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

# FORM 10-K

**(Mark One)**

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

**For the Fiscal Year Ended December 31, 2018**

**OR**

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

**For the Transition Period from_____ to _____**

**Commission File Number: 001-37708**

# Syndax Pharmaceuticals, Inc.

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

| **Delaware** | **2834** | **32-0162505** |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation or Organization)** | **(Primary Standard Industrial Classification Code Number)** | **(I.R.S. Employer Identification Number)** |

**35 Gatehouse Drive, Building D, Floor 3**
**Waltham, Massachusetts 02451**

**(781) 419-1400**

**(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)**

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

| **Title of Each Class** | **Name of Each Exchange on Which Registered** |
|---|---|
| **Common Stock, par value $0.0001 per share** | **Nasdaq Global Select 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 ☒

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to the filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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

| | | | |
|---|---|---|---|
| Large Accelerated Filer | ☐ | Accelerated Filer | ☒ |
| Non-accelerated Filer | ☐ | Smaller Reporting Company | ☒ |
| Emerging growth company | ☒ | | |

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

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

As of June 30, 2018, the last day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately $118.0 million, based on the closing price of the registrant's common stock on June 30, 2018. Shares of the registrant's common stock held by each officer and director and each person known to the registrant to own 10% or more of the outstanding common stock of the registrant have been excluded in that such persons may be deemed affiliates. This determination of affiliate status is not a determination for other purposes.

As of March 6, 2019, there were 25,000,740 shares of common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive proxy statement for its 2019 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2018, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical fact are "forward-looking statements" for purposes of this Annual Report on Form 10-K. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "could," "estimate," "expects," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative or plural of those terms, and similar expressions.

Forward-looking statements include, but are not limited to, statements about:

- our estimates regarding our expenses, future revenues, anticipated capital requirements and our needs for additional financing;
- the timing of the progress and receipt of data from the Phase 1b/2 clinical trials of entinostat in hormone receptor positive, human epidermal growth factor receptor 2 negative (HR+, HER2-) breast cancer;
- the timing of the progress and receipt of data from the Phase 3 clinical trial of entinostat in advanced HR+, HER2- breast cancer;
- the timing of the progress and receipt of data from the Phase 1 clinical trial of SNDX-6352 and the potential use of SNDX-6352 to treat various cancer indications;
- the timing of the progress and receipt of data from the Phase 1b clinical trial of SNDX-6352 in chronic Graft Versus Host Disease (cGVHD);
- the timing of the filing of our Investigational New Drug application of SNDX-5613 and the potential use of SNDX-5613 to treat acute leukemias;
- the scope, timing of the commencement, progress and receipt of data from any other clinical trials that we and our collaborators may conduct;
- our ability to replicate results in future clinical trials;
- our expectations regarding the potential safety, efficacy or clinical utility of our product candidates;
- our ability to obtain and maintain regulatory approval for our product candidates and the timing or likelihood of regulatory filings and approvals for such candidates;
- our ability to maintain our licenses with Bayer Pharma AG, Kyowa Hakko Kirin Co., Ltd., UCB Biopharma Sprl and Vitae Pharmaceuticals, Inc., a subsidiary of Allergan plc;
- the potential milestone and royalty payments under certain of our license agreements;
- the implementation of our strategic plans for our business and development of our product candidates;
- the scope of protection we establish and maintain for intellectual property rights covering our product candidates and our technology;
- the market adoption of our product candidates by physicians and patients; and
- developments relating to our competitors and our industry.

Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part I, Item 1A, "Risk Factors," below and for the reasons described elsewhere in this Annual Report on Form 10-K. Any forward-looking statement in this Annual Report on Form 10-K reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions. Given these uncertainties, you should not rely on these forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, our information may be incomplete or limited and we cannot guarantee future results. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

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

In this Annual Report on Form 10-K, unless otherwise stated or as the context otherwise requires, references to “Syndax,” “the Company,” “we,” “us,” “our” and similar references refer to Syndax Pharmaceuticals, Inc. and its wholly owned subsidiaries. This Annual Report on Form 10-K also contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies’ trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

## PART I

### Item 1. BUSINESS

### Our Company

We are a clinical-stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Our lead product candidate, entinostat is a once-weekly, oral, small molecule, Class I HDAC inhibitor currently being evaluated in a Phase 3 clinical trial in combination with exemestane for advanced hormone receptor positive, or HR+, human epidermal growth factor receptor 2 negative, or HER2-, breast cancer, an indication for which it has been granted breakthrough therapy designation by the FDA. Entinostat has been shown to block the function of immune suppressive cells in the tumor microenvironment, and is being evaluated in combination with several approved PD-1/PD-L1 antagonists, including in Phase 1b/2 clinical trials combining entinostat with *Keytruda*® (pembrolizumab) from Merck & Co., Inc. for non-small cell lung cancer and melanoma; and with *Tecentriq*® (atezolizumab) from Genentech, Inc., a member of the Roche Group, for advanced HR+, HER2- breast cancer.

Our second clinical-stage product candidate, SNDX-6352, is a monoclonal antibody that targets the colony stimulating factor-1 receptor, or CSF-1R, a cell surface protein thought to control the survival and function of monocytes and macrophages. In many cancers, inhibition of CSF-1R will reduce the number of immunosuppressive tumor-associated macrophages, or TAMs, and enable an immune response against tumors. We expect topline results and a recommended Phase 2 dose, or RP2D, and schedule from the Phase 1/1b trial of SNDX-6352, alone or in combination with *Imfinzi*® (durvalumab), from AstraZeneca plc, in the second quarter of 2019. We are also expecting topline results and a RP2D and schedule from the Phase 1 trial of SNDX-6352 in patients with chronic graft versus host disease, or cGVHD, in the fourth quarter of 2019.

In the third quarter of 2018, development of our portfolio of preclinical, orally-available, small molecule inhibitors of the interaction of Menin with the mixed lineage leukemia, or MLL, protein led to our selection of a lead compound, SNDX-5613, to continue through IND-enabling studies. We are developing SNDX-5613 as a targeted therapy to potentially treat two genetically defined acute leukemias: (i) mixed lineage leukemia-rearranged, or MLLr, a genetically-defined subset of acute leukemias with chromosomal rearrangements in the MLL gene; and (ii) acute myeloid leukemia, or AML, with a mutated nucleophosmin 1, or NPM1, characterized by a somatic mutation in the NPM1 gene, or NPM1c. We expect to file an IND with the FDA in the second quarter of 2019 and initiate a Phase 1 clinical trial in leukemia patients having relapsed or refractory MLLr or NPM1c AML soon after.

We plan to continue to leverage the technical and business expertise of our management team and scientific collaborators to opportunistically license, acquire and develop additional cancer therapies to expand our pipeline.

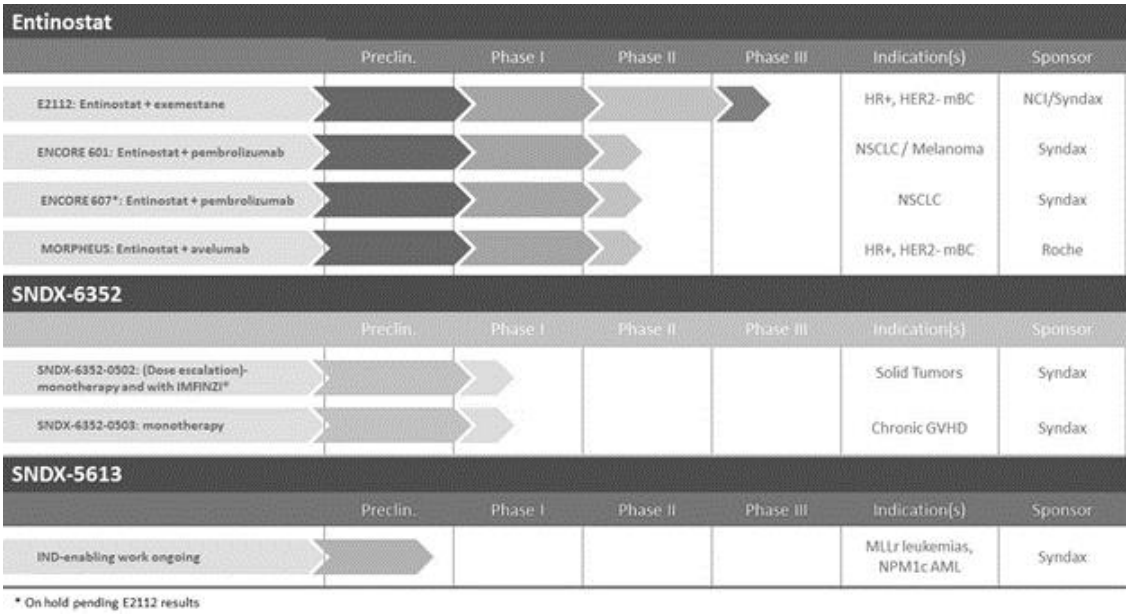
### Our Strategy

We are developing entinostat, SNDX-6352 and SNDX-5613 for use in multiple cancer and potentially other indications in combination with complementary therapeutic drugs and potentially as single agents. Key elements of our strategy include:

- Develop and obtain regulatory approval for entinostat in combination with hormone therapy in advanced HR+, HER2- breast cancer. Based on the positive results from our Phase 2b clinical trial, we received breakthrough therapy designation from the FDA for entinostat in combination with exemestane in advanced HR+ breast cancer. We believe that the submission of the overall survival, or OS, results of the Phase 3 clinical trial, if successful, would be sufficient for regulatory approval of entinostat in the United States.
- Develop SNDX-5613 for the treatment of MLL-r driven malignancies. We believe that SNDX-5613 has the potential to treat at least two genetically defined acute leukemias: (i) MLLr, a genetically-defined subset of acute leukemias with chromosomal rearrangements in the MLL gene; and (ii) NPM1c AML, characterized by a somatic mutation in the NPM1 gene. We conducted preclinical studies in 2018 and plan to file an IND in the second quarter of 2019.

- Establish entinostat as the combination therapy of choice with immune checkpoint inhibitors, initially PD-1 and PD-L1 inhibitors, by conducting clinical trials in patients where we believe the response to PD-1 or PD-L1 inhibitors can be improved. To that end, we have entered into non-exclusive collaborations with Merck, Genentech, and Merck KGaA and Pfizer. We are currently prioritizing our resources ahead of the Phase 3 clinical trial OS readout, at which time we will make a determination on next steps for the immuno-oncology combination program.
- Develop SNDX-6352 as monotherapy and in combination in one or more tumor types. We are currently looking to establish a recommended phase 2 dose for use of SNDX-6352 as a monotherapy or combination agent in solid tumors. We are also conducting a Phase 1 trial of SNDX-6352 as a monotherapy in patients with cGVHD.
- Leverage the technical and business expertise of our management team and scientific collaborators to license, acquire and develop additional cancer therapies to expand our pipeline. We acquired the exclusive rights to SNDX-6352 in 2016 and to SNDX-5613 in 2017. We intend to continue leveraging the collective talent within our organization and network of advisors to guide our pipeline expansion and development plans.

**Our Pipeline**




**Entinostat**

Entinostat is our oral, small molecule product candidate that has direct effects on both cancer cells and immune regulatory cells, potentially enhancing the body's immune response to tumors. The favorable safety profile of entinostat has been demonstrated in clinical trials in more than 1,200 cancer patients. The long half-life of entinostat allows for continuous exposure to therapy potentially resulting in positive efficacy benefits without corresponding cytotoxic effects. Another benefit of entinostat's long half-life is the potential to minimize the frequency of dosing and reduce the severity and frequency of adverse events. Based on entinostat's ability to reverse hormone resistance, alter cancer stem cells, and modulate immunosensitivity, we believe entinostat may have broad applications in tumor types which have become resistant to hormone and/or immunotherapy.

Entinostat has also been shown to enhance the immune system's ability to identify and target tumor cells. It is now widely accepted that many tumors have the ability to evade the immune system either through direct cellular interactions and recruitment of immuno-suppressive cells to the area surrounding the tumor, or through parallel evasion-mechanisms focused on the interaction between the T cell with other immune cells found within the surrounding tumor microenvironment. Entinostat has been observed to decrease the population of immuno-suppressive cells known as myeloid-derived suppressor cells, or MDSCs, and regulatory T cells, or Tregs, which localize in the area surrounding the tumor and block T cells from killing cancer cells, while sparing the cytotoxic T cells. Through blocking the immuno-suppressive effects of MDSCs and Tregs, we believe entinostat has the potential to be used synergistically with therapies such as immune checkpoint inhibitors, resulting in the increased ability of the T cells to attack the tumor.

***Entinostat in Advanced HR+ Breast Cancer***

We are evaluating entinostat in an ongoing Phase 3 clinical trial testing exemestane in combination with entinostat versus exemestane in combination with placebo in patients with advanced HR+, HER2- breast cancer. ECOG-ACRIN Cancer Research Group, or ECOG-ACRIN, is conducting this clinical trial under sponsorship and funding support from the National Cancer Institute, or NCI. The Phase 3 clinical trial was designed to determine whether the addition of entinostat to exemestane improves progression-free survival, or PFS, OS, or both in patients who have previously progressed after treatment with standard-of-care hormonal agents.

