13.19 million in the aggregate in such calendar year, and (5) any additional payments in such calendar year shall be paid 65.0% to Curis Royalty and 35.0% to the Purchasers.

The Oberland Purchase Agreement also provides that, so long as an event of default by Curis Royalty has not occurred under the security agreement, if Curis Royalty recovers any monetary award or settlement or any other non-ordinary course lump sum payment made in respect of the royalty and royalty-related payments owed by Genentech under the Genentech collaboration agreement that does not specifically relate to any calendar period, then such payment or other recovery shall be allocated in the following order: (1) Curis Royalty shall receive payments to satisfy Curis' royalty obligations to certain academic institutions up to a specified percentage cap, (2) the Purchasers shall receive 100.0% of all such payments up to an amount equal to the product of $13.19 million and the number of full calendar years, and any fraction thereof, in the period beginning on the first day of the calendar quarter in which such payment or other recovery is received and ending on December 31, 2028, subject to certain exceptions, and (3) any additional payment shall be paid 65.0% to Curis Royalty and 35.0% to the Purchasers. Following an event of default under the security agreement, the Agent has the right to stop all allocations of payments that would have otherwise been allocated to Curis Royalty pursuant to the foregoing two paragraphs and instead retain all such payments.

In addition, the Oberland Purchase Agreement provides that after the occurrence of an event of default by Curis Royalty under the security agreement, as described below, the Purchasers shall have the option, for a period of 180 days, to require Curis Royalty to repurchase the Purchased Receivables at a price, referred to as the Put/Call Price, equal to a percentage, beginning at a low triple digit percentage and increasing over time up to a low-mid triple digit percentage of the sum of the upfront purchase price and any portion of the milestone payments paid in a lump sum by the Purchasers, if any, minus certain payments previously received by the Purchasers with respect to the Purchased Receivables. Additionally, Curis Royalty shall have the option at any time to repurchase the Purchased Receivables at the Put/Call Price as of the date of such repurchase.

The Oberland Purchase Agreement will terminate upon the earlier to occur of (i) the date on which Curis Royalty's rights to receive the Purchased Receivables owed by Genentech under the Genentech collaboration agreement have terminated in their entirety and (ii) the date on which payment in full of the Put/Call Price is received by the Purchasers pursuant to the Purchasers' exercise of their put option or Curis Royalty's exercise of its call right as described above.

Pursuant to the security agreement, Curis Royalty granted to the Agent a first priority lien and security interest in all of its assets and all real, intangible and personal property, including all of its right, title and interest in and to the Erivedge royalty payments pursuant to a security agreement. The security interest secures the obligations of Curis Royalty arising under the Oberland Purchase Agreement, the security agreement or otherwise with respect to the due and prompt payment of (i) an amount equal to the Put/Call Price and (ii) all fees, costs, expenses, indemnities and other payments of Curis Royalty under or in respect of the Oberland Purchase Agreement and the security agreement. Additionally, in connection with the transaction, Curis granted to the Agent a first priority lien and security interest of Curis' equity interest in Curis Royalty pursuant to a

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pledge agreement. For further discussion, please refer to “Part II, Item 9B. Other Information - Royalty Interest Purchase Agreement.”

Corporate Information

We were organized as a Delaware corporation in February 2000. We began our operations in July 2000 upon the completion of the merger of Creative BioMolecules, Inc., Ontogeny, Inc. and Reprogenesis, Inc. Our principal executive office is located at 4 Maguire Road, Lexington, MA 02421 and our telephone number is (617) 503-6500. Curis™ and the Curis logo are trademarks or registered trademarks of Curis, and Erivedge® is a trademark of Genentech. This annual report on Form 10-K may also contain trademarks and trade names of others.

Website Access to Reports

We maintain a website with the address www.curis.com. We are not including the information contained in our website as part of, or incorporating it by reference into, this annual report on Form 10-K. Our website address is included in this annual report on Form 10-K as an inactive textual reference only. We make available free of charge through our website our annual reports on Form 10-K, our quarterly reports on Form 10-Q, our current reports on Form 8-K and any such amendments to those reports as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the Securities and Exchange Commission, or the SEC. The SEC maintains a website, www.sec.gov, that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. The public may read and copy any materials we file with the Securities and Exchange Commission at the SEC’s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. The public may obtain information on the operation of the public reference room by calling 1-800-SEC-0330. In addition, we provide paper copies of our filings free of charge upon request. We also make available on our website our corporate governance guidelines, the charters for our audit committee, compensation committee and nominating and corporate governance committee, and our code of business conduct and ethics, and such information is available in print to any stockholder of Curis who requests it.

Intellectual Property

Our policy is to obtain and enforce the patents and proprietary technology rights that are key to our business. We intend to continue to file U.S. and foreign patent applications to protect technology, inventions and improvements that are considered important to the development of our business. We will be able to protect our proprietary technologies from unauthorized use by third parties only to the extent that our proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets.

In the U.S., as of December 31, 2018, we have 80 issued or allowed patents expiring on various dates between 2019 and 2036 as well as numerous pending patent applications. We have foreign counterpart patent filings for most of our U.S. issued patents and patent applications. These patents and patent applications are directed to various inventions including compositions of matter, methods of making and using these compositions for multiple applications, methods for drug screening and discovery, developmental biological processes, and patents which relate to our proprietary technologies.

Fimepinostat and other Targeted Drug Candidates. As of December 31, 2018, we have 28 issued U.S. patents that expire on various dates between 2027 and 2032, including patents covering the composition of matter for fimepinostat, which expires in 2032. We also have several U.S. and foreign utility patent applications directed to our novel small molecules. Our patents and patent applications cover compositions of matter, methods of manufacturing these molecules, formulations, and methods of using these molecules to treat a variety of therapeutic indications. We intend to continue to file additional U.S. and foreign applications as the programs progress.

CA-170, CA-4948, CA-327 and Aurigene Collaboration Programs. In conjunction with the October 2015 exercise of options to license the PDL1/VISTA and IRAK-4 programs, the October 2016 exercise of our option to license the PDL1/TIM3 program under this collaboration, and the March 2018 exercise of our option to the fourth program in immuno-oncology, we obtained world-wide (except for India and Russia) exclusive licenses to the Aurigene intellectual property relevant to the program. The portfolio consists of filings which cover various genera of compounds from each program and methods of use thereof. As of December 31, 2018, there are ten issued or allowed U.S. patents included in such filings.

Erivedge and the Hedgehog Signaling Pathway. As of December 31, 2018, we have 36 issued or allowed U.S. patents expiring on various dates between 2019 and 2033, which relate to the Hedgehog signaling pathway, including patents covering Erivedge's composition of matter, which expires in 2028. Our patents and patent applications cover proteins, and certain small molecule agonists and inhibitors of the Hedgehog signaling pathway, drug screening and discovery methods, as well as methods of using Hedgehog proteins, antibodies or small molecules to activate or inhibit the Hedgehog signaling pathway for a

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variety of therapeutic indications or diagnostic uses. In addition, we have filed foreign patent applications corresponding to many of the aforementioned U.S. filings that could provide additional patent protection for products that activate or inhibit the Hedgehog signaling pathway.

Our academic and research institution collaborators have certain rights to publish data and information regarding their discoveries to which we have rights. While we believe that the prepublication access to the data developed by our collaborators pursuant to our collaboration agreements will be sufficient to permit us to apply for patent protection in the areas in which we are interested in pursuing further research, there is considerable pressure on such institutions to rapidly publish discoveries arising from their efforts. This may affect our ability to obtain patent protection in the areas in which we may have an interest. In addition, these collaboration agreements typically contain provisions that provide us with, at a minimum, an option to license the institution's rights to intellectual property arising from the collaboration.

We are party to various license agreements that give us rights to commercialize various technologies, particularly our Hedgehog signaling pathway technologies, and to use technologies in our research and development processes. The consideration payable in exchange for these licenses includes up-front fees, issuances of shares of common stock, annual royalties, milestone payments and royalties on net sales by our sub-licensees and us. The licensors may terminate these agreements if we fail to meet certain diligence requirements, fail to make payments or otherwise commit a material breach that is not cured after notice.

In addition, we depend upon trade secrets, know-how and continuing technological advances to develop and maintain our competitive position. To maintain the confidentiality of trade secrets and proprietary information, we require our employees, scientific advisors, consultants and collaborators, upon commencement of a relationship with us, to execute confidentiality agreements and, in the case of parties other than our research and development collaborators, to agree to assign their inventions to us. These agreements are designed to protect our proprietary information and to grant us ownership of technologies that are developed in connection with their relationship to us.

Research and Development Program

As of December 31, 2018, our research and development group consisted of 21 employees, including medical doctors, molecular biologists, cell biologists, and other clinical or scientific disciplines who seek to identify and develop new applications for our existing proprietary portfolio.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, pricing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA approves and regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;

- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;

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- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA, requesting marketing for one or more proposed indications;
- review of the candidate product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current good manufacturing practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, and the purity and stability of the drug substance, as well as in vitro and animal studies to assess the potential safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Applicants usually must complete some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

The IND and IRB Processes

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their voluntary informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is

designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend

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an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with FDA certain regulatory requirements in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee or DSMB. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not

interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded

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access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their voluntary informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

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

- Phase 1. The drug is initially introduced into a small number of healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition (e.g., cancer) and tested for safety, dosage tolerance, absorption, distribution, metabolism, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- Phase 2. The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage, and regimen.
- Phase 3. These clinical trials are commonly referred to as “pivotal” studies, which denotes a study which presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.
- Phase 4. Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the

integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

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Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2019 is $2.6 million for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2019 is $0.3 million. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to certain performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for NMEs for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing, such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. The FDA must implement a protocol to expedite review of responses to inspection reports

pertaining to certain drug applications, including applications for drugs in a shortage or drugs for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must

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approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Finally, with passage of the 21st Century Cures Act, or Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy (as defined in the Cures Act) that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the

surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an

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expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

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

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

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;

- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as

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reflected in the product's prescribing information. In the United States, healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementation regulations, as well as the Drug Supply Chain Security Act, or DSCSA, which regulates the distribution of and tracing of prescription drugs and prescription drug samples at the federal level, and sets minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCSA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Drug Price Competition, Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing

process validation data and quality control procedures. ANDAs are “abbreviated” because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is “bioequivalent” to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if “the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug...”

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Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

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To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time. For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with drug sponsors. The legislation requires FDA to meet with drug sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless and until FDA promulgates a regulation stating otherwise, the pediatric data requirements do not apply to products with orphan designation.

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product, are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act of 1983, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or

more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product.) A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product

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generally will be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another orphan drug under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. The new legislation reverses prior precedent holding that the Orphan Drug Act

unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Patent Term Restoration and Extension

A patent claiming a new drug product of use may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half 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 ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Drugs in Europe and other Foreign Jurisdictions

In addition to regulations in the United States, a manufacturer is subject to a variety of regulations in foreign jurisdictions to the extent the manufacturer chooses to sell any drug products in those foreign countries. Even if a manufacturer obtains FDA approval of a product, it must still obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. To obtain regulatory approval of an investigational drug or biological product in the European Union (EU), a manufacturer must submit a marketing authorization application to the European Medicines Agency or EMA. For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, clinical trials are to be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Clinical Trial Approval in the EU

Requirements for the conduct of clinical trials in the European Union including Good Clinical Practice, or GCP, are set forth in the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the E.U. member states. Under this system, approval must be obtained from the competent national authority of each E.U. member state in which a study is planned to be conducted. To this end, a CTA is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, the E.U. passed the new Clinical Trials Regulation (EU) No 536/2014, which will replace the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the European Union, the new E.U. clinical trials legislation was passed as a regulation that is directly applicable in all E.U. member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable. According to the current plans of EMA, the new Clinical Trials Regulation will become applicable in 2019.The Clinical Trials Directive 2001/20/EC will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

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The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the E.U. portal; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states; a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I is assessed jointly by all member states concerned, and Part II is assessed separately by each member state concerned); strictly defined deadlines for the assessment of clinical trial applications; and the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

PRIME Designation in the EU

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The Priority Medicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products (CHMP) or Committee for Advanced Therapies (CAT) are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Marketing Authorization

To obtain marketing approval of a product under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the European Medicines Agency, or EMA, is responsible for conducting the initial assessment of a product. The CHMP is
also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member
states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and

concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

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Within this framework, manufacturers may seek approval of hybrid medicinal products under Article 10(3) of Directive 2001/83/EC. Hybrid applications rely, in part, on information and data from a reference product and new data from appropriate pre-clinical tests and clinical trials. Such applications are necessary when the proposed product does not meet the strict definition of a generic medicinal product, or bioavailability studies cannot be used to demonstrate bioequivalence, or there are changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration of the generic product compared to the reference medicinal product. In such cases the results of tests and trials must be consistent with the data content standards required in the Annex to the Directive 2001/83/EC, as amended by Directive 2003/63/EC.

Hybrid medicinal product applications have automatic access to the centralized procedure when the reference product was authorized for marketing via that procedure. Where the reference product was authorized via the decentralized procedure, a hybrid application may be accepted for consideration under the centralized procedure if the applicant shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation, or the granting of a community authorization for the medicinal product is in the interest of patients at the community level.

A marketing authorization may be granted only to an applicant established in the EU. Regulation No. 1901/2006 provides that prior to obtaining a marketing authorization in the EU, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

Regulatory Data Exclusivity in the European Union

In the European Union, innovative medicinal products authorized in the EU on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity . During this period, applicants for authorization of generics of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to ten years' market exclusivity. During this ten-year period no generic of this medicinal product can be placed on the EU market. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals in the EU

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU Member State. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the EU Member State with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the EU Member State decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU Member State which delivered the marketing authorization within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Similar to the U.S., both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations.

The holder of an EU marketing authorization for a medicinal product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. These rules can impose on central marketing authorization holders for medicinal products the obligation to conduct a labor-intensive collection of data regarding the risks and benefits of marketed products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies.

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The manufacturing process for medicinal products in the EU is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Similarly, the distribution of medicinal products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States.

In the EU, the advertising and promotion of our products are subject to EU Member States' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

Pediatric Studies and Exclusivity

Prior to obtaining a marketing authorization in the European Union, applicants must demonstrate compliance with all measures included in an EMA approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so called Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the Centralized Procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC.

Orphan Drug Designation and Exclusivity in the EU

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated an orphan medicinal product 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 EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition. Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and in addition a range of

other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

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Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom (U.K.) voted in favor of leaving the European Union (commonly referred to as “Brexit”). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate on the deadline, which was initially March 29, 2019 (two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union) and is currently expected to be extended to either April 12, 2019 or May 22, 2019; however, the terms and duration of any such extension are uncertain at this time. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on the given deadline without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

Since the regulatory framework for pharmaceutical products in the U.K. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the U.K.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Even if our drug candidate is approved, sales of our products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, drug candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover our drug candidate could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and

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reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. 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 a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services, or HHS, will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and 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 products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Outside the United States, ensuring adequate coverage and payment for our drug candidate will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our drug candidate or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval.

For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions.

Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new

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products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. 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 products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted regulatory approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits 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;
- the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, or ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are 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 health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some

circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. The ACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2024 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the

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repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole”. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

Competition

Our drug candidates, if approved, will compete with existing and new products being developed by others for treatment of the same indications. Competition in the development of human therapeutics and, in particular, human therapeutics that target signaling pathways to treat cancers, is intense and rapidly evolving. Our competitors include large pharmaceutical and biopharmaceutical companies, as well as specialized biotechnology firms, that are developing cancer therapies in the same indications as we are. Many competitors have substantially greater research, development, manufacturing, marketing, and financial capabilities, than we do. Successful development and commercialization of products depends on the ability to differentiate the benefits of our products (e.g. efficacy, safety, dosing, route of administration, convenience, and cost-effectiveness) over competing drug or biologic therapies.

There are several companies developing drug candidates that target the same molecular targets and signaling pathways, and in some cases the same cancer indications, that are being pursued by us and our collaborators. We believe our primary competitors by molecular target are as follows:

Fimepinostat: We are not aware of other molecules in clinical testing that are designed as one chemical entity to target both HDAC and PI3K. However, there are commercially-available drugs that individually target HDAC. For example, commercially available HDAC inhibitors include Farydak™ (panobinostat) which is produced by Novartis International AG, Zolinza™ (vorinostat), which is produced by Merck & Co., Istodax™ (romidepsin), which is produced by Celgene Corporation, Beleodaq™ (belinostat) which is produced by Spectrum Pharmaceuticals and Depakine™ (valproate sodium), which is produced by Sanofi. In addition, there are several companies testing novel HDAC inhibitors in clinical trials, including among others, Mirati Therapeutics (mocetinostat), Syndax Pharmaceuticals, Inc. (entinostat), MEI Pharma, Inc. (pracinostat), Regenacy Pharmaceuticals, LLC (ricolinostat), Italfarmaco S.p.A. (givinostat), Celleron Therapeutics (CXD101), Viracta Therapeutics, Inc. (nanatinostat), Xynomic Pharmaceuticals (abexinostat), and HUYA Bioscience International (HBI-8000). There are multiple companies testing various PI3K inhibitors, both isoform specific and pan-PI3K inhibitors, which are in various stages of clinical development. There are currently three approved isoform specific PI3K inhibitors on the market, Zydelig™ (idelalisib), which is marketed by

Gilead Sciences, Aliqopa® (copanlisib), which is marketed by Bayer AG, and Copiktra™ (duvelisib), which is marketed by Verastem, Oncology. Other companies developing PI3K inhibitors include Adlai Nortye (buparlisib) Novartis International AG (alpelisib,CDZ173/leniolisib), Genentech / Roche (RG6114/GDC-0077), Takeda Pharmaceutical Company (TAK-117), GlaxoSmithKline plc (GSK2636771), Pfizer, (gedatolisib/PF-05212384), Sanofi (voxtalisib/XL765/SAR245409), TG Therapeutics, (umbralisib/TGR-1202), and Incyte Corporation (INCB050465).
Licensed Programs Under Aurigene Collaboration. We are aware of multiple other companies that are developing IRAK4 inhibitors for oncology indications, including: Pfizer Inc., Nimbus Discovery/Genentech, TG Therapeutics Inc., Merck & Co., Bristol Myers Squibb Company and Amgen, Inc. In addition, there are multiple approved drugs that target PD1/ PDL1

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interactions, including Bristol-Myers Squibb Company's Opdivo™, Merck & Co., Inc.'s Keytruda™, Roche's Tecentriq™, Merck & Co., Inc. and Pfizer Inc.'s, Bavencio™ and AstraZeneca plc's Imfinzi™.

Erivedge. In 2015, Sun Pharmaceuticals Industries Ltd's sonidegib (Odomzo®), a Hedgehog signaling pathway inhibitor indicated for the treatment of adult patients with locally advanced BCC that has recurred following surgery or radiation, or those who are not candidates for surgery or radiation, received regulatory approvals in the United States and European Union. Other commercially available Hedgehog pathway inhibitors include Pfizer Inc.'s glasdegib (Daurismo™). We are aware of several other biotechnology and pharmaceutical companies that have drug development programs relating to compounds that modulate the Hedgehog signaling pathway, including: Eli Lilly and Company (taladegib / LY2940680), Exelixis, Inc./Bristol-Myers Squibb Company (BMS-833923 / XL139), PellePharm Inc. (patidegib), and Senhwa BiosciencesInc. (silmitasertib / CX-4945).

Many competing companies have financial, marketing and human resource capacities that are substantially greater than our own, which may provide these competitors with significant advantages over us. Others have extensive experience in undertaking clinical trials, in obtaining regulatory approval to market products, in manufacturing products on a large scale and in effectively promoting products to healthcare providers, health plans and consumers which may enhance their competitive position relative to ours. In addition to competing with pharmaceutical and biotechnology companies, the products that we are developing would also compete with those being developed by academic and research institutions, government agencies and other public organizations. Any of these organizations may discover new therapies, seek patent protection or establish collaborative arrangements for products and technologies that compete with our products and technologies.

The technologies underlying the development of human therapeutic products are expected to continue to undergo rapid and significant advancement and unpredictable changes. Accordingly, our technological and commercial success will be based, among other things, on our ability to develop proprietary positions in key scientific areas and efficiently evaluate potential product opportunities.

The timing of a product's introduction may be a major factor in determining eventual commercial success and profitability. Early entry may have important advantages in gaining product acceptance and market share. Accordingly, we believe the relative speed with which we or any current or future collaborator(s) can complete preclinical and clinical testing, obtain regulatory approvals, and supply commercial quantities of a product will have an important impact on our competitive position, both in the U.S. and abroad. Other companies may succeed in developing similar products that are introduced earlier, are more effective, or are produced and marketed more effectively, or at a minimum obtain a portion of the market share. For example, our competitors may discover, characterize and develop important targeted cancer molecules before we do, which could have a material adverse effect on any of our related research programs. If research and development by others renders any of our products obsolete or noncompetitive, then our potential for success and profitability may be adversely affected.

For some of our programs, we rely on, or intend to rely on, strategic collaborators for support in our research programs and for preclinical evaluation and clinical development of our potential products and manufacturing and marketing of any products. Our strategic collaborators may conduct multiple product development efforts within each disease area that is the subject of our strategic collaboration with them. Our strategic collaboration agreements may not restrict the strategic collaborator from pursuing competing internal development efforts. Any of our drug candidates, therefore, may be subject to competition with a drug candidate under development by a strategic collaborator.

Manufacturing and Supply

We do not have our own manufacturing capabilities. We currently rely on collaborators or subcontractors, and we have no plans to develop our own manufacturing capability. Instead, we plan to continue to rely on corporate collaborators or subcontractors to manufacture products. If any of our current or planned collaborators or subcontractors encounters regulatory compliance problems or enforcement actions for their own or a collaborative product, it could have a material adverse effect on our business prospects.

We employ a material sourcing strategy that complies with regulatory requirements for building increasing amounts of quality into the product, beginning with raw materials and following through to packaged drug product for clinical use. Starting materials for the drug substance are typically sourced from qualified suppliers, and their production is

conducted under our supervision. Where appropriate, redundant suppliers are added to ensure availability of key materials

Drug substance and product production, and subsequent packaging, labeling and distribution for all of our development candidates are conducted in the various locations under GMP controls.

Sales and Marketing

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We have no sales, marketing or distribution experience or infrastructure and we have no current plans to develop such capabilities. We currently plan to rely on corporate collaborators for product sales, marketing and distribution.

Employees

As of December 31, 2018, we had 31 full-time employees, of whom 7 hold a Ph.D. or other advanced scientific or medical degree. Of our employees, 21 are currently involved in research and development. None of our employees is a party to a collective bargaining agreement, and we consider our relations with our employees to be good.

Segment Reporting

We are engaged solely in the discovery and development of innovative drug candidates for the treatment of human cancers. Accordingly, we have determined that we operate in one operating segment.

Executive Officers of the Registrant

Our executive officers as of March 26, 2019 are as follows:

Name	Age	Position
James Dentzer	52	President and Chief Executive Officer
Robert Martell, M.D., Ph.D.	56	Head of Research and Development

James Dentzer

Mr. Dentzer has served on our board of directors and as our President, Chief Executive Officer, Secretary and Treasurer since September 2018. From March 2018 to September 2018, Mr. Dentzer served as our Chief Operating Officer, Chief Financial Officer, Secretary, and Treasurer. Mr. Dentzer joined the Company in March 2016 as Chief Administrative Officer, Chief Financial Officer, Secretary, and Treasurer. From December 2013 to December 2015, Mr. Dentzer served as Chief Financial Officer of Dicerna Pharmaceuticals, Inc., an RNA interference-based biopharmaceutical company. From March 2010 to December 2013, Mr. Dentzer was the Chief Financial Officer of Valeritas, Inc., a commercial-stage medical technology company. From October 2006 to October 2009, Mr. Dentzer was the Chief Financial Officer of Amicus Therapeutics, Inc., a biotechnology company. In prior positions, Mr. Dentzer spent six years as corporate controller of Biogen and six years in various senior financial roles at E.I. du Pont de Nemours and Company in the U.S. and Asia. Mr. Dentzer holds a B.A. in philosophy from Boston College and an M.B.A. from the University of Chicago.

Robert Martell, M.D., Ph.D.

Dr. Martell has served as our Head of Research & Development since June 2018 and has been an Attending Physician at Tufts Medical Center since September 2015. From September 2011 to May 2018, Dr. Martell served on our board of directors.

Dr. Martell is a co-founder of Epi-Cure Pharmaceuticals, a privately held early-stage biotechnology company, and has served on its board of directors and as president from June 2016 to August 2018. From September 2015 to May 2018, Dr. Martell has served as Associate Chief for the Division of Hematology/Oncology and on faculty at Tufts University School of Medicine. From September 2012 until June 2015, Dr. Martell served as Chief Medical Officer at Tesaro, Inc., a biopharmaceutical company developing Zejula and Varubi. During this time, he also held the position of an Adjunct Associate Professor of Medicine at the Tufts University School of Medicine, and was a practicing medical oncologist at Tufts Medical Center. From September 2009 to September 2012, Dr. Martell was an Associate Professor at Tufts Medical Center, serving as both the Director of the Neely Center for Clinical Cancer Research, overseeing oncology clinical research, and the Leader of the Cancer Center's Program in Experimental Therapeutics, where he was responsible for developing the center's phase I oncology clinical development program. From May 2005 to July 2009, Dr. Martell served as Vice President and Chief Medical Officer of MethylGene, a publicly-traded biotechnology company focused on the development of cancer therapeutics. From November 2002 to May 2005, Dr. Martell also served as Director of Oncology Global Clinical Research at Bristol-Myers Squibb Company, a biopharmaceutical company developing Sprycel, Erbitux and Ixempra. From July 2001 to May 2005, Dr. Martell served concurrently as Assistant Clinical Professor of Oncology at Yale University School of Medicine and Staff Physician at the Veterans Affairs hospital. From July 2000 to October 2002, Dr. Martell worked at Bayer Corporation, Pharmaceutical Division, where he oversaw phase I and phase II clinical studies of Nexavar. Dr. Martell received a B.A. in chemistry from Kalamazoo College, a Ph.D. in pharmacology from the University of Michigan, and an M.D. from Wayne State

University. He completed his internal medicine internship and residency and medical oncology fellowship at Duke University Medical Center.

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ITEM 1A. RISK FACTORS

You should carefully consider the following risk factors, in addition to other information included in this annual report on Form 10-K. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 4 of this annual report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occurs, our business, financial condition, and results of operations and future growth prospects could be materially and adversely affected.

RISKS RELATING TO OUR FINANCIAL RESULTS AND NEED FOR FINANCING

We have incurred substantial losses, expect to continue to incur substantial losses for the foreseeable future and may never generate significant revenue or achieve profitability.

We have incurred significant annual net operating losses in every year since our inception. We expect to continue to incur significant and increasing net operating losses for at least the next several years. Our net losses were $32.6 million and $53.3 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $984.8 million. We have not completed the development of any drug candidate on our own. Other than Erivedge®, which is being commercialized and further developed by Genentech and Roche under our June 2003 collaboration with Genentech, we may never have a drug candidate approved for commercialization. We have financed our operations to date primarily through public offerings and private placements of our common stock, other debt financings, and amounts received through various licensing and collaboration agreements. We have devoted substantially all of our financial resources and efforts to research and development and general and administrative expense to support such research and development. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' (deficit) equity and working capital.

We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials with respect to drug candidates;
- seek to identify and develop additional drug candidates;
- acquire or in-license other drug candidates or technologies;
- seek regulatory and marketing approvals for our drug candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various drugs for which we may obtain marketing approval, if any;
- require the manufacture of larger quantities of drug candidates for clinical development and, potentially, commercialization;
- maintain, expand, and protect our intellectual property portfolio;
- hire and retain additional personnel, such as clinical, quality control and scientific personnel; and
- add equipment and physical infrastructure as may be required to support our research and development programs.

Our ability to become and remain profitable depends on our ability to generate significant revenue. Our only current source of revenues is comprised of licensing and royalty revenues that we earn under our collaboration with Genentech related to the development and commercialization of Erivedge. In addition, a portion of our royalty and royalty-related revenues under our collaboration with Genentech will be paid to TPC Investments I LP and TPC Investments II LP, or the Purchasers, pursuant to the royalty interest purchase agreement we and Curis Royalty entered into with the Purchasers and Lind SA LLC, or Agent, on March 22, 2019, or the Oberland Purchase Agreement.

We do not expect to generate significant revenues other than those related to Erivedge unless and until we are, or any collaborator is, able to obtain marketing approval for, and successfully commercialize, one or more of our drug candidates other than Erivedge. Successful commercialization will require achievement of key milestones, including initiating and successfully completing clinical trials of our drug candidates, obtaining marketing approval for these drug candidates, manufacturing, marketing, and selling those drugs for which we, or any of our collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our drugs from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues and whether or when we might achieve

profitability. We and any collaborators may never succeed in these activities and, even if we do, or any collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability. Our failure to become

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and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of drug candidates, or continue our operations and cause a decline in the value of our common stock.

We will require substantial additional capital, which may be difficult to obtain, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our drug development programs or commercialization efforts.

We will require substantial funds to continue our research and development programs and to fulfill our planned operating goals. Our planned operating and capital requirements currently include the support of our current and future research and development activities for fimepinostat, CA-170, and CA-4948 as well as development candidates we have and may continue to license under our collaboration with Aurigene. We will require substantial additional capital to fund the further development of these programs, as well as to fund our general and administrative costs and expenses. Moreover, under our collaboration, license and option agreement with Aurigene, we are required to make milestone, royalty and option fee payments for discovery, research and preclinical development programs that will be performed by Aurigene, which impose significant potential financial obligations on us. The collaboration includes multiple programs, and we have the option to exclusively license compounds once a development candidate is nominated within each respective program.

Based upon our current operating plan, we believe that our existing cash, cash equivalents and short-term investments of $24.3 million as of December 31, 2018, plus our net proceeds of $27.5 million from the upfront consideration we received in connection with entering into the Oberland Purchase Agreement will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2020. We expect that we will need to raise additional capital or incur indebtedness to continue to fund our operations in the future. Our ability to raise additional funds will depend on financial, economic and market conditions, many of which are outside of our control, and we may be unable to raise financing when needed, or on terms favorable to us. If necessary funds are not available, we may have to delay, reduce the scope of, or eliminate some of our development programs, potentially delaying the time to market for, or preventing the marketing of any of our product candidates which could adversely affect our business prospects, and we may be unable to continue operations.

Furthermore, there are a number of factors that may affect our future capital requirements and further accelerate our need for additional working capital, many of which are outside our control, including the following:

- unanticipated costs in our research and development programs;
- the timing and cost of obtaining regulatory approvals for our drug candidates and maintaining compliance with regulatory requirements;
- the timing and amount of option exercise fees, milestone payments, royalties and other payments, including payments due to licensors, including Aurigene, for patent rights and technology used in our drug development programs;
- the costs of commercialization activities for any of our drug candidates that receive marketing approval, to the extent such costs are our responsibility, including the costs and timing of establishing drug sales, marketing, distribution and manufacturing capabilities;
- unplanned costs to prepare, file, prosecute, defend and enforce patent claims and other patent-related costs, including litigation costs and technology license fees; and
- unexpected losses in our cash investments or an inability to otherwise liquidate our cash investments due to unfavorable conditions in the capital markets.

In connection with the Oberland Purchase Agreement, we transferred and encumbered certain royalty and royalty-related payments on commercial sales of Erivedge, Curis Royalty granted a first priority lien and security interest in all of its assets, including its rights to the Erivedge royalty payments, and we granted the Purchasers a first priority lien and security interest in our equity interest in Curis Royalty. As a result, in the event of a default by us or Curis Royalty we could lose all retained rights to future royalty and royalty-related payments, we could be required to repurchase the Purchased Receivables at a price that is a multiple of the payments we have received, and our ability to enter into future arrangements may be inhibited, all of which could have a material adverse effect on our business, financial condition and stock price.

Pursuant to the Oberland Purchase Agreement, the Purchasers acquired the rights to a portion of certain royalty and royalty-related payments excluding a portion of non-US royalties retained by Curis Royalty, referred to as the Purchased Receivables, owed by Genentech under our collaboration agreement with Genentech. In connection with entering into the

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Oberland Purchase Agreement, Curis Royalty and the Agent entered into a security agreement and Curis and the Purchasers entered into a pledge agreement.

Following an event of default under the security agreement entered into between Curis Royalty and the Agent in connection with the transaction, the Agent has the right to stop all allocations of payments that would have otherwise been allocated to Curis Royalty pursuant to the Oberland Purchase Agreement and instead retain all such payments. In addition, the Oberland Purchase Agreement provides that after the occurrence of an event of default by Curis Royalty under the security agreement, as described below, the Purchasers shall have the option, for a period of 180 days, to require Curis Royalty to repurchase the Purchased Receivables at a price, referred to as the Put/Call Price, equal to a percentage, beginning at a low triple digit percentage and increasing over time up to a low-mid triple digit percentage, of the sum of the upfront purchase price and any portion of the milestone payments paid in a lump sum by the Purchasers, if any, minus certain payments previously received by the Purchasers with respect to the Purchased Receivables.

Pursuant to the security agreement, Curis Royalty granted to the Agent a first priority lien and security interest in all of its assets and all real, intangible and personal property, including all of its right, title and interest in and to the Erivedge royalty payments. The security interest secures the obligations of Curis Royalty arising under the Oberland Purchase Agreement, the security agreement or otherwise with respect to the due and prompt payment of (i) an amount equal to the Put/Call Price and (ii) all fees, costs, expenses, indemnities and other payments of Curis Royalty under or in respect of the Oberland Purchase Agreement and the security agreement.

The obligations of Curis Royalty under the Oberland Purchase Agreement may be accelerated upon the occurrence of an event of default under the security agreement (subject to certain cure periods), including:

- any royalty and royalty-related payments to be remitted into a certain Curis Royalty designated account controlled by the Agent pursuant to a control agreement, referred to as the royalty account, into which all royalty and royalty-related payments must be paid by Curis or Curis Royalty are not so remitted in accordance with the Oberland Purchase Agreement;
- any representation or warranty made by Curis or Curis Royalty in the Oberland Purchase Agreement or any other transaction document proves to be incorrect or misleading in any material respect when made;
- a default by Curis or Curis Royalty in the performance of affirmative and negative covenants set forth in the Oberland Purchase Agreement or any other transaction document;
- a default by Curis in the performance or observance of its indemnity obligations under the Oberland Purchase Agreement;
- the failure by Genentech to pay material amounts owed under the Genentech collaboration agreement because of an actual breach or default by Curis under the Genentech collaboration agreement;
- the failure of the security agreement to create a valid and perfected first priority security interest in any of the collateral;
- a material breach or default by Curis under our agreement with Curis Royalty pursuant to which we transferred our rights to the royalty revenues under the Genentech collaboration agreement to Curis Royalty;
- the voluntary or involuntary commencement of bankruptcy proceedings by either Curis or Curis Royalty and other insolvency related events;
- any materially adverse effect on the binding nature of any of the Oberland Purchase Agreement, Security Agreement, Pledge Agreement or other transaction documents, the Genentech collaboration agreement or our agreement with Curis Royalty;
- any person shall be designated as an independent director of Curis Royalty other than in accordance with Curis Royalty's limited liability company operating agreement; or
- Curis shall at any time cease to own, of record and beneficially, 100% of the equity interests in Curis Royalty.