To confirm the PFS and OS benefits observed in the Phase 2b clinical trial, we collaborated with ECOG-ACRIN to develop and conduct the Phase 3 clinical trial, E2112. ECOG-ACRIN is conducting the trial under sponsorship and funding support from the NCI. We are providing financial and operational support for the Phase 3 clinical trial under a Cooperative Research and Development Agreement, or CRADA, with the NCI and a separate agreement with ECOG-ACRIN. The trial is a randomized, double-blind, placebo-controlled trial of entinostat in combination with exemestane compared to exemestane and a placebo. The protocol for the Phase 3 clinical trial was reviewed and agreed upon by the FDA under a Special Protocol Assessment, or SPA, agreement with the NCI in January 2014.

Syndax, the NCI and ECOG-ACRIN designed the trial to evaluate whether the addition of entinostat to exemestane improves PFS, OS or both PFS and OS in patients with advanced HR+, HER2- breast cancer who have previously progressed after treatment with standard of care hormonal agents such as NSAIs or Faslodex. In November 2017, ECOG-ACRIN notified us that the Data Safety Monitoring Committee, or DSMC, completed the final PFS analysis and the first interim analysis for OS. The results of this analysis are held confidentially by the ECOG-ACRIN study statistician and the DSMC until the trial completed enrollment.

In October 2018, we announced that enrollment in E2112 concluded, with a total of 608 patients enrolled. ECOG-ACRIN and NCI conducted the primary analysis of PFS after 247 PFS events occurred among the initial 360 patients enrolled and informed us that the trial did not meet the high statistical hurdle for the first primary endpoint of improving PFS. Although a positive result on PFS would have provided the earliest regulatory filing opportunity, it does not impact the potential for the trial to achieve the OS endpoint. Following the most recent interim OS analysis also conducted by the trial's DSMC in October 2018, ECOG-ACRIN informed us that the trial is continuing as planned, with the next interim analysis for the OS primary endpoint scheduled for the second quarter of 2019.

The DSMC will conduct additional interim analyses every six months until either it observes an OS benefit, or the final target number of events occur. E2112 was designed, and obtained breakthrough therapy designation for this indication, based on positive Phase 2b OS results. Any positive OS assessment would enable us to file for full regulatory approval.

***Entinostat in Immuno-Oncology***

Entinostat is currently being studied in clinical trials across a broad range of solid tumors, including breast, non-small cell lung cancer, or NSCLC, melanoma, ovarian and microsatellite stable colorectal carcinoma, or MSS-CRC.

We are working in collaboration with Merck to study the combination of entinostat with Merck's immune checkpoint inhibitor, *Keytruda*, in a Phase 1b/2 clinical trial (ENCORE 601) of up to approximately 202 patients with NSCLC, melanoma or MSS-CRC. The primary objective of the Phase 1b portion of the trial was to determine the dose-limiting toxicities, or DLT, maximum tolerated dose, or MTD, and the RP2D of entinostat given in combination with *Keytruda*, which we confirmed as weekly oral doses of 5 mg. The Phase 1b portion of the clinical trial also characterized the effect of the combination therapy on numerous biomarkers, including expression of PD-1 and PD-L1, the number and function of different types of T cells and the number of MDSCs. We are assessing these biomarkers both in peripheral blood and in serial tumor biopsies. We announced safety data, data from the Phase 1b portion and initiated patient enrollment in the Phase 2 portion in 2016.

The Phase 2 portion employs a two-stage design in which a defined minimum number of responders must be seen in the first stage for the cohort to advance to full enrollment in the second stage. The first stage of the Phase 2 portion of the trial was designed to evaluate the results from these first cohorts and make an informed decision around expanding and progressing any, all or none of the cohorts into the next stage of the trial only after attaining a certain pre-specified and meaningful level of objective response in each cohort. We have completed enrollment of the first stage of the Phase 2 portion for all four cohorts.

In the first half of 2017, both the PD-L1 pretreated melanoma and PD-L1 pretreated NSCLC cohorts of ENCORE 601 met the pre-specified objective response threshold and progressed to the second stage of the trial. The melanoma cohort completed enrollment after the addition of 42 patients for a total of 55 patients enrolled. We shared data in the second quarter of 2018 at the American Society of Clinical Oncology annual meeting, showing that a total of six confirmed partial responses and three unconfirmed partial responses were observed in the 34 evaluable patients at the time of the data cut-off.

Similarly, the cohort enrolling PD-L1 pretreated NSCLC patients enrolled an additional 39 patients in the second stage of the trial. Enrollment completed with a total of 70 patients in this arm and we presented the full clinical data set in the third quarter of 2018 at the World Conference on Lung Cancer. At the time of data cut-off, there were seven confirmed partial responses among the overall population of 72 efficacy-evaluable patients, for a ten percent objective response rate, a median duration of response of 5.3 months, and a median PFS of 2.8 months. In October 2018, we announced plans to commence a focused, biomarker-driven, randomized registration trial in NSCLC comparing the entinostat-*Keytruda* combination to standard of care chemotherapy in patients whose disease has progressed after both platinum-based chemotherapy and PD-1 antagonist therapy. We have recently completed a full portfolio prioritization assessment and have determined to place the initiation of this trial on hold until we receive final OS results from E2112.

In the second half of 2017, we announced that the cohort enrolling PD-L1 naïve NSCLC patients also met the established criteria to advance to stage two, however due to the changing landscape in this patient population, we decided to not progress this cohort into the second stage of the Phase 2 trial. The first stage of the Phase 2 portion of the MSS-CRC cohort completed enrollment in the third quarter of 2017 and we completed the expanded enrollment to 37 patients in the third quarter of 2018. Based on the lack of activity observed to date in this indication, we have decided not to advance to the second stage of the study.

We also entered into a collaboration with Genentech to evaluate the safety, tolerability and preliminary efficacy of entinostat in combination with Genentech's immune checkpoint inhibitor, *Tecentriq*, in a Phase 1b/2 clinical trial, ENCORE 602, of patients with triple-negative breast cancer, or TNBC. The Phase 1b portion established the safety and RP2D of entinostat of in the combination and completed in November 2016. The Phase 2 portion, which opened in December 2016, has PFS as the primary endpoint with response rate, duration of response, time to response and OS as secondary end points. This trial did not meet its primary endpoint of statistically significant improvement in PFS for the combination regimen versus *Tecentriq* monotherapy. The Phase 2 trial randomized 81 patients to receive 1200 mg *Tecentriq* every three weeks in combination with either 5 mg of entinostat (n=40) or placebo (n=41) once weekly.

In January 2018, we entered into a second clinical collaboration with Genentech to evaluate the combination of entinostat with *Tecentriq* in patients with HR+, HER2- metastatic breast cancer in a Phase 1b/2, open-label, multicenter, randomized trial that will enroll patients with metastatic HR+, HER2- breast cancer who have experienced disease progression during or following treatment with a CDK4/6 inhibitor. Genentech is responsible for conducting the trial and has initiated patient enrollment.

We also entered into a collaboration with Ares Trading, S.A., a subsidiary of Merck KGaA, Darmstadt, Germany, and Pfizer Inc. to evaluate the safety, tolerability and preliminary efficacy of entinostat in combination with *Bavencio*® (avelumab), their monoclonal antibody targeting PD-L1, in a Phase 1b/2 clinical trial, ENCORE 603, of patients with ovarian cancer. The Phase 1b portion established the safety of weekly, oral entinostat in combination with *Bavencio*. The Phase 2 portion, which began in the third quarter of 2017, is a randomized, double-blind, placebo-controlled trial with PFS as the primary endpoint and response rate, duration of response, time to response and OS as secondary end points. This trial did not meet its primary endpoint of a statistically significant improvement in PFS for the combination regimen compared with *Bavencio* monotherapy. The Phase 2 trial randomized 126 patients to receive 10 mg/kg *Bavencio* every two weeks in combination with either 5 mg of entinostat (N=85) or placebo (N=41) once weekly.

We designed these series of immune-oncology trials to test whether entinostat could enhance the activity of PD1 pathway antagonists across a number of immunologic environments. NSCLC and melanoma represent settings where the tumors are infiltrated with T cells, MSS-CRC and TNBC are characterized as excluded where the T cells cannot enter the tumor and organize around the edges of the tumor, and ovarian cancer which is characterized by having an absence of T-cells. The data that we have received thus far from clinical trials of entinostat in immuno-oncology suggests that entinostat has the ability to overcome resistance in PD-1 refractory patients in NSCLC and melanoma, but was not supportive of continued study in MSS-CRC, TNBC and ovarian cancer. We believe that results to date from our ENCORE program support that entinostat's beneficial effect is evident in tumors that have been infiltrated with T cells, or inflamed tumors, and not in the other immunologic settings.

Additionally, entinostat is being evaluated in over 10 ongoing and additional planned investigator-sponsored clinical trials that are designed to provide further validation of entinostat's immuno-modulatory activity in various other immuno-responsive tumors. We believe that there may be further opportunities through these and additional collaborations to expand the indications in which entinostat may target immunologic mechanisms of resistance to cancer therapies.

**SNDX-6352**

SNDX-6352 is a humanized monoclonal antibody that binds with high affinity to CSF-1R. CSF-1R is expressed on the surface of specific immuno-suppressive cells (e.g., TAMs) known to play a role in the growth, survival, and metastases of cancer. Inhibition of CSF-1R is thought to disrupt the activity of TAMs, resulting in a decrease in the immunosuppressive environment immediately surrounding the tumor, or tumor micro-environment. This mode of action is thought to make CSF-1R inhibitors well suited for use in combination with checkpoint inhibitors, particularly in cancers where there may be limited activity of immune checkpoint inhibitors as monotherapy. We believe that SNDX-6352 has the potential to be used to treat a variety of cancers in combination with entinostat and with other oncology agents, including immune checkpoint inhibitors, radiation, and chemotherapy.

We are developing SNDX-6352 to bind to CSF-1R and block the ability of CSF-1 and IL-34 to bind to and activate CSF-1R signaling. Our near-term focus is to rapidly establish proof of concept that SNDX-6352 can provide meaningful clinical benefit to patients in one or more tumor types when combined with standard of care therapies for a given indication. We intend to conduct clinical trials in patients with tumor types having clear unmet needs (e.g., NSCLC, TNBC, prostate, melanoma, pancreatic, ovarian, bladder) and where we believe that the inhibition of TAMs via CSF-1R inhibition will produce meaningful benefits for patients, such as chronic graft versus host disease.

We commenced SNDX-6352-502, a Phase 1 dose escalation trial, in the third quarter of 2017. In addition to assessing safety at increasing doses of SNDX-6352, this trial will provide information on the concentration of SNDX-6352 and levels of CSF-1, IL-34 and non-classical monocytes in the blood. We are conducting the trial at multiple centers in the United States and expect to complete enrollment in this Phase 1 trial by the end of second

quarter of 2019. We expect to utilize the safety assessment of SNDX-6352 to determine the starting dose for subsequent clinical trials testing multiple doses of SNDX-6352 as a single agent and in combinations.

In early 2018, we expanded SNDX-6352-502 to include a Phase 1b dose escalation study evaluating the safety of SNDX-6352 in combination with *Imfinzi*, AstraZeneca's human monoclonal antibody directed against PD-L1. These cohorts will also provide information on pharmacokinetic and pharmacodynamic effects of the combination. We anticipate identifying the RP2D and schedule for SNDX-6352 in combination with *Imfinzi* in the second quarter of 2019.

In the fourth quarter of 2018, we opened enrollment in SNDX-6352-503, a Phase 1 dose escalation trial of SNDX-6352 in patients with cGVHD. The objectives of this trial are to evaluate the safety and preliminary efficacy of SNDX-6352 in cGVHD and to identify a RP2D and schedule. We expect to receive initial results in the fourth quarter of 2019.

**SNDX-5613**

SNDX-5613 is a potent, orally active inhibitor of the high affinity interaction site on menin with the protein MLL1. This specific interaction is a key driver for two genetically defined acute leukemias: (i) MLLr and (ii) NPM1c AML. Both diseases have a poor prognosis with an unmet need. In preclinical testing, SNDX-5613 has demonstrated complete tumor regression and profound, dose-dependent survival benefit in leukemic models of disease. SNDX-5613 is a targeted therapy that we are developing initially as a treatment for leukemia patients having relapsed or refractory MLLr or NPM1c AML. We anticipate filing an IND in the second quarter of 2019 and initiating the clinical program shortly thereafter.

**Market and Competition**

***Entinostat in Advanced HR+ Breast Cancer***

Patients in the United States with advanced HR+ breast cancer are treated with hormone therapies with the goal to prolong OS and to delay treatment with more toxic chemotherapies. Hormone therapies are designed to inhibit estrogen stimulation of advanced HR+ breast cancers. Due to limited efficacy of hormone therapies in the advanced HR+ breast cancer setting, multiple lines of treatment are typically used, with each additional line of hormone therapy resulting in a shorter PFS and lower OS. The cause of resistance is multi-factorial and results in tumor progression independent of estrogen stimulation. In 2016, approximately 34,000 patients with HR+ breast cancer were treated with a hormone therapy as second-line or later treatment in the United States. The median OS for advanced HR+ breast cancer in the second-line setting is approximately two years.