Upon the occurrence and continuance of an event of default under the security agreement, the Agent may exercise its rights and remedies under the security agreement with respect to Curis Royalty and to the collateral pledged thereunder, including, among other things, acceleration of the obligations under the security agreement, the sale or other realization of the collateral and performance of Curis Royalty's obligations under the purchase and sale agreement. Additionally, Curis granted to the Agent a first priority lien and security interest of Curis' equity interest in Curis Royalty pursuant to a pledge agreement. Upon the occurrence and continuance of an event of default under the security agreement, the Agent may exercise its rights and

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remedies under the pledge agreement with respect to the equity interests, including, among other things, the rights to receive distributions and exercise voting with respect to the equity interests and to sell or otherwise realize upon the collateral in satisfaction of the obligations. The exercise by the Agent of the foregoing rights shall be deemed to constitute an exercise by the Purchasers of their put option under the Oberland Purchase Agreement.

If any of the above events of default were to occur, Curis Royalty may not have sufficient funds to pay the Put/Call price and the Agent could foreclose on the secured royalty and royalty-related payment stream and/or our equity interests in Curis Royalty. In such an event, we could lose our right to royalty and royalty-related payments not transferred to the Purchasers pursuant to the Oberland Purchase Agreement and we could lose our rights in Curis Royalty. In addition, in the event Genentech exercises its set-off rights against royalty payments to Curis Royalty pursuant to our collaboration agreement with Genentech, we may be required to satisfy our royalty-sharing obligations to the Purchasers with amounts from our working capital. The Oberland Purchase Agreement also contains exculpation and indemnification obligations of Curis and Curis Royalty on behalf of the Agent and the Purchasers. Further, the encumbrance of all of Curis Royalty's assets, including the right to royalties from sales of Erivedge, and our equity interests in Curis Royalty pursuant to the security agreement and pledge agreement, respectively, may inhibit us from raising additional funds or entering into other strategic arrangements. Any of these consequence of an event of default could have a material adverse effect on our business, financial condition and stock price.

The amount of royalty revenue we received from sales of Erivedge has been adversely affected by a competing drug, and may further be affected in the future.

Pursuant to the terms of our collaboration agreement with Genentech, our subsidiary Curis Royalty is entitled to receive royalties on net sales of Erivedge that range from 5% to 7.5% based upon global Erivedge sales by Roche and Genentech. The royalty rate applicable to Erivedge may be decreased in certain specified circumstances, including when a competing drug product that binds to the same molecular target as Erivedge is approved by the applicable country's regulatory authority and is being sold in such country by a third party for use in the same indication as Erivedge, or when there is no issued intellectual property covering Erivedge in a territory in which sales are recorded. During the third quarter of 2015, the FDA and the CHMP, approved an additional Hedgehog signaling pathway inhibitor marketed by Sun Pharmaceuticals, sonidegib (Odomzo®), for the treatment of adults with locally advanced BCC.

Sales of sonidegib (Odomzo®) were first recorded in the U.S. during the fourth quarter of 2015 and, accordingly, Genentech has reduced royalties on its net sales in the U.S. of Erivedge from 5-7.5% to 3-5.5%. Furthermore, we anticipate that Genentech will reduce by 2% royalties on net sales of Erivedge outside of the United States on a country-by-country basis to the extent that sonidegib is approved by the applicable country's regulatory authority and is being sold in such country. We also believe that sales of sonidegib have, and are likely to continue to, adversely affect sales of Erivedge, including those in the U.S. and ex-U.S. countries, and which would adversely affect the resulting revenue we may receive from Genentech. A decrease in sales of Erivedge, or in the royalty rate that we receive for sales of Erivedge could adversely affect our operating results.

Fluctuations in our quarterly and annual operating results could adversely affect the price of our common stock.

Our quarterly and annual operating results may fluctuate significantly. Some of the factors that may cause our operating results to fluctuate on a period-to-period basis include:

- payments we may be required to make to collaborators such as Aurigene to exercise license rights and satisfy milestones and royalty obligations;
- the status of, and level of expenses incurred in connection with, our programs, including development costs relating to fimepinostat, CA-4948 and CA-170, as well as funding programs that we have licensed or may in the future license and develop under our collaboration with Aurigene;
- fluctuations in sales of Erivedge and related royalty and milestone payments, including fluctuations resulting from the sales of competing drug products such as sonidegib, which is approved in the U.S. and Europe for the treatment of locally advanced BCC and is now being marketed and sold by Sun Pharmaceuticals Industries Ltd., or Sun Pharmaceuticals;
- any intellectual property infringement lawsuit or other litigation in which we may become involved;

- the implementation of restructuring and cost-savings strategies;
- the occurrence of an event of default under the Oberland Purchase Agreement;
- the implementation or termination of collaboration, licensing, manufacturing or other material agreements with third parties, and non-recurring revenue or expenses under any such agreement; and

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- compliance with regulatory requirements.

If the estimates we make and the assumptions on which we rely in preparing our financial statements prove inaccurate, our actual results may vary significantly.

Our financial statements have been prepared in accordance with GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges taken by us, and disclosures related thereto. Such estimates and judgments include the carrying value of our property, the value of equipment and intangible assets, revenue recognition, and the value of certain liabilities, the repayment term of our loan from HealthCare Royalty, for periods prior to its termination, and stock-based compensation expense. We base our estimates and judgments on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. However, these estimates and judgments, and their underlying assumptions, may change over time. Accordingly, our actual financial results may vary significantly from the estimates contained in our financial statements.

For a further discussion of the estimates and judgments that we make and the critical accounting policies that affect these estimates and judgments, see “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates” set forth in this report.

RISKS RELATING TO THE DEVELOPMENT AND COMMERCIALIZATION OF OUR DRUGS

The therapeutic efficacy of our drug candidates is unproven in humans, and we may not be able to successfully develop and commercialize drug candidates pursuant to these programs.

Our drug candidates, including fimepinostat, CA-4948 and CA-170, are novel chemical entities and their potential benefit as therapeutic cancer drugs is unproven. Our ability to generate revenues from these drug candidates, which we do not expect will occur in the short term, if ever, will depend heavily on their successful development and commercialization, which is subject to many potential risks. For example, our drug candidates may not prove to be effective inhibitors of the molecular targets they are being designed to act against, and may not demonstrate in patients any or all of the pharmacological benefits that may have been demonstrated in preclinical studies. These drug candidates may interact with human biological systems in unforeseen, ineffective or harmful ways. If the FDA determines that any of our drug candidates are associated with significant side effects or have characteristics that are unexpected, we may need to delay or abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

Moreover, many drug candidates that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound or resulted in their removal from the market. As a result of these and other risks described herein that are inherent in the development and commercialization of novel therapeutic agents, we may not successfully maintain third party licensing or collaboration transactions with respect to, or successfully commercialize, drug candidates, in which case we will not achieve profitability and the value of our stock may decline.

We depend heavily on the success of our most advanced drug candidates. All of our drug candidates are still in early clinical or preclinical development. Preclinical studies and clinical trials of our drug candidates may not be successful. If we are unable to commercialize our drug candidates or experience significant delays in doing so, our business will be materially harmed.

Our ability to generate drug candidate(s) and/or drug product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our most advanced drug candidates, including fimepinostat, CA-4948 and CA-170. The success of our drug candidates will depend on many factors, including the following:

- successful enrollment in, and completion of, ongoing and future clinical trials of fimepinostat, CA-4948, CA-170 and other compounds that we may develop under our collaboration agreement with Aurigene;
- Aurigene’s ability to successfully discover and preclinically develop other drug candidates under the collaboration agreement;
- a safety, tolerability and efficacy profile that is satisfactory to the FDA or any comparable foreign regulatory authority for marketing approval;

- receipt of requisite marketing approvals from applicable regulatory authorities;

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- the extent of any required post marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third party raw materials suppliers and manufacturers;
- establishment of arrangements with third party manufacturers to obtain finished drug products that is appropriately packaged for sale;
- adequate ongoing availability of raw materials and drug products for clinical development and any commercial sales;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the U.S. and internationally;
- protection of the rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully market, commercialize, or distribute our most advanced drug candidate, which would materially harm our business.

If clinical trials of any future drug candidates that we, or any collaborators, may develop fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or any collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these drug candidates.

We, and any collaborators, are not permitted to commercialize, market, promote or sell any drug candidate in the U.S. without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the European Medicines Agency, or the EMA, impose similar requirements. We, and any collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our drug candidates in humans before we will be able to obtain these approvals.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our drug candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events or undesirable side effects that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a drug candidate may not continue development or is not approvable. It is possible that even if one or more of our drug candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a drug candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by our drug candidates, or we may mistakenly believe that our drug candidates are toxic or not well tolerated when that is not in fact the case.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any collaborators, and impair our ability to generate revenues from drug sales, regulatory and commercialization milestones and royalties. Moreover, if we, or any collaborators, are required to conduct additional clinical trials or other testing of our drug candidates beyond the trials and testing that we or they contemplate, if we, or they, are unable to successfully complete clinical trials of our drug candidates or other testing, or the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or there are unacceptable safety concerns associated with our drug candidates, we, or any future collaborators, may:

- incur additional unplanned costs;
- be delayed in obtaining marketing approval for our drug candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;

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- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the drug from the market after obtaining marketing approval.

Our failure to successfully initiate and complete clinical trials of our drug candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our drug candidates would significantly harm our business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, drug candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, any drug candidates that we may develop could cause us, any collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our drug candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If any of our drug candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any collaborators, may need to abandon development or limit development of that drug candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

If we, or any collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our drug candidates, potential clinical development, marketing approval or commercialization of our drug candidates could be delayed or prevented.

We, or any collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent clinical development, marketing approval or commercialization of our current drug candidates or any future drug candidates that we, or any collaborators, may develop, including:

- regulators or institutional review boards may not authorize us, any collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or any collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our drug candidates may produce unfavorable or inconclusive results;
- we, or any collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon drug development programs;
- the number of patients required for clinical trials of our drug candidates may be larger than we, or any collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any collaborators, anticipate;
- our estimates of the patient populations available for study may be higher than actual patient numbers and result in our inability to sufficiently enroll our trials;
- the cost of planned clinical trials of our drug candidates may be greater than we anticipate;
- our third-party contractors or those of any collaborators, including those manufacturing our drug candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any collaborators in a timely manner or at all;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- we, or any collaborators, may have to delay, suspend or terminate clinical trials of our drug candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the drug candidate;
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regulators or institutional review boards may require that we, or any collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or

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their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the drug candidate or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;

- the FDA or comparable foreign regulatory authorities may disagree with our, or any collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or any collaborators, enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Drug development costs for us, or any collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our drug candidates. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we, or any collaborators, may have the exclusive right to commercialize our drug candidates or allow our competitors, or the competitors of any collaborators, to bring drugs to market before we, or any collaborators, do and impair our ability, or the ability of any collaborators, to successfully commercialize our drug candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our drug candidates.

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

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the availability of approved therapeutics for the relevant disease;
- the proximity of patients to clinical sites;
- the eligibility criteria and design for the trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

In addition, many of our competitors have ongoing clinical trials for drug candidates that could be competitive with our drug candidates. Patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates or rely upon treatment with existing therapies that may preclude them from eligibility for our clinical trials.

Our inability, or the inability of any future collaborators, to enroll a sufficient number of patients for our, or their, clinical trials could result in significant delays or may require us or them to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials, including for clinical trials of fimepinostat, CA-4948 and CA-170, may result in increased development costs for our drug candidates, which could cause the value of our stock price to decline.

Results of preclinical studies and early clinical trials may not be predictive of results of future late stage clinical trials. We cannot assure you that we will be able to replicate in human clinical trials the results we observed in animal models. Moreover, the outcome of preclinical studies and early clinical trials may not be predictive of the success of

later clinical trials,

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and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a drug and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their drug candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the drug candidates. Even if we, or any collaborators, believe that the results of clinical trials for our drug candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our drug candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same drug candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our drug candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced drug candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

Interim, “top-line,” initial, and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted, and audit and verification procedures could result in material changes to the final data.

From time to time, we publish interim, “top-line,” initial, or preliminary data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Initial, preliminary or “top-line” data also remain subject to audit and verification procedures that may result in the final data being materially different from the data we previously published. As a result, interim, "top-line," initial, and preliminary data should be viewed with caution until the final data are available. Material adverse changes between such data and final published data could significantly harm our business prospects.

We have never obtained marketing approval for a drug candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our current drug candidates or any future drug candidates that we, or any future collaborators, may develop.

We have never obtained marketing approval for a drug candidate. It is possible that the FDA may refuse to accept for substantive review any new drug applications, or NDAs, that we submit for our drug candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our drug candidates. If the FDA does not accept or approve our NDAs for any of our drug candidates, it may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA-required trials or studies, approval of any NDA or application that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our drug candidates or any companion diagnostics, generating revenues and achieving and sustaining profitability. If any of these outcomes occurs, we may be forced to abandon our development efforts for our drug candidates, which could significantly harm our business.

Even if any drug candidates that we, or any collaborators, may develop receive marketing approval, we or others may later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any collaborators, to market the drug.

Clinical trials of any drug candidates we may develop will be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any collaborator, may indicate an apparent positive effect of a drug candidate that is greater than the actual positive effect, if any, or

alternatively fail to identify undesirable side effects. If, following approval of a drug candidate, we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials;

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- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the drug may become less competitive; and
- our reputation may suffer.

Any of these events could harm our business and operations, and could negatively impact our stock price.

Even if our drug candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

We have never commercialized a drug, and even if one of our drug candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching drugs or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third-party payors on the benefits of our drug candidates may require significant resources and may not be successful. If any of our drug candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable.

The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the drug;
- the potential advantages of the drug compared to competitive therapies;
- the prevalence and severity of any side effects;
- whether the drug is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability, or the ability of any future collaborators, to offer the drug for sale at competitive prices;
- the drug’s convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the drug;
- limitations or warnings, including distribution or use restrictions, contained in the drug’s approved labeling;
- the strength of sales, marketing and distribution support;
- changes in the standard of care for the targeted indications for the drug; and
- availability and amount of coverage and reimbursement from government payors, managed care plans and other third-party payors.

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

Because we have limited financial and managerial resources, we focus on research programs and drug candidates that we believe may have the best potential in certain specific indications. As a result, we may delay or forgo pursuit of certain opportunities with our other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future proprietary research and development programs and drug candidates for specific indications may not yield any commercially viable drug candidates. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing

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or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate.

We have no sales, marketing, or distribution experience and, as such, plan to rely primarily on third parties who may not successfully market or sell any drugs we develop.

We have no sales, marketing, or drug distribution experience or capabilities. If we receive required regulatory approvals to commercialize any of our drug candidates, we plan to rely primarily on sales, marketing and distribution arrangements with third parties, including our collaborative partners. For example, as part of our agreements with Genentech, we have granted Genentech the exclusive rights to distribute drugs resulting from such collaboration, and Genentech is currently commercializing Erivedge. We may have to enter into additional marketing and/or sales arrangements in the future and we may not be able to enter into these additional arrangements on terms that are favorable to us, if at all. In addition, we may have limited or no control over the sales, marketing, and distribution activities of these third parties, and sales through these third parties could be less profitable for us than direct sales. These third parties could sell competing drugs and may devote insufficient sales efforts or resources to our drugs. Our future revenues will be materially dependent upon the successful efforts of these third parties.

We may seek to independently market and sell drugs that are not already subject to agreements with other parties. If we undertake to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

- we may not be able to attract and build a significant and skilled marketing staff or sales force;
- the cost of establishing a marketing staff or sales force may not be justifiable in light of the revenues generated by any particular drug; and
- our direct sales and marketing efforts may not be successful.

We face substantial competition, and our competitors may discover, develop or commercialize drugs before or more successfully than we do.

Our drug candidates face competition from existing and new technologies and drugs being developed by biotechnology, medical device, and pharmaceutical companies, as well as universities and other research institutions. For example, there are several companies developing drug candidates that target the same molecular targets that we are targeting or that are testing drug candidates in the same cancer indications that we are testing. For example, while we are not aware of other molecules in clinical testing that are designed as one chemical entity to target both PI3K and HDAC, there are commercially-available drugs that individually target PI3K or HDAC and there are multiple companies testing PI3K or HDAC inhibitors that are in various stages of clinical development.

We are aware of multiple other companies that are developing IRAK4 inhibitors for oncology indications, including: Nimbus Discovery, Inc., TG Therapeutics, Inc., Merck & Co., Inc., Ligand Pharmaceuticals, Inc., AstraZeneca plc, Rigel Pharmaceuticals, Inc., and Bayer AG. In addition, there are multiple approved products on the market that inhibit PD1/PDL1, including Bristol-Myers Squibb Company’s Opdivo,™ Merck & Co., Inc.'s Keytruda,™ Roche Holding AG's Tecentriq,™ Merck & Co., Inc., KGaA / Pfizer Inc.'s Bavencio™, AstraZeneca plc’s Imfinzi™, Regeneron Pharmaceuticals, Inc./Sanofi S.A.'s Libtayo™, and a number of drug candidates in various stages of development (by Novartis AG, TESARO Inc., and others). We are also aware of multiple other companies developing drugs to target TIM3, including Novartis AG, Incyte Corporation, TESARO, Inc., Bristol-Myers Squibb Company, Eli Lilly and Company, and others.

We are aware of several companies that have clinical development programs relating to compounds that modulate the Hedgehog signaling pathway and may compete with Erivedge, including : Pfizer Inc. (glasdegib / PF-04449913), Eli Lilly and Company/Igynta (taladegib / LY2940680), Exelixis, Inc./Bristol-Myers Squibb Company (BMS-833923 / XL139), PellePharm, Inc. (patidegib), Novartis International AG/Sun Pharmaceuticals (LEQ-506) and Cyclone Pharmaceuticals Inc./Senhwa Biosciences Inc. (silmitasertib / CX-4945). Furthermore, sonidegib (Odomzo™) is marketed by Sun Pharmaceuticals, for the treatment of adults with locally advanced BCC. Under the terms of our collaboration agreement with Genentech, our royalty on sales of Erivedge has been reduced as a result of sales of sonidegib.

Many of our competitors have substantially greater capital resources, research and development staffs and facilities, and more extensive experience than we have. As a result, efforts by other biotechnology, medical device and

pharmaceutical companies could render our programs or drugs uneconomical or result in therapies superior to those that we develop alone or with a collaborator. For those programs that we have selected for internal development, we face competition from companies that are more experienced in drug development and commercialization, obtaining regulatory approvals and drug manufacturing. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Other smaller companies may also prove to be significant

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competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, any of these companies may be more successful in obtaining collaboration agreements or other monetary support, approval and commercialization of their drugs and/or may develop competing drugs more rapidly and/or at a lower cost.

If we are not able to compete effectively, then we may not be able, either alone or with others, to advance the development and commercialization of our drug candidates, which would adversely affect our ability to grow our business and become profitable.

Even if we, or any collaborators, are able to commercialize any drug candidate that we, or they, develop, the drug may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business.

The commercial success of our drug candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our drug candidates will be paid by third-party payors, including government health care programs and private health insurers. If coverage is not available, or reimbursement is limited, we, or any collaborators, may not be able to successfully commercialize our drug candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the U.S., no uniform policy of coverage and reimbursement for drugs exists among third-party payors and coverage and reimbursement levels for drugs can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our drugs to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or drug licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay commercial launch of the drug, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the drug in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize successfully any of our drug candidates will depend in part on the extent to which coverage and adequate reimbursement for these drugs and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the U.S. and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell our drug candidates profitably. These payors may not view our drugs, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our drugs, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for drugs, which could result in lower than anticipated drug revenues. If the prices for our drugs, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory

authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. An inability to promptly obtain coverage and adequate payment rates from both government-

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funded and private payors for any of our drug candidates for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of any drugs that we may develop.

Product liability claims are inherent in the process of researching, developing and commercializing human healthcare drugs and could expose us to significant liabilities and prevent or interfere with the development or commercialization of our drug candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the drug, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our drug candidates. Regardless of their merit or eventual outcome, such liability claims would require us to spend significant time, money and other resources to defend such claims, and could result in:

- decreased demand for our drug candidates or drugs that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend resulting litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the reduced ability or inability to commercialize any drugs that we may develop.

Although we currently have product liability insurance for our clinical trials, this insurance is subject to deductibles and coverage limitations and may not be adequate in scope to protect us in the event of a successful drug liability claim. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we commercialize any drug that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our drug candidates, which could harm our business, financial condition, results of operations and prospects.

RISKS RELATING TO OUR DEPENDENCE ON THIRD PARTIES

We are reliant on Genentech and Roche for the successful development and commercialization of Erivedge. If Genentech and Roche do not successfully commercialize Erivedge for advanced BCC or develop Erivedge for other indications, our future prospects may be substantially harmed.

Erivedge is FDA-approved for people with advanced BCC in the U.S. Erivedge is also approved in over 60 foreign countries. Genentech and/or Roche have filed regulatory submissions seeking approval to commercialize Erivedge for this same indication. Our levels of revenue in each period and our near-term prospects substantially depend upon Genentech's ability to successfully continue to commercialize Erivedge for patients with advanced BCC and to demonstrate its superiority over existing therapies and standards of care. The further development and commercialization of Erivedge could be unsuccessful if:

- Erivedge becomes no longer accepted as safe, efficacious, cost-effective and preferable for the treatment of advanced BCC to current therapies in the medical community and by third-party payors;
- Genentech and/or Roche fail to continue to apply the necessary financial resources and expertise to manufacturing, marketing and selling Erivedge for advanced BCC, and to regulatory approvals for this indication outside of the U.S.;
- Genentech and/or Roche do not continue to develop and implement effective marketing, sales and distribution strategies and operations for development and commercialization of Erivedge for advanced BCC;
- Genentech and/or Roche do not continue to develop, validate and maintain a commercially viable manufacturing process for Erivedge that is compliant with current good manufacturing practices;

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- Genentech and/or Roche do not successfully obtain third party reimbursement and generate commercial demand that results in sales of Erivedge for advanced BCC in any geographic areas where requisite approvals have been, or may be, obtained;
- we, Genentech, or Roche encounter third-party patent interference, derivation, inter partes review, post-grant review, reexamination or patent infringement claims with respect to Erivedge;
- Genentech and/or Roche do not comply with regulatory and legal requirements applicable to the sale of Erivedge for advanced BCC;
- competing drug products are approved for the same indications as Erivedge, such as is the case with sonidegib, which is being marketed and sold by Sun Pharmaceutical, both in the U.S. and abroad for the treatment of adults with locally advanced BCC;
- new safety risks are identified;
- Erivedge does not demonstrate acceptable safety and efficacy in current or future clinical trials, or otherwise does not meet applicable regulatory standards for approval in indications other than advanced BCC;
- Genentech and/or Roche determine to re-prioritize Genentech's commercial or development programs and reduce or terminate Genentech's efforts on the development or commercialization of Erivedge; or
- Genentech does not exercise its first right to maintain or defend intellectual property rights associated with Erivedge.

In addition, pursuant to the terms of the Oberland Purchase Agreement, a portion of our royalty and royalty-related revenues under our collaboration with Genentech will be paid to the Purchasers.

We depend on third parties for the research and, as applicable, development and commercialization of certain programs. If one or more of our collaborators fails or delays in developing or, as applicable, commercializing drug candidates based upon our technologies, our business prospects and operating results would suffer and our stock price would likely decline.

Pursuant to our collaboration with Genentech, we have granted to Genentech exclusive rights to develop and commercialize drugs based upon our Hedgehog signaling pathway technologies. In addition, pursuant to our collaboration agreement with Aurigene, Aurigene may develop various immuno-oncology, selected precision oncology and other potential targets which we will have the option to license and advance into clinical trials. Collaborations involving our drug candidates, including our collaborations with Aurigene and Genentech, pose the following risks to us:

- Our collaborators each have significant discretion in determining the efforts and resources that they will apply to their respective collaboration with us. If a collaborator fails to allocate sufficient time, attention and resources to our collaboration, the successful development and commercialization of drug candidates under such collaboration is likely to be adversely affected. For example, we are dependent on Aurigene to successfully discover and advance preclinical programs from which we may exercise our option to license drug candidates for future development.
- Our collaborators may develop and commercialize, either alone or with others, drugs that are similar to or competitive with the drug candidates that are the subject of our respective collaborations. For example, Genentech and Roche are involved in the commercialization of many cancer medicines and are seeking to develop several other cancer drug therapies, and Aurigene has other active cancer-focused discovery programs and has also entered into license agreements with other companies that focus on cancer therapies.
- Our collaborators may change the focus of their development and commercialization efforts or pursue higher-priority programs.
- Our collaborators may enter into one or more transactions with third parties, including a merger, consolidation, reorganization, sale of substantial assets, sale of substantial stock or change of control. Any such transaction could divert the attention of our collaborative partner's management and adversely affect its ability to retain and motivate key personnel who are important to the continued development of the programs under such collaboration. In addition, an acquirer could determine to reprioritize our collaborator's development programs such that our collaborator ceases to diligently pursue the development of our programs, and/or terminates our collaboration.
- Our collaborators may, under specified circumstances, terminate their collaborations with us on short notice and for circumstances outside of our control, which could make it difficult for us to attract new collaborators or adversely affect how we are perceived in the scientific, biotech, pharma and financial communities.

- Our collaborators may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights, or expose us to potential liability.

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- Disputes may arise between collaborators and us regarding ownership of or other rights in the intellectual property generated in the course of the collaborations.
- If any of our collaborators were to breach or terminate its arrangement with us, the development and commercialization of the affected drug candidate or program could be delayed, curtailed or terminated.

If Genentech and other third parties are not successful in commercializing products that reach successful development, our revenues and business will suffer.

As development of certain of our drug candidates advance, we must begin to plan for their launch and commercial distribution. Potential competitors may have substantially greater financial and other resources and may be able to expend more funds and effort than Genentech or other third parties engaged by us in marketing competing products. There can be no assurance that Genentech or other third parties will succeed in commercializing our products, or that the pricing of our products will allow us to generate significant revenues. There can be no assurance that Genentech or other third parties engaged to commercialize our products will devote sufficient resources to marketing and commercialization of our products. Genentech's or third party's failure to successfully commercialize our products will have a material adverse effect on our business and financial condition.

We may not be successful in establishing additional strategic collaborations, which could adversely affect our ability to develop and commercialize drug candidates.

We intend to seek corporate collaborators or licensees for the further development and commercialization of one or more of our drug candidates in one or more geographic territories, particularly in territories outside of the U.S. We do not currently have the resources or capacity to advance these programs into later stage clinical development (i.e., Phase 3) or commercialization on our own, but we are seeking to build such a capacity to enable us to retain development and certain commercial rights to most of our programs in at least the U.S., should we elect to do so. Our success will depend, in part, on either our ability to build such capacity, or our ability to enter into one or more collaborations for our drug candidates. We face significant competition in seeking appropriate collaborators and a number of recent business combinations in the biotechnology and pharmaceutical industry may result in a reduced number of potential future collaborators. In addition, collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. Moreover, we may not be successful in our efforts to establish a collaboration or other alternative arrangements because our research and development pipeline may be insufficient, our programs may be deemed to be at too early of a stage of development for collaborative effort and/or third parties may not view our drug candidates and programs as having the requisite potential to demonstrate safety and efficacy or as sufficiently differentiated compared to existing or emerging treatments. We are also restricted under the terms of certain of our existing collaboration agreements from entering into collaborations regarding or otherwise developing drug candidates that are similar to the drug candidates that are subject to those agreements, such as developing drug candidates that inhibit the same molecular target. In addition, collaboration agreements that we enter into in the future may contain further restrictions on our ability to enter into potential collaborations or to otherwise develop specified drug candidates. Even if we are successful in our efforts to establish new collaborations, the terms that we agree upon may not be favorable to us and such collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner, or at all.

Moreover, if we fail to establish and maintain additional collaborations related to our drug candidates:

- the development of certain of our current or future drug candidates may be terminated or delayed;
- our cash expenditures related to development of certain of our current or future drug candidates would increase significantly and we may need to seek additional financing;
- we may be required to hire additional employees or otherwise develop additional expertise, such as clinical, regulatory, sales and marketing expertise, for which we have not budgeted;
- we will have to bear all of the risk related to the development of any such drug candidates; and

- our future prospects may be adversely affected and our stock price could decline.

We rely in part on third parties to conduct clinical trials of our internally-developed drug candidates, and if such third parties perform inadequately, including failing to meet deadlines for the completion of such trials, research or testing, then we will not be able to successfully develop and commercialize drug candidates and grow our business.

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We rely heavily on third parties such as consultants, clinical investigators, contract research organizations and other similar entities to complete certain aspects of our preclinical testing and clinical trials and provide services in connection with such clinical trials, and expect to continue to do so for the foreseeable future. Despite having contractual remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. These third parties may not complete activities on schedule, or at all, or may not conduct our clinical trials in accordance with the established clinical trial protocol or design. In addition, the FDA and its foreign equivalents require us to comply with certain standards, referred to as "good clinical practices," and applicable regulatory requirements, for conducting, recording and reporting the results of clinical trials. These requirements assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties does not relieve us of these responsibilities and requirements. If any of our third party contractors do not comply with good clinical practices or other applicable regulatory requirements, we may not be able to use the data and reported results from the applicable trial. Any failure by a third party to conduct our clinical trials as planned or in accordance with regulatory requirements could delay or otherwise adversely affect our efforts to obtain regulatory approvals for and commercialize our drug candidates.

We depend on third parties to produce our drug candidates, and if these third parties do not successfully formulate or manufacture these drug candidates, our business will be harmed.

We have no internal manufacturing experience or capabilities, and therefore cannot manufacture any of our drug candidates on either a clinical or commercial scale. In order to continue to develop drug candidates, apply for regulatory approvals, and commercialize drugs, we or any collaborators must be able to manufacture drug candidates in adequate clinical and commercial quantities, in compliance with regulatory requirements, including those related to quality control and quality assurance, at acceptable costs and in a timely manner. The manufacture of our drug candidates may be complex, difficult to accomplish and difficult to scale-up when large-scale production is required. Manufacture may be subject to delays, inefficiencies and low yields of quality drugs. The cost of manufacturing some of our drug candidates may make them prohibitively expensive.

To the extent that we or any collaborators seek to enter into manufacturing arrangements with third parties, we and such collaborators will depend upon these third parties to perform their obligations in a timely and effective manner and in accordance with government regulations. We may be unable to establish any agreements with contract manufacturers or to
do so on acceptable terms. Contract manufacturers may breach their manufacturing agreements because of factors beyond our and our collaborators' control or may terminate or fail to renew a manufacturing agreement based on their own business priorities, becoming costly and/or inconvenient for us and our collaborators. Even if we are able to establish agreements with
contract manufacturers, reliance on contract manufacturers entails additional risks, including:

- manufacturing delays if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them, or if unforeseen events in the manufacturing process arise;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

Any manufacturing problem, the loss of a contract manufacturer or any loss of storage could be disruptive to our operations, delay our clinical trials and, if our products are approved for sale, result in lost sales.

Any contract manufacturers with whom we or our collaborators enter into manufacturing arrangements will be subject to ongoing periodic, unannounced inspection by the FDA and state and foreign agencies or their designees to ensure

strict compliance with current good manufacturing practices and other governmental regulations and corresponding foreign standards. Any failure by contract manufacturers, collaborators, or us to comply with applicable regulations could result in sanctions being imposed, including fines, injunctions, civil penalties, denial by regulatory authorities of marketing approval for drug candidates, delays, suspension or withdrawal of approvals, imposition of clinical holds, seizures or recalls of drug candidates, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business. If we or a collaborator need to change manufacturers, the FDA and corresponding foreign regulatory agencies must approve

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any new manufacturers in advance. This would involve testing and pre-approval inspections to ensure compliance with FDA and foreign regulations and standards.

If third-party manufacturers fail to perform their obligations, our competitive position and ability to generate revenue may be adversely affected in a number of ways, including;

- we, and any collaborators, may not be able to initiate or continue certain preclinical and/or clinical trials of our drug candidates under development;
- we, and any collaborators, may be delayed in submitting applications for regulatory approvals for our drug candidates; and
- we, and any collaborators, may not be able to meet commercial demand for any approved drug products.

Because we rely on a limited number of suppliers for the raw materials used in our drug candidates, any delay or interruption in the supply of such raw materials could lead to delays in the manufacture and supply of our drug candidates.

We rely on third parties to supply certain raw materials necessary to produce our drug candidates for preclinical studies and clinical trials. There are a small number of suppliers for certain raw materials that we use to manufacture our drug candidates. We purchase these materials from our suppliers on a purchase order basis and do not have long-term supply agreements in place. Any reliance on suppliers may involve several risks, including a potential inability to obtain critical materials and reduced control over production costs, delivery schedules, reliability and quality. Any unanticipated disruption to our contract manufacturing caused by problems at suppliers could delay shipment of our product candidates, increase our cost of goods sold and result in lost sales with respect to any approved products. Although we generally do not begin a preclinical study or clinical trial unless we believe we have a sufficient supply of a drug candidate to complete such study or trial, any significant delay in the supply of raw materials for our drug candidates for a preclinical study or an ongoing clinical trial due to the need to replace a third-party supplier could considerably delay completion of certain preclinical studies and/or clinical trials. Moreover, if we are unable to purchase sufficient raw materials after regulatory approval for our drug candidates, the commercial launch of our drug candidates could be delayed, or there could be a supply shortage, each of which would impair our ability to generate revenues from their sale.

Any contamination in our manufacturing process, shortages of raw materials or failure of any of our key suppliers to deliver necessary components could result in delays in our clinical development or marketing schedules.

Any contamination could materially adversely affect our ability to produce drug candidates on schedule and could, therefore, harm our results of operations and cause reputational damage. A material shortage, contamination, recall or restriction on the use of substances in the manufacture of our drug candidates, or the failure of any of our key suppliers to deliver necessary components required for the manufacture of our drug candidates, could adversely impact or disrupt the commercial manufacture or the production of clinical material, which could materially and adversely affect our development timelines and our business, financial condition, results of operations, and future prospects.

RISKS RELATING TO EMPLOYEE MATTERS AND MANAGING GROWTH

If we are not able to attract and retain key management and scientific personnel and advisors, we may not successfully develop our drug candidates or achieve our other business objectives.

We depend upon our senior management team. The loss of the service of any of the key members of our senior management may significantly delay or prevent the achievement of drug development and other business objectives. Our officers all serve pursuant to “at will” employment arrangements and can terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. In the future, we may be dependent on other members of our management, scientific and development team.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. If we lose one or more of our executive officers or other key employees, our ability to successfully implement our business strategy could be seriously harmed. Furthermore, replacing executive officers or other key employees may be difficult and take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, market

and commercialize drugs successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similarly qualified

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personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our drug candidates will be limited.

We may seek to acquire complementary businesses and technologies or otherwise seek to expand our operations and grow our business, which may divert management resources and adversely affect our financial condition and operating results.

We may seek to expand our operations, including through internal growth and/or the acquisition of businesses and technologies that we believe are a strategic complement to our business model. We may not be able to identify suitable acquisition candidates or expansion strategies and successfully complete such acquisitions or successfully execute any such other expansion strategies. We may never realize the anticipated benefits of any efforts to expand our business. Furthermore, the expansion of our business, either through internal growth or through acquisitions, poses significant risks to our existing operations, financial condition and operating results, including:

- a diversion of management attention from our existing operations;
- increased operating complexity of our business, requiring greater personnel and resources;
- significant additional cash expenditures to expand our operations and acquire and integrate new businesses and technologies;
- unanticipated expenses and potential delays related to integration of the operations, technology and other resources of any acquired companies;
- uncertainty related to the value, benefits or legitimacy of intellectual property or technologies acquired;
- retaining and assimilating key personnel and the potential impairment of relationships with our employees;
- incurrence of debt, other liabilities and contingent liabilities, including potentially unknown contingent liabilities; and
- dilutive stock issuances.

RISKS RELATING TO OUR INTELLECTUAL PROPERTY

We may not be able to obtain and maintain patent protection for our technologies and drugs, our licensors may not be able to obtain and maintain patent protection for the technology or drugs that we license from them, and the patent protection we or they do obtain may not be sufficient to stop our competitors from using similar technology.

The long-term success of our business depends in significant part on our ability to:

- obtain patents to protect our technologies and discoveries;
- protect trade secrets from disclosure to competitors;
- operate without infringing upon the proprietary rights of others; and
- prevent others from infringing on our proprietary rights.

The patent positions of pharmaceutical and life science companies, including ours, are generally uncertain and involve complex legal, scientific and factual questions. The laws, procedures and standards that the U.S. Patent and Trademark Office and various foreign intellectual property offices use to grant and maintain patents, and the standards that courts use to interpret patents, are not always applied predictably or uniformly and have changed in significant ways and are expected to continue to change. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the U.S. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Consequently, the level of protection, if any, that will be obtained and provided by our patents if we attempt to enforce them, and they are challenged, is uncertain.

Patents may not issue from any of the patent applications that we own or license. If patents do issue, the type and extent of patent claims issued to us may not be sufficient to protect our technology from exploitation by our competitors. Our patents also may not afford us protection against competitors with similar technology. Assuming the other requirements for

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patentability are met, currently, the first to file a patent application is generally entitled to the patent. Prior to March 16, 2013, in the U.S., patent applications were subject to a "first to invent" rule of law. Applications filed on or after March 16, 2013 (with the exception of certain applications claiming priority to applications filed prior to March 16, 2013, such as continuations and divisionals) are subject to new laws including a "first to file" rule of law. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Additionally, how the U.S. Patent & Trademark Office and U.S. courts will interpret the new laws remains significantly uncertain at this time. We cannot be certain that any existing or future application will be subject to the "first to file" or "first to invent" rule of law, that we were the first to make the inventions claimed in our existing patents or pending patent applications subject to the prior laws, or that we were the first to file for patent protection of such inventions subject to the new laws.

We may not have rights under patents that may cover one or more of our drug candidates. Patents of others may overlap with our own patents regarding one or more of our drug candidates. In some cases, these patents may be owned or controlled by third-party competitors and may prevent or impair our ability to exploit our technology. As a result, we or our current or potential future collaborative partners may be required to obtain licenses under third-party patents to develop and commercialize some of our drug candidates. If we are unable to secure licenses to such patented technology on acceptable terms, we or our collaborative partners may not be able to develop and commercialize the affected drug candidate or candidates.

It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or drugs that we license from third parties and are reliant on our licensors. For example, while under our collaboration with Aurigene we have established a joint patent team to coordinate efforts on patent filing, prosecution, maintenance and other patent matters, we do not control the patent process until we have exercised our option to obtain an exclusive license on a program-by-program basis. If we do not control the filing, prosecution of certain patent rights, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business.

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

We may become involved in expensive and unpredictable patent litigation or other contentious intellectual property proceedings, which could result in liability for damages or require us to cease our development and commercialization efforts.

There are substantial threats of litigation and other adversarial opposition proceedings regarding patent and other intellectual property rights in the pharmaceutical and life science industries. We may become a party to patent litigation or other proceedings regarding intellectual property rights.

Situations that may give rise to patent litigation or other disputes over the use of our intellectual property include:

- initiation of litigation or other proceedings against third parties to enforce our patent rights, to seek to invalidate the patents held by third parties or to obtain a judgment that our drug candidates do not infringe such third parties' patents;
- participation in interference and/or derivation proceedings to determine the priority of invention if our competitors file U.S. patent applications that claim technology also claimed by us;
- initiation of opposition, reexamination, post grant review or inter partes review proceedings by third parties that seek to limit or eliminate the scope of our patent protection;
-

initiation of litigation by third parties claiming that our processes or drug candidates or the intended use of our drug candidates infringes their patent or other intellectual property rights; and

- initiation of litigation by us or third parties seeking to enforce contract rights relating to intellectual property that may be important to our business.

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Any patent litigation or other proceeding, even if resolved favorably, will likely require us to incur substantial costs and be a distraction to management. Some of our competitors may be able to sustain the cost of such litigation or other proceedings more effectively than we can because of their substantially greater financial resources. In addition, our collaborators and licensors may have rights to file and prosecute claims of infringement of certain of our intellectual property, and we are reliant on them. If a patent litigation or other intellectual property proceeding is resolved unfavorably, we or any collaborative partners may be enjoined from manufacturing or selling our future drugs without a license from the other party and be held liable for significant damages. Moreover, we may not be able to obtain required licenses on commercially acceptable terms or any terms at all. In addition, we could be held liable for lost profits if we are found to have infringed a valid patent, or liable for treble damages if we are found to have willfully infringed a valid patent. Litigation results are highly unpredictable, and we or any collaborative partner may not prevail in any patent litigation or other proceeding in which we may become involved. Any changes in, or unexpected interpretations of, the patent laws may adversely affect our ability to enforce our patent position. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could damage our ability to compete in the marketplace.

We face risks relating to the enforcement of our intellectual property rights in China and India that could adversely affect our business.

We have conducted chemical development work through contract research agreements with contract research organizations, or CROs, in China and India. We seek to protect our intellectual property rights under this arrangement through, among other things, non-disclosure and assignment of invention covenants. Enforcement of intellectual property rights and confidentiality protections in China may not be as effective as in the U.S. or other countries. Policing unauthorized use of proprietary technology is difficult and expensive, and we might need to resort to litigation to enforce or defend patents issued to us or to determine the enforceability, scope and validity of our proprietary rights or those of others. The experience and capabilities of Chinese courts in handling intellectual property litigation vary, and outcomes are unpredictable. Further, such litigation may require significant expenditure of cash and management efforts and could harm our business, financial condition and results of operations. An adverse determination in any such litigation will impair our intellectual property rights and may harm our business, prospects and reputation.

In addition, we collaborate with Aurigene, an Indian company, in the development of new therapeutic compounds. Some or all of the intellectual property arising from this collaboration may be developed by Aurigene's employees, consultants, and third-party contractors, and we have an option right under the collaboration agreement to obtain exclusive licenses to Aurigene's rights in this intellectual property. Accordingly, our rights depend in part on Aurigene's contracts with its employees and contractors and Aurigene's ability to protect its trade secrets and other confidential information in India, both before and after we exercise our option to obtain exclusive license rights on a program-by-program basis. Enforcement of intellectual property rights and confidentiality protections in India may not be as effective as in the U.S. or other countries. Policing unauthorized use of proprietary technology is difficult and expensive, and we or Aurigene might need to resort to litigation to protect our trade secrets and confidential information. The experience and capabilities of Indian courts in handling intellectual property litigation vary, and outcomes are unpredictable. Further, such litigation may require significant expenditure of cash and management efforts and could harm our business, financial condition and results of operations. An adverse determination in any such litigation would impair our intellectual property rights and may harm our business, prospects and reputation.

If we are unable to keep our trade secrets confidential, our technology and proprietary information may be used by competitors.

We rely heavily on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect this information through confidentiality and intellectual property license or assignment provisions in agreements with our employees, consultants and other third-party contractors, including our contract research agreements with CROs in China and India, as well as through other security measures. Similarly, our agreement with Aurigene requires Aurigene to enter into such agreements with its employees, consultants, and other third-party contractors. The confidentiality and intellectual property provisions of our agreements and security measures may be breached, and we or they may not have adequate remedies for any such

breach. In addition, our trade secrets may otherwise become known or be independently developed by competitors.

If we fail to comply with our obligations in the agreements under which we license rights to technology from third parties, we could lose license rights that are important to our business.

We are party to agreements that provide us licenses of intellectual property or sharing of rights to intellectual property that is important to our business, and we may enter into additional agreements in the future that provide us licenses to valuable technology. These licenses, including our agreement with Aurigene, impose, and future licenses may impose, various commercialization, milestone and other obligations on us, including the obligation to terminate our use of licensed subject

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matter under certain contingencies. If a licensor becomes entitled to, and exercises, termination rights under a license, we would lose valuable rights and could lose our ability to develop our drugs. We may need to license other intellectual property to commercialize future drugs. Our business may suffer if any current or future licenses terminate, if the licensors fail to abide by the terms of the license or fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid, or if we are unable to enter into necessary licenses on acceptable terms.

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

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

RISKS RELATING TO REGULATORY APPROVAL AND MARKETING OF OUR DRUG CANDIDATES AND OTHER LEGAL COMPLIANCE MATTERS

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of some or all of our drug candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize a drug candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drugs are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. We, and any future collaborators, are not permitted to market our drug candidates in the U.S. or in other countries until we, or they, receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside the U.S. Our drug candidates are in various stages of development and are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for any of our drug candidates in the U.S. or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the U.S. and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the drug candidate’s safety and efficacy. Securing marketing approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA or other regulatory authorities may determine that our drug candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. Moreover, the FDA or other regulatory authorities may fail to approve the companion diagnostics we contemplate developing with partners. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted drug application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a drug candidate. Any marketing approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

Any delay in obtaining or failure to obtain required approvals could negatively affect our ability or that of any future collaborator to generate revenue from the particular drug candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

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Failure to obtain marketing approval in foreign jurisdictions would prevent our drug candidates from being marketed abroad. Any approval we are granted for our drug candidates in the U.S. would not assure approval of our drug candidates in foreign jurisdictions.

In order to market and sell our drugs in the European Union and other foreign jurisdictions, we, and any future collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U.S., a drug must be approved for reimbursement before the drug can be approved for sale in that country. We, and any future collaborators, may not obtain approvals from regulatory authorities outside the U.S. on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may file for marketing approvals but not receive the necessary approvals to commercialize our drugs in any market.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate on the deadline, which was initially March 29, 2019 (two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union) and is currently expected to be extended to either April 12, 2019 or May 22, 2019; however, the terms and duration of any such extension are uncertain at this time. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on the given deadline without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occurs, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our drug candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving competing drugs.

Regulatory authorities in some jurisdictions, including the U.S. and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the U.S. We, or any future collaborators, may seek orphan drug designations for drug candidates and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a drug candidate, we, or they, may not be able to obtain orphan drug exclusivity for that drug candidate. Generally, a drug with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same drug for that indication for the applicable exclusivity period. The applicable exclusivity

period is seven years in the U.S. and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a drug, that exclusivity may not effectively protect the drug from competition because different drugs can be approved for the same condition and the same drug can be approved for different conditions. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for

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the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Even if we, or any future collaborators, obtain marketing approvals for our drug candidates, the terms of approvals and ongoing regulation of our drugs may limit how we manufacture and market our drugs, which could impair our ability to generate revenue.

Once marketing approval has been granted, an approved drug and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our drug candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the drug's approved labeling. Thus, we and any future collaborators will not be able to promote any drugs we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved drugs and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any future collaborators, receive marketing approval for one or more of our drug candidates, we, and any future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, drug surveillance and quality control.

If we, and any future collaborators, are not able to comply with post-approval regulatory requirements, we, and any future collaborators, could have the marketing approvals for our drugs withdrawn by regulatory authorities and our, or any future collaborators', ability to market any future drugs could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any of our drug candidates for which we, or any future collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, or any future collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our drugs following approval.

Any of our drug candidates for which we, or any future collaborators, obtain marketing approval, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such drug, among other things, will be subject to ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the drug may be marketed or to the conditions of approval, including the requirement to implement an FDA-sanctioned Risk Evaluation and Mitigation Strategy.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a drug. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or any future collaborators, do not market any of our drug candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to

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warnings or enforcement action for off-label marketing. Violation of the U.S. Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our drugs or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such drugs, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a drug;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the drugs from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of drugs;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of drugs;
- drug seizure; or
- injunctions or the imposition of civil or criminal penalties.

We may seek a Breakthrough Therapy designation for one or more of our drug candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process.

We may seek a Breakthrough Therapy designation for one or more of our drug candidates. A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drug candidates that have been designated Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated Breakthrough Therapies by the FDA may also be eligible for priority review if supported by clinical data at the time the NDA is submitted to the FDA.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe that one of our drug candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. Even if we receive Breakthrough Therapy designation, the receipt of such designation for a drug candidate may not result in a faster development or regulatory review or approval process compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our drug candidates qualify as Breakthrough Therapies, the FDA may later decide that the drug candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Receipt of Fast Track designation for one or more of our drug candidates, such as fimepinostat, may not actually lead to a faster development or regulatory review or approval process.

If a drug is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a drug sponsor may apply for FDA Fast Track designation. We have received Fast Track designation for the development of fimepinostat in adult patients with relapsed or refractory ("R/R") diffuse large B-cell lymphoma ("DLBCL") after two or more lines of systemic therapy. However, Fast Track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe for fimepinostat or any other product candidate that may receive Fast Track designation. We may

not experience a faster development or regulatory

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review or approval process with Fast Track designation compared to conventional FDA procedures. The FDA may withdraw Fast Track designation for fimepinostat or any other product candidate that may receive Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track designation alone for fimepinostat or any other product candidate does not guarantee qualification for the FDA's priority review procedures.

Under the CURES Act and the Trump Administration's regulatory reform initiatives, the FDA's policies, regulations and guidance may be revised or revoked and that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U.S. or abroad. For example, certain policies of the Trump Administration may impact our business and industry. Namely, the Trump Administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. An under-staffed FDA could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. Moreover, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and Budget on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations, however it is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely,

including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including the 35-day period between December 22, 2018 and January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs again, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval and commercialize our drug candidates and affect the prices we, or they, may obtain.

In the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any drugs for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved drugs.

Among the provisions of the Patient Protection and Affordable Care Act, or Affordable Care Act ("ACA"), of potential importance to our business and our drug candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2024 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop commercialize product candidates.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise.

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Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provision. We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

The costs of prescription pharmaceuticals in the U.S. has also been the subject of considerable discussion in the U.S., and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. The pricing of prescription pharmaceuticals is also subject to governmental control outside the U.S. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired. In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. 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.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services (“HHS”) will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers’ ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with

drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and

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individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and 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 products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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

Governments outside the U.S. tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, such as the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we, or any future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

We may be subject to certain healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

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

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;

False Claims Laws. The federal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including those from 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;

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing or attempting to execute a scheme to defraud any healthcare benefit program;

HIPAA and HITECH. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act, also imposes obligations on certain types of individuals and entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

False Statements Statute. The federal false statements statute prohibits 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;

Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the U.S. Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and

investment interests; and

Analogous State and Foreign Laws. Analogous state laws and regulations, such as state anti-kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services

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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. Many state laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Foreign laws also govern the privacy and security of health information in many circumstances.

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States, such as the U.K. Bribery Act 2010, or the Bribery Act. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation (GDPR), which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements has required and will continue to require significant time, resources and a review of our technologies,

systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices or lead to government enforcement actions, private litigation or significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

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

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We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

We have adopted a Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics mandates compliance with the FCPA and other anti-corruption laws applicable to our business throughout the world. However, we cannot assure you that our employees and third party intermediaries will comply with this code or such anti-corruption laws. Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

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

Our drug products and other materials are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Exports of our drugs and solutions outside of the U.S. must be made in compliance with these laws and regulations. If we fail to comply with these laws and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges, fines, which may be imposed on us and responsible employees or managers, and, in extreme cases, the incarceration of responsible employees or managers. In addition, changes in our drugs or solutions or changes in applicable export or import laws and regulations may create delays in the introduction, provision, or sale of our drugs and solutions in international markets, prevent customers from using our drugs and solutions or, in some cases, prevent the export or import of our drugs and solutions to certain countries, governments or persons altogether. Any limitation on our ability to export, provide, or sell our drugs and solutions could adversely affect our business, financial condition and results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for

failure to comply with such laws and regulations.

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 hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

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In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the most recent global financial crisis, could result in a variety of risks to our business, including weakened demand for our drug candidate and our ability to raise additional capital when needed on acceptable terms, if at all. This is particularly true in the European Union, which is undergoing a continued severe economic crisis. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payors or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Our internal computer systems and information technology, or those of our collaborators or other contractors or consultants, may fail, suffer interruptions or suffer security breaches, which could result in a material disruption of our drug development programs and harm to our business.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures.

In addition, we, and our collaborators, contractors or consultants, rely on information technology networks and systems, including the Internet, to process, transmit and store clinical trial data and other electronic information, and manage or support a variety of business processes, including operational and financial transactions and records, personal identifying information, payroll data and workforce scheduling information. We purchase some of our information technology from vendors, on whom our systems depend. We rely on commercially available systems, software, tools and monitoring to provide security for the processing, transmission and storage of company and customer information. Although we have taken steps to protect the security of our information systems and the data maintained in those systems, no such measures can eliminate the possibility of the systems' improper functioning or the improper access or disclosure of confidential or personally identifiable information such as in the event of cyber-attacks. Security breaches, whether through physical or electronic break-ins, computer viruses, ransomware, impersonation of authorized users, attacks by hackers or other means, can create system disruptions or shutdowns or the unauthorized disclosure of confidential information. Additionally, outside parties may attempt to fraudulently induce employees, collaborators, or other contractors or consultants to disclose sensitive information or take other actions, including making fraudulent payments or downloading malware, by using “spoofing” and “phishing” emails or other types of attacks. Our employees may be targeted by such fraudulent activities. Outside parties may also subject us to distributed denial of services attacks or introduce viruses or other malware through “trojan horse” programs to our users’ computers in order to gain access to our systems and the data stored therein. Because the techniques used to obtain unauthorized access, disable or degrade service, or sabotage systems change frequently and continuously become more sophisticated, often are not recognized until launched against a target and may be difficult to detect for a long time, we may be unable to anticipate these techniques or to implement adequate preventive or detective measures.

If company, clinical, personal or otherwise protected information is improperly accessed, tampered with or distributed, we may face significant financial exposure, including incurring significant costs to remediate possible injury to the affected parties. We may also be subject to sanctions and civil or criminal penalties if we are found to be in violation of the privacy or security rules under federal, state, or international laws protecting confidential information. While we have not experienced any such material system failure, accident, service interruption or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or

other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Any failure to maintain proper functionality and security of our internal computer and information systems could result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, interrupt our operations, damage our reputation, subject us to liability, claims or regulatory penalties, harm our competitive position and delay the further development and commercialization of our drug candidates.

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Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. 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, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

RISKS RELATING TO OUR COMMON STOCK

If we fail to meet the requirements for continued listing on the Nasdaq Global Market, our common stock could be delisted from trading, which would decrease the liquidity of our common stock and our ability to raise additional capital.

Our common stock is currently listed on the Nasdaq Global Market. We are required to meet specified requirements to maintain our listing on the Nasdaq Global Market, including a minimum market value of listed securities of $50,000,000, a minimum total assets and total revenues of $50,000,000, a minimum bid price of $1.00 per share for our common stock, and other continued listing requirements.

On December 27, 2018, we received a deficiency letter from the Staff of Nasdaq notifying us that our Market Value of Listed Securities (“MVLS”) had closed for the last 30 consecutive business days below the minimum $50,000,000 requirement for continued listing on the Nasdaq Global Market pursuant to Nasdaq Listing Rule 5450(b)(2)(A) (the “Minimum MVLS Requirement”). The Staff also noted in its letter that we are not in compliance with Nasdaq Listing Rule 5450(b)(3)(A), which requires listed companies to have total assets and total revenue of at least $50,000,000 each for the most recently completed fiscal year or for two of the three most recently completed fiscal years.

In accordance with Nasdaq Listing Rule 5810(c)(3)(C), we have 180 calendar days from our receipt of the deficiency letter to regain compliance with the Minimum MVLS Requirement (the “Compliance Period”). The expiration of the compliance period is June 25, 2019 (the "Compliance Expiration Date”). In order to regain compliance, our MVLS must close at $50,000,000 or more for a minimum of ten consecutive business days during the Compliance Period. In its letter, the Staff advised us that if at any time during the Compliance Period our MVLS closes at $50,000,000 or more for a minimum of 10 consecutive business days, the Staff will provide written confirmation of compliance and this matter will be closed. In the event the Company fails to regain compliance prior to the Compliance Expiration Date, we will receive written notification that our securities are subject to delisting from the Nasdaq Global Market (a “Delisting Notice”). At that time, we may appeal the Staff’s delisting determination to a Nasdaq Listing Qualifications Panel (“Panel”). We expect that our stock would remain listed pending the Panel’s decision. However, there can be no assurance that, if we do appeal the delisting determination by the Staff to the Panel, that such appeal would be successful.

In January 2018, we received a deficiency letter from the Staff that notified us that, for the 30 consecutive business days prior to January 2, 2018, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Global Market and provided us an initial period of 180 calendar days, or until July 2, 2018, to regain compliance with the minimum bid price requirement by maintaining a minimum bid price of at least $1.00 for a minimum of ten consecutive business days. On May 29, 2018, we effected a 1-for 5 reverse stock split of our common stock. As a result of the reverse stock split, the per share market price of our common stock increased and, from May 30 to June 12, 2018 (10 consecutive business days), the closing bid price of

our common stock exceeded $1.00 per share. Accordingly, on June 13, 2018, we received a notice from Nasdaq indicating that we have regained compliance with Listing Rule 5450(a)(1) as of such date.

There can be no assurance that we can regain, or maintain in the future, compliance with the Nasdaq continued listing requirements. If we fail to satisfy the Nasdaq Global Market's continued listing requirements, we may transfer to the Nasdaq Capital Market, which generally has lower financial requirements for initial listing, to avoid delisting, or, if we fail to meet its listing requirements, the OTC Bulletin Board. However, we may not be able to satisfy the initial listing requirements for the Nasdaq Capital Market. A transfer of our listing to the Nasdaq Capital Market or having our common stock trade on the OTC

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Bulletin Board could adversely affect the liquidity of our common stock. Any such event could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price.

Our stock price may fluctuate significantly and the market price of our common stock could drop below the price paid by our investors.

The trading price of our common stock has been volatile and is likely to continue to be volatile in the future. For example, our stock traded within a range of a high price of $23.70 and a low price of $0.60 per share for the period January 1, 2013 through March 19, 2019. The stock market, particularly in recent years, has experienced significant volatility with respect to pharmaceutical and biotechnology company stocks. Prices for our stock will be determined in the marketplace and may be influenced by many factors, including:

- the timing and result of clinical trials of our drug candidates;
- the success of, and announcements regarding, existing and new technologies and/or drug candidates by us or our competitors;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- market conditions in the biotechnology and pharmaceutical sectors;
- rumors relating to us or our collaborators or competitors;
- commencement or termination of collaborations for our development programs;
- litigation or public concern about the safety of our drug candidates;
- actual or anticipated variations in our quarterly operating results and any subsequent restatement of such results;
- the amount and timing of any royalty revenue we receive from Genentech related to Erivedge;
- actual or anticipated changes to our research and development plans;
- deviations in our operating results from the estimates of securities analysts;
- entering into new collaboration agreements or termination of existing collaboration agreements;
- adverse results or delays in clinical trials being conducted by us or any collaborators;
- any intellectual property disputes or other lawsuits involving us;
- third-party sales of large blocks of our common stock;
- sales of our common stock by our executive officers, directors or significant stockholders;
- equity sales by us of our common stock to fund our operations;
- the loss of any of our key scientific or management personnel;
- FDA or international regulatory actions;
- limited trading volume in our common stock;
- general economic and market conditions, including recent adverse changes in the domestic and international financial markets; and
- the other factors described in this "Risk Factors" section.

While we cannot predict the individual effect that these factors may have on the price of our common stock, these factors, either individually or in the aggregate, could result in significant variations in price during any given period of time.

In the past, securities class action litigation has often been instituted against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources.

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We and our collaborators may not achieve projected research, development, commercialization and marketing goals in the time frames that we or they announce, which could have an adverse impact on our business and could cause our stock price to decline.

We set goals for, and make public statements regarding, the timing of certain accomplishments, such as the commencement and completion of preclinical studies, and clinical trials, and other developments and milestones relating to our business and our collaboration agreements. Our collaborators may also make public statements regarding their goals and expectations for their collaborations with us. The actual timing of any such events can vary dramatically due to a number of factors including delays or failures in our and our current and potential future collaborators' preclinical studies or clinical trials, the amount of time, effort and resources committed to our programs by all parties, and the inherent uncertainties in the regulatory approval and commercialization process. As a result:

- our or our collaborators' preclinical studies and clinical trials may not advance or be completed in the time frames we or they announce or expect;
- we or our collaborators may not make regulatory submissions, receive regulatory approvals or commercialize approved drugs as predicted; and
- we or our collaborators may not be able to adhere to our or their current schedule for the achievement of key milestones under any programs.

If we or any collaborators fail to achieve research, development and commercialization goals as planned, our business could be materially adversely affected and the price of our common stock could decline.

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a company undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. Changes in our stock ownership, some such changes being out of our control, may have resulted or could in the future result in an ownership change. The changes of ownership will result in net operating loss and research and development credit carryforwards that we expect to expire unutilized. If additional limitations were to apply, utilization of a portion of our net operating loss and tax credit carryforwards could be further limited in future periods and a portion of the carryforwards could expire before being available to reduce future income tax liabilities.

Comprehensive changes to the U.S. tax code made by 2017's tax reform law could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law legislation, commonly referred to as the Tax Cuts and Jobs Act (the "TCJA"), that significantly revised the Internal Revenue Code of 1986, as amended. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the TCJA remains uncertain and our business and financial condition could be adversely affected. In addition, how various states will respond to the TCJA continues to be uncertain. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including as a result of applying the provisions of the

TCJA (as such provisions may be elaborated on or further developed in guidance, regulations and technical corrections pertaining to the TCJA), changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in

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tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

Future sales of shares of our common stock, including by employees and large stockholders or pursuant to our sales agreement with Cowen or our universal shelf registration statement could result in dilution to our stockholders and negatively affect our stock price.

Most of our outstanding common stock can be traded without restriction at any time. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock.

As of December 31, 2018, Aurigene beneficially owned approximately 16.5% of our outstanding common stock. Subject to certain restrictions, Aurigene is able to sell its common shares in the public market from time to time without registering them, subject to certain limitations on the timing, amount and method of those sales imposed by Rule 144 under the Securities Act of 1933, as amended. Pursuant to our registration rights agreement with Aurigene, Aurigene has the right, subject to certain conditions and with certain exceptions, to require us to file registration statements covering the common shares it owns or to include those common shares in registration statements that we may file. Following their registration and sale under the applicable registration statement, those shares would become freely tradable. By exercising its registration rights and selling a large number of shares common stock, Aurigene could cause the price of our common stock to decline. In addition, the perception in the public markets that sales by Aurigene might occur could also adversely affect the market price of our common stock.

We have a significant number of shares that are subject to outstanding options and in the future we may issue additional options, warrants or other derivative securities convertible into our common stock. The exercise of any such options, warrants or other derivative securities, and the subsequent sale of the underlying common stock, could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

We currently have on file with the SEC a “universal” shelf registration statement which allows us to offer and sell registered common stock, preferred stock, and warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. In July 2015, we entered into a sales agreement with Cowen, pursuant to which, from time to time, we may offer and sell through Cowen up to $30.0 million of the common stock registered under the shelf registration statement pursuant to one or more “at the market” offerings. In addition, with our prior written approval, Cowen may sell these shares of common stock by any other method permitted by law, including in privately negotiated transactions.

Sales of substantial amounts of shares of our common stock or other securities by our employees and other shareholders, by Cowen pursuant to our sales agreement, under our universal shelf registration statement or otherwise could dilute our stockholders, lower the market price of our common stock and impair our ability to raise capital through the sale of equity securities.

If we are not able to maintain effective internal controls under Section 404 of the Sarbanes-Oxley Act, our business and stock price could be adversely affected.

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls, and requires our independent registered accounting firm to attest to the effectiveness of our internal controls. Any failure by us to maintain the effectiveness of our internal controls in accordance with the requirements of Section 404 of the Sarbanes-Oxley Act, as such requirements exist today or may be modified, supplemented or amended in the future, could have a material adverse effect on our business, operating results and stock price.

We do not intend to pay dividends on our common stock, and any return to investors will come, if at all, only from potential increases in the price of our common stock.

We have never declared nor paid cash dividends on our common stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. In addition, the terms of any future debt or credit agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Insiders have substantial influence over us and could cause us to take actions that may not be, or refrain from taking actions that may be, in our best interest or in the best interest of our shareholders.

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As of December 31, 2018, we believe that our directors, executive officers and principal stockholders, together with their affiliates, owned, in the aggregate, approximately 17.3% of our outstanding common stock including approximately 16.5% of our outstanding common stock owned by, Aurigene. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs, such as:

- the composition of our board of directors;
- the adoption of amendments to our certificate of incorporation and bylaws;
- the approval of mergers or sales of substantially all of our assets;
- our capital structure and financing; and
- the approval of contracts between us and these shareholders or their affiliates, which could involve conflicts of interest.

This concentration of ownership could harm the market price of our common stock by:

- delaying, deferring or preventing a change in control of our company and making some transactions more difficult or impossible without the support of these shareholders, even if such transactions are beneficial to other shareholders;
- impeding a merger, consolidation, takeover or other business combination involving our company; or
- entrenching our management or the board of directors.

Moreover, the interests of these shareholders may conflict with the interests of other shareholders, and we may be required to engage in transactions that may not be agreeable to or in the best interest of us or other shareholders.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock may depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. A lack of research coverage or adverse coverage may negatively impact the market price of our common stock. In addition, if one or more of our current or potential future analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more of our current or potential future analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

A decline in our stock price may affect future fundraising efforts.

We currently have no drug revenues, and depend entirely on funds raised through other sources. One source of such funding is future debt and/or equity offerings. Our ability to raise funds in this manner depends upon, among other things, our stock price, which may be affected by numerous factors including without limitation capital market conditions, evaluation of our stock by securities analysts, numerous factors including without limitation development programs, and the overall status of our business, finances and operations.

We have anti-takeover defenses that could delay or prevent an acquisition that our stockholders may consider favorable, or prevent attempts by our stockholders to replace or remove current management, which could result in a decline in the price of our common stock.

Provisions of our certificate of incorporation, our bylaws, and Delaware law may deter unsolicited takeovers or delay or prevent changes in control of our management, including transactions in which our stockholders might otherwise receive a premium for their shares over then-current market prices. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interest. For example, we have divided our board of directors into three classes that serve staggered three-year terms, we may issue shares of our authorized "blank check" preferred stock, and our stockholders are limited in their ability to call special stockholder meetings. In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person who together with his, her, or its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person

became an interested stockholder, unless

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the business combination is approved in a prescribed manner. These provisions could discourage, delay or prevent a change in control.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We currently lease a facility for our administrative, research and development requirements located at 4 Maguire Road in Lexington, Massachusetts consisting of 24,529 square feet. On November 1, 2017, we entered into a second amendment to the lease agreement pursuant to which we extended the lease for an additional two-year period. The second amended lease will expire on February 29, 2020. We believe that our existing facility will be sufficient to meet our current needs and that suitable additional space will be available if and when needed.

ITEM 3. LEGAL PROCEEDINGS

We are currently not a party to any material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

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PART II

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

Market Information. Our common stock is traded on the Nasdaq Global Market under the trading symbol "CRIS."
Holders. On March 19, 2019 the last reported sale price of our common stock per share on the Nasdaq Global Market was $1.46 and there were 171 holders of record of our common stock. The number of record holders may not be representative of the number of beneficial owners because many of the shares of our common stock are held by depositories, brokers or other nominees.
Dividends. We have never declared or paid any cash dividends on our common stock. We currently intend to retain earnings, if any, to support our business strategy and do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the sole discretion of our board of directors after taking into account various factors, including our financial condition, operating results, capital requirements and any plans for expansion.
Issuer Purchases of Equity Securities. None.
Unregistered Sales of Equity Securities. None.
Performance Graph. Not required.

ITEM 6. SELECTED FINANCIAL DATA

Not applicable.

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

The following discussion of our financial condition and results of operations should be read in conjunction with the consolidated financial statements and the related notes appearing elsewhere in this report. This discussion contains forward-looking statements, based on current expectations and related to future events and our future financial performance, that involve risks and uncertainties. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many important factors, including those set forth under Part I, Item 1A, "Risk Factors" and elsewhere in this report. As used throughout this report, the terms "the Company," "we," "us," and "our" re to the business of Curis, Inc. and its wholly-owned subsidiaries, except where the context otherwise requires, and the term "Curis" refers to Curis, Inc. Unless otherwise indicated, all information in this Form 10-K gives effect to a 1-for-5 reverse stock split of Curis' common stock, that became effective on May 29, 2018. All common shares and per share amounts have been adjusted to reflect such reverse stock split.