The FDA has approved the use of *Afinitor*® (everolimus), an inhibitor of mammalian target of rapamycin, for use in combination with exemestane, based on a randomized Phase 3 clinical trial which resulted in a median PFS benefit of 7.8 months for patients receiving *Afinitor*-exemestane and 3.2 months for patients receiving exemestane alone, but no statistically significant improvement in OS.

More recently, the FDA granted approval to three cyclin-dependent kinase 4 and 6, or CDK4/6, inhibitors, *Ibrance*® (palbociclib), *Kisqali*® (ribociclib) and *Verzenio*® (abemaciclib) in combination with endocrine therapy for the treatment of breast cancer in postmenopausal women with metastatic disease. Based on the significant PFS benefit observed in combination with endocrine therapy, these agents have been adopted as standard of care treatment, with patients increasingly receiving a CDK4/6 therapy in the front-line setting.

While the treatment of advanced HR+ breast cancer is evolving given the introduction of multiple combination therapies, we believe physicians will welcome the introduction of a well-tolerated therapy that improves OS, which has not been demonstrated to date for *Afinitor* or the CDK 4/6 inhibitors in combination with hormone therapy. We believe current data suggests that entinostat could demonstrate a favorable benefit-risk profile and an improvement in OS, and thus may become a preferred treatment option for patients with advanced HR+ breast cancer who have stopped responding to their first line endocrine-based regimen.

***Entinostat with Immune Checkpoint Inhibitors in NSCLC, Melanoma***

*NSCLC*

Lung cancer is the leading cause of cancer death among men and women, with more people dying of lung cancer each year than of colon, breast, and prostate cancers combined. According to the American Cancer Society, approximately 80% to 85% of lung cancers are NSCLC; and in 2017, an estimated 222,500 new cases of lung cancer were diagnosed, and an estimated 155,870 people died from lung cancer in the United States. The five-year survival rate for patients with lung cancer generally is 18% and for patients with Stage IV is approximately 5%, indicating a significant need for new therapies that can prolong OS.

Advanced/metastatic NSCLC is a severe disease with a poor prognosis in the majority of patients. Treatment typically included a first-line combination chemotherapy followed by a choice of a second-line therapeutic approach. Most patients receiving first-line chemotherapy will progress within one year of treatment with a median PFS of approximately six to seven months and median OS of approximately 12 to 14 months. In the second-line setting, the median PFS for standard chemotherapy is approximately three to four months and median OS is approximately six to nine months.

However, even as the development of these immune checkpoint inhibitors represent a significant advance for NSCLC patients, most patients may still see their disease progress and the proportion of treated patients with low PD-L1 expression who respond to approved regimens is quite low (approximately 10%). We believe with these disease-progressing patients and low response rates, there is significant room to improve upon the benefit of PD-L1 inhibitors through combinations with drugs, like entinostat, that target immune modulation through complementary mechanisms.

There are other PD-L1 inhibitors being developed to treat NSCLC, such as Merck KGaA/Pfizer's *Bavencio*, BeiGene, Ltd.'s BGB-A317, and Sanofi/Regeneron's cemiplimab which are in Phase 3 trials. The clinical development programs for these PD-L1 inhibitors have been designed to understand the broad impact they could have across NSCLC, including chemotherapy-naive and previously treated patients, as well as earlier stage patients. We anticipate the immune checkpoint inhibitors will be available for use across the spectrum of advanced NSCLC patients.

However, even as the development of these immune checkpoint inhibitors represent a significant advance for NSCLC patients, most patients may still see their disease progress and the proportion of treated patients with low PD-L1 expression who respond to approved regimens is quite low (approximately 10%). We believe with these disease-progressing patients and low response rates, there is significant room to improve upon the benefit of PD-L1 inhibitors through combinations with drugs, like entinostat, that target immune modulation through complementary mechanisms.

*Melanoma*

The incidence of malignant melanoma in most developed countries has risen faster than any other cancer type since the mid-1950s. In 2011, the average survival duration for patients with Stage IV melanoma, in which the melanoma has metastasized, was only six to ten months; and the five-year survival rate for such patients was 16%. Although this rate had not changed in some time, a recent major advance for melanoma came with the development and approval of drugs such as *Zelboraf*® (vemurafenib), *Tafinlar*® (dabrafenib) and *Mekinist*® (trametinib), for patients with a mutated BRAF gene, which is a human gene that encodes a protein called B Raf.

Melanoma is a particularly immune-responsive tumor, and thus, immunotherapy of melanoma has developed as a dynamic field for clinical research. To date, immunotherapies such as *Yervoy*® (ipilmumab), *Keytruda* and *Opdivo*® (nivolumab), have been approved for the treatment of malignant melanoma patients with unresectable or metastatic disease. However, in this tumor type as well, the immunotherapies represent a significant advance for only a small proportion of patients, leaving significant room to improve upon the benefit of immune checkpoint inhibitors through combinations with drugs, like entinostat, that target immune modulation through complementary mechanisms.

***SNDX-6352 in GVHD***

GVHD is a condition that can develop after an allogeneic hematopoietic stem cell transplant, HSCT, whereby donated cells, graft, view the recipient's, host's, tissue as foreign and attack. The chronic form of GVHD, cGVHD, can occur months or years after transplant and is the leading cause of late morbidity and mortality after allogeneic HSCT. U.S. incidence of cGVHD is approximately 5,000 patients, or 30-70% of HSCT recipients.

cGVHD can affect many different organs or tissues, including skin, eyes, lungs, gastrointestinal tract, genitourinary tract and neuromuscular system. The first line of therapy for cGVHD is typically corticosteroids, though approximately 50% of patients may require treatment with additional systemic therapies, such as extracorporeal photopheresis, cytostatic agents such as mycophenolate moftetil, methotrexate, and immunmodulators such as rituximab, IL-2. *Imbruvica*® (ibrutinib), a BTK inhibitor, is the only FDA-approved therapy for cGVHD and is indicated for use after one or more lines of therapy. *Imbruvica* received approval based on Phase 1/2 clinical trial data that showed a 68% overall response rate, with 48% of responses lasting 20 weeks or longer and reduced dependence on steroids for most patients. Significant unmet need remains for these patients as no agent has demonstrated an improvement in long-term outcomes.

***SNDX-5613***

*Rationale for Targeting MLLr*

MLLr leukemias arise by rare, spontaneous translocations at the MLL1 locus (11q23). It is estimated that approximately 10% of AML and ALL harbor this MLL-re-arrangement with a worldwide incidence of approximately 4,000 cases per year. These translocations generate oncogenic fusion proteins with more than 90 different MLL fusions currently known. All MLL fusion proteins bind with high affinity to the chromatin associated protein menin through a conserved N-terminal sequence. This specific interaction with menin enables an aberrant transcription program that drives leukemic transformation. In pre-clinical animal models, small molecule inhibitors of the menin-MLL interaction have demonstrated deep and durable single agent treatment effects in multiple leukemic xenografts harboring MLL fusions. Inhibiting the menin-MLL1 interaction represents a novel targeted strategy for the treatment of MLLr leukemias.

*Rationale for Targeting Nucleophosmin 1 Mutant AML*

NPM1 is among the most frequently mutated genes in AML, found in approximately 30% of AML cases for an incidence of approximately 20,000 cases per year. Mutations in NPM1 lead to the aberrant cytoplasmic localization of the mutants, termed NPM1c. Loss of NPM1c from the nucleus leads to suppression of differentiation and enables a leukemic transcription program that relies critically on the menin-MLL1 complex to drive and maintain the program. As a result, NPM1c harboring cells are sensitive to menin-MLL interaction inhibitors. In NPM1c cells, inhibition of the menin-MLL interaction suppresses the leukemic transcription program, causing growth arrest, terminal differentiation and cell death. In animal models, small molecule inhibitors of the menin-MLL interaction have demonstrated deep and durable single agent treatment effects in multiple NPM1c xenografts. Based on these findings, blocking the menin-MLL1 interaction represents a novel targeted strategy for the treatment of NPM1c AML.

**Collaborations**

***Clinical Collaborations in Immuno-Oncology***

We have entered into several clinical collaborations in immuno-oncology, as we have further described below. To the extent that any inventions arise from such a collaboration, each party will solely own inventions relating to its drug alone, and the parties will jointly own any inventions relating to the combination of the two drugs. In most cases, clinical data from the trial will be jointly owned. In general, either party may terminate the applicable collaboration agreement for the other party's uncured material breach. In addition, either party may terminate the applicable agreement if it determines that the trial may unreasonably affect patient safety, or if a regulatory authority withdraws the approval to conduct a trial or takes an action that prevent such party from supplying its drug, or if the other party or its employees are sanctioned under certain healthcare-related laws, or if such party decides to discontinue development of its drug.

***Merck—MSD International GmbH***

In March 2015, we entered into a clinical trial collaboration and supply agreement with MSD International GmbH, an affiliate of Merck, under which we will conduct a clinical trial evaluating entinostat in combination with Merck's drug *Keytruda* in patients with NSCLC and melanoma. We are the sponsor of the clinical trial. Merck is supplying *Keytruda* for use in the clinical trial. Neither party will have any obligation to reimburse any costs incurred by the other party, except that a party may be required to reimburse the manufacturing costs of the other party upon certain early termination events.

***Genentech***

In August 2015, we entered into a combination study collaboration agreement with Genentech under which we will conduct a clinical trial evaluating entinostat in combination with Genentech's drug *Tecentriq* in patients with TNBC. We are the sponsor of the clinical trial. Genentech supplied *Tecentriq* for use in the clinical trial. Each party will perform its obligations under the agreement at its own expense, including its internal costs. In March 2019, we announced that this trial did not meet its primary endpoint of statistically significant improvement in PFS for the combination regimen versus *Tecentriq* monotherapy.

In January 2018, we entered into a combination study collaboration agreement with Genentech under which Genentech will conduct a clinical trial evaluating entinostat in combination with Genentech's drug *Tecentriq* in patients with HR+, HER2-, metastatic breast cancer. Genentech is the sponsor of the clinical trial. We are supplying entinostat for use in the clinical trial. Each party will perform its obligations under the agreement at its own expense, including its internal costs.

***Merck KGaA and Pfizer***

In December 2015, we entered into a clinical trial collaboration and supply agreement with Merck KGaA and Pfizer under which we will conduct a clinical trial evaluating entinostat in combination with an investigational monoclonal antibody, *Bavencio*, in patients with ovarian cancer. *Bavencio* is being developed collaboratively by Merck KGaA and Pfizer, which are together treated as a single party for purposes of this agreement. We are the sponsor of the clinical trial. Merck KGaA and Pfizer supplied *Bavencio* for use in the clinical trial. In March 2019, we announced that this did not meet its primary endpoint of a statistically significant improvement in PFS for the combination regimen compared with *Bavencio* monotherapy.

***Nektar Therapeutics***

In May 2018, we entered into a clinical trial collaboration agreement with Nektar under which we agreed to conduct a clinical trial evaluating entinostat in combination with Nektar's proprietary IL2-based, CD122-biased agonist known as NKTR-214, in patients with metastatic melanoma. In January 2019, we agreed with Nektar not to advance the proposed clinical trial and the parties terminated the agreement. There were no costs associated with terminating the agreement.

***NCI and Investigator Collaborations***

***Collaborative Research and Development Agreement with the NCI related to Entinostat***

Our collaboration with the NCI is governed by a CRADA between us and the NCI. The CRADA was originally signed by Mitsui Pharmaceuticals, Inc., or Mitsui, and was then assigned to Schering AG following Schering AG's acquisition of Mitsui. In 2007, Schering AG, then known as Bayer Schering Pharma AG), agreed to assign the CRADA to us in connection with the execution of a license, development and commercialization agreement, or the Bayer license agreement, with Bayer.

Under the CRADA, as amended, the NCI sponsors clinical studies on entinostat using researchers at the NCI as well as NCI-funded researchers at other institutions, including ECOG-ACRIN and JHU. In return, we receive access to the data generated in these clinical studies, and we are obligated to supply the clinical trial sites with sufficient quantities of entinostat. Additionally, we are required to make an annual payment to a particular NCI laboratory to help support certain research studies related to this and other clinical trial. We have no other payment obligations under the CRADA.

We own any intellectual property generated in the course of the collaboration with the NCI, or Collaboration IP, to the extent that Collaboration IP is generated by our employees. We also have an exclusive option to obtain an exclusive or non-exclusive commercialization license under Collaboration IP generated by the NCI. With respect to any Collaboration IP that is owned by or licensed to us, we have agreed to grant the United States government a non-exclusive license to practice or have practiced this Collaboration IP throughout the world by or on behalf of the government for research or other government purposes.

Either party may terminate the CRADA either by mutual consent or unilaterally upon advance written notice to the other party. Absent such early termination, the CRADA will expire on May 21, 2019. As we have in the past, we expect to renew the CRADA at that time.