Overview

We are a biotechnology company focused on the development of first-in-class and innovative therapeutics for the treatment of cancer. Our clinical stage drug candidates are:

- Fimepinostat (CUDC-907), our internally-developed drug candidate for which our clinical studies in patients with relapsed refractory DLBCL including those with MYC alterations are ongoing. Fimepinostat was granted Orphan Drug Designation in April 2015 and Fast Track Designation in May 2018 by the FDA for the treatment of DLBCL. We are planning a Phase 1 combination study with venetoclax in DLBCL patients with alterations in both MYC and the BCL2 gene, also referred to as double-hit lymphoma, with planned enrollment commencing in the first half of 2019. We expect to report initial clinical data from this combination study in the second half of 2019;
- CA-4948, for which, in January 2018 we initiated a dose escalating clinical trial in patients with non-Hodgkin lymphomas, including those with MYD88 alterations. We expect to report initial Phase 1 clinical data from this study in mid-year 2019; and
- CA-170, for which we are currently conducting a clinical study in patients with advanced solid tumors and lymphomas. We have amended the current protocol for the study to include mesothelioma patients. We announced in January 2019 that we have begun enrollment of these patients and expect to report initial clinical data from this study with respect to mesothelioma in the second half of 2019.

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Our pipeline also includes CA-327, which is a pre-Investigational New Drug, or IND, stage oncology drug candidate. In March 2018, we exercised our option to license a fourth program, which is an immuno-oncology program, from our collaboration partner Aurigene.

In addition, we are party to a collaboration with F. Hoffmann-La Roche Ltd, or Roche, and Genentech Inc., or Genentech, a member of the Roche Group, under which Roche and Genentech are commercializing Erivedge, a first-in-class orally-administered small molecule Hedgehog signaling pathway inhibitor. Erivedge (vismodegib) is approved for the treatment of advanced basal cell carcinoma, or BCC.

Finally, on January 18, 2015, we entered into a collaboration agreement with Aurigene, a specialized, discovery-stage biotechnology company and wholly-owned subsidiary of Dr. Reddy's Laboratories for the discovery, development and commercialization of small molecule compounds in the areas of immuno-oncology and precision oncology, which we refer to as the Aurigene agreement, which was amended in September 2016. As of December 31, 2018, we have licensed four programs under the Aurigene collaboration.

1. IRAK4 Program - a precision oncology program of small molecule inhibitors of IRAK4. The development candidate is CA-4948, an orally available small molecule inhibitor of IRAK4.
2. PD1/VISTA Program - an immuno-oncology program of small molecule antagonists of PD1 and VISTA immune checkpoint pathways. The development candidate is CA-170, an orally available small molecule antagonist of VISTA and PDL1.
3. PD1/TIM3 Program - an immuno-oncology program of small molecule antagonists of PD1 and TIM3 immune checkpoint pathways. The development candidate is CA-327, an orally available small molecule antagonist of PDL1 and TIM3.
4. In March 2018, we exercised our option to license a fourth program, which is an immuno-oncology program.

Based on our clinical development plans for our pipeline, we intend to predominantly focus our available resources on the continued development of fimepinostat, as well as CA-4948 and CA-170 in collaboration with Aurigene in the near term.

We recently implemented a reduction of costs and re-allocation of resources from preclinical activities to clinical activities to strengthen focus on clinical development. We expect the net result of expense reductions in pre-clinical R&D and G&A expenditure and targeted increases in clinical operations to result in a total cash burn reduction from approximately $11 million to $8 million per quarter.

Recent Developments

Royalty Interest Purchase Agreement

On March 22, 2019, we and our wholly-owned subsidiary Curis Royalty LLC, or Curis Royalty, entered into a royalty interest purchase agreement or the Oberland Purchase Agreement, with TPC Investments I LP and TPC Investments II LP, referred to as the Purchasers, each of which is a Delaware limited partnership managed by Oberland Capital Management LLC, and Lind SA LLC, referred to as the Agent, a Delaware limited liability company managed by Oberland Capital Management, LLC, as collateral agent for the Purchasers, pursuant to which we sold to the Purchasers a portion of our rights to receive royalties and royalty-related payments from Genentech on potential net sales of Erivedge®.

As upfront consideration for the purchase of the royalty rights the Purchasers paid $65.0 million to Curis Royalty at closing less certain transaction expenses. Curis Royalty will also be entitled to receive up to approximately $70.7 million in milestone payments based on sales of Erivedge as follows: (i) $17.2 million if the Purchasers and Curis Royalty receive aggregate royalty payments pursuant to the Oberland Purchase Agreement in excess of $18.0 million during the calendar year 2021, subject to certain exceptions and (ii) $53.5 million if the Purchasers receive payments pursuant to the Oberland Purchase Agreement in excess of $117.0 million on or prior to December 31, 2026.

Concurrently with the closing of the Oberland Purchase Agreement Curis Royalty used a portion of the proceeds to terminate and repay in full the loan with Healthcare Royalty. In connection with such termination, Curis Royalty paid approximately $37.2 million to satisfy its remaining loan obligations to HealthCare Royalty, including approximately $33.8 million in principal balance on the loan and $3.4 million in accrued and unpaid interest and prepayment fees. Curis Royalty also used a portion of the proceeds to pay transaction costs of approximately $0.3 million, resulting in net proceeds of approximately $27.5 million. For further discussion please refer to "Part II, Item

9B. Other Information - Royalty Interest Purchase Agreement."

Our Collaborations and License Agreements

Our current collaborations and license agreements are summarized as follows:

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Aurigene

In January 2015, we entered into an exclusive collaboration agreement with Aurigene for the discovery, development and commercialization of small molecule compounds in the areas of immuno-oncology and selected precision oncology targets. Under the collaboration agreement, Aurigene granted us an option to obtain exclusive, royalty-bearing licenses to relevant Aurigene technology to develop, manufacture and commercialize products containing certain of such compounds anywhere in the world, except for India and Russia, which are territories retained by Aurigene.

In connection with the collaboration agreement, we issued to Aurigene 3,424,026 shares of our common stock, valued at $24.3 million at the time of issuance, in partial consideration for the rights granted to us under the collaboration agreement, which we recognized as expense during the year ended December 31, 2015. The shares were issued pursuant to a stock purchase agreement with Aurigene dated January 18, 2015.

In September 2016, we and Aurigene entered into an amendment to the collaboration agreement. Under the terms of the amendment, in exchange for the issuance by us to Aurigene of 2,041,666 shares of our common stock, Aurigene waived payment of up to a total of $24.5 million in potential milestones and other payments associated with the first four programs in the collaboration that may have become due from us under the collaboration agreement. To the extent any of these waived milestones or other payments are not payable by us, for example in the event one or more of the milestone events do not occur, we will have the right to deduct the unused waived amount from any one or more of the milestone payment obligations tied to achievement of commercial milestone events. The amendment also provides that, in the event supplemental program activities are performed by Aurigene, we will provide up to $2.0 million of additional funding for each of the third and fourth licensed program. The shares were issued pursuant to a stock purchase agreement with Aurigene dated September 7, 2016.

As of December 31, 2018, we have exercised our option to license the following four programs under the collaboration:

1. IRAK4 Program - a precision oncology program of small molecule inhibitors of IRAK4. The development candidate is CA-4948, an orally available small molecule inhibitor of IRAK4.
2. PD1/VISTA Program - an immuno-oncology program of small molecule antagonists of PD1 and VISTA immune checkpoint pathways. The development candidate is CA-170, an orally available small molecule antagonist of VISTA and PDL1.
3. PD1/TIM3 Program - an immuno-oncology program of small molecule antagonists of PD1 and TIM3 immune checkpoint pathways. The development candidate is CA-327, an orally available small molecule antagonist of PDL1 and TIM3.
4. In March 2018, we exercised our option to license a fourth program, which is an immuno-oncology program.

For each of our licensed programs (as described above) we are obligated to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize at least one product in each of the U.S., specified countries in the European Union and Japan, and Aurigene is obligated to use commercially reasonable efforts to perform its obligations under the development plan for such licensed program in an expeditious manner.

Subject to specified exceptions, we and Aurigene agreed to collaborate exclusively with each other on the discovery, research, development and commercialization of programs and compounds within immuno-oncology for an initial period of approximately two years from the effective date of the collaboration agreement. At our option, and subject to specified conditions, we may extend such exclusivity for up to three additional one-year periods by paying to Aurigene additional exclusivity option fees on an annual basis. We exercised the first one-year exclusivity option in the first quarter of 2017. The fee for this exclusivity option exercise was $7.5 million, which we paid in two equal installments in the first and third quarters of 2017. We have elected not to further exercise our exclusivity option and thus did not make the $10.0 million payment required for this additional exclusivity in 2018. As a result of our election to not further exercise our exclusivity option, we are no longer operating under the broad immuno-oncology exclusivity with Aurigene.

Since January 2015, we have paid $14.5 million in research payments, and have waived $19.5 million in milestones under the terms of the 2016 amendment.

For each of the IRAK4, PD1/VISTA, PD1/TIM3 programs, and the fourth immuno-oncology program, we have remaining unpaid or unwaived payment obligations of $42.5 million per program, related to regulatory approval and commercial sales milestones, plus specified additional payments for approvals for additional indications, if any. We have agreed to pay Aurigene tiered royalties on our and our affiliates' annual net sales of products at percentage rates ranging from the high single digits up to 10%, subject to specified reductions.

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We have agreed to make certain payments to Aurigene upon our entry into sublicense agreements on any program(s), including:

- with respect to amounts that we and our affiliates receive from sublicensees under a licensed program in the U.S. or the European Union, a declining percentage of non-royalty sublicense revenues that is dependent on the stage of the most advanced product for such licensed program at the time the sublicense is granted, including, for example 25% of such amounts following our initiation of a Phase 2 clinical study and 15% of such amounts after initiation of the first pivotal study. This sharing will also extend to royalties that we receive from sublicensees, subject to minimum royalty percentage rates that we are obligated to pay to Aurigene, which generally range from mid-to-high single-digit royalty percentage rates up to 10%;
- with respect to sublicensing revenues we and our affiliates receive from sublicensees under a licensed program in Asia, 50% of such sublicensing revenues, including both non-royalty sublicensee revenues and royalties that we receive from sublicensees; and
- with respect to non-royalty sublicensing revenues we and our affiliates receive from sublicensees under a licensed program outside of the U.S., the European Union and Asia, a percentage of such non-royalty sublicense revenues ranging from 30% to 50%. We are also obligated to share 50% of royalties that we receive from sublicensees that we receive in these territories.

Our royalty payment obligations (including those on sales by sublicensees) under the collaboration agreement with respect to a product in a country will expire on a product-by-product and country-by-country basis on the later of: (i) expiration of the last-to-expire valid claim of the Aurigene patents covering the manufacture, use or sale of such product in such country; and (ii)10 years from the first commercial sale of such product in such country.

For additional information regarding the terms and termination provisions of this agreement, see "Business—Collaborations and License Agreements—Aurigene Agreement."

Genentech Hedgehog Signaling Pathway Collaboration Agreement

In 2003, we entered into a collaborative research, development and license agreement with Genentech, which we refer to as the collaboration agreement.

Under the terms of our collaboration agreement with Genentech, we granted Genentech an exclusive, global, royalty-bearing license, with the right to sublicense, to make, use, sell and import molecules capable of inhibiting the Hedgehog signaling pathway (including small molecules, proteins and antibodies) for human therapeutic applications, including cancer therapy. Genentech subsequently granted a sublicense to Roche for non-U.S. rights to Erivedge, other than in Japan where such rights are held by Chugai. Genentech and Roche are responsible for worldwide clinical development, regulatory affairs, manufacturing and supply, formulation, and sales and marketing.

We are eligible to receive up to an aggregate of $115.0 million in contingent cash milestone payments, exclusive of royalty payments, in connection with the development of Erivedge or another small molecule hedgehog pathway inhibitor, assuming the successful achievement by Genentech and Roche of specified clinical development and regulatory objectives. Of this amount, we have received $59.0 million to date.

In addition to the contingent cash milestone payments, our wholly-owned subsidiary, Curis Royalty, is entitled to a royalty on net sales of Erivedge that ranges from 5% to 7.5% based upon global Erivedge sales by Roche and Genentech. The royalty rate applicable to Erivedge may be decreased by 2% on a country-by-country basis in certain specified circumstances, including when a competing product that binds to the same molecular target as Erivedge is approved by the applicable country's regulatory authority in another country and is being sold in such country by a third party for use in the same indication as Erivedge, or, when there is no issued intellectual property covering Erivedge in a territory in which sales are recorded. During the third quarter of 2015, the FDA and the CHMP, approved another Hedgehog signaling pathway inhibitor, Odomzo® (sonidegib), which is marketed by Sun Pharmaceutical Industries Ltd., for use in locally advanced BCC. Accordingly, Genentech reduced royalties to Curis Royalty on its net sales in the United States of Erivedge by 2% since the fourth quarter of 2015 and we anticipate that Genentech will reduce by 2% royalties on net sales of Erivedge outside of the United States on a country-by-country basis to the extent that sonidegib is approved by the applicable country's regulatory authority and is being sold in such country. However, pursuant to the Oberland Purchase Agreement, Curis has retained its rights with respect to the 2% of royalties that are subject to such reduction in countries where such reduction has not occurred, subject to the terms

and conditions of the Oberland Purchase Agreement, which we refer to as the “Retained Royalty Amounts”.

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We recognized $10.4 million of royalty revenue from Genentech's net sales of Erivedge during the year ended December 31, 2018, and have recognized an aggregate of $48.3 in royalty revenues since Erivedge was approved.

As a result of our licensing agreements with various universities, we are obligated to make payments to university licensors on royalties that Curis Royalty earns in all territories (other than Australia) in an amount that is equal to 5% of the royalty payments received from Genentech. This obligation endures on a country-by-country basis for a period of 10 years from the first commercial sale of Erivedge, which occurred in February 2012 in the U.S. For royalties that we earn from Roche's sales of Erivedge in Australia, we will be obligated to make payments to university licensors of 2% of Roche's direct net sales in Australia until the expiration of the Australian patent in April 2019, after which time the amount will decrease to 5% of the royalty payments that Curis Royalty receives from Genentech for the remainder of the period ending 10 years from the first commercial sale of Erivedge. Cost of royalty revenues were $0.6 million during the year ended December 31, 2018. As of December 31, 2018, we have paid an aggregate of $2.6 million to university licensors since Erivedge was approved.

In November 2012, we formed a wholly-owned subsidiary, Curis Royalty, which received a $30.0 million loan at an annual interest rate of 12.25% pursuant to a credit agreement between Curis Royalty and BioPharma Secured Debt Fund II Sub, S. à r. l., a Luxembourg limited liability company managed by Pharmakon Advisors, or BioPharma-II. In connection with the loan, we transferred to Curis Royalty our rights to receive royalty and royalty related payments on the commercial sales of Erivedge that we receive from Genentech, and any payment made by Genentech to us pursuant to Genentech's indemnification obligations under the collaboration agreement. The loan and accrued interest was being repaid by Curis Royalty using such royalty and royalty related payments. The loan constituted an obligation of Curis Royalty and was non-recourse to Curis.

Under the terms of the credit agreement, quarterly royalty and royalty-related payments from Genentech were first applied to pay interest and second, principal on the loan from BioPharma-II. As a result of the loan received from BioPharma-II, we continued to record royalty revenue from Genentech but expect such revenues would have been used to pay down such loan until it is repaid in full. Curis Royalty retained the right to royalty payments related to sales of Erivedge following repayment of the loan.

In March 2017, we and Curis Royalty entered into a credit agreement with HealthCare Royalty Partners III, L.P., or HealthCare Royalty, for the purpose of refinancing the loan from BioPharma-II. HealthCare Royalty made a $45.0 million loan at an interest rate of 9.95% to Curis Royalty, which was used, in part, to pay off $18.4 million in remaining loan obligations to BioPharma-II under the prior loan with the residual proceeds of $26.6 million distributed to us as sole equity member of Curis Royalty. As of December 31, 2018, Curis Royalty owed HealthCare Royalty a total of $35.8 million, which was comprised of principal and accrued interest. On March 22, 2019, we terminated, and repaid in full all amounts outstanding under, the loan with HealthCare Royalty. For further discussion, please refer to "Part II, Item 9B. Other Information - Royalty Interest Purchase Agreement."

In connection with our termination of the credit agreement with HealthCare Royalty, we and Curis Royalty entered into the Oberland Purchase Agreement. For further discussion, please refer to "Part II, Item 9B. Other Information - Royalty Interest Purchase Agreement."

The Leukemia & Lymphoma Society

In November 2011, we entered into an agreement with Leukemia and Lymphoma Society ("LLS"), pursuant to which LLS agreed to provide us with up to $4.0 million in payments to support our ongoing development of fimepinostat, subject to the achievement of specified milestones.

In August 2015, we entered into an amendment of the November 2011 agreement with LLS. Under the amendment, LLS agreed to provide advisory services regarding both the fimepinostat and IRAK4 programs, and LLS is no longer obligated to make further milestone payments related to ongoing clinical development of fimepinostat.

We agreed to make up to $1.7 million in future payments to LLS, which represents the aggregate payments previously received from LLS under the November 2011 agreement, pursuant to achievement of certain objectives, including a licensing, sale, or other similar transaction, as well as regulatory and commercial objectives, in each case related to the fimepinostat program in hematological malignancies. However, if fimepinostat does not continue to meet its clinical safety endpoints in ongoing and future clinical trials in the defined field, or fails to obtain necessary regulatory

approvals, all funding provided to us by LLS will be considered a non-refundable grant.

Liquidity

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Since our inception, we have funded our operations primarily through private and public placements of our equity securities, license fees, contingent cash payments, research and development funding from our corporate collaborators, debt financings and the monetization of certain royalty rights. We have never been profitable on an annual basis, and have an accumulated deficit of $984.8 million as of December 31, 2018. For the year ended December 31, 2018 we incurred a loss of $32.6 million and used $30.1 million of cash in operations. We expect that our cash, cash equivalents and short-term investments as of December 31, 2018 plus net proceeds from the upfront consideration we received in connection with our entering into the Oberland Purchase Agreement, will enable us to fund our operating expenses and capital requirements, based upon our current operating plan, into the second half of 2020.

We will need to generate significant revenues to achieve profitability, and do not expect to achieve profitability in the foreseeable future, if at all. For a further discussion of our liquidity and funding requirements, see “Liquidity and Capital Resources - Funding Requirements.”

Key Drivers

We believe that near-term key drivers to our success will include:

- our ability to successfully plan, finance and complete current and planned clinical trials for fimepinostat, CA-4948 and CA-170 as well as for such clinical trials to generate favorable data;
- Aurigene’s ability to advance additional preclinical immuno-oncology, and precision oncology drug candidates, and our ability to license these programs from Aurigene and further progress them clinically;
- Genentech and Roche’s ability to continue to successfully commercialize Erivedge in advanced BCC in the United States and in other global territories; and
- our ability to raise the substantial additional financing required to fund our operations through our at-the-market sale facility with Cowen or other potential financing.

In the longer term, a key driver to our success will be our ability, and the ability of any current or future collaborator or licensee, to successfully develop and commercialize additional drug candidates.

Financial Operations Overview

General. Our future operating results will largely depend on the progress of drug candidates currently in our research and development pipeline. The results of our operations will vary significantly from year to year and quarter to quarter and depend on, among other factors, the cost and outcome of any preclinical development or clinical trials then being conducted. For a discussion of our liquidity and funding requirements, see “Liquidity” and “Liquidity and Capital Resources - Funding Requirements.”

Debt. In December 2012, our wholly-owned subsidiary, Curis Royalty LLC, or Curis Royalty, entered into a $30 million credit agreement with BioPharma Secured Debt Fund II Sub, S. à r. l., a Luxembourg limited liability company managed by Pharmakon Advisors, or BioPharma-II, at an annual interest rate of 12.25% collateralized with certain future Erivedge royalty and royalty-related payment streams.

In connection with the loan, we transferred to Curis Royalty our right to receive royalty and royalty-related payments from Genentech. The loan and accrued interest was an obligation of Curis Royalty, with no recourse to us, to be repaid using the royalty and royalty-related payments from Genentech. To secure repayment of the loan, Curis Royalty granted a first priority lien and security interest (subject only to permitted liens) to BioPharma-II in all of its assets and all real, intangible and personal property, including all of its right, title and interest in and to the royalty and royalty-related payments. Under the terms of the credit agreement, quarterly royalty and royalty-related payments received by Curis Royalty from Genentech were first applied to pay interest and second, principal on the loan from BioPharma-II. As a result of the loan received from BioPharma-II, we continued to record royalty revenue from Genentech but expect such revenues would have been used to pay down such loan until it is repaid in full. Curis Royalty retained the right to royalty payments related to sales of Erivedge following repayment of the loan.

In March 2017, we and Curis Royalty, entered into a new credit agreement, referred to as the credit agreement, with HealthCare Royalty Partners III L.P., or HealthCare Royalty, a Delaware limited partnership managed by Healthcare Royalty Management, LLC, for the purpose of refinancing the prior loan from BioPharma-II. On the effective date of

the credit agreement with Healthcare Royalty, the prior loan was terminated in its entirety.

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Pursuant to the credit agreement, HealthCare Royalty made a $45.0 million loan at an annual interest rate of 9.95% to Curis Royalty, which was used to pay off the approximate $18.4 million in remaining loan obligations to BioPharma-II under the prior loan. The remaining proceeds of the loan of $26.6 million were distributed to us as sole equity holder of Curis Royalty. As of December 31, 2018, the outstanding principal and interest due under the loan was $35.8 million. On March 22, 2019, we terminated, and repaid in full all amounts outstanding under the loan with HealthCare Royalty.

In connection with the termination and repayment in full of the loan with HealthCare Royalty, we entered in the Oberland Purchase Agreement. Upon closing of the Oberland Purchase Agreement, Curis Royalty received an upfront purchase price of $65.0 million from the Purchasers, approximately $33.8 million of which was used to pay off the remaining loan principal to HealthCare Royalty, and $3.7 million of which was used to pay transaction costs, including $3.4 million to HealthCare Royalty in accrued and unpaid interest and prepayment fees under the loan, resulting in net proceeds of $27.5 million. Curis Royalty will also be entitled to receive milestone payments of (i) $17.2 million if the Purchasers and Curis Royalty receive aggregate royalty payments pursuant to the Oberland Purchase Agreement in excess of $18.0 million during the calendar year 2021, subject to certain exceptions, and (ii) $53.5 million if the Purchasers receive payments pursuant to the Oberland Purchase Agreement in excess of $117.0 million on or prior to December 31, 2026, which milestone payments may each be paid, at the option of the Purchasers, in a lump sum in cash or out of the Purchaser's portion of future payments under the Oberland Purchase Agreement. For further discussion please refer to "Part II, Item 9B. Other Information - Royalty Interest Purchase Agreement."

Revenue. We do not expect to generate any revenues from our direct sale of products for several years, if ever. Substantially all of our revenues to date have been derived from license fees, research and development payments, and other amounts that we have received from our strategic collaborators and licensees, including royalty payments. Since the first quarter of 2012, we have recognized royalty revenues related to Genentech's sales of Erivedge and we expect to continue to recognize royalty revenue in future quarters from Genentech's sales of Erivedge in the U.S. and Roche's sales of Erivedge outside of the U.S. However, a portion of our royalty and royalty-related revenues under our collaboration with Genentech will be paid to the Purchasers, pursuant to the Oberland Purchase Agreement. The Oberland Purchase Agreement will terminate upon the earlier to occur of (i) the date on which Curis Royalty's rights to receive the Purchased Receivables owed by Genentech under the Genentech collaboration agreement have terminated in their entirety and (ii) the date on which payment in full of the put/call price is received by the Purchasers pursuant to the Purchasers' exercise of their put option or Curis Royalty's exercise of its call right as described in "Part II, Item 9B. Other Information - Royalty Interest Purchase Agreement."

We could receive additional milestone payments from Genentech, provided that contractually-specified development and regulatory objectives are met. Also, we could receive milestone payments from the Purchasers, provided that contractually-specified royalty payment amounts are met within applicable time periods. Our only source of revenues and/or cash flows from operations for the foreseeable future will be royalty payments that are contingent upon the continued commercialization of Erivedge under this collaboration, and contingent cash payments for the achievement of clinical, development and regulatory objectives, if any, are met, under our existing collaboration with Genentech. Our receipt of additional payments under our existing collaboration with Genentech cannot be assured, nor can we predict the timing of any such payments, as the case may be.

Cost of Royalty Revenues. Cost of royalty revenues consists of all expenses incurred that are associated with royalty revenues that we record as revenues in our consolidated statements of operations and comprehensive loss. These costs currently consist of payments we are obligated to make to university licensors on royalties that Curis Royalty receives from Genentech on net sales of Erivedge. In all territories other than Australia, our obligation is equal to 5% of the royalty payments that we receive from Genentech for a period of 10 years from the first commercial sale of Erivedge, which occurred in February 2012 in the U.S. In addition, for royalties that Curis Royalty receives from Roche's sales of Erivedge in Australia, we will be obligated to make payments to university licensors of 2% of Roche's direct net sales in Australia until expiration of the patent in April 2019. After April 2019, the amount we are obligated to pay will decrease to 5% of the royalty payments that Curis Royalty receives from Genentech.

Research and Development. Research and development expense consists of costs incurred to develop our drug candidates. These expenses consist primarily of:

- salaries and related expenses for personnel, including stock-based compensation expense;
- costs of conducting clinical trials, including amounts paid to clinical centers, clinical research organizations and consultants, among others;
- other outside service costs including costs of contract manufacturing;
- sublicense payments;

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- the costs of supplies and reagents;
- occupancy and depreciation charges;
- certain payments that we make to Aurigene under our collaboration agreement, including, for example, option exercise fees and milestone payments; and
- payments that we are obligated to make to certain third-party university licensors upon our receipt of payments from Genentech related to the achievement of clinical development and regulatory objectives under our collaboration agreement.

We expense research and development costs as incurred. We are currently incurring research and development costs under our Hedgehog signaling pathway inhibitor collaboration with Genentech related to the maintenance of third-party licenses to certain background technologies.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect that our research and development expenses will increase substantially over the next several years as we conduct our clinical trials of fimepinostat, CA-4948 and CA-170; prepare regulatory filings for our product candidates; continue to develop additional product candidates; and potentially advance our product candidates into later stages of clinical development.

The successful development and commercialization of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates. This uncertainty is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the scope, quality of data, rate of progress and cost of clinical trials and other research and development activities undertaken by us or our collaborators;
- the results of future preclinical studies and clinical trials;
- the cost and timing of regulatory approvals and maintaining compliance with regulatory requirements;
- the cost and timing of establishing sales, marketing and distribution capabilities;
- the cost of establishing clinical and commercial supplies of our drug candidates and any products that we may develop;
- the effect of competing technological and market developments; and
- the cost and effectiveness of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

Any changes in the outcome of any of these variables with respect to the development of our product candidates could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to delay our clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time to complete clinical development of that product candidate. We may never obtain regulatory approval for any of our product candidates. Drug commercialization will take several years and millions of dollars in development costs.

A further discussion of some of the risks and uncertainties associated with completing our research and development programs on schedule, or at all, and some consequences of failing to do so, are set forth under “Part I, Item 1A—Risk Factors.”

General and Administrative. General and administrative expense consists primarily of salaries, stock-based compensation expense and other related costs for personnel in executive, finance, accounting, business development, legal, information technology, corporate communications and human resource functions. Other costs include facility costs not otherwise included in research and development expense, insurance, and professional fees for legal, patent and accounting services. Patent costs include certain patents covered under collaborations, a portion of which is reimbursed by collaborators and a portion of which is borne by us.

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Critical Accounting Policies and Estimates

The preparation of our consolidated financial statements in conformity with accounting principles generally accepted in the United States requires that we make estimates and assumptions that affect the reported amounts and disclosure of certain assets and liabilities at our balance sheet date. Such estimates and judgments include the carrying value of property and equipment and intangible assets, revenue recognition, the value of certain liabilities, debt classification and stock-based compensation. We base our estimates on historical experience and on various other factors that we believe to be appropriate under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in our consolidated financial statements, we believe that the following accounting policies are critical to understanding the judgments and estimates we use in preparing our financial statements:

Revenue Recognition

Our business strategy includes entering into collaborative license and development agreements with biotechnology and pharmaceutical companies for the development and commercialization of our drug candidates. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon achievement of clinical development and regulatory objectives, and royalties on product sales. As of January 1, 2018 we have adopted the provisions of the Financial Accounting Standards Board, or FASB, Codification Topic 606, Revenue from Contracts with Customers, or Topic 606. This guidance supersedes the provisions of FASB Codification Topic 605, Revenue Recognition.

Under the new guidance, a company can adopt Topic 606 using either the full retrospective method or the modified retrospective method. Under the full retrospective method, a company recasts the amount by which each financial statement line item presented in the current filing is affected as if the new guidance has always existed. Under the modified retrospective method, prior year financial statements would not need to be recast. Instead, a company applies the cumulative effect of initially applying the new standard as an adjustment to the opening retained earnings balance. We performed a detailed accounting assessment to quantify the effect of the transition from the former guidance to the new guidance and concluded that there was no material effect on our consolidated financial statements under either the full retrospective or the modified retrospective methods. We concluded that we will elect the modified retrospective method to avoid restatement of prior filings.

There are multiple options for the transition method under the new guidance, one of which allows a company to apply this guidance retrospectively either to all contracts at the date of initial application or only to contracts that are not completed contracts at the date of initial application. We have elected to apply the guidance to only contracts that are not completed contracts as of January 1, 2018. Our only contract not completed as of January 1, 2018 is our collaboration agreement with Genentech (see Note 3 of the notes to our consolidated financial statements included elsewhere in this annual report on Form 10-K). We assessed the potential effects to the consolidated financial statements and retained earnings and have concluded that, upon adoption of the new standard, there was no material impact.

License Fees and Multiple Element Arrangements. If a license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from non-refundable, up-front fees allocated to the license at such time as the license is transferred to the licensee and the licensee is able to use, and benefit from, the license. For licenses that are bundled 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 from non-refundable, up-front fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

If we are involved in a steering committee as part of a multiple element arrangement, we assess whether our involvement constitutes a performance obligation or a right to participate. Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort

required in an arrangement and the period over which we expect to complete our aggregate performance obligations. Appropriate methods of measuring progress include output methods and input methods. In determining the appropriate method for measuring progress, we consider the nature of service that we promise to transfer to the customer. When we decide

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on a method of measurement, we will apply that single method of measuring progress for each performance obligation satisfied over time and will apply that method consistently to similar performance obligations and in similar circumstances.

If we cannot reasonably measure our progress toward complete satisfaction of a performance obligation because we lack reliable information that would be required to apply an appropriate method of measuring progress, but we can reasonably estimate when the performance obligation ceases or the remaining obligations become inconsequential and perfunctory, then revenue is not recognized until we can reasonably estimate when the performance obligation ceases or becomes inconsequential. Revenue is then recognized over the remaining estimated period of performance. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement.

Contingent Research Milestone Payments. Under the new guidance, there exists a constraint on the amount of variable consideration included in the transaction price in that either all, or a portion, of an amount of variable consideration should be included in the transaction price. The variable consideration amount should be included only to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. The assessment of whether variable consideration should be constrained is largely a qualitative one that has two elements: the likelihood of a change in estimate, and the magnitude thereof. Variable consideration is not constrained if the potential reversal of cumulative revenue recognized is not significant, for example.

If the consideration in a contract includes a variable amount, a company will estimate the amount of consideration in exchange for transfer of promised goods or services. The consideration also can vary if a company's entitlement to the consideration is contingent on the occurrence or nonoccurrence of a future event. We consider contingent research milestone payments to fall under the scope of variable consideration, which should be estimated for revenue recognition purposes at the inception of the contract and reassessed ongoing at the end of each reporting period.

We assess whether contingent research milestones should be considered variable consideration that should be constrained and thus not part of the transaction price. This includes an assessment of the probability that all or some of the milestones revenue could be reversed when the uncertainty around whether or not the achievement of each milestone is resolved, and the amount of reversal could be significant.

GAAP provides factors to consider when assessing whether variable consideration should be constrained. All of the factors should be considered, and no factor is determinative. We consider all relevant factors.

Reimbursement of Costs. Reimbursement of research and development costs by third party collaborators is recognized as revenue over time provided we have determined that we transfer control (i.e. perform the services) of a service over time and, therefore, satisfy a performance obligation according to the provisions outlined in the ASC 606-10-25-27, Revenue Recognition.

Royalty Revenue. Since the first quarter of 2012, we have recognized royalty revenues related to Genentech's and Roche's sales of Erivedge. For arrangements that include sales-based royalties, including milestone payments based on the level 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). We expect to continue recognizing royalty revenue from Genentech's sales of Erivedge in the U.S. and in other markets where Genentech and Roche successfully obtain marketing approval, if any (see Note 3). However, a portion of Erivedge royalties will be paid to the Purchasers under the Oberland Purchase Agreement (see Note 16).

Deferred Revenue. Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets. Significant judgments are required in the application of revenue recognition guidance. Short-term deferred revenue would consist of amounts that are expected to be recognized as revenue, or applied against future co-development costs, within the next fiscal year. Amounts that we expect will not be recognized in the next fiscal year would be classified as long-term deferred revenue. However, this estimate would be based on our operating plan as of the balance sheet date and on our estimated performance periods under the collaboration in which we have recorded deferred revenues. If our operating plan or our estimated performance period would change, we could recognize a different amount of deferred revenue over the reporting

period.

With respect to each of the foregoing areas of revenue recognition, we exercise significant judgment in determining whether an arrangement contains multiple elements, and, if so, how much revenue is allocable to each element. In addition, we exercise our judgment in determining when our significant obligations have been met under such agreements and the specific time periods over which we recognized revenue, such as non-refundable, up-front license fees. To the extent that actual facts and circumstances differ from our initial judgments, our revenue recognition with respect to such transactions would change accordingly and any such change could affect our reported financial results.

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Stock-based Compensation

We account for stock-based compensation transactions using a grant-date fair-value-based method under FASB Codification Topic 718, Compensation—Stock Compensation.

We have recorded employee and director stock-based compensation expense of $3.9 million and $5.4 million for the years ended December 31, 2018 and 2017, respectively. We estimate that our stock-based compensation expense will increase in 2019 as we have granted, and expect that we may continue to grant options, in 2019 that could increase the amount of stock-based compensation ultimately recognized. The amount of the incremental employee stock-based compensation expense attributable to 2019 employee stock options to be granted will depend primarily on the number of stock options granted, the fair market value of our common stock at the respective grant dates, and the specific terms of the stock options.

We measure compensation cost for stock-based compensation at fair value, including our estimate of forfeitures, and recognize the expense as compensation expense over the period that the recipient is required to provide service in exchange for the award, which generally is the vesting period. We use the Black-Scholes option pricing model to measure the fair value of stock options. This model requires significant estimates related to the award's expected life and future stock price volatility of the underlying equity security. In determining the amount of expense to be recorded, we estimate forfeiture rates for awards, based on the probability that employees will complete the required service period. We estimate the forfeiture rate based on historical experience. If actual forfeitures differ significantly from our estimates, additional adjustments to compensation expense may be required in future periods. Ultimately, the actual expense recognized over the vesting period will only be for those shares that vest.

Fair Value Measurements

We have adopted the provisions of the FASB Codification Topic 820, Fair Value Measurements and Disclosures. Topic 820 provides a framework for measuring fair value under GAAP and requires expanded disclosures regarding fair value measurements. GAAP defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Market participants are buyers and sellers in the principal market that are (i) independent, (ii) knowledgeable, (iii) able to transact, and (iv) willing to transact.

GAAP requires the use of valuation techniques that are consistent with the market approach, the income approach and/or the cost approach. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets and liabilities. The income approach uses valuation techniques to convert future amounts, such as cash flows or earnings, to a single present amount on a discounted basis. The cost approach is based on the amount that currently would be required to replace the service capacity of an asset (replacement cost). Valuation techniques should be consistently applied. GAAP also establishes a fair value hierarchy which requires an entity to maximize the use of observable inputs, where available, and minimize the use of unobservable inputs when measuring fair value. The standard describes three levels of inputs that may be used to measure fair value:

Level 1 Quoted prices in active markets for identical assets or liabilities.

Level 2 Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Our cash equivalents and short- and long-term investments have been classified as either Level 1 or Level 2 assets. We do not hold any asset-backed or auction rate securities. Short-term accounts receivable and accounts payable are reflected in the consolidated financial statements at net realizable value, which approximates fair value due to the short-term nature of these instruments.

While we believe our valuation methodologies are appropriate and consistent with other market participants, the use of different methodologies or assumptions to determine the fair value of certain financial instruments could result in a different estimate of fair value at the reporting date.

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Long-lived Assets

Long-lived assets consist primarily of property and equipment and goodwill. Property and equipment is stated at cost and depreciated over the estimated useful lives of the related assets using the straight-line method. Determining the economic lives of property and equipment requires us to make significant judgments that can materially impact our operating results. If it were determined that the carrying value of our other long-lived assets might not be recoverable based upon the existence of one or more indicators of impairment, we would measure an impairment based on application of the FASB Codification Topic 360-10-05, Impairment or Disposal of Long-Lived Assets.

We evaluate our goodwill for impairment at least annually or more frequently if an indicator of potential impairment exists. In performing our evaluations of impairment, we determine fair value using widely accepted valuation techniques, including discounted cash flows. These calculations contain uncertainties as they require us to make assumptions related to future cash flows, projected useful lives of assets and the appropriate discount rate to reflect the risk inherent in future cash flows. We must also make assumptions regarding industry economic factors and the profitability of future business strategies. If actual results are not consistent with our estimates and assumptions used in estimating future cash flows and asset fair values, we may be exposed to a material impairment charge. As a single reporting unit, we completed our annual goodwill impairment tests in December 2018 and 2017, and determined that as of those dates our fair value exceeded the carrying value of our net assets. Accordingly, no goodwill impairment was recognized in either of the years ended December 31, 2018 or 2017.

Debt Classification

In December 2012, our wholly-owned subsidiary, Curis Royalty, received a $30.0 million loan at an annual interest rate of 12.25% pursuant to a credit agreement between Curis Royalty and BioPharma-II. In connection with the loan, we transferred to Curis Royalty our right to receive certain future royalty and royalty-related payments on the commercial sales of Erivedge that we received from Genentech. The loan and accrued interest was being repaid by Curis Royalty using such royalty and royalty-related payments. In March 2017, we and Curis Royalty entered into a new credit agreement with HealthCare Royalty Partners III, L.P., or HealthCare Royalty, for the purpose of refinancing and terminating the loan from BioPharma-II. Accordingly, HealthCare Royalty made a $45.0 million loan at an annual interest rate of 9.95% to Curis Royalty, which was used in part to pay off $18.4 million in remaining loan obligations to BioPharma-II under the prior loan with the residual proceeds of $26.6 million distributed to us as sole equity member of Curis Royalty.

The final maturity date of the HealthCare Royalty loan was the earlier of such date as the principal is paid in full, or Curis Royalty's rights to receive royalties under the collaboration agreement with Genentech terminate. On March 22, 2019, we terminated and repaid in full all amounts outstanding under the HealthCare Royalty loan, consisting of approximately $33.8 million to repay in full the remaining loan principal and approximately $3.4 million to HealthCare Royalty in accrued and unpaid interest and prepayment fees.

Our discussion of our critical accounting policies is not intended to be a comprehensive discussion of all of our accounting policies. In many cases, the accounting treatment of a particular transaction is specifically dictated by generally accepted accounting principles, with no need for management's judgment in their application. There are also areas in which management's judgment in selecting any available alternative would not produce a materially different result.

Results of Operations (all amounts rounded to the nearest thousand)

Years Ended December 31, 2018 and 2017

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

	For the Year Ended December 31,		Percentage Increase/ (Decrease)	
	2018	2017	2018 v. 2017	
Revenues	$10,428	$9,898	5	%
Cost of royalty revenues	563	496	13	%

Research and development	24,413	45,096	(46	)%
General and administrative	14,785	14,066	5	%
Total other expense, net	3,242	3,557	(9	)%
Net loss	$(32,575)	$(53,317)	39	%

Revenues

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Total revenues are summarized as follows

	For the Year Ended December 31,		Percentage Increase/ (Decrease)
	2018	2017	2018 v. 2017
REVENUES:			
Royalties	10,421	9,849	6 %
Research and development, net	7	49	(85)%
Total revenues	$10,428	$9,898	5 %

Total revenues increased by $0.5 million, or 5%, to $10.4 million for the year ended December 31, 2018 as compared to $9.9 million for the year ended December 31, 2017, related to an increase in royalty revenues arising from Genentech and Roche's net sales of Erivedge during the current year as compared to the prior year period.

Cost of Royalty Revenues. Cost of royalty revenues increased by $0.1 million, to $0.6 million for the year ended December 31, 2018 as compared to $0.5 million for the year ended December 31, 2017. The increase reflects our obligation to make payments to two university licensors on royalties that Curis Royalty earns on Genentech's net sales of Erivedge, which increased in 2018 as compared to 2017.

Research and Development Expenses. Research and development expenses are summarized as follows:

	For the Year Ended December 31,		Percentage Increase/ (Decrease)
	2018	2017	2018 v. 2017
Direct research and development expenses	$10,941	$31,468	(65)%
Employee-related expenses	11,378	11,752	(3)%
Facilities, depreciation and other expenses	2,094	1,876	12 %
Total research and development expenses	$24,413	$45,096	(46)%

Our total research and development expenses decreased by $20.7 million, or 46%, to $24.4 million for the year ended December 31, 2018, as compared to $45.1 million for the prior year. Direct research and development expenses decreased $20.5 million for the year ended December 31, 2018 as compared to the prior year period, which was primarily due to aggregate payments to Aurigene of $7.5 million, for an exclusivity option which were paid in 2017 as well as decreased costs related to ongoing clinical activities for CA-170. These costs included decreased clinical site, patient, clinical research organization, formulation and manufacturing and consulting costs for our ongoing Phase 1 clinical trial. Employee-related expenses decreased $0.4 million for the year ended December 31, 2018 as compared to the prior year period, which was primarily due to a reduction in headcount which occurred in the fourth quarter of 2018.

We expect that a majority of our research and development expenses for the foreseeable future will be incurred in connection with our efforts to advance our programs, including clinical and preclinical development costs, option exercise fees, and potential payments upon achievement of certain milestones.

General and Administrative Expenses. General and administrative expenses are summarized as follows:

	For the Year Ended December 31,		Percentage Increase/ (Decrease)
	2018	2017	2018 v. 2017
Personnel	$5,277	$4,620	14 %
Occupancy and depreciation	553	460	20 %
Legal services	2,906	2,055	41 %

Professional and consulting services	2,142	1,835	17	%
Insurance costs	409	404	1	%
Other general and administrative expenses	869	819	6	%
Stock-based compensation	2,630	3,873	(32	)%
Total general and administrative expenses	$14,785	$14,066	5	%

General and administrative expenses increased by $0.7 million, or 5%, during the year ended December 31, 2018 as compared to the prior year. The increase in general administrative expense was driven primarily by higher personnel, legal,

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professional and consulting services and other administrative expenses, offset by lower stock-based compensation for the period.

Other Expense (Income). For the years ended December 31, 2018 and 2017, interest expense was $3.9 million and $4.0 million, respectively. The decrease in interest expense in the current year was related to a lower principal balance on Curis Royalty's outstanding debt with HealthCare Royalty, which was refinanced in the first quarter of 2017. For the years ended December 31, 2018 and 2017, interest income was $0.7 million and $0.5 million, respectively.

Net Loss Applicable to Common Stockholders

As a result of the foregoing, we incurred a net loss applicable to common stockholders of $32.6 million for the year ended December 31, 2018 and $53.3 million for the year ended December 31, 2017.

Liquidity and Capital Resources

We have financed our operations primarily through private and public placements of our equity securities, license fees, contingent cash payments and research and development funding from our corporate collaborators, debt financings, and the monetization of certain royalty rights.

All references to shares of common stock outstanding, average number of shares outstanding and per share amounts in these consolidated financial statements and notes to consolidated financial statements have been restated to reflect the reverse stock split on a retroactive basis.

Public Offering of Common Stock

On September 18, 2017, we entered into an underwriting agreement with Baird as underwriter, under which we issued and sold 4,000,000 shares of our common stock. The offering price to the public was $9.25 per share, and the underwriter agreed to purchase the shares from us pursuant to the underwriting agreement at a price of $8.90 per share. We received net proceeds from the sale of the shares, after deducting the underwriting discounts and commissions and estimated offering expenses, of $35.3 million. We incurred offering expenses of $0.3 million related to this transaction.

Placement of Equity Securities

On July 2, 2015, we entered into a sales agreement with Cowen and Company, or Cowen, pursuant to which we may sell from time to time up to $30.0 million of our common stock through an "at-the-market" equity offering program, under which Cowen will act as sales agent. Subject to the terms and conditions of the sales agreement, Cowen may sell the common stock by methods deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on the Nasdaq Global Market, on any other existing trading market for the common stock, or to or through a market maker other than on an exchange. We are not obligated to sell any of the common stock under this sales agreement. Either Cowen or we may at any time suspend solicitations and offers under the sales agreement upon notice to the other party. The sales agreement may be terminated at any time by either party upon written notice to the other party, in the manner specified in the sales agreement. The aggregate compensation payable to Cowen will be 3% of the gross sales price of the common stock sold pursuant to the sales agreement. The shares sold under the sales agreement have been issued and sold pursuant to the universal shelf registration statement on Form S-3, filed with the Securities and Exchange Commission on July 2, 2015. The remaining shares that may be sold under the sales agreement are expected to be issued and sold, if at all, pursuant to the currently effective universal shelf registration statement on Form S-3, filed with the Securities and Exchange Commission on May 3, 2018. As of December 31, 2018, we have sold an aggregate of 420,796 shares of common stock pursuant to this sales agreement, for net proceeds of $6.2 million.

Debt Financing

In December 2012, our wholly-owned subsidiary, Curis Royalty, received a $30.0 million loan, at an annual interest rate of 12.25%, pursuant to a credit agreement with BioPharma-II. In connection with the loan, we transferred to Curis Royalty our right to receive certain future royalty and royalty-related payments on the commercial sales of Erivedge that we may receive from Genentech. The loan and accrued interest was being repaid by Curis Royalty using such royalty and royalty-related payments. The loan constituted an obligation of Curis Royalty, and was non-recourse to us. The final maturity date of the loan was the earlier of such date that the principal was paid in full, or Curis Royalty's right to receive royalties under the collaboration agreement with Genentech was terminated.

In March 2017, we and Curis Royalty entered into a credit agreement with HealthCare Royalty for the purpose of refinancing our and Curis Royalty's existing royalty financing arrangement with BioPharma-II. On the effective date of the credit agreement with Healthcare Royalty, the prior loan was terminated in its entirety. Pursuant to the credit agreement,

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HealthCare Royalty made a $45.0 million loan at an annual interest rate of 9.95% to Curis Royalty, which was used to pay off the $18.4 million in remaining loan obligations to BioPharma-II under the prior loan. The residual proceeds of the loan were distributed to us as sole equity member of Curis Royalty. The final maturity date of the loan was the earlier of such date that the principal is paid in full, or Curis Royalty's right to receive royalties under the collaboration agreement with Genentech is terminated.

Payments to HealthCare Royalty for the year ended December 31, 2018 totaled $10.0 million, of which $6.1 million has been applied to the principal, and the remainder satisfying interest obligations. As of December 31, 2018, Curis Royalty owed a total of $35.8 million, gross of issuance costs, to HealthCare Royalty, including accrued interest. On March 22, 2019, we terminated, and repaid all amounts outstanding under the loan with HealthCare Royalty. For further discussion please refer to “Part II, Item 9B. Other Information - Royalty Interest Purchase Agreement."

Milestone Payments and Monetization of Royalty Rights

We have received aggregate milestone payments totaling $59.0 million under our collaboration with Genentech since 2012. In addition, we began receiving royalty revenues in 2012 in connection with Genentech’s sales of Erivedge in the U.S. and Roche’s sales of Erivedge outside of the U.S. Erivedge royalty revenues received after December 2012 have been used to repay Curis Royalty’s outstanding principal and interest under the loans due to BioPharma-II and HealthCare Royalty. A portion of Erivedge royalty and royalty-related revenue payments will be paid to the Purchasers pursuant to the Oberland Purchase Agreement. We also remain entitled to receive any contingent payments upon achievement of clinical development objectives and royalty payments related to sales of Erivedge pursuant to our collaboration agreement with Genentech and certain contingent payments upon achievement of contractually-specified royalty revenue payment amounts related to sales of Erivedge pursuant to the Oberland Purchase Agreement. Upon receipt of any such payments, as well as on royalties received in any territory other than Australia, we are required to make payments to certain university licensors totaling 5% of these amounts. In addition, for royalties that Curis Royalty receives from Roche’s sales of Erivedge in Australia, we are obligated to make payments to university licensors of 2% of Roche’s direct net sales in Australia until the expiration of the patent in April 2019. After April 2019, the amount we are obligated to pay will decrease to 5% of the royalty payments that Curis Royalty receives from Genentech.

At December 31, 2018, our principal sources of liquidity consisted of cash, cash equivalents, and investments of $24.3 million, excluding our restricted investments of $0.2 million. Our cash and cash equivalents are highly liquid investments with a maturity of three months or less at date of purchase, and consist of investments in money market funds with commercial banks and financial institutions, as well as short-term commercial paper and government obligations. We maintain cash balances with financial institutions in excess of insured limits.

Cash Flows

Cash flows for operations have primarily been used for salaries and wages for our employees, facility and facility-related costs for our office and laboratory, fees paid in connection with preclinical and clinical studies, laboratory supplies, consulting fees and legal fees. We expect that costs associated with clinical studies will increase in future periods.

Net cash used in operating activities of $30.1 million during the year ended December 31, 2018 was primarily the result of our net loss for the period of $32.6 million, offset by non-cash charges consisting of stock-based compensation, amortization of debt issuance costs, and depreciation, totaling $4.2 million. Accounts payable and accrued and other liabilities increased $1.9 million, accounts receivable decreased $0.2 million related to an decrease in fourth quarter Erivedge royalties, and prepaid expenses and other assets increased $0.2 million.

Net cash used in operating activities of $48.4 million during the year ended December 31, 2017 was primarily the result of our net loss for the period of $53.3 million, offset by non-cash charges consisting of the stock issuance to Aurigene as partial consideration for the collaboration agreement with Aurigene, stock-based compensation, and depreciation totaling $5.7 million. Accounts payable and accrued and other liabilities increased $0.4 million, accounts receivable increased $0.6 million related to an increase in Erivedge royalties and prepaid expenses and other assets increased $0.3 million.

We expect to continue to use cash in operations as we seek to advance our drug candidates and our programs under our collaboration agreement with Aurigene. In addition, in the future we may owe royalties and other contingent payments to our licensors based on the achievement of developmental milestones, product sales and other specified objectives.

Investing activities provided cash of $21.4 million and used cash of $3.6 million for the years ended December 31, 2018 and 2017, respectively, resulting primarily from net investment activity from purchases and sales or maturities of investments for the respective periods. The decrease in purchases of investments during the year ended December 31, 2018 resulted from operational funding requirements in 2018.

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Financing activities used cash of $6.0 million for the year ended December 31, 2018. We made principal payments on Curis Royalty's loan to HealthCare Royalty of $6.1 million, and received $0.1 million in proceeds from the sale of common stock related to our share based compensation plans.

Financing activities provided cash of $64.2 million for the year ended December 31, 2017. We received $26.6 million in net proceeds from our loan with HealthCare Royalty, $41.5 million in net proceeds from our underwritten public offering of common stock and at-the-market sales pursuant to our sales agreement with Cowen and $1.1 million from the exercise of stock options and purchases under our employee stock purchase plan during the same period. These proceeds were offset by the principal payments on Curis Royalty’s loans with BioPharma-II and HealthCare Royalty of $5.0 million in the aggregate.

Funding Requirements

We have incurred significant losses since our inception. As of December 31, 2018, we had an accumulated deficit of approximately $984.8 million. We will require substantial funds to continue our research and development programs and to fulfill our planned operating goals. In particular, our currently planned operating and capital requirements include the need for working capital to support our research and development activities for fimepinostat, CA-4948, CA-170 and other programs under our collaboration with Aurigene, and to fund our general and administrative costs and expenses. We anticipate that our existing cash, cash equivalents and investments at December 31, 2018 plus net proceeds from the upfront consideration we received in connection with entering into the Oberland Purchase Agreement, should enable us to maintain our planned operations into the second half of 2020.We will need to raise additional capital or incur indebtedness to continue to fund our operations in the future. Our ability to raise additional funds will depend on financial, economic and market conditions, many of which are outside of our control, and we may be unable to raise financing when needed, or on terms favorable to us. If necessary funds are not available, we may have to delay, reduce the scope of, or eliminate some of our development programs, potentially delaying the time to market for, or preventing the marketing of, any of our product candidates, which could adversely affect our business prospects, and we may be unable to continue our operations. Factors that may affect our planned future capital requirements and accelerate our need for additional working capital include the following:

- unanticipated costs in our research and development programs;
- the timing and cost of obtaining regulatory approvals for our drug candidates and maintaining compliance with regulatory requirements;
- the timing and amount of option exercise fees, milestone payments, royalties and other payments, including payments due to licensors, including Aurigene, for patent rights and technology used in our drug development programs;
- the costs of commercialization activities for any of our drug candidates that receive marketing approval, to the extent such costs are our responsibility, including the costs and timing of establishing drug sales, marketing, distribution and manufacturing capabilities;
- unplanned costs to prepare, file, prosecute, defend and enforce patent claims and other patent-related costs, including litigation costs and technology license fees; and
- unexpected losses in our cash investments or an inability to otherwise liquidate our cash investments due to unfavorable conditions in the capital markets.

Subject to specified exceptions, we and Aurigene agreed to collaborate exclusively with each other on the discovery, research, development and commercialization of programs and compounds within immuno-oncology for an initial period of approximately two years from the effective date of the collaboration agreement. At our option, and subject to specified conditions, we may extend such exclusivity for up to three additional one-year periods by paying to Aurigene additional exclusivity option fees on an annual basis. We exercised the first one-year exclusivity option in 2017. The fee for this exclusivity option exercise was $7.5 million, which we paid in two equal installments in 2017. We elected not to exercise our exclusivity option in 2018 and did not make the $10.0 million payment required for this additional exclusivity in 2018. As a result of this election to not further exercise our exclusivity option, we no longer operate under the broad immuno-oncology exclusivity with Aurigene. In 2019 we have elected not to further exercise our exclusivity option related to the IRAK4 and PD1/VISTA programs and thus will not be making the $2.0 million payment required for this continued exclusivity.

We have historically derived a portion of our operating cash flow from our receipt of milestone payments under collaboration agreements with third parties. However, we cannot predict whether we will receive additional milestone payments under existing or future collaborations or arrangements.

To become and remain profitable, we, either alone or with collaborators, must develop and eventually commercialize one or more drug candidates with significant market potential. This will require us to be successful in a range of challenging

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activities, including completing preclinical testing and clinical trials of our drug candidates, obtaining marketing approval for these drug candidates, manufacturing, marketing and selling those drugs for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. Other than Erivedge, which is being commercialized by Genentech and Roche, our most advanced drug candidates are currently only in early clinical testing.

For the foreseeable future, we will need to spend significant capital in an effort to develop and commercialize products and we expect to incur substantial operating losses. Our failure to become and remain profitable would, among other things, depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our research and development programs or continue our operations.

Contractual Obligations

As of December 31, 2018 we had contractual obligations and other commitments as follows:

	Payment Due By Period (amounts in 000's)				
	Total	Less than One Year	One to Three Years	Three to Five Years	More than Five Years
Debt obligations under credit agreement (1)	$46,492	$ 10,037	$ 21,619	$ 14,836	$ —
Operating lease obligations (2)	1,170	1,002	168	—	—
Outside service obligations (3)	795	450	345	—	—
Licensing obligations (4)	404	320	84	—	—
Total future obligations	$48,861	$ 11,809	$ 22,216	$ 14,836	$ —

(1) As of December 31, 2018, the outstanding balance, including interest, on the debt was $35.8 million. The above amounts reflect management's estimates as of December 31, 2018 of repayments, including accrued interest payments, based on the terms of Curis Royalty's credit facility with HealthCare Royalty, and assumptions about potential future Erivedge royalties. In March 2019 we terminated and repaid all amounts outstanding under the loan with HealthCare Royalty. For further discussion please refer to "Part II, Item 9B. Other Information - Royalty Interest Purchase Agreement."

(2) We are party to a lease agreement with the Trustees of Lexington Office Realty Trust pursuant to which we lease 24,529 square feet of property for office, research and laboratory space located at 4 Maguire Road in Lexington, Massachusetts. The term of the lease agreement commenced on December 1, 2010 and, pursuant to a second amendment to the lease agreement on November 1, 2017, it will expire on February 29, 2020. The total remaining cash obligation for the base rent over the second amended term of the lease agreement is approximately $1.2 million. In addition to the base rent, we are responsible for our share of operating expenses and real estate taxes, in accordance with the terms of the lease agreement. Amounts include contractual rent payments as defined in the agreement.

(3) Outside service obligations consist of agreements we have with outside labs, consultants and various other service organizations. Obligations to clinical research organizations, medical centers and hospitals conducting our clinical trials are included in our financial statements for costs incurred as of December 31, 2018. Our obligations under these types of arrangements are limited to actual costs incurred for services performed and do not include any contingent or milestone payments.

(4) Licensing obligations include only obligations that are known to us as of December 31, 2018. In the future, we may owe royalties and other contingent payments to our licensors based on the achievement of developmental milestones, product sales, and other specified objectives. These future obligations, including those related to Aurigene, Genentech, Debiopharm and LLS, are not reflected in the table above as these payments are contingent upon achievement of developmental and commercial milestones, the likelihood and timing of which cannot be reasonably estimated at this time. These contingent obligations are further described under the "Our Collaborations and License Agreements" section.

Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements as of December 31, 2018.

Inflation

We believe that inflation has not had a significant impact on our revenue and results of operations since inception.

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New Accounting Pronouncements

See Note 2 to our consolidated financial statements included in Part II, Item 8, “Financial Statements and Supplementary Data,” of this annual report on Form 10-K for a description of recent accounting pronouncements applicable to our business.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not required.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Management’s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) or 15d-15(f) promulgated under the Securities Exchange Act of 1934, as amended, as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of management and our board of directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

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

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2018. In making this assessment our management used the criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO.

Based on our assessment, management concluded that, as of December 31, 2018, our internal control over financial reporting is effective based on the criteria established in Internal Control—Integrated Framework (2013) issued by COSO.

The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, who has issued an attestation report on our internal control over financial reporting that appears herein.

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Report of Independent Registered Public Accounting Firm
To the Board of Directors and Stockholders of Curis, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Curis, Inc. and its subsidiaries (the “Company”) as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, stockholders’ equity and cash flows for the years then ended, including the related notes (collectively referred to as the “consolidated financial statements”). We also have audited the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management’s Report on Internal Control over Financial Reporting appearing under Item 8. Our responsibility is to express opinions on the Company’s consolidated financial statements and on the Company's internal control over financial reporting 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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements 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. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Emphasis of matter

As discussed in Note 1 to the consolidated financial statements, the Company will require additional financing to fund planned future operations. Management’s plans in regard to this matter are described in Note 1.

Definition and Limitations of Internal Control over Financial Reporting

A company’s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company’s internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the

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

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

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 26, 2019

We have served as the Company's auditor since 2002.

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CURIS, INC. AND SUBSIDIARIES
Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31,	
	2018	2017
ASSETS		
Current Assets:		
Cash and cash equivalents	$23,636	$38,288
Investments	634	21,944
Accounts receivable	2,864	3,073
Prepaid expenses and other current assets	827	989
Total current assets	27,961	64,294
Property and equipment, net	267	366
Long-term investment—restricted	153	153
Goodwill	8,982	8,982
Other assets	2	3
Total assets	$37,365	$73,798
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$2,909	$5,423
Accrued liabilities	3,457	2,793
Current portion of long-term debt, net	6,884	5,886
Total current liabilities	13,250	14,102
Long-term debt, net	28,600	35,669
Other long-term liabilities	11	34
Total liabilities	41,861	49,805
Stockholders' Equity:		
Common stock, $0.01 par value—67,500,000 shares authorized, 33,159,253 shares issued and outstanding at December 31, 2018; 45,000,000 shares authorized, 33,075,949 shares issued and 32,831,380 shares outstanding at December 31, 2017	332	331
Additional paid-in capital	980,012	977,453
Treasury stock, at cost, 0 shares at December 31, 2018 and 244,569 shares at December 31, 2017	—	(1,524)
Accumulated deficit	(984,840)	(952,265)
Accumulated other comprehensive loss	—	(2)
Total stockholders' equity	(4,496)	23,993
Total liabilities and stockholders' equity	$37,365	$73,798

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

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CURIS, INC. AND SUBSIDIARIES
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Years Ended December 31,	
	2018	2017
Revenues:		
Royalties	$10,421	$9,849
Research and development, net	7	49
Total revenues	10,428	9,898
Costs and Expenses:		
Cost of royalties	563	496
Research and development	24,413	45,096
General and administrative	14,785	14,066
Total costs and expenses	39,761	59,658
Loss from operations	(29,333)	(49,760)
Other (Expense) Income:		
Interest income	684	513
Other expense	—	(104)
Interest expense	(3,926)	(3,966)
Total other expense, net	(3,242)	(3,557)
Net loss	$(32,575)	$(53,317)
Net Loss per Common Share (Basic and Diluted)	$(0.98)	$(1.79)
Weighted Average Common Shares (Basic and Diluted)	33,118,393	29,826,693
Net Loss	$(32,575)	$(53,317)
Other comprehensive gain, net of tax:		
Unrealized gain on marketable securities	2	2
Comprehensive loss	$(32,573)	$(53,315)

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

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CURIS, INC. AND SUBSIDIARIES
Consolidated Statements of Stockholders' Equity
(In thousands, except share data)

	Common Stock		Additional Paid-in Capital	Treasury Stock	Accumulated Deficit	Accumulated Other Comprehensive Income/(Loss)	Total Stockholders' Equity
	Shares	Amount					
Balance, December 31, 2016	28,469,330	$ 285	$929,642	$(1,524)	$(898,948)	$ (4)	$ 29,451
Issuances of common pursuant to sales of shares in the Company's public offering, net of $0.3 million of issuance costs	4,000,000	40	35,131	—	—	—	35,171
Issuances of common pursuant to sales of shares from the Company's ATM, net of $0.2 million of commissions	420,796	4	6,194	—	—	—	6,198
Issuances of common stock upon the exercise of stock options and for purchases under the ESPP	190,700	2	1,169	—	—	—	1,171
Exercise of stock options settled in shares	(4,877)	—	(42)	—	—	—	(42)
Recognition of employee stock-based compensation	—	—	5,365	—	—	—	5,365
Non-employee stock-based compensation expense, including mark-to-market	—	—	(6)	—	$—	—	(6)
Other comprehensive gain	—	—	—	—	—	2	2
Net loss	—	—	—	—	(53,317)	—	(53,317)
December 31, 2017	33,075,949	331	977,453	(1,524)	(952,265)	(2)	23,993
Issuance of stock under grant of restricted stock awards	294,250	3	(3)	—	—	—	—
Issuances of common stock upon the exercise of stock options and for purchases under the ESPP	101,623	1	142	—	—	—	143
Recognition of employee stock-based compensation	—	—	3,941	—	—	—	3,941
Cancellation of restricted stock awards	(68,000)	(1)	1	—	—	—	—
Retirement of Treasury Stock	(244,569)	(2)	(1,522)	1,524	—	—	—
Other comprehensive gain	—	—	—	—	—	2	2
Net loss	—	—	—	—	(32,575)	—	(32,575)
Balance, December 31, 2018	33,159,253	$ 332	$980,012	$—	$(984,840)	$ —	$ (4,496)

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

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CURIS, INC. AND SUBSIDIARIES
Consolidated Statements of Cash Flows
(In thousands)

	Years Ended December 31,	
	2018	2017
Cash Flows from Operating Activities:		
Net loss	$(32,575)	$(53,317)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	177	235
Stock-based compensation expense	3,940	5,359
Amortization of debt issuance costs	35	144
Non-cash interest income	(147)	(53)
Loss on sale of fixed assets	7	—
Changes in operating assets and liabilities:		
Accounts receivable	209	(614)
Prepaid expenses and other assets	162	267
Accounts payable and accrued and other liabilities	(1,873)	(376)
Total adjustments	2,510	4,962
Net cash used in operating activities	(30,065)	(48,355)
Cash Flows from Investing Activities:		
Purchases of investments	(26,741)	(51,121)
Sales/maturities of investments	48,200	47,679
Expenditures for property and equipment	(85)	(188)
Net cash provided by (used in) investing activities	21,374	(3,630)
Cash Flows from Financing Activities:		
Proceeds from issuance of common stock associated with offerings, net of issuance costs (see Note 11)	—	41,546
Proceeds from issuance of common stock under the Company’s share-based compensation plans	143	1,138
Proceeds from new credit agreement with HealthCare Royalty	—	45,000
Payment of debt issuance costs	—	(192)
Payment on termination of former credit agreement with BioPharma	—	(18,303)
Payments made on Curis Royalty’s debt	(6,104)	(4,954)
Net cash (used in)/provided by financing activities	(5,961)	64,235
Net (decrease)/increase in cash and cash equivalents	(14,652)	12,250
Cash and cash equivalents, beginning of period	38,288	26,038
Cash and cash equivalents, end of period	$23,636	$38,288
Supplemental cash flow data:		
Cash paid for interest	$3,919	$3,942

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

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Notes to Consolidated Financial Statements

(1) Nature of Business

Curis, Inc. is a biotechnology company focused on the development of first-in-class and innovative therapeutics for the treatment of cancer. As used throughout these consolidated financial statements, the term “the Company” refers to the business of Curis, Inc. and its wholly-owned subsidiaries, except where the context otherwise requires, and the term “Curis” refers to Curis, Inc.

The Company conducts its research and development programs both internally and through strategic collaborations. The Company’s clinical stage drug candidates are fimepinostat, CA-4948, and CA-170:

- Fimepinostat is currently being explored in clinical studies in patients with MYC-altered diffuse large B-cell lymphoma (DLBCL) and solid tumors and has been granted Orphan Drug Designation and Fast Track Designation for the treatment of DLBCL by the U.S. Food and Drug Administration, or FDA in April 2015 and May 2018, respectively. The Company is planning a combination study with venetoclax in DLBCL patients with alterations in both MYC and the BCL2 gene, also referred to as double-hit lymphoma, with planned enrollment commencing in the first half of 2019. The Company expects to report initial clinical data from this combination study in the second half of 2019.
- CA-4948 is being tested in a dose escalating clinical trial in patients with non-Hodgkin lymphomas, including those with myeloid differentiation primary response 88, or MYD88, alterations. The Company expects to report initial clinical data from this study in mid-year 2019.
- CA-170 is currently undergoing testing in a clinical study in patients with advanced solid tumors and lymphomas. The Company has amended the current protocol for the study to include mesothelioma patients. The Company announced in January 2019 that it had begun enrollment of these patients and expects to report initial clinical data from this study with respect to mesothelioma in the second half of 2019.

The Company’s pipeline also includes CA-327, which is a pre-Investigational New Drug (“IND”) stage oncology drug candidate. The Company is party to a collaboration with F. Hoffmann-La Roche Ltd, or Roche, and Genentech Inc., or Genentech, a member of the Roche Group, under which Roche and Genentech are commercializing Erivedge, a first-in-class orally-administered small molecule Hedgehog signaling pathway inhibitor. Erivedge (vismodegib) is approved for the treatment of advanced basal cell carcinoma, or BCC.

In January 2015, and as amended in September 2016, the Company entered into a collaboration, option and license agreement focused on immuno-oncology and selected precision oncology targets with Aurigene Discovery Technologies Limited, or "Aurigene".