***Clinical Trial Agreement with Eastern Cooperative Oncology Group***

In March 2014, we entered into a clinical trial agreement with Eastern Cooperative Oncology Group, a contracting entity for ECOG-ACRIN, which describes the parties' obligations with respect to the NCI-sponsored pivotal Phase 3 clinical trial of entinostat. Under the terms of the clinical trial agreement, ECOG-ACRIN is performing this clinical trial in accordance with the clinical trial protocol and a mutually agreed scope of work. In January 2015, we amended the agreement to provide for additional patient site reimbursement funds, which will be paid based on milestone-based payments. We will provide a fixed level of financial support for the clinical trial through an upfront payment of $0.7 million and a series of time- and milestone-based payments of up to $1.0 million each that are comprised of milestone payments through the completion of enrollment and time-based payments through the completion of patient monitoring post-enrollment. In addition, we are obligated to supply entinostat and placebo to ECOG-ACRIN for use in the clinical trial. From the second quarter of 2016 through the fourth quarter of 2018, we have entered into a number of amendments to the agreement to provide for additional study activities resulting in an increase of the contractual obligation of $5.1 million. We have agreed to provide this additional financial support to fund the additional activities required to ensure that the E2112 clinical trial will satisfy FDA registration requirements. As of December 31, 2018, our aggregate payment obligations under this agreement are approximately $24.5 million; and our remaining obligations under this agreement were $9.6 million over an estimated period of approximately three years.

ECOG-ACRIN owns data and inventions from the Phase 3 clinical trial. We have access to the data generated in the clinical trial, both directly from ECOG-ACRIN under the clinical trial agreement, as well as from the NCI through our agreement with it. Additionally, ECOG-ACRIN has granted us a non-exclusive license to any inventions or discoveries that are derived from entinostat as a result of its use during the clinical trial, along with a first right to negotiate an exclusive license to any of these inventions or discoveries.

Either party may terminate the clinical trial agreement in the event of an uncured material breach by the other party or if the FDA or NCI withdraws the authorization to perform the clinical trial in the United States. The parties may jointly terminate the clinical trial agreement if the parties agree that safety-related issues support termination.

***Collaborative Research and Development Agreement with the NCI related to Entinostat and SNDX-6352***

In September 2016, we entered into a collaboration with the NCI related to both entinostat and SNDX-6352 is governed by a CRADA between us and the NCI. Under the CRADA, the NCI sponsors clinical studies on entinostat and SNDX-6352 using researchers at the NCI as well as NCI-funded researchers at other institutions. In return, we receive access to the data generated in these clinical studies, and we are obligated to supply the clinical trial sites with sufficient quantities of entinostat and SNDX-6352. Additionally, we are required to make an annual payment to a particular NCI laboratory to help support certain research studies related to this and other clinical trial. We have no other payment obligations under the CRADA.

We own all intellectual property generated during the collaboration with the NCI, or 6352 Collaboration IP, to the extent that 6352 Collaboration IP is generated by our employees. We also have an exclusive option to obtain an exclusive or non-exclusive commercialization license under 6352 Collaboration IP generated by the NCI. With respect to any 6352 Collaboration IP that is owned by or licensed to us, we have agreed to grant the United States government a non-exclusive license to practice or have practiced this 6352 Collaboration IP throughout the world by or on behalf of the government for research or other government purposes.

**License Agreement**

***Kyowa Hakko Kirin***

In December 2014, we entered into a license, development and commercialization agreement with Kyowa Hakko Kirin Co., Ltd., or KHK, under which KHK received an exclusive license under our intellectual property rights to develop and commercialize entinostat in Japan and Korea. This license includes a sublicense under the rights we received under the Bayer license agreement. If we acquire or develop any other anti-cancer drug that, like entinostat, is a selective inhibitor of Class I HDAC, such drug will be included in this license as well. We will manufacture and supply entinostat to KHK during the term of the agreement, and such obligation may continue for a longer period if KHK continues to sell entinostat following expiration of the agreement or termination of the agreement for our breach. During the term of the agreement, subject to certain exceptions, each party is prohibited from commercializing in the Japan and Korea any other selective inhibitor of Class I HDACs for the same indication as entinostat, with all forms of cancer being treated as the same indication.

We received an upfront license fee of $17.5 million, and KHK purchased 536,049 shares of our Series B-1 Preferred Stock for an aggregate price of approximately $7.5 million. We are eligible to receive up to $50.0 million in development and regulatory milestone payments and up to $25.0 million in sales milestone payments. In October 2017, we announced that KHK dosed the first patient in a randomized, double-blind, placebo-controlled, pivotal Phase 2 trial of entinostat (designated KHK2375 by KHK), in combination with exemestane versus exemestane plus placebo in Japanese patients with advanced or recurrent HR+, HER2- breast cancer. Enrollment of the first patient in this trial triggered a $5 million milestone payment to us from KHK.

KHK will pay us a transfer price for the supply of entinostat as well as royalties on net sales of entinostat above a specified threshold each calendar year by KHK, its affiliates and sublicensees in the low single digits. Royalty payment obligations will be payable in each country in the KHK territory until the later to occur of (i) the date that all valid claims of the last effective license patent in such country expires or is abandoned, withheld or otherwise invalidated and (ii) 15 years from the date of first commercial sale of entinostat in such country. Any payments owed to Bayer as a result of KHK's development and commercialization of entinostat in the KHK territory will be made by us out of the payments we receive from KHK.

The agreement with KHK will expire with respect to each country in the KHK territory upon the expiration of all royalty payment obligations in such country. In addition, we may terminate the agreement in its entirety upon written notice to KHK if KHK or any affiliate commences any action or proceeding that challenges the validity, enforceability or scope of any licensed patent in the KHK territory. KHK may terminate the agreement in its entirety for convenience at any time upon advance notice to us. Either party may terminate the agreement for the other party's uncured material breach, or bankruptcy or related actions or proceedings. If we commit an uncured material breach of certain provisions of the agreement, KHK may, instead of terminating the agreement, elect to continue the agreement in full force and effect except certain payments to us will be reduced.

**Sales and Marketing**

We intend to create a commercial infrastructure to support sales of our product candidates in the United States. Our targeted sales force will focus on a well-defined group of medical oncologists, primarily in the non-hospital and academic settings, who are responsible for the care and treatment of cancer patients. We expect to manage sales, marketing and distribution through internal resources and third-party relationships. While we may commit significant financial and management resources to commercial activities, we would also consider collaborating with one or more pharmaceutical companies to enhance our commercial capabilities. Outside the United States, we plan to rely on our current partners and may seek additional pharmaceutical partners for sales and marketing activities.

**Manufacturing**

We do not own or operate manufacturing facilities for the production of entinostat, SNDX-6352 or SNDX-5613, and we do not have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for all of our required raw materials, active pharmaceutical ingredients and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationship for the manufacture of commercial supplies. If entinostat, SNDX-6352 or SNDX-5613 is approved by any regulatory agency, we intend to enter into agreements with a third-party contract manufacturer and one or more backup manufacturers for the commercial production of such product. Development and commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA and the regulatory agencies of other jurisdictions in which we are seeking approval.

**Intellectual Property**

***Patents and Property Rights***

Through licensed intellectual property and our owned intellectual property, we seek patent protection in the United States and internationally for our product candidates, their methods of use and processes for their manufacture, as well as for other technologies, where appropriate. Our policy is to actively seek to protect our proprietary position by, among other things, filing patent applications in the United States and abroad claiming our proprietary technologies that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

We cannot be sure that patents will be granted with respect to any of our owned or licensed pending patent applications or with respect to any patent applications filed by us or our licensors in the future, nor can we be sure that any of our existing owned or licensed patents or any patents that may be granted to us or to our licensors in the future will protect our technology. Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for the technologies that we consider important to our business, defend our patents, preserve the confidentiality of our trade secrets, operate our business without infringing the patents and proprietary rights of third parties, and prevent third parties from infringing our proprietary rights.

***Entinostat Patent Portfolio***

We strive to protect entinostat with multiple layers of patents. As of December 31, 2018, our portfolio included one owned U.S. provisional patent applications jointly owned with The Regents of the University of Colorado, five owned pending U.S. non-provisional patent applications, one owned allowed U.S. patent, five granted non-U.S. patents (including one Canadian patent jointly owned with The Regents of the University of Colorado), including a European Patent validated in seven countries, and 65 non-U.S. pending patent applications (including two pending international patent applications under the Patent Cooperation Treaty, or PCT). Also, we have filed national phase applications in the Eurasia Regional Patent Office, Ukraine and Georgia based on our owned PCT application directed to treatment of selected breast cancer patients with a combination of entinostat and exemestane. We have assigned our rights to the application we filed in the Eurasia Regional Patent Office to Domain Russia Investments Limited, or DRI. We have also assigned our rights to the applications we filed in Ukraine and Georgia to NovaMedica LLC, or NovaMedica. We have also filed national phase applications based on

our owned PCT application directed to treatment of selected breast cancer patients with the combination of entinostat and exemestane in the U.S. Patent and Trademark Office, or USPTO, the European Patent Office, or EPO, China, India, Australia, Canada, Japan, South Korea, South Africa, Brazil and Mexico. Our owned entinostat patent portfolio includes pending U.S. and ex-U.S. patent applications directed to methods of treating cancer patients by administration of entinostat according to selected dosing regimens, methods of treating cancer patients by administration of entinostat in combination with an HER2 inhibitor, methods of treating lung cancer patients by administration of entinostat in combination with an EGFR inhibitor, and treatments with entinostat combined with anti PD-1 or anti PD-L1 antibodies. Our owned pending U.S. provisional and PCT applications relate to entinostat and CSF-1 or CSF-1R combination therapies and patient selection for combination therapy comprising entinostat and a second therapeutic agent, respectively. If issued, patents based on our owned pending U.S. applications and non-U.S. filings based on our owned PCT applications would expire between April 2029 and May 2039.

The patent portfolio we licensed from Bayer contains a number of issued U.S. and foreign patents as well as patent applications pending outside the United States. A number of the patents and patent applications we licensed from Bayer are directed to entinostat while other patents and patent applications are directed to compounds other than entinostat. As of December 31, 2018, the portfolio we licensed from Bayer included seven issued U.S. patents, 62 granted non-U.S. patents and 17 patent applications pending in non-U.S. patent offices. For example, the portfolio we licensed from Bayer includes reissue U.S. Patent RE39,754, which covers a genus of benzamide compounds including entinostat or SNDX-275. RE39,754 is a composition of matter patent having an initial term which expired in September 2017.

The portfolio we licensed from Bayer also includes U.S. Patent 7,973,166, or the ’166 patent, which covers a crystalline polymorph of entinostat which is referred to as crystalline polymorph B, the crystalline polymorph used in the clinical development of entinostat. Many compounds can exist in different crystalline forms. A compound which in the solid state may exhibit multiple different crystalline forms is called polymorphic, and each crystalline form of the same chemical compound is termed a polymorph. A new crystalline form of a compound may arise, for example, due to a change in the chemical process or the introduction of an impurity. Such new crystalline forms may be patented. By comparison, the U.S. Patent RE39,754, which expired in September 2017, covers the chemical entity of entinostat and any crystalline or non-crystalline form of entinostat. On March 7, 2014, our licensor Bayer applied for reissue of the ‘166 patent. The reissue application sought to add three additional inventors to the ‘166 patent. The reissue was granted as RE45,499 on April 28, 2015, at which time the original ‘166 patent was surrendered. The reissue patent has the same force and effect as the original ‘166 patent and the same August 2029 expiration date.

Of the 62 foreign-granted patents we licensed from Bayer, 26 are foreign counterparts of the ‘166 patent (now RE45,499) that cover crystalline polymorph B, the granted European patent comprises 37 national countries that all been validated, and the granted Eurasian patent comprises nine countries that have all been validated. Likewise, 15 of the 17 pending foreign applications are counterparts of the ‘166 crystalline polymorph B patent. Other patents and patent applications in the licensed Bayer portfolio cover methods of treatment by administration of entinostat. For example, U.S. Patent 7,317,028, which expired in October 2017, covers methods of treating selected cancers by administration of entinostat; U.S. Patent 7,687,525, which also expired in September 2017, covers methods of treating autoimmune disease by administration of entinostat; U.S. Patent 6,320,078, which expires in July 2019, covers methods of manufacturing entinostat; U.S. Patent No. 8,026,239, which expired in September 2017, covers methods of treating certain malignant tumors by administration of a compound within a subgenus of benzamide compounds including entinostat; U.S. Patent RE40,703, which expired in September 2017, covers a subgenus of benzamide compounds that does not include entinostat; and U.S. Patent 6,794,392, which expired in September 2017, covers a subgenus of benzamide compounds that does not include entinostat.

***SNDX-6352 Patent Portfolio***

We have also in-licensed from UCB a patent portfolio directed to SNDX-6352, an IND-ready anti-CSF-1R monoclonal antibody. As of December 31, 2018, the SNDX-6352 composition-of-matter patent portfolio included one granted U.S. non-provisional patent application, two allowed non-U.S. applications, four granted non-U.S. patents and 33 non-U.S. pending patent applications. If issued, patents based on the in-licensed pending U.S. application and non-U.S. applications covering SNDX-6352 would expire in August 2034. Our in-licensed patent portfolio also includes pending U.S. and non-U.S. patent applications directed to methods for the treatment and/or prophylaxis of fibrotic disease by administration of an inhibitor of CSF-1R activity, methods for the treatment and/or prophylaxis of inflammatory bowel disease, or IBD, by administration of an inhibitor of CSF-1R activity, and liquid pharmaceutical compositions of anti-CSF-1R antibodies. If issued, patents based on these pending applications would expire between November 2024 and February 2036. Further, the in-licensed portfolio includes three non-U.S. patents directed to methods of treating solid tumors by administration of an inhibitor of CSF-1R activity. The three patents will expire in October 2020.