The collaboration with Aurigene is comprised of multiple programs, and the Company has the option to exclusively license each program, including data, intellectual property and compounds associated therewith, once a development candidate is nominated within such program. In October 2015, the Company exercised options to license two programs under this collaboration. The first licensed program is in the immuno-oncology field and the Company has named CA-170, an orally-available small molecule antagonist of two immune checkpoints, V-domain Ig suppressor of T-cell activation (VISTA) and programmed death ligand-1 (PDL1), as the development candidate from this program. The second licensed program is in the precision oncology field and the Company has named CA-4948, an orally-available small molecule inhibitor of Interleukin-1 receptor-associated kinase 4 (IRAK4) as the development candidate. In October 2016, the Company exercised its option to license a third program in the collaboration, and designated CA-327, a distinct orally available small molecule antagonist of two immune checkpoints PDL1 and T-cell immunoglobulin and mucin domain containing protein-3 (TIM3) as the development candidate from this program. In March 2018, the Company exercised its option to license a fourth program, which is an immuno-oncology program.

The Company operates in a single reportable segment, which is the research and development of innovative cancer therapeutics. The Company expects that any products that are successfully developed and commercialized would be used in the healthcare industry and would be regulated in the United States by the FDA and in overseas markets by similar regulatory authorities.

The Company is subject to risks common to companies in the biotechnology industry as well as risks that are specific to the Company’s business, including, but not limited to: the Company’s ability to advance and expand its research and

development programs; the Company's reliance on Aurigene to successfully discover and preclinically develop drug candidates under the parties' collaboration agreement; the Company's reliance on Roche and Genentech to successfully commercialize Erivedge in the approved indication of advanced BCC and to progress its clinical development in indications other than BCC; the Company's ability to obtain adequate financing to fund its operations; the ability of the Company and its wholly-owned subsidiary, Curis Royalty, LLC, or Curis Royalty, to satisfy the terms of the royalty interest purchase agreement, or the Oberland Purchase Agreement, with TPC Investments I LP and TPC Investments II LP, referred to as the Purchasers, each of which is a Delaware limited partnership managed by Oberland Capital Management, LLC, and Lind SA LLC, referred to as the

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Agent, a Delaware limited liability company managed by Oberland Capital Management, LLC, as collateral agent for the Purchasers; the Company's ability to obtain and maintain necessary intellectual property protection; development by the Company's competitors of new or better technological innovations; the Company's dependence on key personnel; the Company's ability to comply with regulatory requirements; the Company's ability to obtain and maintain applicable regulatory approvals and commercialize any approved product candidates, and the Company's ability to execute on its overall business strategies.

The Company's future operating results will largely depend on the progress of drug candidates currently in its development pipeline and the magnitude of payments that it may receive and make under its current and potential future collaborations. The results of the Company's operations have varied and will likely continue to vary significantly from year to year and quarter to quarter and depend on a number of factors, including, but not limited to: the timing, outcome and cost of the Company's preclinical studies and clinical trials for its drug candidates; Aurigene's ability to successfully discover and develop preclinical programs under the Company's collaboration with Aurigene, as well as the Company's decision to exclusively license and further develop programs under this collaboration; Roche and Genentech's ability to successfully commercialize Erivedge; and positive results in Roche and Genentech's ongoing clinical trials.

The Company has incurred losses and negative cash flows from operations since its inception. As of December 31, 2018, the Company had an accumulated deficit of approximately $984.8 million, incurred a loss of $32.6 million and used $30.1 million of cash in operations. The Company expects to continue to generate operating losses in the foreseeable future. The Company anticipates that its $24.3 million of existing cash, cash equivalents and investments at December 31, 2018 plus the net proceeds of $27.5 million from the upfront consideration it received in connection with entering into the Oberland Purchase Agreement, will be sufficient to fund its operating expenses and capital requirements, based upon its current operating plan, for at least the next twelve months from the issuance date of the financial statements. The Company will need to raise additional capital or incur indebtedness to continue to fund its operations in the future. The Company's ability to raise additional funds will depend, among other factors, on financial, economic and market conditions, many of which are outside of its control and it may be unable to raise financing when needed, or on terms favorable to the Company. If necessary funds are not available, the Company may have to delay, reduce the scope of, or eliminate some of its development programs, potentially delaying the time to market for or preventing the marketing of any of its product candidates.

Reverse Stock Split

On May 29, 2018, the Company effected a 1-for-5 reverse stock split of its common stock. All references to shares of common stock outstanding, average number of shares outstanding and per share amounts for all periods presented in the accompanying financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split on a retroactive basis (see Note 11).

(2) Summary of Significant Accounting Policies

(a) USE OF ESTIMATES

The preparation of the Company's consolidated financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts and disclosure of revenue, expenses and certain assets and liabilities at the balance sheet date. Such estimates include revenue recognition, including estimates of the performance obligations under the Company's collaboration agreements; the estimated repayment term of the Company's debt and related short- and long-term classification; the collectability of receivables; the carrying value of property and equipment and intangible assets; the assumptions used in the Company's valuation of stock-based compensation and the value of certain investments and liabilities. Actual results may differ from such estimates.

(b) CONSOLIDATION

The accompanying consolidated financial statements include the Company and its wholly-owned subsidiaries, Curis Royalty (see Note 10) and Curis Securities Corporation, Inc. The Company has eliminated all intercompany transactions in each of the years ended December 31, 2018 and 2017.

(c) REVENUE RECOGNITION

The Company’s business strategy includes entering into collaborative license and development agreements with biotechnology and pharmaceutical companies for the development and commercialization of the Company’s drug candidates. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon achievement of clinical development and regulatory objectives, and royalties on product sales. As of January 1, 2018 the Company follows the provisions of the Financial Accounting Standards Board, or FASB, Codification Topic 606, Revenue from Contracts with Customers, or Topic 606. This guidance supersedes the provisions of FASB Codification Topic 605, Revenue Recognition.

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Under the new guidance, a company can adopt Topic 606 using either the full retrospective method or the modified retrospective method. Under the full retrospective method, a company recasts the amount by which each financial statement line item presented in the current filing is affected as if the new guidance has always existed. Under the modified retrospective method, prior year financial statements would not need to be recast. Instead, a company applies the cumulative effect of initially applying the new standard as an adjustment to the opening retained earnings balance. The Company performed a detailed accounting assessment to quantify the effect of the transition from the former guidance to the new guidance and concluded that there was no material effect on its consolidated financial statements under either the full retrospective or the modified retrospective methods. The Company concluded that it will elect the modified retrospective method to avoid restatement of prior filings.

There are multiple options for the transition method under the new guidance, one of which allows a company to apply this guidance retrospectively either to all contracts at the date of initial application or only to contracts that are not completed contracts at the date of initial application. The Company has elected to apply the guidance to only contracts that are not completed contracts as of January 1, 2018. The Company's only contract not completed as of January 1, 2018 is its collaboration agreement with Genentech (see Note 3). The Company assessed the potential effects to the consolidated financial statements and retained earnings and has concluded that, upon adoption of the new standard, there was no material impact.

License Fees and Multiple Element Arrangements

If a license to its intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company will recognize revenues from non-refundable, up-front fees allocated to the license at such time as the license is transferred to the licensee and the licensee is able to use, and benefit from, the license. For licenses that are bundled 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 from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, will adjust the measure of performance and related revenue recognition.

If the Company is involved in a steering committee as part of a multiple element arrangement, the Company assesses whether its involvement constitutes a performance obligation or a right to participate. Steering committee services that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which the Company expects to complete its aggregate performance obligations.

Appropriate methods of measuring progress include output methods and input methods. In determining the appropriate method for measuring progress, the Company considers the nature of service that it promises to transfer to the customer. When the Company decides on a method of measurement, the Company will apply that single method of measuring progress for each performance obligation satisfied over time and will apply that method consistently to similar performance obligations and in similar circumstances.

If the Company cannot reasonably measure its progress toward complete satisfaction of a performance obligation because the Company lacks reliable information that would be required to apply an appropriate method of measuring progress, but it can reasonably estimate when the performance ceases or the remaining obligations become inconsequential and perfunctory, then revenue is not recognized until the Company can reasonably estimate when the performance obligation ceases or becomes inconsequential. Revenue is then recognized over the remaining estimated period of performance.

Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company is expected to complete its performance obligations under an arrangement.

Contingent Research Milestone Payments

Under the new guidance, there exists a constraint on the amount of variable consideration included in the transaction price in that either all, or a portion, of an amount of variable consideration should be included in the transaction price. The variable consideration amount should be included only to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. The assessment of whether variable consideration should be constrained is

largely a qualitative one that has two elements: the likelihood of a change in estimate, and the magnitude thereof. Variable consideration is not constrained if the potential reversal of cumulative revenue recognized is not significant, for example.

If the consideration in a contract includes a variable amount, a company will estimate the amount of consideration in exchange for transfer of promised goods or services. The consideration also can vary if a company's entitlement to the

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consideration is contingent on the occurrence or nonoccurrence of a future event. The Company considers contingent research milestone payments to fall under the scope of variable consideration, which should be estimated for revenue recognition purposes at the inception of the contract and reassessed ongoing at the end of each reporting period.
The Company assesses whether contingent research milestones should be considered variable consideration that should be constrained and thus not part of the transaction price. This includes an assessment of the probability that all or some of the milestones revenue could be reversed when the uncertainty around whether or not the achievement of each milestone is resolved, and the amount of reversal could be significant.
GAAP provides factors to consider when assessing whether variable consideration should be constrained. All of the factors should be considered, and no factor is determinative. The Company considers all relevant factors.
Reimbursement of Costs
Reimbursement of research and development costs by third party collaborators is recognized as revenue over time provided the Company has determined that it transfers control (i.e. performs the services) of a service over time and, therefore, satisfies a performance obligation according to the provisions outlined in ASC 606-10-25-27, Revenue Recognition.
Royalty Revenue
Since the first quarter of 2012, the Company has recognized royalty revenues related to Genentech’s and Roche’s sales of Erivedge. For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and where 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). The Company expects to continue recognizing royalty revenue from Genentech’s sales of Erivedge in the U.S. and in other markets where Genentech and Roche successfully obtain marketing approval, if any (see Notes 4(a) and 10). However, a portion of potential Erivedge royalties will be paid to the Purchasers pursuant to the Oberland Purchase Agreement (see Note 16).
Deferred Revenue
Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets. Significant judgments are required in the application of revenue recognition guidance. Short-term deferred revenue would consist of amounts that are expected to be recognized as revenue, or applied against future co-development costs, within the next fiscal year. Amounts that the Company expects will not be recognized in the next fiscal year would be classified as long-term deferred revenue. However, this estimate would be based on the Company's operating plan as of the balance sheet date and on its estimated performance periods under the collaboration in which the Company has recorded deferred revenues. If the Company's operating plan or its estimated performance period would change, the Company could recognize a different amount of deferred revenue over the reporting period.
With respect to each of the foregoing areas of revenue recognition, the Company exercises significant judgment in determining whether an arrangement contains multiple elements, and, if so, how much revenue is allocable to each element. In addition, the Company exercises its judgment in determining when its significant obligations have been met under such agreements and the specific time periods over which it recognized revenue, such as non-refundable, up-front license fees. To the extent that actual facts and circumstances differ from the Company's initial judgments, its revenue recognition with respect to such transactions would change accordingly and any such change could affect its reported financial results.
Summary
During the years ended December 31, 2018 and 2017, total gross revenues were 100% from the Company’s collaboration with Genentech.
(d) RESEARCH AND DEVELOPMENT
Research and development expense consists of costs incurred to discover, research and develop drug candidates. These expenses primarily include: (1) salaries and related expenses for personnel including stock-based compensation expense; (2) outside service costs, including clinical research organizations and contract manufacturing costs, among others; (3) sublicense payments; and (4) the costs of supplies and reagents, consulting, and occupancy and

depreciation charges. The Company expenses research and development costs as they are incurred.
The Company recognizes cost of royalties on Erivedge royalty revenue earned from Genentech related to obligations to third-party university licensors. The Company is also incurring research and development expenses under this collaboration related to the maintenance of these third-party licenses to certain background technologies. In addition, the Company records

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research and development expense for obligations to certain third-party university licensors upon earning payments from Genentech related to the achievement of clinical development and regulatory objectives under this collaboration.

(e) CASH EQUIVALENTS AND INVESTMENTS

Cash equivalents consist of short-term, highly liquid investments purchased with original maturities of three months or less. All other liquid investments are classified as marketable securities. The Company's short-term investments are marketable securities with original maturities of greater than three months from the date of purchase, but less than twelve months from the balance sheet date, and long-term investments are marketable securities with original maturities of greater than twelve months from the balance sheet. Marketable securities consist of commercial paper, corporate bonds and notes, and government obligations. All of the Company's investments have been designated available-for-sale and are stated at fair value with any unrealized holding gains or losses included as a component of stockholders' equity and any realized gains and losses recorded in the statement of operations in the period during which the securities are sold.

Unrealized gains and temporary losses on investments are included in accumulated other comprehensive income (loss) as a separate component of stockholders' equity. Realized gains and losses, dividends and interest income are included in other income (expense). Any premium or discount arising at purchase is amortized and/or accreted to interest income.

(f) LONG-LIVED ASSETS OTHER THAN GOODWILL

Long-lived assets other than goodwill consist of property and equipment. The aggregate net balances for these long-lived assets were $0.3 million and $0.4 million as of December 31, 2018 and 2017, respectively. The Company applies the guidance in FASB Codification Topic 360-10-05, Impairment or Disposal of Long-Lived Assets. If it were determined that the carrying value of the Company's other long-lived assets might not be recoverable based upon the existence of one or more indicators of impairment, the Company would measure an impairment based on the difference between the carrying value and fair value of the asset. The Company did not recognize any material impairment charges for the years ended December 31, 2018 or 2017.

Purchased equipment is recorded at cost. The Company does not currently hold any leased equipment. Depreciation and amortization are provided on the straight-line method over the estimated useful lives of the related assets or the remaining terms of the leases, whichever is shorter, as follows:

Asset Classification	Estimated Useful Life
Laboratory equipment, computers and software	3-5 years
Leasehold improvements	Lesser of life of the lease or the life of the asset
Office furniture and equipment	5 years

(g) GOODWILL

As of both December 31, 2018 and 2017, the Company had recorded goodwill of $9.0 million. The Company applies the guidance in the FASB Codification Topic 350, Intangibles—Goodwill and Other. During each of December 2018 and 2017, the Company completed its annual goodwill impairment tests and determined that the Company represented a single reporting unit and as of those dates the fair value of the Company exceeded the carrying value of its net assets. Accordingly, no goodwill impairment was recognized for the years ended December 31, 2018 and 2017.

(h) TREASURY STOCK

On May 31, 2002, the Company announced that its board of directors had approved the repurchase of up to $3.0 million of the Company's common stock. The Company accounted for its common stock repurchases as treasury stock under the cost method. In 2002, the Company repurchased 209,541 shares of its common stock at a cost of $0.9 million pursuant to this repurchase program.

Each of the Company's now-expired 2000 Stock Incentive Plan and the current Amended and Restated 2010 Stock Incentive Plan generally allow participants to purchase common stock upon the exercise of a stock option by delivery of shares of Company common stock held directly by the participant, with such shares of common stock valued at the closing price on the Nasdaq Global Market, or Nasdaq, on the date of exercise. On certain instances in the past, the Company has accounted for the value of the common stock remitted to the Company in satisfaction of the exercise price as treasury stock under the cost method. As of December 31, 2017, the Company had repurchased an aggregate

of 244,569 shares of its common stock at a total cost of $1.5 million. During the first quarter of 2018, the Company retired 244,569 shares of common stock at a total cost of $1.5 million.

(i) BASIC AND DILUTED LOSS PER COMMON SHARE

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Basic and diluted net losses per share were determined by dividing net loss by the weighted average number of common shares outstanding during the period. Diluted net loss per common share is the same as basic net loss per common share for all periods presented, as the effect of the potential common stock equivalents is antidilutive due to the Company's net loss position for all periods presented. Antidilutive securities consist of stock options outstanding as of the respective reporting period. Antidilutive securities as of December 31, 2018 and 2017 consisted of the following

	For the Year Ended December 31,	
	2018	2017
Stock options outstanding	3,714,394	3,206,858
Total antidilutive securities	3,714,394	3,206,858

(j) STOCK-BASED COMPENSATION

The Company accounts for stock-based compensation transactions using a grant-date fair-value-based method under FASB Codification Topic 718, Compensation-Stock Compensation.

The Company has recorded employee and director stock-based compensation expense of $3.9 million and $5.4 million for the years ended December 31, 2018 and 2017, respectively. The Company estimates that its stock-based compensation expense will increase in 2018 as it has granted, and expects that it may continue to grant options, in 2018 that could increase the amount of stock-based compensation ultimately recognized. The amount of the incremental employee stock-based compensation expense attributable to 2018 employee stock options to be granted will depend primarily on the number of stock options granted, the fair market value of the Company's common stock at the respective grant dates, and the specific terms of the stock options.

The Company measures compensation cost for stock-based compensation at fair value, including an estimate of forfeitures and recognizes the expense as compensation expense over the period that the recipient is required to provide service in exchange for the award, which generally is the vesting period. The Company uses the Black-Scholes option pricing model to measure the fair value of stock options. This model requires significant estimates related to the award's expected life and future stock price volatility of the underlying equity security. In determining the amount of expense to be recorded, the Company also estimates forfeiture rates for awards, based on the probability that employees will complete the required service period. The Company estimates the forfeiture rate based on historical experience. If actual forfeitures differ significantly from the Company's estimates, additional adjustments to compensation expense may be required in future periods. Ultimately, the actual expense recognized over the vesting period will only be for those shares that vest.

(k) OPERATING LEASES

The Company currently has one facility located at 4 Maguire Road in Lexington, Massachusetts under a noncancellable operating lease agreement for office and laboratory space. The rent payments for this facility escalate over the lease term and the Company expenses its obligations under this lease agreement on a straight-line basis over the term of the lease (see Note 10(a)).

(l) CONCENTRATION OF RISK

Financial instruments, which potentially subject the Company to concentrations of credit risk, consist principally of cash and cash equivalents, short- and long-term investments. The Company invests directly in commercial paper of financial institutions and corporations with A-/Aa3 or better long-term ratings and A-1/P-1 short term debt ratings and U.S. Treasury securities. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company's credit risk related to investments is reduced as a result of the Company's policy to limit the amount invested in any one issue.

The Company's accounts receivable at December 31, 2018 represents amounts due from collaborators, primarily for royalties earned on sales of Erivedge by Genentech and Roche.

The Company relies on third parties to supply certain raw materials necessary to produce its drug candidates, including fimepinostat, CA-4948, and CA-170, for preclinical studies and clinical trials. There are a small number of suppliers for certain raw materials that the Company uses to manufacture its drug candidates.

(m) COMPREHENSIVE LOSS

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Comprehensive loss is comprised of net loss and other comprehensive income (loss). Other comprehensive income (loss) includes unrealized holding gains and losses arising during the period on available-for-sale securities that are not other-than-temporarily impaired.

(n) NEW ACCOUNTING PRONOUNCEMENTS

Recently Issued and Adopted

In June 2018, the Financial Accounting Standard Board (“FASB”) issued Accounting Standard Update (“ASU”) 2018-07, Compensation - Stock Compensation: Improvements to Nonemployee Share-based Payment Accounting, which simplifies the accounting for nonemployee share-based payment transactions resulting from expanding the scope of ASC 718, Compensation - Stock Compensation (“ASC 718”). The standard will be effective for annual reporting periods and interim periods within those annual periods, beginning after December 15, 2018, and early adoption is permitted, but no earlier than an entity's adoption date of ASC 606, Revenue from Contracts with Customers (“ASC 606”). The Company did not have any outstanding nonemployee awards as of June 30, 2018, and adopted this update as of that date. There is no material impact on the Company's consolidated financial statements.

In May 2017, the FASB issued ASU 2017-09, Scope of Modification Accounting, which clarifies the scope under which modification accounting should be applied to a share-based payment award under ASC 718. The standard will be effective for annual reporting periods and interim periods within those annual periods, beginning after December 15, 2017, and early adoption is permitted for interim or annual periods beginning after January 1, 2017. As such, the Company adopted this standard as of January 1, 2018 and concluded there was no material impact on its consolidated financial statements.

In January 2017, the FASB issued ASU 2017-04, Simplifying the Test for Goodwill Impairment, which simplifies the subsequent measurement of goodwill under the current standard in testing the interim or annual impairment of goodwill. The standard will be effective for annual reporting periods and interim periods within those annual periods, beginning after December 15, 2019, and early adoption is permitted for interim or annual periods beginning after January 1, 2017. As such, the Company adopted this standard as of January 1, 2018 and concluded there was no material impact on its consolidated financial statements.

In August 2016, the FASB issued ASU 2016-15, Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments, which helps to clarify the diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows under ASC 230, Statement of Cash Flows (“ASC 230”), by addressing eight specific cash flow issues. The standard will be effective for annual reporting periods and interim periods within those annual periods, beginning after December 15, 2017, and early adoption is permitted for interim or annual periods. As such, the Company adopted this standard as of January 1, 2018 and concluded there was no material impact on its consolidated financial statements.

In January 2016, the FASB issued ASU 2016-01, Recognition and Measurement of Financial Assets and Financial Liabilities, which amends prior guidance on accounting for equity investments and financial liabilities. The new standard amends certain aspects of accounting and disclosure requirements for financial instruments, including the requirement that equity investments with readily determinable fair values be measured at fair value with changes in fair value recognized in results of operations. The new standard does not apply to investments accounted for under the equity method of accounting or those that result in consolidation of the investee. Equity investments that do not have readily determinable fair values may be measured at fair value or at cost minus impairment adjusted for changes in observable prices. A financial liability that is measured at fair value in accordance with the fair value option is required to be presented separately in other comprehensive income for the portion of the total change in the fair value resulting from change in the instrument-specific credit risk. In addition, a valuation allowance should be evaluated on deferred tax assets related to available-for-sale debt securities in combination with other deferred tax assets. The guidance is effective for fiscal years beginning after December 15, 2017, and interim periods within such years. As such, the Company adopted this standard as of January 1, 2018 and concluded there was no material impact on its consolidated financial statements.

In May 2014, the FASB issued new revenue recognition guidance in ASU 2014-09, for entities, providing a single, comprehensive model to account for revenue arising from contracts with customers. In addition, the FASB recently issued ASUs 2016-08, 2016-10, 2016-12, 2016-20 and 2017-13, all of which are further clarifying amendments to

ASU 2014-09. This new standard provides a five step framework whereby revenue is recognized when promised goods or services are transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The new standard also requires significantly expanded disclosures regarding the qualitative and quantitative information of an entity's nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers. Two adoption methods are permitted: retrospectively to all prior reporting periods presented, with certain practical expedients permitted; or retrospectively with the cumulative effect of initially adopting the ASU recognized at the date of initial application. The Company adopted the modified retrospective method. To date, the Company's sources of collaboration and

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other revenue have primarily been collaboration agreements. The most significant differences between Topic 606 and previous guidance for license and collaboration revenue are: (i) allocating consideration to performance obligations; and (ii) estimating and determining the timing of recognition of variable consideration received from licensees, including up-front license payments, contingent milestones and royalties. The guidance is effective for interim and annual periods beginning after December 15, 2017 and early adoption is permitted. The Company has adopted the guidance as of January 1, 2018. The Company has evaluated the impact that ASU 2014-09 may have on the financial position and results of operations and has concluded that the adoption of this guidance has no material impact on its consolidated financial statements. For more detail, see Note 2(c) above, Revenue Recognition.

Recently Issued, Not Yet Adopted

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurement, which modified the disclosure requirements for fair value measurement under ASC 820. The standard will be effective for annual reporting periods and interim periods within those annual periods, beginning after December 15, 2019, and early adoption is permitted. The Company is currently evaluating the effects of this standard and does not expect that adoption of this standard will have a material impact on its consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, Leases. In addition, the FASB recently issued ASUs 2018-10 and 2018-11, all of which are further clarifying amendments to ASU 2016-02. The standard requires organizations that lease assets to recognize on the balance sheet assets or liabilities, as applicable, for the rights and obligations created by those leases. Additionally, the guidance modifies current guidance for lessor accounting and leveraged leases, and is effective for fiscal years beginning after December 15, 2018, and interim periods within such years. Early adoption is permitted, but the Company does not anticipate electing early adoption. The Company completed its assessment of the current state of accounting for leases, and determined that the adoption of this standard will require us to recognize the fair value of the office space leased. This recognition will increase both total assets and liabilities in the consolidated financial statements in the Company's 2019 fiscal year. The Company estimates the increase in both total assets and liabilities to be approximately $1.1 million.

(o) SEGMENT REPORTING

The Company is engaged solely in the discovery and development of innovative drug candidates for the treatment of human cancers. Accordingly, the Company has determined that it operates in one operating segment.

(3) Research and Development Collaborations

(a) Genentech

In June 2003, the Company licensed its proprietary Hedgehog pathway technologies to Genentech for human therapeutic use. The primary focus of the collaborative research plan has been to develop molecules that inhibit the Hedgehog pathway for the treatment of various cancers. The collaboration is currently focused on the development of Erivedge, which is being commercialized by Genentech in the U.S. and by Genentech's parent company, Roche, in several other countries for the treatment of advanced BCC. Pursuant to the agreement, the Company is eligible to receive up to an aggregate of $115.0 million in contingent cash milestone payments, exclusive of royalty payments, in connection with the development of Erivedge or another small molecule Hedgehog pathway inhibitor, assuming the successful achievement by Genentech and Roche of specified clinical development and regulatory objectives. Of this amount, the Company has received $59.0 million in cash milestone payments as of December 31, 2018.

In addition to these payments and pursuant to the collaboration agreement, the Company, is entitled to a royalty on net sales of Erivedge that ranges from 5% to 7.5%. The royalty rate applicable to Erivedge may be decreased by 2% on a country-by-country basis in certain specified circumstances, including when a competing product that binds to the same molecular target as Erivedge is approved by the applicable regulatory authority in another country and is being sold in such country, by a third party for use in the same indication as Erivedge, or, when there is no issued intellectual property covering Erivedge in a territory in which sales are recorded. In 2015, the FDA and the European Medicine Agency’s Committee for Medicinal Products for Human Use, approved another Hedgehog signaling pathway inhibitor, Odomzo® (sonidegib), which is marketed by Sun Pharmaceutical Industries Ltd., for use in locally advanced BCC. Beginning in the fourth quarter of 2015, Genentech applied the 2% royalty reduction on U.S. sales of Erivedge as a result of the first commercial sale of Odomzo® in the U.S. and the Company anticipates that Genentech

will reduce by 2% royalties on net sales of Erivedge outside of the United States on a country-by-country basis to the extent that sonidegib is approved by the applicable country's regulatory authority and is being sold in such country. However, pursuant to the Oberland Purchase Agreement, Curis has retained its rights with respect to the 2% of royalties that are subject to such reduction in countries where such reduction has not occurred, subject to the terms and conditions of the Oberland Purchase Agreement (the “Retained Royalty Amounts”).

In November 2012, the Company formed a wholly-owned subsidiary, Curis Royalty, to receive a $30.0 million loan, at an annual interest rate of 12.25%, pursuant to a credit agreement between Curis Royalty and BioPharma Secured Debt Fund II

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Sub, S. à r. l., a Luxembourg limited liability company managed by Pharmakon Advisors, or BioPharma-II (see Note 9). In connection with the loan, the Company transferred to Curis Royalty its right to receive royalty and royalty-related payments from Genentech. The loan and accrued interest was an obligation of Curis Royalty, with no recourse to the Company, to be repaid using the royalty and royalty-related payments from Genentech.

In March 2017, the Company and Curis Royalty entered into a new credit agreement with HealthCare Royalty Partners III, L.P., or HealthCare Royalty, for the purpose of refinancing and terminating the loan from BioPharma-II. Accordingly, HealthCare Royalty made a $45.0 million loan at an annual interest rate of 9.95% to Curis Royalty, which was used in part to pay off $18.4million in remaining loan obligations to BioPharma-II under the prior loan with the residual proceeds of $26.6 million distributed to the Company as sole equity member of Curis Royalty. The final maturity date of the loan was the earlier of such date that the principal is paid in full, or Curis Royalty's right to receive royalties under the collaboration agreement with Genentech is terminated. On March 22, 2019, the Company and Curis Royalty terminated, and repaid in full all amounts outstanding under, the loan with HealthCare Royalty.

The Company has identified the following performance obligations related to the Genentech collaboration:

1.To grant the license for its Hedgehog antagonist programs and to provide service on both a steering committee and co-development steering committee. This performance obligation has been satisfied and only contingent royalty revenue remains to be recognized in the future.

2.To provide reimbursable research and development services. This performance obligation has been satisfied and no revenue remains to be recognized in the future.

The Company recognized $10.4 million and $9.8 million in royalty revenue under the Genentech collaboration during the year ended December 31, 2018 and 2017, respectively. The Company also recorded $0.6 million and $0.5 million, respectively, as cost of royalty revenues within the costs and expenses section of its consolidated statements of operations and comprehensive loss during these same periods. Cost of royalty revenues is comprised of the 5% of the royalties earned by Curis Royalty with respect to Erivedge outside Australia, and 2% direct net sales in Australia (subject to decrease on expiration of the patent in April 2019 to 5% of the royalty payments that Curis Royalty receives from Genentech, through February 2022), that the Company is obligated to pay to university licensors.

As further discussed in Note 16, a portion of royalty revenues received from Genentech on net sales of Erivedge will be paid to the Purchasers pursuant to the Oberland Purchase Agreement. The Company recorded research and development revenue of $0.1 million and $0.2 million, respectively, related to expenses incurred by the Company on behalf of Genentech that were paid by the Company and for which Genentech is obligated to reimburse the Company. Genentech incurred expenses of $0.1 million and $0.2 million, respectively, under this collaboration for which the Company is obligated to reimburse to Genentech, and which the Company has recorded as contra-revenues which have been net against research and development revenues in its consolidated statements of operations and comprehensive loss. The Company will continue to recognize revenue for expense reimbursement as such reimbursable expenses are incurred, provided that the provisions of the ASC 606 are met.

The Company has recorded as amounts receivable from Genentech under this collaboration, comprised primarily of Erivedge royalties earned in the fourth quarters of 2018 and 2017 of $2.9 million and $3.0 million as of December 31, 2018 and 2017, respectively, in "accounts receivable" in the Company's current assets section of its consolidated balance sheets.

(b) Aurigene

In January 2015, the Company entered into an exclusive collaboration agreement with Aurigene for the discovery, development and commercialization of small molecule compounds in the areas of immuno-oncology and selected precision oncology targets. Under the collaboration agreement, Aurigene granted the Company an option to obtain exclusive, royalty-bearing licenses to relevant Aurigene technology to develop, manufacture and commercialize products containing certain of such compounds anywhere in the world, except for India and Russia, which are territories retained by Aurigene.

In connection with the collaboration agreement, the Company issued to Aurigene 3,424,026 shares of its common stock valued at $24.3 million in partial consideration for the rights granted to the Company under the collaboration agreement, which the Company recognized as expense during the year ended December 31, 2015. The shares were issued pursuant to a stock purchase agreement with Aurigene dated January 18, 2015.

In September 2016, the Company and Aurigene entered into an amendment to the collaboration agreement. Under the terms of the amendment, in exchange for the issuance by the Company to Aurigene of 2,041,666 shares of its common stock, Aurigene waived payment of up to a total of $24.5 million in potential milestones and other payments associated with the first four programs in the collaboration that may have become due from the Company under the collaboration agreement. To the extent any of these waived milestones or other payments are not payable by the Company, for example in the event one or more of the milestone events do not occur, the Company will have the right to deduct the unused waived amount from any one or more of the milestone payment obligations tied to achievement of commercial milestone events. The amendment also provides

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that, in the event supplemental program activities are performed by Aurigene, the Company will provide up to $2.0 million of additional funding for each of the third and fourth licensed program. The shares were issued pursuant to a stock purchase agreement with Aurigene dated September 7, 2016.

As of December 31, 2018, the Company has exercised its option to license the following four programs under the collaboration:

1. IRAK4 Program - a precision oncology program of small molecule inhibitors of IRAK4. The development candidate is CA-4948, an orally available small molecule inhibitor of IRAK4.
2. PD1/VISTA Program - an immuno-oncology program of small molecule antagonists of PD1 and VISTA immune checkpoint pathways. The development candidate is CA-170, an orally available small molecule antagonist of VISTA and PDL1.
3. PD1/TIM3 Program - an immuno-oncology program of small molecule antagonists of PD1 and TIM3 immune checkpoint pathways. The development candidate is CA-327, an orally available small molecule antagonist of PDL1 and TIM3.
4. In March 2018, the Company exercised its option to license a fourth program, which is an immuno-oncology program.

For each of our licensed programs (as described above) we are obligated to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize at least one product in each of the U.S., specified countries in the European Union and Japan, and Aurigene is obligated to use commercially reasonable efforts to perform its obligations under the development plan for such licensed program in an expeditious manner.

Subject to specified exceptions, Aurigene and the Company agreed to collaborate exclusively with each other on the discovery, research, development and commercialization of programs and compounds within immuno-oncology for an initial period of approximately two years from the effective date of the collaboration agreement. At the Company's option, and subject to specified conditions, it may extend such exclusivity for up to three additional one-year periods by paying to Aurigene additional exclusivity option fees on an annual basis. The Company exercised the first one-year exclusivity option in the first quarter of 2017. The fee for this exclusivity option exercise was $7.5 million, which the Company paid in two equal installments in the first and third quarters of 2017. The Company has elected not to further exercise its exclusivity option and thus did not make the $10.0 million payment required for this additional exclusivity in 2018. As a result of the Company's election to not further exercise its exclusivity option, Curis is no longer operating under broad immuno-oncology exclusivity with Aurigene. The Company has, however, as provided in the agreement, elected to exercise its option to extend exclusivity on a program-by-program, year-by-year, basis for the IRAK4 Program and the PD1/VISTA Program, both of the licensed programs currently in clinical trials.

Since January 2015, the Company has paid $14.5 million in research payments and has waived $19.5 million in milestone payments under the terms of the 2016 amendment.

For each of the IRAK4, PD1/VISTA,PD1/TIM3 programs, and the fourth immuno-oncology program: the Company has remaining unpaid or unwaived payment obligations of $42.5 million per program, related to regulatory approval and commercial sales milestones, plus specified additional payments for approvals for additional indications, if any.

In addition to the collaboration agreement, in June 2017, the Company entered into a master development and manufacturing agreement with Aurigene for the supply of drug substance and drug product, under which it has made cash payments to Aurigene of $0.6 million in 2018 and $0.8 million in 2017.

(4) Fair Value of Financial Instruments

The Company has adopted the provisions of the FASB Codification Topic 820, Fair Value Measurements and Disclosures. Topic 820 provides a framework for measuring fair value under GAAP and requires expanded disclosures regarding fair value measurements. GAAP defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Market participants are buyers and sellers in the principal market that are (i) independent, (ii) knowledgeable, (iii) able to transact, and (iv) willing to transact.