***Menin Asset Patent Portfolio***

We have in-licensed from Vitae Pharmaceuticals, Inc., a subsidiary of Allergan, a patent portfolio directed to a series of selective preclinical inhibitors targeting the binding interaction of Menin with MLL-r. As of December 31, 2018, the in-licensed portfolio included two pending U.S. applications and 29 non-U.S. pending patent applications (including pending PCT application) covering composition of matter and methods of treating, e.g., MLL. If issued, patents based on the in-licensed applications would expire between December 2036 and September 2037.

***Patent Term***

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the earliest non-provisional application or PCT application.

In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. The term of a patent that covers an approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the development and regulatory review process. To obtain a patent extension in the United States, the term of the relevant patent must not have expired before the extension application, the patent cannot have been extended previously under this law, an application for extension must be submitted, the product must be subject to regulatory review prior to its commercialization, and the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product. If our future products contain active ingredients which have not been previously approved, we may be eligible for a patent term extension in the United States. In the United States, we expect to seek extension of patent terms under the Drug Price Competition and Patent Term Restoration Act of 1984, which permits a patent term extension of up to five years beyond the expiration of the patent for patent claims covering a new chemical entity. If patent extensions are available to us outside of the United States, we would expect to file for a patent term extension in applicable jurisdictions.

**In-Licensed Intellectual Property**

***License, Development and Commercialization Agreement with Bayer***

In March 2007, we entered into the Bayer license agreement pursuant to which we obtained a worldwide, exclusive license to develop and commercialize entinostat and any other products containing the same active ingredient. The Bayer license agreement, as amended, permits us to use entinostat or other licensed products for the treatment of any human disease, and we are obligated to use commercially reasonable efforts to develop, manufacture and commercialize licensed products for all commercially reasonable indications. Initially, Bayer manufactured and supplied our requirements of entinostat, but effective May 2012, manufacturing rights and responsibility for entinostat was transferred to us, by mutual agreement of the parties.

In connection with the execution of the Bayer license agreement, we paid Bayer an upfront license fee of $2.0 million. We are also obligated to pay up to approximately $50.0 million in the aggregate upon obtaining certain milestones in the development and marketing approval of entinostat, assuming that we pursue at least two different indications for entinostat or any other licensed product.

We are also obligated to pay Bayer up to $100.0 million in aggregate sales milestones, and a tiered single-digit royalty on net sales by us, our affiliates and sublicensees of entinostat and any other licensed products under the Bayer license agreement. We are obligated to pay Bayer these royalties on a country-by-country basis for the life of the relevant licensed patents covering such product or 15 years after the first commercial sale of such product in such country, whichever is longer. We cannot determine the date on which our royalty payment obligations to Bayer would expire because no commercial sales of entinostat have occurred and the last-to-expire relevant patent covering entinostat in a given country may change in the future.

The Bayer license agreement will remain in effect until the expiration of our royalty obligations under the agreement in all countries. Upon expiration of the agreement our licenses become fully paid-up and irrevocable. Either party may terminate the Bayer license agreement in its entirety or with respect to certain countries in the event of an uncured material breach by the other party. Either party may terminate the Bayer license agreement if voluntary or involuntary bankruptcy proceedings are instituted against the other party, if the other party makes an assignment for the benefit of creditors, or upon the occurrence of other specific events relating to the insolvency or dissolution of the other party. Bayer may terminate the Bayer license agreement if we seek to revoke or challenge the validity of any patent licensed to us by Bayer under the Bayer license agreement or if we procure or assist a third party to take any such action.

***License Agreement with UCB***

In July 2016, we entered into a license agreement with UCB, or the UCB license agreement, under which UCB granted us a worldwide, sublicenseable, exclusive license to UCB6352, which the Company refers to as SNDX-6352, an IND-ready anti-CSF-1R monoclonal antibody. The UCB license agreement permits us to use SNDX-6352 or other licensed products for all human uses, including treatment, prevention and diagnostic uses, in all indications, diseases, conditions or disorders, and we are obligated to use commercially reasonable efforts to develop, obtain regulatory approval and commercialize a certain licensed product.

In consideration for the license grant, we made a nonrefundable upfront payment of $5.0 million to UCB in the third quarter of 2016. Additionally, subject to the achievement of certain milestone events, we may be required to pay UCB up to $119.5 million in one-time development and regulatory milestone payments over the term of the UCB license agreement. In the event that we or any of our affiliates or sublicensees commercializes SNDX-6352, we will also be obligated to pay UCB low double-digit royalties on sales, subject to reduction in certain circumstances, as well as up to an aggregate of $250.0 million in potential one-time, sales-based milestone payments based on achievement of certain annual sales thresholds. Under certain circumstances, we may be required to share a percentage of non-royalty income from sublicensees, subject to certain deductions, with UCB. We are solely responsible for the development and commercialization of SNDX-6352, except that UCB is performing a limited set of transitional chemistry, manufacturing and control tasks related to SNDX-6352.

Each party may terminate the UCB license agreement for the other party's uncured material breach or insolvency; and we may terminate the UCB license agreement at will at any time upon advance written notice to UCB. UCB may terminate the UCB license agreement if we or any of our affiliates or sublicensees institutes a legal challenge to the validity, enforceability, or patentability of the licensed patent rights. Unless terminated earlier in accordance with its terms, the UCB license agreement will continue on a country-by-country and product-by-product basis until the later of: (i) the expiration of all of the licensed patent rights in such country; (ii) the expiration of all regulatory exclusivity applicable to the product in such country; and (iii) 10 years from the date of the first commercial sale of the product in such country.

***License Agreement with Vitae Pharmaceuticals, Inc.***

In October 2017, we entered into a license agreement with Vitae Pharmaceuticals, Inc., a subsidiary of Allergan, or the Allergan License Agreement, under which Allergan granted us an exclusive, sublicenseable, worldwide license to, preclinical, orally-available, small molecule inhibitors of the interaction of Menin with the MLL protein, or the Menin Assets. We made a nonrefundable upfront payment of $5.0 million to Allergan in the fourth quarter of 2017. Additionally, subject to the achievement of certain milestone events, we may be required to pay Allergan up to an aggregate of $99 million in one-time development and regulatory milestone payments over the term of the Allergan License Agreement. In the event that we or any of its affiliates or sublicensees commercializes the Menin Assets, we will also be obligated to pay Allergan low single to low double-digit royalties on sales, subject to reduction in certain circumstances, as well as up to an aggregate of $70.0 million in potential one-time, sales-based milestone payments based on achievement of certain annual sales thresholds. Under certain circumstances, we may be required to share a percentage of non-royalty income from sublicensees, subject to certain deductions, with Allergan. We are solely responsible for the development and commercialization of the Menin Assets.

Each party may terminate the Allergan License Agreement for the other party's uncured material breach or insolvency; and we may terminate the Allergan License Agreement at will at any time upon advance written notice to Allergan. Allergan may terminate the Allergan License Agreement if we or any of its affiliates or sublicensees institutes a legal challenge to the validity, enforceability, or patentability of the licensed patent rights. Unless terminated earlier in accordance with its terms, the Allergan License Agreement will continue on a country-by-country and product-by-product basis until the later of: (i) the expiration of all of the licensed patent rights in such country; (ii) the expiration of all regulatory exclusivity applicable to the product in such country; and (iii) 10 years from the date of the first commercial sale of the product in such country.

***Confidential Information and Inventions Assignment Agreements***

We require our employees and consultants to execute confidentiality agreements upon the commencement of employment, consulting or collaborative relationships with us. These agreements provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not disclosed to third parties except in specific circumstances.

In the case of employees, the agreements provide that all inventions resulting from work performed for us, utilizing our property or relating to our business and conceived or completed by the individual during employment shall be our exclusive property to the extent permitted by applicable law. Our consulting and service agreements also provide for assignment to us of any intellectual property resulting from services performed for us.

**Government Regulation and Product Approval**

***United States Government Regulation***

In the United States, the FDA regulates drugs and biologics under the Federal Food, Drug, and Cosmetic Act, or FDCA, the Public Health Service Act, and related regulations. Drugs and biologics are also subject to other federal, state and local statutes and regulations. The FDA and comparable regulatory agencies in state and local jurisdictions impose substantial requirements upon, among other things, the testing, development, manufacture, quality control, safety, purity, potency, labeling, storage, distribution, record keeping and reporting, approval, import and export, advertising and promotion, and postmarket surveillance of drugs and biologics.

***Biopharmaceutical Product Development Process***

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

- completion of extensive preclinical laboratory tests and animal studies in accordance with applicable regulations, including the FDA's good laboratory practice, or GLP regulations;
- submission of an IND application which must become effective before clinical trials may begin;
- performance of adequate and well-controlled human clinical trials in accordance with applicable regulations, including the FDA's current good clinical practice, or GCP, regulations to establish the safety and efficacy of the proposed drug for its intended use or uses;
- submission to the FDA of an NDA for a new drug product or a Biologics License Application, or BLA, for biologics;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to accept the application for filing and review;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the drug or biologic is produced to assess compliance with the FDA's current Good Manufacturing Practices, or cGMP, regulations to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of an NDA or BLA; and
- FDA review and approval of an NDA or BLA prior to any commercial marketing or sale of the biopharmaceutical product in the United States.

Before testing any compounds with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry and formulation, as well as animal studies to assess the potential safety, toxicity profile and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

Prior to commencing the first clinical trial in humans, an IND must be submitted to the FDA, and the IND must become effective. A sponsor must submit preclinical testing results to the FDA as part of the IND and the FDA must evaluate whether there is an adequate basis for testing the drug in humans. The IND automatically becomes effective 30 days after receipt by the FDA unless the FDA within the 30-day time period raises concerns or questions about the submitted data or the conduct of the proposed clinical trial and places the IND on clinical hold. In such case, the IND application sponsor must resolve any outstanding concerns with the FDA before the clinical trial may begin. A separate submission to the existing IND application must be made for each successive clinical trial to be conducted during product development. Further, an independent Institutional Review Board, or IRB, for each site proposing to conduct the clinical trial must review and approve the protocol and informed consent for any clinical trial before it commences at that site. Informed consent must also be obtained from each study subject. Regulatory authorities, an IRB, a data safety monitoring board or the trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the participants are being exposed to an unacceptable health risk.

Human clinical trials are typically conducted in three sequential phases that may overlap:

- Phase 1—The drug is initially given to healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- Phase 2—The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases or conditions and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3—Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall benefit-risk ratio of the product and to provide an adequate basis for product approval by the FDA.

Post-approval studies, or Phase 4 clinical trials, may be conducted after initial marketing approval. These studies may be required by the FDA as a condition of approval and are used to gain additional experience from the treatment of patients in the intended therapeutic indication. The FDA also has express statutory authority to require post-market clinical studies to address safety issues.

The FDCA permits the FDA and an IND sponsor to agree in writing on the design and size of clinical studies intended to form the primary basis of a claim of effectiveness in an NDA or BLA. An SPA agreement is not a guarantee of product approval by the FDA or approval of any permissible claims about the product. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement. In particular, the SPA agreement is not binding on the FDA if previously unrecognized public health concerns later come to light, other new scientific concerns regarding product safety or efficacy arise, the IND sponsor fails to comply with the protocol agreed upon, or the relevant data, assumptions, or information provided by the IND sponsor when requesting an SPA agreement change, are found to be false statements or misstatements, or are found to omit relevant facts. An SPA agreement may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA, or if the FDA determines that a substantial scientific issue essential to determining the safety or effectiveness of the drug was identified after the testing began.

Some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated checkpoints based on access to certain data from the study. A sponsor may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate 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 include developed methods for testing the identity, strength, quality and purity of the finished product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

***FDA Review and Approval Processes***

In order to obtain approval to market a biopharmaceutical product in the United States, a marketing application must be submitted to the FDA that provides data establishing to the FDA's satisfaction the safety and effectiveness of the investigational drug for the proposed indication. Each NDA or BLA submission requires a substantial user fee payment unless a waiver or exemption applies. The application includes all relevant data available from pertinent nonclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators.

The FDA will initially review an NDA or BLA for completeness before it accepts it for filing. The FDA has 60 days from its receipt of an application to determine whether the application will be accepted for filing based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. If it is not, the FDA may refuse to file the application and request additional information, in which case the application must be resubmitted with the supplemental information, and review of the application is delayed. After an NDA or BLA submission is accepted for filing, the FDA reviews the application to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and, if so, under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Upon the filing of an NDA or BLA, the FDA may grant a priority review designation to a product, which sets the target date for FDA action on the application at 6 months, rather than the standard 10 months. Priority review is given for drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. Priority review designation does not change the scientific or medical standard for approval or the quality of evidence necessary to support approval.

Before approving an NDA or BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA may inspect one or more clinical sites to assure compliance with GCP.

After the FDA completes its initial review of an NDA or BLA, it will communicate to the sponsor that the product is approved, or it will issue a complete response letter to communicate that the application will not be approved in its current form and inform the sponsor of changes that must be made or additional clinical, nonclinical or manufacturing data that must be received before the application can be approved.

Even if a product candidate receives regulatory approval, the approval may be limited to specific disease states, patient populations and dosages, or might contain significant limitations on use in the form of warnings, precautions or contraindications, or in the form of onerous risk management plans, restrictions on distribution, or post-marketing study requirements. For example, the FDA may require Phase 4 testing, which involves clinical trials designed to further assess a drug's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also determine that a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of an NDA must submit a proposed REMS, and the FDA will not approve an NDA without an approved REMS, if required.

***Expedited Review Programs***

Among other programs, the FDA may expedite the review of a product candidate designated as a breakthrough therapy, which is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A sponsor may request the FDA to designate a drug as a breakthrough therapy at the time of, or any time after, the submission of an IND application for the drug. If the FDA designates a drug as a breakthrough therapy, it must take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the drug; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and taking steps to ensure that the design of the clinical trials is as efficient as practicable, when scientifically appropriate, such as by minimizing the number of patients exposed to a potentially less efficacious treatment. The FDA may rescind a breakthrough therapy designation in the future if further clinical development later shows that the criteria for designation are no longer met.

Breakthrough therapy designation does not change the standards for approval, but may expedite the development or review process.

***Post-Approval Requirements***

If and when approved, any products manufactured or distributed by us or on our behalf will be subject to continuing regulation by the FDA, including requirements for record-keeping, reporting of adverse experiences and submitting annual reports.

Biopharmaceutical manufacturers are required to register their facilities with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs, which impose certain quality processes, manufacturing controls and documentation requirements upon us and our third-party manufacturers in order to ensure that the product is safe, has the identity and strength, and meets the quality and purity characteristics that it purports to have. The FDA and certain states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including technology capable of tracking and tracing product as it moves through the distribution chain. We cannot be certain that we or our present or future suppliers will be able to comply with the cGMP and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, fail to approve any application, shut down manufacturing operations or withdraw approval of an application, or we may recall the product from distribution. Noncompliance with cGMP or other requirements can result in issuance of warning letters, civil and criminal penalties, seizures and injunctive action.

The FDA closely regulates the labeling, marketing and promotion of drugs and biologics. While doctors are free to prescribe any drug approved by the FDA for any use, a company can only make claims relating to safety and efficacy of a drug that are consistent with FDA approval, and the company is allowed to actively market a drug only for the particular use and treatment approved by the FDA. In addition, any claims we make for our products in advertising or promotion must be appropriately balanced with important safety information and otherwise be adequately substantiated. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising, injunctions and potential civil and criminal penalties. Government regulators recently have increased their scrutiny of the promotion and marketing of drugs.

***Coverage and Reimbursement***

In both domestic and foreign markets, sales of any products for which we may receive regulatory approval will depend in part upon the availability of coverage and adequate reimbursement to healthcare providers from third-party payors. Such third-party payors include government health programs, such as Medicare and Medicaid, as well as managed care organizations, private health insurers and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are available. Assuming coverage is granted, the reimbursement rates paid for covered products might not be adequate. Even if favorable coverage status and adequate reimbursement rates are attained, less favorable coverage policies and reimbursement rates may be implemented in the future. The marketability of any products for which we may receive regulatory approval for commercial sale may suffer if the government and other third-party payors fail to provide coverage and adequate reimbursement to allow us to sell such products on a competitive and profitable basis. For example, under these circumstances, physicians may limit how much or under what circumstances they will prescribe or administer such products, and patients may decline to purchase them. This, in turn, could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition, and future success.

In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies. Such pressure, along with the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union, will likely put additional downward pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions, governmental laws and regulations related to government healthcare programs, healthcare reform, and pharmaceutical coverage and reimbursement policies.

The market for any product candidates for which we may receive regulatory approval will depend significantly on the degree to which these products are listed on third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement to the extent products for which we may receive regulatory approval are covered under a pharmacy benefit or are otherwise subject to a formulary. The industry competition to be included on such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. In addition, because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming and costly process. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. We may be required to provide scientific and clinical support for the use of any product to each third-party payor separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. We cannot be certain that our product candidates will be considered cost-effective. This process could delay the market acceptance of any product candidates for which we may receive approval and could have a negative effect on our future revenues and operating results.

***Federal and State Fraud and Abuse and Data Privacy and Security Laws and Regulations***

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state laws restrict business practices in the pharmaceutical industry. These laws include anti-kickback and false claims laws and regulations as well as data privacy and security laws and regulations. The laws that will affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in return for the purchase, recommendation, leasing or furnishing of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, amended the intent requirement of the federal Anti-Kickback Statute so that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;
- federal civil and criminal false claims laws, including, without limitation, the False Claims Act, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other government payors that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The Affordable Care Act provides, and recent government cases against pharmaceutical manufacturers support, the view that federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, may implicate the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing a scheme or making false or fraudulent statements to defraud any healthcare benefit program, regardless of the payor (e.g., public or private);
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers, known as covered entities, and their respective business associates, individuals or entities that perform certain services on behalf of a covered entity that involves the use or disclosure of individually identifiable health information;

- the federal Physician Payments Sunshine Act, which 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 Centers for Medicare & Medicaid Services, or CMS, information related to: (i) payments or other "transfers of value" made to physicians and teaching hospitals; and (ii) ownership and investment interests held by physicians and their immediate family members;
- state law equivalents of each of the above federal laws, state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or to adopt compliance programs as prescribed by state laws and regulations, or that otherwise restrict payments that may be made to healthcare providers, State laws that require manufactures to report pricing information regarding certain drugs, state and local laws that require the registration of pharmaceutical sales representatives, and state laws that govern the privacy and security of health information, which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

We may also be subject to federal and state laws that govern the privacy and security of other personal information, including federal and state consumer protection laws, state data security laws, and data breach notification laws. A data breach affecting sensitive personal information, including health information, could result in significant legal and financial exposure and reputational damages.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge, investigation or legal action under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal, and administrative penalties, including, without limitation, damages, fines, individual imprisonment, disgorgement, exclusion from participation in government healthcare programs, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations.

To the extent that any of our product candidates receive approval and are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, international data protection laws (including the General Data Protection Directive ((EU) 2016/679) on the protection of individuals with regard to the processing of personal data and on the free movement of such data as well as EU member state implementing legislation), and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

***Healthcare Reform***

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, then President Obama signed into law the Affordable Care Act, which substantially changes the way healthcare will be financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. Among the provisions of the Affordable Care Act of importance to our business, including, without limitation, our ability to commercialize, and the prices we may obtain for, any of our product candidates that are approved for sale, are the following:

- an annual, nondeductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;

- expansion of healthcare fraud and abuse laws, including the federal 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 now agree to offer 70% point-of- sale discounts off negotiated prices;
- 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 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.

There have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect such challenges to continue. In July 2018, CMS published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under its risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by the U.S. Congress as part of the Tax Cuts and Jobs Act of 2017 Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act.

Further, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains additional drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid and to eliminate cost-sharing for generic drugs for low-income patients. The Trump administration also released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019. While some of these and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly 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.

The full impact on our business of the Affordable Care Act and other new laws is uncertain but may result in additional reductions in Medicare and other healthcare funding. Nor is it clear whether other legislative changes will be adopted, if any, or how such changes would affect the demand for our products once commercialized.

***Regulations Outside of the United States***

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our product candidates to the extent we choose to sell any products outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. As in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution would apply to any product that is approved outside the United States.

***Other Regulations***

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

**Employees**

As of March 6, 2019, we had 38 full-time employees. Of the full-time employees, 24 were primarily engaged in research and development activities and 13 have an M.D. or Ph.D. degree. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

**Corporate and Other Information**

We were incorporated in Delaware in 2005. In 2011, we established a wholly owned subsidiary in the United Kingdom and in 2014 we established a wholly owned U.S. subsidiary. There have been no material activities for these entities to date. We currently operate in one segment.

Our principal executive offices are located at 35 Gatehouse Drive, Building D, Floor 3, Waltham, Massachusetts 02451 and our telephone number is (781) 419-1400. Our corporate website address is www.syndax.com. Information contained on or accessible through our website is not a part of this Annual Report, and the inclusion of our website address in this Annual Report is an inactive textual reference only.

We file electronically with the SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make available on our website at www.syndax.com, under “Investors,” free of charge, copies of these reports as soon as reasonably practicable after filing or furnishing these reports with the SEC.

**Item 1A. Risk Factors**

*This Annual Report on Form 10-K contains forward-looking information based on our current expectations. Because our business is subject to many risks and our actual results may differ materially from any forward-looking statements made by or on behalf of us, this section includes a discussion of important factors that could affect our business, operating results, financial condition and the trading price of our common stock. You should carefully consider these risk factors, together with all of the other information included in this Annual Report on Form 10-K as well as our other publicly available filings with the Securities and Exchange Commission.*

**Risks Related to Our Business and Industry**

***If the Phase 3 clinical trial of entinostat in combination with exemestane in advanced HR+, HER2- breast cancer patients fails to demonstrate safety and efficacy to the satisfaction of regulatory authorities or does not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of entinostat.***

Before obtaining marketing approval from regulatory authorities for the sale of entinostat, we or our collaborators must conduct extensive trials to demonstrate the safety and efficacy of entinostat in humans. We have entered into an arrangement with ECOG-ACRIN to conduct the Phase 3 clinical trial of entinostat in combination with exemestane in advanced HR+, HER2- breast cancer patients. The NCI designed the trial to measuring two primary endpoints, progression-free survival, or PFS, and overall survival, or OS. We received the final PFS analysis from ECOG-ACRIN in October 2018 and we expect to receive the final OS analysis no later than the end of 2020. In October 2018, ECOG-ACRIN informed us that the trial did not achieve the high statistical hurdle for the first primary endpoint of improving PFS, which would have provided the earliest regulatory filing opportunity. In accordance with the trial protocol, ECOG-ACRIN is confidentially holding the findings from the PFS analysis until reporting final OS results. We will not be able to submit an NDA unless and until we receive data demonstrating that the trial has achieved the primary endpoint for OS. In addition, based on scientific advice that we received from the European Medicines Agency in March 2014, the current Phase 3 clinical trial may not be sufficient to receive regulatory approval in Europe for entinostat to treat advanced HR+, HER2- breast cancer, and it is unclear whether we would be able to complete an alternate clinical trial that would be sufficient.

Despite the results reported in our Phase 2b clinical trial for entinostat in advanced estrogen receptor positive, or ER+, breast cancer, we do not know whether the Phase 3 clinical trial in advanced HR+, HER2- breast cancer will demonstrate adequate efficacy and safety to result in regulatory approval to market entinostat in any particular cancer indications or jurisdiction. Additionally, while we do not expect that there will be overlapping toxicities between entinostat and exemestane, we cannot be certain that we will not observe these toxicities or unexpected adverse drug reactions in the Phase 3 clinical trial.

Clinical testing is expensive and difficult to design and implement, can take many years to complete and is inherently uncertain as to the outcome. A failure of one or more trials can occur at any stage of testing. The outcome of preclinical studies and early clinical trials may not accurately predict the success of later trials, and interim results of a trial do not necessarily predict final results. For example, with the emergence of the new therapies such as Verzenio, Kisqali and Ibrance, patients enrolled in the Phase 3 clinical trial may be different than those enrolled in our previous Phase 2b clinical trial in that they may have received a CDK 4/6 inhibitor prior to our trial and therefore may respond differently to treatment with entinostat. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced trials due to lack of efficacy or unacceptable safety profiles, notwithstanding promising results in earlier trials.

***The failure of ECOG-ACRIN or the NCI to adequately perform its obligations and responsibilities in the conduct of the Phase 3 clinical trial or to meet expected deadlines could substantially harm our business because we may not obtain regulatory approval for entinostat in a timely manner, or at all.***

We have entered into an arrangement with ECOG-ACRIN, pursuant to which it, with sponsorship and funding support by the NCI, is conducting the Phase 3 clinical trial of entinostat in combination with exemestane in advanced HR+, HER2- breast cancer patients. While we provide operational and logistical support for the trial, we have limited control of their activities. We cannot control whether ECOG-ACRIN will devote sufficient time and resources to the trial, including as a result of any reduction or delay in government funding or sponsorship of the activities of ECOG-ACRIN or the NCI. If ECOG-ACRIN or the NCI does not successfully carry out its obligations and responsibilities or meet expected deadlines or if the quality or accuracy of the clinical data that ECOG-ACRIN obtains is compromised due to the failure to adhere to GCPs, clinical protocols, regulatory requirements or for other reasons, the Phase 3 clinical trial may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, entinostat. As a result, our results of operations and the commercial prospects for entinostat would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Although the Phase 3 clinical trial is being conducted by ECOG-ACRIN, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on ECOG-ACRIN does not relieve us of our regulatory responsibilities. We are required to comply with Good Clinical Practice, or GCP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and foreign regulatory authorities for any product in clinical development. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we fail to comply with applicable GCP, the clinical data generated in our trials may be deemed unreliable and the FDA or foreign regulatory authorities may require us to perform additional trials before approving our marketing applications. We cannot assure that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our trials comply with GCP requirements. In addition, we must conduct our trials with products produced under current Good Manufacturing Practices regulations, or cGMP requirements. Failure to comply with any of these regulations may require us to repeat preclinical and clinical trials, which would delay the regulatory development process.