GAAP requires the use of valuation techniques that are consistent with the market approach, the income approach and/or the cost approach. The market approach uses prices and other relevant information generated by market

transactions involving identical or comparable assets and liabilities. The income approach uses valuation techniques to convert future amounts, such as cash flows or earnings, to a single present amount on a discounted basis. The cost approach is based on the amount that currently would be required to replace the service capacity of an asset (replacement cost). Valuation techniques should be consistently applied. GAAP also establishes a fair value hierarchy which requires an entity to maximize the use of observable

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inputs, where available, and minimize the use of unobservable inputs when measuring fair value. The standard describes three levels of inputs that may be used to measure fair value:

Level 1 Quoted prices in active markets for identical assets or liabilities.

Level 2 Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

In accordance with the fair value hierarchy, the following table shows the fair value as of December 31, 2018 and 2017 of those financial assets and liabilities that are measured at fair value on a recurring basis, according to the valuation techniques the Company used to determine their fair value. No financial assets or liabilities are measured at fair value on a nonrecurring basis at December 31, 2018 and 2017.

	Quoted Prices in Active Markets (Level 1)	Other Observable Inputs (Level 2)	Unobservable Inputs (Level 3)	Fair Value
	(in thousands)			
As of December 31, 2018				
Cash equivalents:				
Money market funds	$18,180	$ —	$ —	$18,180
Corporate commercial paper, stock, bonds and notes	—	2,199	—	2,199
Municipal bonds	—	135	—	135
Short-term investments:				
Corporate commercial paper, stock, bonds and notes	—	634	—	634
Total assets at fair value	$18,180	$ 2,968	$ —	$21,148

	Quoted Prices in Active Markets (Level 1)	Other Observable Inputs (Level 2)	Unobservable Inputs (Level 3)	Fair Value
	(in thousands)			
As of December 31, 2017				
Cash equivalents:				
Money market funds	$35,308	$ —	$ —	$35,308
Municipal bonds	—	260	—	260
Short- and long-term investments:				
Corporate commercial paper, stock, bonds and notes	—	21,944	—	21,944
Total assets at fair value	$35,308	$ 22,204	$ —	$57,512

(5) Investments

Cash equivalents consist of short-term, highly liquid investments purchased with original maturities of three months or less. All other liquid investments are classified as marketable securities. The Company’s short-term investments are marketable securities with original maturities of greater than three months from the date of purchase, but less than twelve months from the balance sheet date, and long-term investments are marketable securities with original maturities of greater than twelve months from the balance sheet. Marketable securities consist of commercial paper, corporate bonds and notes, and government obligations. All of the Company’s investments have been designated available-for-sale and are stated at fair value with any unrealized holding gains or losses included as a component of

stockholders' equity and any realized gains and losses recorded in the statement of operations in the period during which the securities are sold.

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Unrealized gains and temporary losses on investments are included in accumulated other comprehensive income (loss) as a separate component of stockholders' equity. Realized gains and losses, dividends and interest income are included in other income (expense). Any premium or discount arising at purchase is amortized and/or accreted to interest income.

The amortized cost, unrealized gains and losses and fair value of investments available-for-sale as of December 31, 2018 are as follows:

	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
Corporate bonds and notes—short-term	$ 634	$ —	$ —	$ 634
Total investments	$ 634	$ —	$ —	$ 634

Short-term investments have maturities ranging from one to twelve months with a weighted average maturity of 0.1 years at December 31, 2018.

The amortized cost, unrealized gains and losses and fair value of investments available-for-sale as of December 31, 2017 are as follows:

	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
Corporate bonds and notes—short-term	$ 21,946	$ —	$ (2)	$ 21,944
Total investments	$ 21,946	$ —	$ (2)	$ 21,944

Short-term investments have maturities ranging from one and twelve months with a weighted average maturity of 0.2 years at December 31, 2017.

At December 31, 2018, Curis held no securities that were in an unrealized loss position for less than 12 months and held one security that was in an unrealized loss position at December 31, 2017. The fair value of this security was $1.5 million at December 31, 2017. Curis held no investments that have been in a continuous unrealized loss position for 12 months or longer at December 31, 2018 or December 31, 2017. The Company evaluated its securities for other-than-temporary impairments based on quantitative and qualitative factors, and it considered the decline in market value for the one debt security as of December 31, 2017 to be primarily attributable to current economic and market conditions at that time.

(6) Stock Plans and Stock Based Compensation

As of December 31, 2018, the Company had two shareholder-approved, share-based compensation plans: (i) the Amended and Restated 2010 Employee Stock Purchase Plan, or the ESPP, adopted by the Board of Directors in April 2017 and approved by shareholders in June 2017, and (ii) the Third Amended and Restated 2010 Stock Incentive Plan, or the 2010 Plan, adopted by the Board of Directors in March 2018 and approved by shareholders in June 2018, which was amended to, among other things, add an additional 2,390,000 shares under the 2010 Plan, and set a new expiration date of May 14, 2028 for the 2010 Plan. New employees are typically issued options as an inducement equity award under Nasdaq Listing Rule 5635(c)(4) outside of the 2010 Plan. Effective May 29, 2018, the number of shares of common stock available for issuance under the plans and the number of shares of common stock issuable upon the exercise of then outstanding options have been adjusted to reflect a 1-for-5 reverse stock split (see Note 11). In the first quarter of 2010, the Company's 2000 Stock Incentive Plan expired in accordance with its terms, and its 2000 Director Stock Option Plan had no available shares remaining under the plan. No additional awards will be made under these plans, although all outstanding awards under these plans will remain in effect until they are exercised or they expire in accordance with their terms.

The Third Amended and Restated 2010 Stock Incentive Plan

The 2010 Plan permits the granting of incentive and non-qualified stock options and stock awards to employees, officers, directors, and consultants of the Company and its subsidiaries at prices determined by the Company's Board of Directors. The Company can issue up to 6,190,000 shares of its common stock pursuant to awards granted under the 2010 Plan. Options become exercisable as determined by the Board of Directors and expire up to 10 years from the date of grant. The 2010 Plan uses a "fungible share" concept under which each share of stock subject to awards granted as options and stock appreciation rights ("SARs"), will cause one share per share under the award to be removed from the available share pool, while each share of stock subject to awards granted as restricted stock, restricted stock

units, other stock-based awards or performance awards where the price charged for the award is less than 100% of the fair market value of the Company's common stock will cause 1.3 shares per share under the award to be removed from the available share pool. As of December 31, 2018, the Company had only granted options to purchase shares of the Company's common stock with an exercise price equal to the closing market

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price of the Company's common stock on the Nasdaq Global Market on the grant date. As of December 31, 2018, 2,595,622 shares remained available for grant under the 2010 Plan.

During the year ended December 31, 2018, the Company's board of directors granted options to purchase 2,072,596 shares of the Company's common stock to officers and employees of the Company under the 2010 Plan. These options vest and become exercisable as to 25% of the shares underlying the award after the first year and as to an additional 6.25% of the shares underlying the award in each subsequent quarter, based upon continued employment over a four-year period, and are exercisable at a price equal to the closing price of the Company's common stock on the Nasdaq Global Market on the grant dates.

Also during the year ended December 31, 2018, the Company's board of directors granted restricted stock awards, or RSAs, to officers of the Company for an aggregate amount of 109,250 shares of the Company's common stock under the 2010 Plan. These RSAs will vest as to 25% of the shares underlying the RSA on the first anniversary of the date of grant and as to an additional 25% annually thereafter until all such shares become vested, based upon continued service to the Company over a four-year period.

During the year ended December 31, 2018, the Company's board of directors granted RSAs to its non-employee directors for an aggregate amount of 185,000 shares of the Company's common stock under the 2010 Plan. These RSAs will vest as to 100% of the shares underlying the RSA on the first anniversary of the date of grant, subject to continued service to the Company over the course of such year.

Nonstatutory Inducement Grants

For certain new employees the Company issued options as an inducement equity award under Nasdaq Listing Rule 5635(c)(4) outside of the 2010 Plan. The option will vest as to 25% of the shares underlying the option on the first anniversary of the grant date, and as to an additional 6.25% of the shares underlying the option on each successive three-month period thereafter. During the year ended December 31, 2018, the Company's board of directors granted inducement equity awards of 92,000 shares of common stock. These options were granted at a weighted average exercise price of $2.35, which is based on the closing market price of the Company's common stock on the Nasdaq Global Market on the grant date.

Employee and Director Grants

Vesting Tied to Service Conditions

In determining the fair value of stock options, the Company generally uses the Black-Scholes option pricing model. As discussed below, for employee stock options with market performance conditions, the Company uses a Monte Carlo simulation valuation model. The Black-Scholes option pricing model employs the following key assumptions for employee and director options awarded during each of the following years:

	For the Year Ended December 31,	
	2018	2017
Expected term (years)—Employees	5.5	5.5
Expected term (years)—Officers	5.5	5.5
Expected term (years)—Directors	N/A	6.3
Risk-free interest rate	2.5-3.0%	2.0-2.1%
Expected volatility	66-73%	63-64%
Expected dividend yield	None	None

The expected volatility is based on the annualized daily historical volatility of the Company's stock price for a time period consistent with the expected term of each grant. Management believes that the historical volatility of the Company's stock price best represents the future volatility of the stock price. The risk-free rate is based on the U.S. Treasury yield in effect at the time of grant for the expected term of the respective grant. The Company has not historically paid cash dividends, and does not expect to pay cash dividends in the foreseeable future.

The stock price volatility and expected terms utilized in the calculation involve management's best estimates at that time, both of which impact the fair value of the option calculated under the Black-Scholes methodology and, ultimately, the expense that will be recognized over the life of the option. GAAP also requires that the Company

recognize compensation expense for only the portion of options that are expected to vest. Therefore, management calculated an estimated annual pre-vesting forfeiture rate that is derived from historical employee termination behavior since the inception of the Company, as adjusted. If the actual number of forfeitures differs from those estimated by management, additional adjustments to compensation expense may be required in future periods.

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A summary of stock option activity under the 2010 Plan, the 2000 Stock Incentive Plan, the 2000 Director Stock Option Plan, and Nonstatutory Inducement Grants is summarized as follows:

	Number of Shares	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding, December 31, 2017	3,206,858	$ 12.08		
Granted	2,072,596	2.56		
Exercised	—	—		
Canceled	(1,565,060)	9.91		
Outstanding, December 31, 2018	3,714,394	$ 7.68	6.38	$ —
Exercisable at December 31, 2018	1,776,293	$ 11.90	3.52	$ —
Vested and unvested expected to vest	3,347,440	$ 8.23	6.06	$ —

At December 31, 2018, the weighted average grant-date fair values of stock options granted with standard vesting terms during the years ended December 31, 2018 and 2017 were $1.46 and 1.43 per share of common stock underlying such stock options, respectively. As of December 31, 2018, there was approximately $3.5 million, including the impact of estimated forfeitures, of unrecognized compensation cost related to unvested employee stock option awards outstanding under the Company's 2010 Plan that is expected to be recognized as expense over a weighted average period of 3.5 years. There were no employee stock options exercised during the year ended December 31, 2018. The intrinsic value of employee stock options exercised during the year ended December 31, 2017 was $1.0 million.

The following table presents a summary of outstanding RSAs under the 2010 Plan as of December 31, 2018:

	Number of Shares	Weighted Average Grant Date Fair Value
Outstanding, December 31, 2017	—	—
Awarded	294,250	3.45
Vested	—	—
Forfeited	(68,000)	3.45
Outstanding, December 31, 2018	226,250	3.45

As of December 31, 2018, there were 226,250 shares outstanding covered by RSAs that are expected to vest. The weighted average fair value of these shares of restricted stock was $3.45 per share and the aggregate fair value of these shares of restricted stock was approximately $1.0 million. As of December 31, 2018, there were approximately $0.1 million of unrecognized compensation costs, net of estimated forfeitures, related to RSAs granted to officers and non-employee directors, which are expected to be recognized as expense over a remaining weighted average period of 0.61 years.

Second Amended and Restated 2010 Employee Stock Purchase Plan (ESPP)

The Company has reserved 2,000,000 of its shares of common stock for issuance under the ESPP. Eligible employees may purchase shares of the Company's common stock at 85% of the lower closing market price of the common stock at the beginning of the enrollment period or ending date of the any purchase period within a two-year enrollment period, as defined. The Company has four six-month purchase periods per each two-year enrollment period. If, within any one of the four purchase periods in an enrollment period, the purchase period ending stock price is lower than the stock price at the beginning of the enrollment period, the two-year enrollment resets at the new lower stock price. This aspect of the plan was amended in 2017. Prior to 2017, the plan included two six-month purchase period per year with no defined enrollment period. As of December 31, 2018, 231,053 shares were issued under the ESPP, of which 101,623 were issued during 2018. As of December 31, 2018, there were 1,768,947 shares available for future purchase

under the ESPP.

For the years ended December 31, 2018 and 2017, the Company recorded compensation expense related to its ESPP and calculated the fair value of shares expected to be purchased under the ESPP using the Black-Scholes models with the following assumptions:

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	For the Year Ended December 31,	
	2018	2017
Compensation expense recognized under ESPP	$ 173	$ 268
Expected term	6-24 months	6-24 months
Risk-free interest rate	2.1-2.7%	1.1-1.8%
Volatility	79-104%	65-76%
Dividends	None	None

Employee Stock-Based Compensation Expense

Stock-based compensation for employee and director stock option grants for the years ended December 31, 2018 and 2017 of $3.9 million and $5.4 million , respectively, was calculated using the above valuation models and has been included in the Company's results of operations. The total fair value of vested stock options for the years ended December 31, 2018 and 2017 was $4.7 million and $3.6 million, respectively.

Total Stock-Based Compensation Expense

For the years ended December 31, 2018 and 2017, the Company recorded employee and non-employee stock-based compensation expense to the following line items in its Costs and Expenses section of the Consolidated Statements of Operations and Comprehensive Loss:

	For the Year Ended December 31,	
	2018	2017
Research and development expenses	$1,310	$1,486
General and administrative expenses	2,630	3,873
Total stock-based compensation expense	$3,940	$5,359

No income tax benefits have been recorded for the years ended December 31, 2018 or 2017, as the Company has recorded a full valuation allowance and management has concluded that it is more likely than not that the net deferred tax assets will not be realized (see Note 12).

(7) Property and Equipment, net

Property and equipment consist of the following:

	December 31,	
	2018	2017
Laboratory equipment, computers and software	$1,753	$1,736
Leasehold improvements	185	185
Office furniture and equipment	354	354
	2,292	2,275
Less—Accumulated depreciation and amortization	(2,025)	(1,909)
Total	$267	$366

The Company recorded depreciation and amortization expense of $0.2 million for each of the years ended December 31, 2018 and 2017.

During the years ended December 31, 2018 and 2017, the Company identified certain of its fully depreciated assets no longer being used. As a result, the Company wrote off gross assets and related accumulated depreciation, totaling $0.1 million for each of the years ended December 31, 2018 and 2017.

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(8) Accrued Liabilities

Accrued liabilities consist of the following:

	December 31,	
	2018	2017
Accrued compensation	$2,774	$2,187
Professional fees	233	148
Accrued interest on debt (see Note 9)	165	193
Other	285	265
Total	$3,457	$2,793

(9) Debt

(a) BioPharma-II

In December 2012, the Company's wholly-owned subsidiary, Curis Royalty, received a $30.0 million loan at an annual interest rate of 12.25% pursuant to a credit agreement between Curis Royalty and BioPharma-II. In connection with the loan, Curis transferred to Curis Royalty its right to receive royalty and royalty-related payments on the commercial sales of Erivedge that it receives from Genentech (see Note 3(a)). The loan and accrued interest was being repaid by Curis Royalty using such royalty and royalty-related payments. To secure repayment of the loan, Curis Royalty granted a first priority lien and security interest (subject only to permitted liens) to BioPharma-II in all of its assets and all real, intangible and personal property, including all of its right, title and interest in and to the royalty and royalty-related payments. The loan constituted an obligation of Curis Royalty, and was non-recourse to Curis. Under the terms of the credit agreement, quarterly royalty and royalty-related payments received by Curis Royalty from Genentech were first applied to pay interest and second, principal on the loan from BioPharma-II. Curis Royalty retained its right to royalty payments related to sales of Erivedge following repayment of the loan.

The final maturity date of the loan was the earlier of the date when the principal was paid in full or the termination of Curis Royalty’s right to receive royalties under the collaboration agreement with Genentech. Because the repayment of the term loan was contingent upon the level of Erivedge royalties received, the short- and long-term classification of the debt was based on the Company’s estimate of the timing of amounts to be repaid. The Company was not able to estimate when the loan would be repaid as repayments were impacted by numerous factors, all of which were beyond the Company’s control. The repayment term could be shortened or extended depending on the actual level of Erivedge royalties received. In addition, if Erivedge royalties were insufficient to pay the accrued interest on the outstanding loan, any unpaid interest outstanding would be added to the principal on a quarterly basis. At any time after January 1, 2017, Curis Royalty was entitled, subject to certain limitations, to prepay the outstanding principal of the loan in whole or in part, at a price equal to 105% of the outstanding principal on the loan, plus accrued but unpaid interest. The loan was paid off and terminated in March 2017.

(b) HealthCare Royalty Partners III

On March 6, 2017, the Company and Curis Royalty entered into a new credit agreement, referred to herein as the credit agreement, with HealthCare Royalty for the purpose of refinancing Curis Royalty’s financing arrangement with BioPharma-II, referred to herein as the prior loan. On March 22, 2017, the prior loan was terminated in its entirety. Pursuant to the credit agreement, HealthCare Royalty made a $45.0 million loan at an interest rate of 9.95% to Curis Royalty, which was used to pay off $18.4 million in remaining loan obligations to BioPharma-II under the prior loan. The remaining proceeds of $26.6 million were distributed to Curis as sole equity holder of Curis Royalty.

Under the terms of the credit agreement with HealthCare Royalty, quarterly Erivedge royalty and royalty-related payments from Genentech were to be first applied to pay, collectively: (i) escrow fees payable by the Company pursuant to an escrow agreement, (ii) the Company’s royalty obligations to academic institutions, (iii) certain expenses incurred by HealthCare Royalty in connection with the credit agreement and related transaction documents, including enforcement of its rights in the case of an event of default under the credit agreement and (iv) expenses incurred by the Company enforcing its right to indemnification under the collaboration agreement. Subsequently, remaining amounts were to be applied first, to pay interest and second, to pay principal on the loan. If royalties owed under the Genentech collaboration agreement were insufficient to pay the accrued interest on the outstanding loan, the unpaid

interest outstanding would be added to the loan principal on a quarterly basis. On March 22, 2019, the Company and Curis Royalty terminated, and repaid all amounts outstanding under, the credit agreement, consisting of approximately $33.8 million in remaining loan principal and approximately $3.4 million in accrued and unpaid interest and prepayment fees.

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(c) Respective Debt Payments to BioPharma-II and HealthCare Royalty Partners III

During the years ended December 31, 2018 and 2017, Curis Royalty made payments totaling $10.0 million and $8.9 million, respectively, of which $6.1 million and $5.0 million have been applied to the principal, respectively, with the remainder applied to accrued interest. As of December 31, 2018, the Company recorded short- and long-term debt of $6.9 and $28.6 million, respectively, and at December 31, 2017, the Company recorded short- and long-term debt of $5.9 million and $35.7 million, respectively, with such amounts recorded within the Company's consolidated balance sheets.

In addition, the Company recorded related accrued interest on its debt of $0.2 million and $0.2 million as of December 31, 2018 and 2017, respectively, with such amounts included in the Company's accrued liabilities section of its consolidated balance sheets. For the years ended December 31, 2018 and 2017, respectively, the Company recognized interest expense related to its debt of $3.9 million and $4.0 million , respectively, in the consolidated statement of operations and comprehensive loss.

At December 31, 2018, the fair value of the principal portion of the debt is estimated as $34.9 million. Due to the assumptions required in estimating future Erivedge royalties, the expected repayment period and weighting of various royalty projection scenarios, the fair value of the debt is measured using Level 3 inputs.

For the year ended December 31, 2018, the Company did not incur any debt issuance costs, however the Company did incur debt issuance costs totaling $0.2 million for the year ended December 31, 2017 in connection with its HealthCare Royalty financing transaction, all of which were incurred directly by the Company. The direct costs incurred by the Company were recorded as contra-debt, which directly reduces the outstanding debt balance on the following table:

	As of December 31,	
	2018	2017
Debt, current	6,920	5,919
Debt issue costs, current	(36)	(33)
Debt, current portion net of issuance costs	$6,884	$5,886
Debt, long-term	28,696	35,802
Debt issue costs, long-term	(96)	(133)
Debt, net of current portion and issuance costs	$28,600	$35,669

All issuance costs will be amortized over the estimated term of the debt using the straight-line method which approximates the effective interest method.

The assumptions used in determining the expected repayment term of the debt and amortization period of the issuance costs requires management to make estimates that could impact the Company's short- and long-term classification of these costs, as well as the period over which these costs will be amortized.

At December 31, 2018, the Company estimates that its future payments of principal on the loan are as follows:

	Principal
2019	$6,920
2020	8,157
2021	9,531
2022	11,008
2023	—
Total payments	35,616
Less current portion, gross	(6,920)
Total long-term debt obligations, gross	$28,696

(10) Commitments

(a) OPERATING LEASES

The Company is party to a lease agreement with the Trustees of Lexington Office Realty Trust pursuant to which the Company leases 24,529 square feet of property that is used for office, research and laboratory space located at 4 Maguire Road in Lexington, Massachusetts.

The term of the 4 Maguire Road lease agreement commenced on December 1, 2010, and was set to expire in February 2018. The Company had the option to extend the term for one additional five-year period upon the Company’s written notice to

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the lessor at least one year and no more than 18 months in advance of the extension. On November 1, 2017, the Company entered into a second amendment to the lease agreement pursuant to which the Company agreed to extend the lease for an additional two-year period. The term of the lease amendment commenced on March 1, 2018, and expires on February 29, 2020. The amendment provides for no option to extend the term beyond the two-year period, nor does it provide an option for early termination of the lease.

The total cash obligations for the base rent over the initial term of the lease agreement and the extended term of the lease agreement were approximately $4.4 million and $2.0 million, respectively. In addition to the base rent, the Company is also responsible for its share of operating expenses and real estate taxes, in accordance with the terms of the lease agreement. The Company has provided a security deposit to the lessor in the form of an irrevocable letter of credit in the original amount of $0.3 million. The original deposit has been reduced throughout the lease term since its inception to $0.2 million during 2018 and 2017, respectively, in accordance with the terms of the lease. These amounts have been classified as the restricted investments in the Company’s Consolidated Balance Sheet as of December 31, 2018 and 2017.

The Company’s remaining operating lease commitments for all leased facilities with an initial or remaining term of at least one year are as follows:

Year Ending December 31,	
2019	$1,002
2020	168
Total minimum payments	$1,170

Rent expense for all operating leases was $0.9 million for the year ended December 31, 2018 and $0.7 million for the year ended December 31, 2017. The related deferred rent is included in accrued liabilities and other long-term liabilities in the Company’s consolidated balance sheet as of December 31, 2018 and 2017.

(b) LICENSE AGREEMENTS

In exchange for the right to use licensed technology in its research and development efforts, the Company has entered into various license agreements. These agreements generally stipulate that the Company pay an annual license fee and is obligated to pay royalties on future revenues, if any, resulting from use of the underlying licensed technology. Such revenues may include, for example, up-front license fees, contingent payments upon collaborators’ achievement of development and regulatory objectives, and royalties. In addition, some of the agreements commit the Company to make contractually defined payments upon the attainment of scientific or clinical milestones. The Company expenses these payments as they are incurred and expenses royalty payments as related future product sales or as royalty revenues are recorded. The Company accrues expenses for scientific and clinical objectives over the period that the work required to meet the respective objective is completed, provided that the Company believes that the achievement of such objective is probable. The Company did not incur license fee expenses within the “Research and development” line item of its “Costs and expenses” section of its consolidated statement of operations for the year ended December 31, 2018. License fee expenses within the “Research and development” line item of the Company's “Costs and expenses” section of its consolidated statement of operations for the year ended December 31, 2017, were $7.5 million. For the years ended December 31, 2018 and 2017, the Company also recognized $0.6 million and $0.5 million as cost of royalty revenues in its Consolidated Statements of Operations and Comprehensive Loss related to such obligations (see Note 3(a)).

(11) Common Stock

(a) Reverse Stock Split

On May 29, 2018 (the “Effective Date”), the Company filed a Certificate of Amendment to the Company’s Restated Certificate of Incorporation with the Secretary of State of the State of Delaware (the “Certificate of Amendment”), which effected, as of 5:00 p.m. Eastern Time on the Effective Date, a 1-for-5 reverse stock split (the “Reverse Stock Split”) of the Company’s issued and outstanding common stock, $0.01 par value per share (the “Common Stock”). As a result of the Reverse Stock Split, every five shares of Common Stock issued and outstanding was converted into one share of Common Stock. No fractional shares were issued in connection with the Reverse Stock Split. Stockholders who would have otherwise been entitled to a fractional share of Common Stock were instead entitled to receive a proportional cash payment.

The Reverse Stock Split proportionately reduced the number of authorized shares of Common Stock. The Reverse Stock Split did not change the par value of the Common Stock or the authorized number of shares of preferred stock of the Company. All outstanding stock options were adjusted as a result of the Reverse Stock Split, as required by the terms of such stock options.

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(b) Treasury Stock Retirement

Since 2002, the Company has repurchased 244,569 shares of common stock at a total cost of $1.5 million. The shares were repurchased through a combination of a repurchase program of up to $3.0 million approved by the Company's board of directors in 2002 and through employee purchases of common stock upon the exercise of stock options by remittance of shares of Company stock. The Company accounts for its common stock repurchases as treasury stock under the cost method.

In March 2018, the Company retired all 244,569 shares of common stock at a total cost of $1.5 million. This was a non-cash transaction and thus only affected the classifications within the stockholders' equity section of the Company's consolidated balance sheet.

(c) 2017 Public Offering of Common Stock

On September 18, 2017, the Company entered into an underwriting agreement with Robert W. Baird & Co., Incorporated, or Baird, as underwriter, pursuant to which the Company sold and issued 4,000,000 shares of the Company’s common stock. The underwriter agreed to purchase the shares from the Company pursuant to the underwriting agreement at a price of $8.90, per share, and the offering price to the public was $9.25 per share. The Company received net proceeds from the sale of the shares, after deducting the underwriting discounts and commissions and estimated offering expenses, of $35.3 million. The Company incurred offering expenses of $0.3 million related to this transaction.

(d) 2015 Sales Agreement with Cowen

On July 2, 2015, the Company entered into a sales agreement with Cowen, pursuant to which the Company may sell from time to time up to $30.0 million of the Company’s common stock through an “at-the-market” equity offering program under which Cowen will act as sales agent. Subject to the terms and conditions of the sales agreement, Cowen may sell the common stock by methods deemed to be an “at-the-market” offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on the Nasdaq Global Market, on any other existing trading market for the common stock or to or through a market maker other than on an exchange. In addition, with the Company’s prior written approval, Cowen may also sell the common stock by any other method permitted by law, including in negotiated transactions. Cowen will use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the Nasdaq Global Market to sell on the Company’s behalf all of the shares requested to be sold by the Company. The Company has no obligation to sell any of the common stock under the sales agreement. Either the Company or Cowen may at any time suspend solicitations and offers under the sales agreement upon notice to the other party. The sales agreement may be terminated at any time by either the Company or Cowen upon written notice to the other party as specified in the sales agreement. The aggregate compensation payable to Cowen shall be 3% of the gross sales price of the common stock sold by Cowen pursuant to the sales agreement. Each party has agreed in the sales agreement to provide indemnification and contribution against certain liabilities, including liabilities under the Securities Act, subject to the terms of the sales agreement. The shares sold under the sales agreement, have been issued and sold pursuant to the universal shelf registration statement on Form S-3, filed with the Securities and Exchange Commission on July 2, 2015. The remaining shares that may be sold under the sales agreement are expected to be issued and sold, if at all, pursuant to the currently effective universal shelf registration statement on Form S-3, filed with the Securities and Exchange Commission on May 3, 2018. The Company did not sell shares of common stock under this sales agreement during the year ended December 31, 2018. The Company sold 420,796 shares of common stock under this sales agreement for net proceeds of $6.2 million during the year ended December 31, 2017.

The shares sold under the sales agreement have been issued and sold pursuant to the universal shelf registration statement on Form S-3, filed with the Securities and Exchange Commission on July 2, 2015. The remaining shares that may be sold under the sales agreement are expected to be issued and sold, if at all, pursuant to the currently effective universal shelf registration statement on Form S-3, filed with the Securities and Exchange Commission on May 3, 2018. As of December 31, 2018, we have sold an aggregate of 420,796 shares of common stock pursuant to this sales agreement, for net proceeds of $6.2 million.

(e) 2018 Charter Amendment

On May 15, 2018, the Company's stockholders approved an increase to the number of authorized shares of our common stock from 45,000,000 shares to 67,500,000 shares.

(12) Income Taxes

For the years ended December 31, 2018 and 2017, the Company did not record any federal or state income tax expense given its continued operating losses.

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A reconciliation between income tax benefit and the expected tax benefit at the statutory rate for the years ended December 31, 2018 and 2017 are as follows:

	For the Year Ended December 31,	
	2018	2017
Statutory federal income tax rate	21.0 %	34.0 %
State income taxes, net of federal benefit	5.9 %	4.4 %
Research and development tax credits	3.8 %	2.7 %
Orphan drug tax credits	3.2 %	10.9 %
Deferred rate change	— %	(104.4)%
Expiration of NOLs/Credits	(13.5)%	— %
Permanent Adjustments and other	(1.1)%	(6.5)%
Change in valuation allowance	(19.3)%	58.9 %
Effective income tax rate	— %	— %

The principle components of the Company’s deferred tax assets at December 31, 2018 and 2017, respectively, are as follows:

	December 31,	
	2018	2017
Deferred Tax Assets:		
NOL carryforwards	$67,068	$63,688
Research and development tax credit carryforwards	15,825	15,340
Orphan drug tax credit carryforwards	16,625	15,580
Depreciation and amortization	10,672	11,663
Capitalized research and development expenditures	33,993	32,550
Stock options	5,783	4,948
Accrued expenses and other	259	155
Total Gross Deferred Tax Asset	150,225	143,924
Valuation Allowance	(150,225)	(143,924)
Net Deferred Tax Asset	$—	$—

For the years ended December 31, 2018 and 2017, the Company had federal net operating losses, or NOLs, of $282.0 and $273.5 million, respectively. The operating losses generated prior to 2018 will expire in years 2019 through 2037, unless previously utilized. The federal operating loss carryforward generated in 2018 can be carried forward indefinitely. For the years ended December 31, 2018 and 2017, the Company had state NOLs of $124.0 and $98.6 million, respectively. The operating losses will expire in years 2019 through 2038, unless previously utilized.

For the years ended December 31, 2018 and 2017, the Company had federal research and development credit carryforwards of $12.3 and $11.6 million, respectively. The credits will expire in the years 2019 through 2037.

For the years ended December 31, 2018 and 2017, the Company had state research and development credit carryforwards of $4.5 and $4.7 million, respectively. The credits will expire in the years 2019 through 2033, unless previously utilized.

For the years ended December 31, 2018 and 2017, the Company had orphan drug tax credit carryforwards of $16.6 and $15.6 million , these credits, if any, relate to qualified expenses incurred for CUDC-907 since receiving the Orphan Drug designation.

As required by U.S. GAAP, the Company’s management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, and has determined that it is more likely than not that the Company will not recognize the benefits of the deferred tax assets. Accordingly, a valuation allowance of approximately $150.2 million has been established at December 31, 2018.

The valuation allowance increased (decreased) approximately $6.3 million and $(31.4) million during the years ended December 31, 2018 and 2017. The current year increase in the valuation allowance is primarily due to the

current year net operating loss offset by the valuation allowance. The decrease in 2017 is primarily due to the impact of the Tax Reform Act on the ending deferred assets which offset the increase in net operating loss carryforwards.

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Utilization of the NOL and research and development, or R&D, credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company has not completed a study to assess whether a change of control has occurred or whether there have been multiple changes of control since the Company's formation because the Company continues to maintain a full valuation allowance on its NOL and R&D credit carryforwards. In addition, there could be additional ownership changes in the future, which may result in additional limitations in the utilization of the carryforward NOLs and credits, and the Company does not expect to have any taxable income for the foreseeable future.

An individual tax position must satisfy for some or all of the benefits of that position to be recognized in a company's financial statements. At December 31, 2018 and 2017, the Company had no unrecognized tax benefits. The Company has not, as yet, conducted a study of its R&D credit carryforwards. This study may result in an adjustment to the Company's R&D credit carryforwards, however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position under Topic 740. A full valuation allowance has been provided against the Company's R&D credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheet or statement of operations if an adjustment were required.

The tax years 2003 through 2018 remain open to examination by major taxing jurisdictions to which the Company is subject, which are primarily in the U.S., as carryforward attributes generated in years past may still be adjusted upon examination by the Internal Revenue Service, or IRS, or state tax authorities if they have or will be used in a future period. The Company is currently not under examination by the IRS or any other jurisdictions for any tax years. The Company recognizes both accrued interest and penalties related to unrecognized benefits in income tax expense. The Company has not recorded any interest or penalties on any unrecognized tax benefits since its inception.

On December 22, 2017 the US government enacted comprehensive tax legislation known as the Tax Cuts and Jobs Act (the "Tax Act"). The Tax Act made significant changes to U.S. corporate income tax laws including a decrease in the corporate income tax rate to 21% effective January 1, 2018.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 ("SAB 118") to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Reform Act. The Company has recognized the provisional tax impacts related to the revaluation of the deferred tax assets and liabilities and included these amounts in its consolidated financial statements for the year ended December 31, 2017. The ultimate impact may differ from these provisional amounts due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued, and actions the Company may take as a result of the Tax Reform Act. The Company completed the accounting for all of the enacted date income tax effects of the Act during 2018. No adjustments were recognized to the provisional amounts recorded at December 31, 2017.

(13) Related Party Transactions

(a) Agreement with Head of Research and Development - Robert E. Martell, M.D., Ph.D.