***If there are delays in completing the Phase 3 clinical trial for entinostat in advanced HR+, HER2- breast cancer, we will be delayed in commercializing entinostat, our development costs may increase and our business may be harmed.***

The Phase 3 clinical trial of entinostat in combination with exemestane in advanced HR+, HER2- breast cancer commenced in the second quarter of 2014, and we expect to receive the final OS analysis no later than the end of 2020. Our product development costs could increase if we experience delays in the overall number of survival events. Significant trial delays also could shorten any periods during which we may have the exclusive right to commercialize entinostat or allow our competitors to bring products to market before we do, which would impair our ability to successfully capitalize on entinostat and may harm our business, results of operations and prospects. Events that may result in a delay or unsuccessful completion of clinical development of entinostat include, among other things:

- unexpectedly high rate of patients withdrawing consent or being lost to follow-up, including patients that withdraw or are lost to follow-up following our announcement in October 2018 that the trial did not achieve the statistical hurdle for the first primary endpoint of improving PFS;
- feedback from the FDA and foreign regulatory authorities, institutional review boards, or IRBs, or the data safety monitoring board, or results from clinical trials that might require modification to a clinical trial protocol;
- imposition of a clinical hold by the FDA or other regulatory authorities, a decision by the FDA, other regulatory authorities, IRBs or the company, or a recommendation by a data safety monitoring board to suspend or terminate trials at any time for safety issues or for any other reason;
- deviations from the trial protocol by clinical trial sites and investigators or failure to conduct the trial in accordance with regulatory requirements;

- failure of third parties, such as ECOG-ACRIN or contract research organizations, or CROs, to satisfy their contractual duties or meet expected deadlines;
- withdrawal of sponsorship of the NCI because of a failure of ECOG-ACRIN to meet certain performance metrics in the clinical trial;
- delays in the testing, validation, manufacturing and delivery of entinostat to the clinical trial sites;
- delays caused by patients dropping out of a trial due to side effects or disease progression;
- unacceptable risk-benefit profile or unforeseen safety issues or adverse drug reactions;
- failure to demonstrate the efficacy of entinostat in this clinical trial; or
- changes in government regulations or administrative actions or lack of adequate funding to continue the trials.

An inability by us to timely complete clinical development could result in additional costs to us or impair our ability to generate product revenues or development, regulatory, commercialization and sales milestone payments and royalties on product sales.

***Although the NCI has entered into a Special Protocol Assessment, or SPA, agreement with the FDA relating to the pivotal Phase 3 clinical trial of entinostat for advanced HR+, HER2- breast cancer, this agreement does not guarantee any particular outcome with respect to regulatory review of the trial or any associated NDA for entinostat.***

The protocol for the pivotal Phase 3 trial of entinostat in combination with exemestane in advanced HR+, HER2- breast cancer was reviewed and agreed upon by the FDA under a SPA agreement with the NCI. The SPA agreement allows for FDA evaluation of whether a clinical trial protocol could form the primary basis of an efficacy claim in support of an NDA. The SPA is an agreement that a Phase 3 clinical trial's design, clinical endpoints, patient population and statistical analyses are sufficient to support the efficacy claim. Agreement on the SPA is not a guarantee of approval; and there is no assurance that the design of, or data collected from, the trial will be adequate to obtain the requisite regulatory approval. In October 2018, ECOG-ACRIN informed us that the trial did not achieve the statistical hurdle for the first primary endpoint of improving PFS, which would have provided the earliest regulatory filing opportunity. Further, obtaining clinical trial data meeting the OS endpoint in satisfaction of the SPA does not guarantee approval. The SPA is not binding on the FDA if public health concerns unrecognized at the time the SPA was entered into become evident or other new scientific concerns regarding product safety or efficacy arise. In addition, upon written agreement of both the FDA and the NCI, the SPA may be changed, and the FDA retains significant latitude and discretion in interpreting the terms of the SPA and any resulting trial data. As a result, we do not know how the FDA will interpret the parties' respective commitments under the SPA, how it will interpret the data and OS results from the pivotal Phase 3 clinical trial, whether the FDA will require that we conduct or complete one or more additional clinical trials to support potential approval or whether entinostat will receive any regulatory approvals. ECOG-ACRIN, with sponsorship and funding support from the NCI, is conducting the pivotal Phase 3 clinical trial, which began enrollment in the second quarter of 2014.

***A breakthrough therapy designation by the FDA for entinostat may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that entinostat will receive marketing approval.***

We received breakthrough therapy designation from the FDA for entinostat when used in combination with exemestane based on the OS results from our completed Phase 2b clinical trial in advanced HR+, HER2- breast cancer. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The Phase 2b trial showed statistically significant improvements in PFS, the primary endpoint, and OS, an exploratory endpoint. Receipt of a breakthrough therapy designation for a drug candidate may not result in a faster development process or review compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, the FDA may later decide that entinostat no longer meets the conditions for qualification or decide that the time period for FDA review will not be shortened. For instance, our Phase 3 trial in HR+, HER2- breast cancer patients failed to achieve one of its primary endpoints of improving PFS. We expect to receive final analysis on the second primary endpoint, OS, no later than the end of 2020. If the results do not confirm the improvement in OS observed in our Phase 2b clinical trial, the FDA may rescind our breakthrough therapy designation.

***We do not currently have any sales, marketing or distribution experience or infrastructure.***

In order to market any approved product candidate in the future, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, as we do not presently have such capabilities. To develop our internal sales, distribution and marketing capabilities, we would have to invest significant amounts of financial and management resources in the future. For drugs where we decide to perform sales, marketing and distribution functions ourselves, we could face a number of challenges, including that:

- we may not be able to attract and build a significant marketing or sales force;
- the cost of establishing, training and providing regulatory oversight for a marketing or sales force may not be justifiable in light of the revenues generated by any particular product;
- our direct or indirect sales and marketing efforts may not be successful; and
- there are significant legal and regulatory risks in drug marketing and sales that we have never faced, and any failure to comply with all legal and regulatory requirements for sales, marketing and distribution could result in enforcement action by the FDA or other authorities that could jeopardize our ability to market the product or could subject us to substantial liability.

Alternatively, we may rely on third parties to launch and market our product candidates, if approved. We may have limited or no control over the sales, marketing and distribution activities of these third parties and our future revenue may depend on the success of these third parties. Additionally, if these third parties fail to comply with all applicable legal or regulatory requirements, the FDA or another governmental agency could take enforcement action that could jeopardize their ability and our ability to market our product candidates.

***We are currently developing several product candidates. If we are unable to successfully complete clinical development of, obtain regulatory approval for and commercialize our product candidates, our business prospects will be significantly harmed.***

Entinostat, SNDX-6352 and SNDX-5613 are currently our only product candidates. Our financial success will depend substantially on our ability to effectively and profitably commercialize our product candidates. In order to commercialize our product candidates, we will be required to obtain regulatory approvals by establishing that each of them is sufficiently safe and effective. The clinical and commercial success of our product candidates will depend on a number of factors, including the following:

- timely commencement and completion of the Phase 1b/2 clinical trials of entinostat in combination with *Keytruda*, *Tecentriq* and the Phase 1/1b clinical trials of SNDX-6352 as a monotherapy and in combination with durvalumab;
- timely completion of the Phase 3 clinical trial in advanced HR+, HER2- breast cancer, which has been significantly slower than we anticipated and will depend substantially upon the satisfactory performance of ECOG-ACRIN and the NCI and other third-party contractors for entinostat;
- whether we are able to complete IND enabling studies for SNDX-5613 and file an IND with the FDA;
- whether we are required by the FDA or foreign regulatory authorities to conduct additional clinical trials;
- the prevalence and severity of adverse drug reactions in any of our clinical trials;
- the ability to demonstrate safety and efficacy of our product candidates for their proposed indications and the timely receipt of necessary marketing approvals from the FDA and foreign regulatory authorities;
- achieving and maintaining compliance with all applicable regulatory requirements;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;

- the effectiveness of our own or our potential strategic collaborators' marketing, sales and distribution strategy and operations in the United States and abroad;
- the ability of our third-party contract manufacturers to produce trial supplies and to develop, validate and maintain a commercially viable manufacturing process that is compliant with cGMP;
- the availability of commercial supplies of therapeutics, including exemestane, *Keytruda*, *Tecentriq* and clinical supplies of investigational drugs, to support the development and marketing of the entinostat therapy as a component of a combination drug regimen for entinostat;
- the availability of commercial supplies of therapeutics, including *Imfinzi*, and clinical supplies of investigational drugs, to support the development and marketing of the SNDX-6352 therapy as a component of a combination drug regimen for SNDX-6352;
- our ability to successfully commercialize our product candidates in the United States and abroad, whether alone or in collaboration with others; and
- our ability to enforce our intellectual property rights in and to our product candidates.

If we fail to obtain regulatory approval for our product candidates, we will not be able to generate product sales, which will have a material adverse effect on our business and our prospects.

***Our strategy of combining entinostat with immune checkpoint inhibitors has undergone limited clinical testing and we may fail to show that the combination is safe and well tolerated and demonstrates additional clinical benefit from the combination.***

Preclinical studies conducted by us and others suggest a strong rationale for combining entinostat with immune checkpoint inhibitors, including PD-1 pathway antagonists, to enhance the immune system's ability to detect and eliminate tumor cells. Our approach is to conduct Phase 1 and 2 clinical trials in patients with tumors that are known to be responsive to PD-1 pathway antagonists and assess both the safety and efficacy of the combination of entinostat plus a PD-1 pathway antagonist. Our initial clinical data is supportive of our hypothesis as we have seen clinical benefit from the combination of entinostat plus pembrolizumab in patients with metastatic melanoma and non-small cell lung cancer. However, we have not yet sufficiently demonstrated a favorable risk-benefit of this combination in patients, and we may be unable to establish sufficient efficacy to warrant regulatory submission and approval.

***Our strategy for developing SNDX-6352 has undergone limited clinical testing and we may fail to show that this drug is safe, well tolerated and provides a clinical benefit for patients.***

Preclinical studies suggest that CSF-1/CSF-1R signaling may be the key regulatory pathway involved in the expansion and infiltration of donor derived macrophages that mediate the disease processes involved in cGVHD. Nonclinical studies and analysis of patient samples indicates that the cGVHD inflammatory disease process is a result of a complex interaction between host and donor immune cells including B cells, and regulatory T cells with M2 differentiated macrophages in target tissue appearing to represent the common distal mediator of fibrosis. Therefore, we hypothesize that a CSF-1R signal inhibitor such as SNDX-6352 may play a meaningful role as a monotherapy agent in the treatment of cGVHD. Our approach is to conduct Phase 1 clinical trial with SNDX-6352 in subjects with active cGVHD who have failed at least two prior lines of therapy. If our initial clinical data lend support for our hypothesis, we plan to continue developing SNDX-6352 in this indication. At this time however, we have not yet sufficiently demonstrated a favorable risk-benefit of SNDX-6352 in patients and we may be unable to establish sufficient efficacy to warrant continued development in this indication.

***Our strategy for developing SNDX-5613 has undergone limited clinical testing and we may fail to show that the drug is safe, well tolerated and a provide clinical benefit for patients.***

Research conducted in the field suggest that MLLr leukemias are driven by the interaction of Menin, a nuclear protein involved in transcription, with MLL-r, a rare, spontaneous fusion between the N-terminus of MLL1 and a host of signaling molecules and nuclear transcription factors. This fusion produces an aberrant transcription program that drives leukemic transformation. In pre-clinical animal models, small molecule inhibitors of the menin-MLL-r interaction, such as SNDX-5613, have demonstrated deep and durable single agent treatment effects in multiple leukemic xenografts harboring MLL fusions. Our approach is to conduct a Phase 1 clinical trial in patients with MLL-r leukemia and assess both the safety and efficacy of SNDX-5613. If our initial clinical data lend support for our hypothesis, we plan to continue developing SNDX-5613 in this indication. At this time however, we have not yet sufficiently demonstrated a favorable risk-benefit of SNDX-5613 in patients, and we may be unable to establish sufficient efficacy to warrant continued development in this indication.

***We may be unable to transfer, qualify and validate an assay for determining peripheral monocyte levels in our forthcoming non-small cell lung cancer, or NSCLC, registration trial.***

In October 2018, we announced that we are proceeding with a registration trial in NSCLC patients whose disease has progressed after both platinum-based combination chemotherapy and a PD-1 antagonist therapy. We designed the trial to both validate a classical monocyte biomarker and demonstrate that the combination therapy of entinostat plus *Keytruda* is superior to standard of care chemotherapy in a high monocyte population. This trial will require testing patients for levels of circulating classical monocytes prior to treatment before assigning them to the appropriate arm of the trial. The assay that our academic collaborators have used to determine circulating levels of classical monocytes has not been developed or validated to the qualifications that the FDA may require for patient selection. We are working to measure circulating levels of cells, including monocytes, but we may not be able to successfully transfer, qualify and validate an assay for determining peripheral monocyte levels that will be acceptable to the FDA. We recently completed a full portfolio prioritization assessment and have determined to place the initiation of this trial on hold until we receive final OS results from E2112.