On October, 17, 2018, the Company entered into an exclusive option and license agreement with Epi-Cure Pharmaceuticals, Inc., ("Epi-Cure") a privately held early-stage biotechnology company. Robert E. Martell, M.D., Ph.D., the Company's Head of Research and Development and a former director of the Company, is a founder of Epi-Cure, was formerly an officer and director of Epi-Cure, and is currently a holder of a convertible promissory note to Epi-Cure. Under the terms of the option and license agreement, Epi-Cure has granted Curis an exclusive option to certain program compounds that may arise during the initial research and development period, and any extension thereof. Upon execution of the option and license agreement, the Company has agreed to pay Epi-Cure an upfront payment of $0.1 million for legal and consulting costs incurred by Epi-Cure in connection with the transaction. Under the terms of the agreement, Epi-Cure will have primary responsibility for conducting research and development activities and Curis will be responsible for funding up to $0.5 million of the research and development program costs and expenses during the initial research and development period. After the end of the initial research and development

period, Curis has sixty days to elect to exercise its option to license the program compounds. If the Company makes this election it will make a $2.0 million license fee payment and will be responsible for the development and commercialization of products that may result from the collaboration. Curis will also make cash payments to Epi-Cure subject to successful achievement of certain patent, development, regulatory, and commercial milestones, up to $63.0 million and will also pay Epi-Cure mid-single digit royalties on net product sales if product candidates derived from this collaboration are successfully developed.

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Epi-Cure has retained the right to opt in to co-develop and share in profits upon initiation of a Phase 2 clinical study, in which event Curis will share in any development costs and profits on a 50/50 basis. Epi-Cure also has the right to opt-out of co-development/co-profit in which case they will receive royalty payments in lieu of profit-sharing.

Each party has the right to terminate the agreement for uncured material breach by the other party. Curis has the right to terminate the agreement for its convenience upon sixty days prior written notice. The agreement also sets forth customary terms regarding each party's intellectual property ownership rights, representations and warranties, indemnification obligations, confidentiality rights and obligations, patent prosecution, and maintenance and defense rights and obligations.

For the period ended December 31, 2018, Curis has paid and expensed $0.1 million of fees related to this agreement.

(b) Agreement with David Tuck

On May 24, 2018, the Company announced that David Tuck, M.D., Chief Medical Officer, provided notice of his intention to retire from the Company, effective as of August 31, 2018. Dr. Tuck subsequently determined to retire on August 3, 2018. The Company and Dr. Tuck entered into a letter agreement on August 1, 2018 (the "Letter Agreement") pursuant to which Dr. Tuck agreed to provide the Company with specified advisory services commencing on August 4, 2018 and extending until May 3, 2019, subject to earlier termination (the "Advisory Period"). In consideration for Dr. Tuck's advisory services, the Company has agreed to (i) pay him a monthly retainer of $35,000 during the Advisory Period and (ii) reimburse him for any pre-approved reasonable, documented out-of-pocket expenses relating to his advisory services. In addition, the Company and Dr. Tuck have agreed to amend his stock option agreements such that his outstanding options will cease to vest as of his date of resignation on August 3, 2018. The Letter Agreement may be terminated (i) at any time upon the mutual written consent of the parties, (ii) at any time by the Company immediately upon Dr. Tuck's breach or threatened breach of the terms of his Invention, Non-Disclosure and Non-Competition Agreement with the Company, or (iii) by the Company at any time upon Dr. Tuck's material breach of the terms of the Letter Agreement and failure to cure such breach within five days after written notice from the Company. In the event of termination of the Letter Agreement, Dr. Tuck will be entitled to payment for services performed and expenses paid or incurred prior to the effective date of termination that have not previously been paid. The Letter Agreement also contains other customary terms and conditions relating to his advisory service.

While the Company may utilize Dr. Tuck's consulting services in the future, the Company deemed the services to be a reduced level of service and not substantive. Under ASC 450, Contingencies, when an employee terminates and enters into a consulting agreement and the services to be provided are not deemed substantive, the transaction should be accounted for as a severance arrangement with no future service requirement. Based on this guidance, the Company recognized $0.3 million of expense during 2018, which represented the total obligation under the Letter Agreement.

(14) Retirement Savings Plan

The Company has a 401(k) retirement savings plan covering substantially all of the Company's employees. For the years ended December 31, 2018 and 2017, the Company made matching contributions of $0.2 million and $0.3 million, respectively.

(15) Selected Quarterly Financial Data (Unaudited)

The following are selected quarterly financial data for the years ended December 31, 2018 and 2017:

	Quarter Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
Revenues	$2,468	$ 2,358	$ 2,847	$ 2,755
Loss from operations	(9,908)	(7,860)	(6,417)	(5,148)
Net loss	(10,747)	(8,664)	(7,223)	(5,941)
Net loss per common share (basic and diluted)	$(0.33)	$ (0.26)	$ (0.22)	$ (0.18)
Weighted average common shares (basic and diluted)	33,053,703	33,135,391	33,161,592	33,121,666

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	Quarter Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Revenues	$2,131	$ 2,061	$ 2,444	$ 3,262
Loss from operations	(15,053)	(13,109)	(14,471)	(7,127)
Net loss	(15,742)	(14,090)	(15,457)	(8,028)
Net loss per common share (basic and diluted)	$(0.55)	$ (0.49)	$ (0.53)	$ (0.24)
Weighted average common shares (basic and diluted)	28,402,352	28,757,341	29,302,839	32,801,650

The net loss amounts presented for the quarters ended March 31, 2017 and September 30, 2017 include milestone payments of $3.8 million made under the Company's collaboration with Aurigene, which were recognized as research and development expenses (see Note 4(b)).

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(16) Subsequent Event

Royalty Interest Purchase Agreement

On March 22, 2019, the Company and Curis Royalty entered into the Oberland Purchase Agreement pursuant to which the Company sold to the Purchasers a portion of its rights to receive royalties from Genentech on potential net sales of Erivedge®.

As upfront consideration for the purchase of the royalty rights, at closing the Purchasers paid to Curis Royalty $65.0 million less certain transaction expenses. Curis Royalty will also be entitled to receive up to approximately $70.7 million in milestone payments based on sales of Erivedge as follows: (i) $17.2 million if the Purchasers and Curis Royalty receive aggregate royalty payments pursuant to the Oberland Purchase Agreement in excess of $18.0 million during the calendar year 2021, subject to certain exceptions and (ii) $53.5 million if the Purchasers receive payments pursuant to the Oberland Purchase Agreement in excess of $117.0 million on or prior to December 31, 2026.

Concurrently with the closing of the Oberland Purchase Agreement Curis Royalty's used a portion of the proceeds to terminate and repay the loan with Healthcare Royalty. In connection with such termination, Curis Royalty paid approximately $37.2 million to satisfy its remaining loan obligations to HealthCare Royalty, including approximately $33.8 million in principal balance on the loan and $3.4 million in accrued and unpaid interest and prepayment fees. Curis Royalty also used a portion of the proceeds to pay transaction costs of approximately $0.3 million, resulting in net proceeds of approximately $27.5 million. For further discussion please refer to "Part II, Item 9B. Other Information - Royalty Interest Purchase Agreement."

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls & Procedures

Our management, with the participation of our chief executive officer, and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2018. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2018, our chief executive officer concluded that, as of such date, our disclosure controls and procedures were effective.

Management's report on internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, is included in Item 8 of this annual report on Form 10-K and is incorporated herein by reference.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2018. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in its 2013 Internal Control—Integrated Framework.

Changes in Internal Control Over Financial Reporting

No changes in our internal control over financial reporting occurred during the fourth quarter of the fiscal year ended December 31, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

Royalty Interest Purchase Agreement

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On March 22, 2019, we and our wholly-owned subsidiary Curis Royalty LLC, or Curis Royalty, entered into a royalty interest purchase agreement, referred to as the Oberland Purchase Agreement, with TPC Investments I LP and TPC Investments II LP, referred to as the Purchasers, each of which is a Delaware limited partnership managed by Oberland Capital Management, LLC and Lind SA LLC, referred to as the Agent, a Delaware limited liability company managed by Oberland Capital Management, LLC, as collateral agent for the Purchasers, for the purpose of providing operating cash flow and extinguishing the credit agreement, dated as of March 6, 2017, among Curis, Curis Royalty and HealthCare Royalty Partners III, L.P., or HealthCare Royalty, referred to as the existing loan. In connection with entering in the Oberland Purchase Agreement, Curis Royalty and the Agent also entered into a security agreement, we and the Agent entered into a pledge agreement and we and Curis Royalty entered into a consent and payment direction letter agreement with Genentech Inc., or Genentech.

Pursuant to the Oberland Purchase Agreement, the Purchasers acquired the rights to a portion of certain royalty and royalty-related payments excluding a portion of non-US royalties retained by Curis Royalty, referred to as the Purchased Receivables, owed by Genentech under our collaboration agreement with Genentech, the rights to which were, transferred from Curis to Curis Royalty in 2012 pursuant to a purchase and sale agreement between Curis and Curis Royalty, referred to as the purchase and sale agreement, in connection with a prior loan from BioPharma Secured Debt Fund II Sub, S.à.r.l. Upon closing of the Oberland Purchase Agreement, Curis Royalty received an upfront purchase price of $65.0 million from the Purchasers, approximately $33.8 million of which was used to pay off the remaining loan principal to HealthCare Royalty under the existing loan, and $3.7 million of which was used to pay transaction costs, including $3.4 million to HealthCare Royalty in accrued and unpaid interest and prepayment fees under the existing loan agreement, resulting in net proceeds of $27.5 million. Curis Royalty will also be entitled to receive milestone payments of (i) $17.2 million if the Purchasers and Curis Royalty receive aggregate royalty payments as described in clauses (4) and (5) of the following paragraph pursuant to the Oberland Purchase Agreement in excess of $18.0 million during the calendar year 2021 and (ii) $53.5 million if the Purchasers receive payments pursuant to the Oberland Purchase Agreement in excess of $117.0 million on or prior to December 31, 2026, which milestone payments may each be paid, at the option of the Purchasers, in a lump sum in cash or out of the Purchaser's portion of future payments under the Oberland Purchase Agreement.

Pursuant to the terms of the Oberland Purchase Agreement, so long as an event of default by Curis Royalty has not occurred under the security agreement, royalty and royalty-related payments owed by Genentech under the Genentech collaboration agreement in each calendar year shall be allocated in the following order: (1) Curis Royalty shall receive, the Retained Royalty Amounts (as previously defined) to the extent actually paid by Genentech under the Genentech collaboration agreement, (2) Curis Royalty shall receive payments to satisfy Curis' royalty obligations to certain academic institutions subject to a specified percentage cap and/or a specified period of time, (3) Curis Royalty shall receive a fixed amount of payments to reimburse intellectual property and other enforcement costs, whether or not actually incurred by us, (4) the Purchasers shall receive 100% of all payments up to $13.19 million in the aggregate in such calendar year, and (5) any additional payments in such calendar year shall be paid 65.0% to Curis Royalty and 35.0% to the Purchasers.

The Oberland Purchase Agreement also provides that, so long as an event of default by Curis Royalty has not occurred under the security agreement, if Curis Royalty recovers any monetary award or settlement or any other non-ordinary course lump sum payment made in respect of the royalty and royalty-related payments owed by Genentech under the Genentech collaboration agreement that does not specifically relate to any calendar period, then such payment or other recovery shall be allocated in the following order: (1) Curis Royalty shall receive payments to satisfy Curis' royalty obligations to certain academic institutions up to a specified percentage cap, (2) the Purchasers shall receive 100% of all such payments up to an amount equal to the product of $13.19 million and the number of full calendar years, and any fraction thereof, in the period beginning on the first day of the calendar quarter in which such payment or other recovery is received and ending on December 31, 2028, subject to certain exceptions, and (3) any additional payment shall be paid 65.0% to Curis Royalty and 35.0% to the Purchasers.

Following an event of default under the security agreement, the Agent has the right to stop all allocations of payments that would have otherwise been allocated to Curis Royalty pursuant to the foregoing two paragraphs and instead retain all such payments.

In addition, the Oberland Purchase Agreement provides that after the occurrence of an event of default by Curis Royalty under the security agreement, as described below, the Purchasers shall have the option, for a period of 180 days, to require Curis Royalty to repurchase the Purchased Receivables at a price, referred to as the Put/Call Price, equal to a percentage, beginning at a low triple digit percentage and increasing over time up to a low-mid triple digit percentage of the sum of the upfront purchase price and any portion of the milestone payments paid in a lump sum by the Purchasers, if any, minus certain payments previously received by the Purchasers with respect to the Purchased Receivables. Additionally, Curis Royalty shall have the option at any time to repurchase the Purchased Receivables at the Put/Call Price as of the date of such repurchase.

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The Oberland Purchase Agreement contains covenants applicable to Curis and Curis Royalty, including certain visitation, information and audits rights granted to the Agent and the Purchasers, restrictions on the conduct of business by Curis and Curis Royalty, including with respect to continued compliance with the Genentech collaboration agreement, and obligations to engage in enforcement and intellectual property defense actions with respect to the Genentech collaboration agreement and the related intellectual property. The Oberland Purchase Agreement also contains covenants solely applicable to Curis Royalty, including restrictions on incurring indebtedness, creating or granting liens, making acquisitions and making specified restricted payments. The Oberland Purchase Agreement also contains customary exculpation and indemnification obligations of Curis and Curis Royalty on behalf of the Agent and the Purchasers. These covenants and indemnities are subject to a number of important exceptions and qualifications. In addition, the Oberland Purchase Agreement contains other customary terms and conditions, including representations and warranties and conditions precedent.

The Oberland Purchase Agreement will terminate upon the earlier to occur of (i) the date on which Curis Royalty's rights to receive the Purchased Receivables owed by Genentech under the Genentech collaboration agreement have terminated in their entirety and (ii) the date on which payment in full of the Put/Call Price is received by the Purchasers pursuant to the Purchasers' exercise of their put option or Curis Royalty's exercise of its call right as described above.

Pursuant to the security agreement, Curis Royalty granted to the Agent a first priority lien and security interest in all of its assets and all real, intangible and personal property, including all of its right, title and interest in and to the Erivedge royalty payments pursuant to a security agreement. The security interest secures the obligations of Curis Royalty arising under the Oberland Purchase Agreement, the security agreement or otherwise with respect to the due and prompt payment of (i) an amount equal to the Put/Call Price and (ii) all fees, costs, expenses, indemnities and other payments of Curis Royalty under or in respect of the Oberland Purchase Agreement and the security agreement.

The obligations of Curis Royalty under the Oberland Purchase Agreement may be accelerated upon the occurrence of an event of default under the security agreement (subject to certain cure periods), including:

- any royalty and royalty-related payments to be remitted into a certain Curis Royalty designated account controlled by the Agent pursuant to a control agreement, referred to as the royalty account, into which all royalty and royalty-related payments must be paid by Curis or Curis Royalty are not so remitted in accordance with the Oberland Purchase Agreement;
- any representation or warranty made by Curis or Curis Royalty in the Oberland Purchase Agreement or any other transaction document proves to be incorrect or misleading in any material respect when made;
- a default by Curis or Curis Royalty in the performance of affirmative and negative covenants set forth in the Oberland Purchase Agreement or any other transaction document;
- a default by Curis in the performance or observance of its indemnity obligations under the Oberland Purchase Agreement;
- the failure by Genentech to pay material amounts owed under the Genentech collaboration agreement because of an actual breach or default by Curis under the Genentech collaboration agreement;
- the failure of the security agreement to create a valid and perfected first priority security interest in any of the collateral;
- a material breach or default by Curis under the purchase and sale agreement;
- the voluntary or involuntary commencement of bankruptcy proceedings by either Curis or Curis Royalty and other insolvency related events;
- any materially adverse effect on the binding nature of any of the Oberland Purchase Agreement, Security Agreement, Pledge Agreement or other transaction documents, the Genentech collaboration agreement or the purchase and sale agreement;
- any person shall be designated as an independent director of Curis Royalty other than in accordance with Curis Royalty's limited liability company operating agreement; or
- Curis shall at any time cease to own, of record and beneficially, 100.0% of the equity interests in Curis Royalty.

Upon the occurrence and continuance of an event of default under the security agreement, the Agent may exercise its rights and remedies under the security agreement with respect to Curis Royalty and to the collateral pledged

thereunder,

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including, among other things, acceleration of the obligations under the security agreement, the sale or other realization of the collateral and performance of Curis Royalty's obligations under the purchase and sale agreement. The exercise by the Agent of the foregoing rights shall be deemed to constitute an exercise by the Purchasers of their put option under the Oberland Purchase Agreement.

Additionally, in connection with the transaction, Curis granted to the Agent a first priority lien and security interest of Curis' equity interest in Curis Royalty pursuant to a pledge agreement. Upon the occurrence and continuance of an event of default under the security agreement, the Agent may exercise its rights and remedies under the pledge agreement with respect to the equity interests, including, among other things, the rights to receive distributions and exercise voting with respect to the equity interests and to sell or otherwise realize upon the collateral in satisfaction of the obligations. The exercise by the Agent of the foregoing rights shall be deemed to constitute an exercise by the Purchasers of their put option under the Oberland Purchase Agreement.

In connection with the transaction, Curis and Curis Royalty have also entered into a consent and payment direction letter agreement with Genentech, referred to as the consent and direction, pursuant to which Genentech consented to the new transaction with the Agent and the Purchasers and the pledge of Curis' equity interest in Curis Royalty to the Agent and agreed that it will make royalty payments under the Genentech collaboration agreement directly to the royalty account. Except as specifically amended or supplemented by the consent and direction letter, the terms and conditions of the Genentech collaboration agreement remain unchanged and in full force and effect.

In connection with entering into the Oberland Purchase Agreement, the existing loan was terminated and paid off in its entirety on March 22, 2019. In connection with such termination, Curis Royalty paid $37.2 million to satisfy its remaining loan obligations to HealthCare Royalty under the existing loan agreement, which included $33.8 million of the outstanding principal amount under the existing loan agreement and accrued and unpaid interest and prepayment fees in an aggregate amount of $3.4 million. The prepayment fees are equal to the amount of interest that would have accrued from the date of prepayment through and including the third anniversary of the closing date of the existing loan.

The representations, warranties and covenants contained in the agreements described above were made only for purposes of such agreements as of the specific dates therein, were solely for the benefit of the parties to such agreements, may be subject to limitations agreed upon by the contracting parties, including being qualified by confidential disclosures made for the purposes of allocating contractual risk between the parties instead of establishing these matters as facts, and may be subject to standards of materiality applicable to the contracting parties that differ from those applicable to investors. Investors are not third-party beneficiaries under the agreements and should not rely on the representations, warranties and covenants or any descriptions thereof as characterizations of the actual state of facts or condition of the parties thereto or any of their respective subsidiaries or affiliates. Moreover, information concerning the subject matter of representations and warranties may change after the date of the agreements, which subsequent information may or may not be fully reflected in our public disclosures.

The foregoing summary descriptions of the Oberland Purchase Agreement, security agreement, pledge agreement and consent and direction do not purport to be complete and are qualified in their entirety by reference to the full text of such agreements, which are filed as Exhibits 10.40, 10.41, 10.42, and 10.43, respectively, of this Annual Report on Form 10-K for the year ended December 31, 2018.

Appointment of Principal Accounting Officer

On March 23, 2019, our Board of Directors appointed William Steinkrauss to the position of principal accounting officer of the Company. Mr. Steinkrauss, age 33, has served as our vice president, treasurer and assistant secretary since January 2019, and prior to that served as our corporate controller and senior director of finance as well as assistant treasurer from August 2016 until January 2019. Mr. Steinkrauss previously served as director of technical accounting and reporting of Ovascience, Inc., a biotechnology company focused on infertility, from June 2015 to August 2016. Prior to that, he was senior manager of technical accounting at Cubist Pharmaceuticals, Inc., a biopharmaceutical company, from November 2012 to May 2015. Prior to joining Cubist Pharmaceuticals, Inc., Mr. Steinkrauss spent five years at PricewaterhouseCoopers, LLP within the transaction services and assurance practices. Mr. Steinkrauss holds a B.S. in accounting and finance and a M.S. in accounting from Boston College. Mr.

Steinkrauss is a certified public accountant.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Information concerning directors that is required by this Item 10 will be set forth in our proxy statement for our 2019 annual meeting of stockholders under the headings “Directors and Nominees for Director,” “Board Committees” and “Section 16(a) Beneficial Ownership Reporting Compliance,” which information is incorporated herein by reference. The information

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concerning our code of ethics is set forth in our proxy statement under the heading “Code of Business Conduct and Ethics.” The name, age, and position of each of our executive officers is set forth under the heading “Executive Officers of the Registrant” in Part I of this Annual Report on Form 10-K, which information is incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

Information required by this Item 11 will be set forth in our proxy statement for our 2019 annual meeting of stockholders under the headings “Executive and Director Compensation and Related Matters,” “Compensation Committee Interlocks and Insider Participation” and “Compensation Committee Report,” which information is incorporated herein by reference.

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

Information required by this Item 12 relating to security ownership of certain beneficial owners and management will be set forth in our 2019 proxy statement under the caption “Security Ownership of Certain Beneficial Owners and Management” and is incorporated herein by reference. Information required by this Item 12 relating to securities authorized for issuance under equity compensation plans will be set forth in our 2019 proxy statement under the caption “Executive and Director Compensation and Related Matters—Securities Authorized for Issuance Under Equity Compensation Plans” and is incorporated herein by reference.

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

Information required by this Item 13 will be set forth in our proxy statement for our 2019 annual meeting of stockholders under the headings “Policies and Procedures for Related Person Transactions,” “Determination of Independence” and “Board Committees,” which information is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Information required by this Item 14 will be set forth in our proxy statement for our 2019 annual meeting of stockholders under the heading “Independent Registered Public Accounting Firm’s Fees and Other Matters,” which information is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a)(1) Financial Statements.

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(a)(2) Financial Statement Schedules.

All schedules are omitted because they are not applicable or the required information is shown in the Financial Statement or Notes thereto.

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(a)(3) List of Exhibits.

Exhibit No.	Description	Link to Filing	Incorporated by Reference			Filed with this 10-K
			Form	SEC Filing Date	Exhibit Number	
	Articles of Incorporation and By-laws					
3.1	Restated Certificate of Incorporation of Curis, Inc., as amended	Link				X
3.2	Certificate of Designations of Curis, Inc.	Link	S-3 (333-50906)	8/10/2001	3.2	
3.3	Amended and Restated By-laws of Curis, Inc.	Link	10-K	2/29/2016	3.3	
	Instruments defining the rights of security holders, including indentures					
4.1	Form of Curis Common Stock Certificate	Link	10-K	3/1/2004	4.1	
	Material contracts—Management Contracts and Compensatory Plans					
#10.1	Employment Agreement, dated March 29, 2016, as amended September 24, 2018 by and between Curis, Inc. and James E. Dentzer.	Link	10-Q	11/1/2018	10.2	
#10.2	Employment Agreement, dated June 2, 2014 as amended March 21, 2018 by and between Curis, Inc. and Ali Fattaey, Ph. D	Link	10-Q	5/3/2018	10.1	
#10.3	Employment Agreement, dated February 29, 2016 as amended March 21, 2018 by and between Curis, Inc. and David Tuck, M.D	Link	10-Q	5/3/2018	10.3	
#10.4	Employment Agreement, dated June 1, 2018, by and between Curis, Inc. and Robert E. Martell, M.D., Ph.D.	Link	10-Q	8/2/2018	10.2	
#10.5	Separation Agreement, dated September 24, 2018, by and between Curis, Inc. and Ali Fattaey, Ph.D.	Link	10-Q	11/1/2018	10.3	
#10.6	Letter Agreement, dated August 1, 2018, by and between Curis, Inc. by and David Tuck, M.D.	Link	10-Q	8/2/2018	10.1	
#10.7	Form of Indemnification Agreement, by and between Curis, Inc. and each non-employee director of the Board of Directors of Curis, Inc.	Link	10-Q	8/7/2014	10.3	
#10.8	Curis 2000 Stock Incentive Plan	Link	S-4/A (333-32446)	5/31/2000	10.71	
#10.9	Curis 2000 Director Stock Option Plan	Link	S-4/A (333-32446)	5/31/2000	10.72	
#10.10	Form of Incentive Stock Option Agreement for awards granted to named executive officers under Curis' 2000 Stock Incentive Plan	Link	10-Q	10/26/2004	10.2	
#10.11	Form of Non-statutory Stock Option Agreement for awards granted to directors and named executive officers under Curis' 2000 Stock Incentive Plan	Link	10-Q	10/26/2004	10.3	
#10.12	Form of Non-statutory Stock Option Agreement for awards granted to non-employee directors under Curis' 2000 Director Stock Option Plan	Link	10-Q	10/26/2004	10.4	

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#10.13	Curis 2010 Stock Incentive Plan		Link	Def 14A	4/16/2010	Exhibit A
#10.14	Curis 2010 Employee Stock Purchase Plan		Link	Def 14A	4/16/2010	Exhibit B
#10.15	Form of Incentive Stock Option Agreement for awards granted to named executive officers under Curis' 2010 Stock Incentive Plan		Link	8-K	6/4/2010	10.1

Exhibit No.	Description	Link to Filing	Incorporated by Reference			Filed with this 10-K
			Form	SEC Filing Date	Exhibit Number	
#10.16	Form of Non-Statutory Stock Option Agreement for awards granted to directors and named executive officers under Curis' 2010 Stock Incentive Plan	Link	8-K	6/4/2010	10.2	
#10.17	Form of Restricted Stock Agreement for awards granted to directors and named executive officers under Curis' 2010 Stock Incentive Plan	Link	8-K	6/4/2010	10.3	
#10.18	Curis Amended and Restated 2010 Stock Incentive Plan, as amended	Link	8-K	5/28/2015	99.1	
#10.19	Form of Incentive Stock Option Agreement for awards granted to named executive officers under Curis' Amended and Restated 2010 Stock Incentive Plan, as amended	Link	10-K	3/8/2018	10.21	
#10.20	Form of Non-Statutory Stock Option Agreement for awards granted to directors and named executive officers under Curis' Amended and Restated 2010 Stock Incentive Plan, as amended	Link	10-K	3/8/2018	10.22	
#10.21	Form of Restricted Stock Agreement for awards granted to directors and named executive officers under Curis' Amended and Restated 2010 Stock Incentive Plan, as amended	Link	10-K	3/8/2018	10.23	
#10.22	Form of Incentive Stock Option Agreement (Online Acceptance) for awards granted to named executive officers under Curis' Amended and Restated 2010 Stock Incentive Plan	Link	10-K	3/9/2017	10.21	
#10.23	Form of Nonstatutory Stock Option Agreement (Online Acceptance) granted to directors and named executive officers under Curis' Amended and Restated 2010 Stock Incentive Plan	Link	10-K	3/9/2017	10.22	
#10.24	Curis Second Amended and Restated 2010 Stock Incentive Plan	Link	8-K	5/22/2017	99.1	
#10.25	Form of Incentive Stock Option Agreement for awards granted to named executive officers under Curis' Second Amended and Restated 2010 Stock Incentive Plan	Link	10-K	3/8/2018	10.27	
#10.26	Form of Non-Statutory Stock Option Agreement for awards granted to directors and named executive officers under Curis' Second Amended and Restated 2010 Stock Incentive Plan	Link	10-K	3/8/2018	10.28	

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#10.27	Form of Restricted Stock Agreement for awards granted to directors and named executive officers under Curis' Second Amended and Restated 2010 Stock Incentive Plan	Link	10-K	3/8/2018	10.29	
#10.28	Form of Nonstatutory Stock Option Agreement - Inducement Grant pursuant to Nasdaq Stock Market Rule 5635(c)(4)	Link	S-8	1/6/2017	99.1	
#10.29	Curis Third Amended and Restated 2010 Stock Incentive Plan	Link	8-K	5/18/2018	99.1	
#10.30	Curis Amended and Restated 2010 Employee Stock Purchase Plan, as amended	Link	10-K	3/8/2018	10.31	

			Incorporated by Reference			
Exhibit No.	Description	Link to Filing	Form	SEC Filing Date	Exhibit Number	Filed with this 10-K
	Material contracts—Leases					
#10.31	Lease, dated September 16, 2010, by and between Curis, Inc. and the Trustees of Lexington Office Realty Trust relating to the premises at 4 Maguire Road, Lexington, Massachusetts	Link	8-K	9/21/2010	10.1	
#10.32	Second Amendment to Lease, dated November 1, 2017, by and between Curis, Inc. and the Trustees of Lexington Office Realty Trust relating to the premises at 4 Maguire Road, Lexington, Massachusetts	Link	10-Q	11/7/2017	10.2	
	Material contracts—Financing Agreements					
†10.33	Credit Agreement, dated November 27, 2012, by and between Curis, Inc., Curis Royalty LLC, a wholly-owned subsidiary of Curis, Inc. and BioPharma Secured Debt Fund II Sub, S.à r.l.	Link	10-K	3/13/2013	10.31	
10.34	Consent and Payment Direction Letter Agreement, dated November 20, 2012 and effective as of December 11, 2012 by and between Curis, Inc., Curis Royalty LLC and Genentech, Inc.	Link	10-K	3/13/2013	10.32	
†10.35	Credit Agreement, dated March 6, 2017, by and between Curis, Inc., Curis Royalty LLC, a wholly-owned subsidiary of Curis, Inc. and HealthCare Royalty Partners III, L.P.	Link	10-K	3/9/2017	10.27	
10.36	Consent and Payment Direction Letter Agreement, dated March 3, 2017 by and between Curis, Inc., Curis Royalty LLC and Genentech, Inc.	Link	10-K	3/9/2017	10.28	
†10.37	Purchase and Sale Agreement, dated as of December 11, 2012 between Curis and Curis Royalty	Link	10-K	3/13/2013	10.33	
10.38	Escrow Agreement, dated December 11, 2012, by and between Curis, Curis Royalty LLC, a wholly-owned subsidiary of Curis, BioPharma Secured Debt Fund II Sub, S.à r.l., a Luxembourg limited liability company managed by Pharmakon Advisors and Boston Private Bank and Trust Company	Link	10-K	3/13/2013	10.34	
10.39	Escrow Agreement, dated March 22, 2017, by and between Curis Royalty LLC, HealthCare Royalty Partners III, L.P., Curis, Inc. and Boston Private Bank and Trust Company	Link	10-Q	5/4/2017	10.1	

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††10.40	Royalty Interest Purchase Agreement, dated March 22, 2019, by and between, Curis, Inc., Curis Royalty LLC, a wholly-owned subsidiary of Curis, Inc., TPC Investments I LP and TPC Investments II LP	Link					X
10.41	Security Agreement, dated March 22, 2019, by and between, Curis Royalty LLC, a wholly-owned subsidiary of Curis, Inc., TPC Investments I LP and TPC Investments II LP	Link					X
10.42	Pledge Agreement, dated March 22, 2019, by and between, Curis, Inc. , TPC Investments I LP and TPC Investments II LP	Link					X
10.43	Consent and Payment Direction Letter Agreement, dated March 22, 2019, by and between Curis, Inc., Curis Royalty LLC and Genentech, Inc.	Link					X
	Material contracts—License and Collaboration Agreements						
†10.44	Collaborative Research, Development and License Agreement, dated June 11, 2003, by and between Curis, Inc. and Genentech, Inc.	Link	10-Q	8/6/2015	10.1		
†10.45	Collaboration, License and Option Agreement, dated January 18, 2015, by and between Curis, Inc. and Aurigene Discovery Technologies Limited	Link	10-K	2/24/2015	10.32		
†10.46	First Amendment to Collaboration, License and Option Agreement, dated September 7, 2016, by and between Curis, Inc. and Aurigene Discovery Technologies Limited	Link	10-Q	11/3/2016	10.2		

Exhibit No.	Description	Link to Filing	Incorporated by Reference				Filed with this 10-K
			Form	SEC Filing Date	Exhibit Number		
	Material contracts—Miscellaneous						
10.47	Sales Agreement, dated July 2, 2015, by and between Curis, Inc. and Cowen and Company, LLC	Link	S-3	7/2/2015	1.2		
10.48	Underwriting Agreement, dated September 13, 2017, by and between Curis, Inc. and Robert W. Baird & Co. Incorporated	Link	8-K	9/15/2017	1.1		
10.49	Common Stock Purchase Agreement, dated January 18, 2015, by and between Curis, Inc. and Aurigene Discovery Technologies Limited	Link	10-K	2/24/2015	10.34		
10.50	Stock Purchase Agreement, dated September 7, 2016, by and between Curis, Inc. and Aurigene Discovery Technologies Limited	Link	10-Q	11/3/2016	10.3		
10.51	Registration Rights Agreement, dated January 18, 2015, by and between Curis, Inc. and Aurigene Discovery Technologies Limited	Link	10-K	2/24/2015	10.35		
10.52	Registration Rights Agreement, dated September 7, 2016, by and between Curis, Inc. and Aurigene Discovery Technologies Limited	Link	10-Q	11/3/2016	10.4		
	Code of Conduct						
14	Amended and Restated Code of Business Conduct and Ethics	Link	10-K	3/8/2018	14		
	Additional Exhibits						
21	Subsidiaries of Curis	Link					X

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23.1	Consent of PricewaterhouseCoopers LLP	Link	X
31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) of the Exchange Act/15d-14(a) of the Exchange Act	Link	X
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a) of the Exchange Act/15d-14(a) of the Exchange Act	Link	X
32.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(b)/15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350	Link	X
32.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(b)/15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350	Link	X
101.INS	XBRL Instance Document		X
101.SCH	XBRL Taxonomy Extension Schema Document		X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document		X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document		X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document		X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document		X

# Indicates management contract or compensatory plan or arrangement.

† Confidential treatment has been granted as to certain portions, which portions have been separately filed with the Securities and Exchange Commission.

†† Confidential treatment has been requested as to certain portions, which portions have been separately filed with the Securities and Exchange Commission.

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ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

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

CURIS, INC.

By: /s/ JAMES DENTZER
James Dentzer
President and Chief Executive Officer

Date: March 26, 2019

Pursuant to the requirements of the Securities Exchange Act of 1934, 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/ JAMES DENTZER James Dentzer	President, Chief Executive Officer and Director (Principal Executive Officer and Principal Financial Officer)	March 26, 2019
/s/ WILLIAM STEINKRAUSS William Steinkrauss	Vice President, Finance (Principal Accounting Officer)	March 26, 2019
/s/ MARTYN D. GREENACRE Martyn D. Greenacre	Chairman of the Board of Directors	March 26, 2019
/s/ KENNETH I. KAITIN Kenneth I. Kaitin	Director	March 26, 2019
/s/ LORI A. KUNKEL Lori A. Kunkel	Director	March 26, 2019
/s/ MARC RUBIN Marc Rubin	Director	March 26, 2019