***If we are or our collaborators are unable to enroll patients in clinical trials, these clinical trials may not be completed on a timely basis or at all.***

The timely completion of clinical trials largely depends on patient enrollment. Many factors affect patient enrollment, including:

- perception about the relative efficacy of our product candidates versus other compounds in clinical development or commercially available;
- evolving standard of care in treating cancer patients;
- the size and nature of the patient population, especially in the case of an orphan indication such as MLL-r acute leukemia;
- the number and location of clinical trial sites enrolled;
- competition with other organizations or our own clinical trials for clinical trial sites or patients;
- the eligibility and exclusion criteria for the trial;
- the design of the trial;
- ability to obtain and maintain patient consents; and
- risk that enrolled subjects will drop out before completion.

As a result of the above factors, there is a risk that our or our collaborators' clinical trials may not be completed on a timely basis or at all.

***We are dependent on Merck, Genentech, Merck KGaA, Pfizer, AstraZeneca and any future collaborators to perform satisfactorily under our agreements.***

Under the agreements with Merck, Genentech, Merck KGaA, Pfizer, AstraZeneca and any future collaborations, we will be dependent on our collaborators' performance of their responsibilities and their cooperation with us. Our collaborators may not perform their obligations under our agreements with them or otherwise cooperate with us. We cannot control whether our collaborators will devote the necessary resources to the activities contemplated by our collaborative agreements, nor can we control the timing of their performance. Our collaborators may choose to pursue existing or alternative technologies in preference to those being developed in collaboration with us. Disputes may arise between us and our collaborators that delay the development and commercialization of our product candidates, disputes that may be difficult and costly to resolve, or may not be resolved. In addition, a collaborator for the potential product may have the right to terminate the collaboration at its discretion. For example, Merck has the right to terminate the Merck agreement for any reason after a specified advance notice period. Any termination may require us to seek a new collaborator, which we may not be able to do on a timely basis, if at all, or may require us to delay or scale back the commercialization efforts or spend additional money to complete the clinical trial. The occurrence of any of these events could adversely affect the commercialization of entinostat and materially harm our business.

If we are unable to enter into additional clinical collaborations with developers of immune checkpoint inhibitors or other combination therapies to explore the same or additional indications, the commercial potential of entinostat and SNDX-6352 could be limited. Such collaborations are complex, and any potential discussions may not result in a definitive agreement for many reasons. For example, whether we reach a definitive agreement for a clinical collaboration will depend, among other things, upon our respective assessments of the other party's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of our clinical trials, the potential market for the combination therapy, the costs and complexities of manufacturing and delivering the potential product to patients, the potential of competing products, and industry and market conditions generally.

***The actions of KHK, Eddingpharm Investment Company Limited and any other current or future sublicensees could adversely affect our business.***

We currently sublicense entinostat to third parties for development and commercialization in certain foreign jurisdictions. Specifically, we have a sublicense agreement with KHK under which we granted KHK an exclusive sublicense to develop and commercialize entinostat in Japan and Korea as well as a sublicense agreement with Eddingpharm under which we granted Eddingpharm an exclusive sublicense to develop and commercialize entinostat in China and select Asian countries. It is possible that any clinical trials conducted by KHK, Eddingpharm and other current or future sublicensees in their respective jurisdictions could have negative results, which in turn could have a material adverse effect on the development of entinostat for development and commercialization in the United States and the rest of the world.

***We are dependent on UCB to comply with the terms of our license agreement for SNDX-6352.***

Our commercial success also depends upon our ability to develop, manufacture, market and sell SNDX-6352. In July 2016, we entered into the UCB license agreement pursuant to which we obtained a worldwide, sublicenseable, exclusive license to SNDX-6352, an IND-ready anti-CSF-1R monoclonal antibody. Under the UCB license agreement, we are dependent on UCB's performance of its responsibilities and its cooperation with us. UCB may not perform its obligations under the UCB license agreement or otherwise cooperate with us. We cannot control whether UCB will devote the necessary resources to its obligations under the UCB license agreement, nor can we control the timing of its performance. Additionally, certain of the rights licensed to us under the UCB license agreement are in-licensed by UCB from third parties. We are dependent on UCB maintaining the applicable third-party license agreements in full force and effect, which may include activities and performance obligations that are not within our control. If any of these third-party license agreements terminate, certain of our rights to develop, manufacture, commercialize or sell SNDX-6352 may be terminated as well. The occurrence of any of these events could adversely affect the development and commercialization of SNDX-6352, and materially harm our business.

***We may be required to relinquish important rights to and control over the development and commercialization of our product candidates to our current or future collaborators.***

Our collaborations, including any future strategic collaborations we enter into, could subject us to a number of risks, including:

- we may be required to undertake the expenditure of substantial operational, financial and management resources;
- we may be required to issue equity securities that would dilute our existing stockholders' percentage of ownership;
- we may be required to assume substantial actual or contingent liabilities;
- we may not be able to control the amount and timing of resources that our strategic collaborators devote to the development or commercialization of our product candidates;
- strategic collaborators may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new version of a product candidate for clinical testing;
- strategic collaborators may not pursue further development and commercialization of products resulting from the strategic collaboration arrangement or may elect to discontinue research and development programs;
- strategic collaborators may not commit adequate resources to the marketing and distribution of our product candidates, limiting our potential revenues from these products;
- disputes may arise between us and our strategic collaborators that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management's attention and consumes resources;
- strategic collaborators may experience financial difficulties;
- strategic collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- business combinations or significant changes in a strategic collaborator's business strategy may also adversely affect a strategic collaborator's willingness or ability to complete its obligations under any arrangement;
- strategic collaborators could decide to move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors; and
- strategic collaborators could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing, our product candidates.

***We may explore strategic collaborations that may never materialize or may fail.***

We may periodically explore a variety of possible strategic collaborations in an effort to gain access to additional product candidates or resources. At the current time, we cannot predict what form such a strategic collaboration might take. We are likely to face significant competition in seeking appropriate strategic collaborators, and strategic collaborations can be complicated and time consuming to negotiate and document. We may enter into strategic collaborations that we subsequently no longer wish to pursue, and we may not be able to negotiate strategic collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any additional strategic collaborations because of the numerous risks and uncertainties associated with establishing them.

***The regulatory approval processes of the FDA and foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. Our inability to obtain regulatory approval for our product candidates could harm our business.***

The time required to obtain approval by the FDA and foreign regulatory authorities is unpredictable, but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any of our product candidates, and it is possible that we will never obtain regulatory approval for our existing product candidates or any future product candidates.

Our product candidates could fail to receive regulatory approval from the FDA or foreign regulatory authorities for many reasons, including but not limited to:

- failure to demonstrate that our product candidates are safe and effective;
- failure of clinical trials to meet the primary endpoints or level of statistical significance required for approval;
- failure to demonstrate that the clinical and other benefits of a product candidate outweigh any of its safety risks;
- disagreement with our interpretation of data from preclinical studies or clinical trials;
- disagreement with the design or implementation of our or our collaborators' trials;
- the insufficiency of data collected from trials of our product candidates to support the submission and filing of an NDA or other submission or to obtain regulatory approval;
- failure to obtain approval of the manufacturing and testing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies;
- receipt of a negative opinion from an advisory committee due to a change in the standard of care regardless of the outcome of the clinical trials; or
- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or foreign regulatory authorities may require more information, including additional preclinical or clinical data, to support approval, which may delay or prevent approval and our commercialization plans, or may cause us to decide to abandon our development program. Even if we were to obtain approval, regulatory authorities may approve one or more of our product candidates for a more limited patient population than we request, may grant approval contingent on the performance of costly post-marketing trials, may impose a risk evaluation and mitigation strategy, or REMS, or foreign regulatory authorities may require the establishment or modification of a similar strategy that may, for instance, restrict distribution of entinostat and impose burdensome implementation requirements on us, or may approve it with a label that does not include the labeling claims necessary or desirable for the successful commercialization of entinostat, all of which could limit our ability to successfully commercialize our product candidates.

***We are not developing entinostat as a monotherapy. A shortage in the supply of exemestane, Keytruda, Tecentriq or other drugs used in combination with entinostat or cessation of development efforts for investigational agents being studied with entinostat could increase our development costs and adversely affect our ability to commercialize entinostat, and any unexpected adverse events with any of the drugs used in combination with entinostat could halt or delay development of entinostat.***

Cancer drugs have from time to time been in short supply and, because many or all of these cancer drugs are also widely used in cancer treatment currently, we will compete with a broad range of healthcare providers and other companies for availability of those drugs. Any shortage of exemestane, *Keytruda*, *Tecentriq* or other drugs that we are testing in combination with entinostat could adversely affect our ability to timely conduct the Phase 3 clinical trial in advanced HR+, HER2- breast cancer, our future potential Phase 3 clinical trial in NSCLC, any future clinical trials in melanoma, and if entinostat receives regulatory approval, to commercialize entinostat for treatment of advanced HR+, HER2- breast cancer, NSCLC, or melanoma. A shortage of supply may also result in an increase, which could be significant, in our costs of procuring exemestane.

Additionally, because entinostat is being developed for use in combination with other cancer treatments, the development of entinostat may be delayed or halted if unexpected adverse events occurring in patients are attributed to entinostat. Likewise, new adverse events emerging from commercialized or development stage drugs being administered with entinostat may limit or halt the potential of such combinations.

***Our product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community to be commercially successful.***

Even if our product candidates receive regulatory approval, they may not gain sufficient market acceptance among physicians, patients, healthcare payors and others in the medical community. Our commercial success also depends on coverage and adequate reimbursement by third-party payors, including government payors, which may be difficult or time-consuming to obtain, may be limited in scope and may not be obtained in all jurisdictions in which we may seek to market our product candidates. The degree of market acceptance will depend on a number of factors, including:

- the efficacy and safety profile as demonstrated in trials;
- the timing of market introduction as well as competitive products;
- the clinical indications for which the product candidate is approved;
- acceptance of the product candidate as a safe and effective treatment by physicians, clinics and patients;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the cost of treatment in relation to alternative treatments;
- pricing and the availability of coverage and adequate reimbursement by third-party payors, including government authorities;
- relative convenience and ease of administration;
- the frequency and severity of adverse events;
- the effectiveness of sales and marketing efforts; and
- unfavorable publicity relating to our product candidates.

If our product candidates are approved but do not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate sufficient revenue to become or remain profitable.

***We rely on third-party suppliers to manufacture and distribute our clinical drug supplies for our product candidates, we intend to rely on third parties for commercial manufacturing and distribution of our product candidates and we expect to rely on third parties for manufacturing and distribution of preclinical, clinical and commercial supplies of any future product candidates.***

We do not currently have, nor do we plan to acquire, the infrastructure or capability to manufacture or distribute preclinical, clinical or commercial quantities of drug substance or drug product, including our existing product candidates. While we expect to continue to depend on third-party manufacturers for the foreseeable future, we do not have direct control over the ability of these manufacturers to maintain adequate manufacturing capacity and capabilities to serve our needs, including quality control, quality assurance and qualified personnel. We are dependent on our third-party manufacturers for compliance with cGMPs and for manufacture of both active drug substances and finished drug products. Facilities used by our third-party manufacturers to manufacture drug substance and drug product for commercial sale must be approved by the FDA or other relevant foreign regulatory agencies pursuant to inspections that will be conducted after we submit our NDA or relevant foreign regulatory submission to the applicable regulatory agency. If our third-party manufacturers cannot successfully manufacture materials that conform to our specifications and/or the strict regulatory requirements of the FDA or foreign regulatory agencies, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. Furthermore, these third-party manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which also exposes our third-party manufacturers to regulatory risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may also affect the regulatory clearance of a third-party manufacturers' facility. If the FDA or a foreign regulatory agency does not approve these facilities for the manufacture of our product candidates, or if it withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would impede or delay our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

***Even if our product candidates receive regulatory approval, they may still face future development and regulatory difficulties.***

Even if we obtain regulatory approval for our product candidates, they would be subject to ongoing requirements by the FDA and foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. The FDA and foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the FDA or foreign regulatory authorities become aware of new safety information after approval of a product candidate, they may require labeling changes or establishment of a REMS or similar strategy, impose significant restrictions on its indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance.

In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including withdrawal of the product from the market or suspension of manufacturing, or we may recall the product from distribution. If we, or our third-party manufacturers, fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;

- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, or refuse to permit the import or export of products.

The occurrence of any event or penalty described above may inhibit our ability to commercialize and generate revenue from the sale of our product candidates.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the Department of Justice, the Department of Health and Human Services' Office of Inspector General, state attorneys general, members of Congress, other government agencies and the public. Violations, including promotion of our products for unapproved (or off-label) uses, may be subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions by the government. Additionally, foreign regulatory authorities will heavily scrutinize advertising and promotion of any product candidate that obtains approval in their respective jurisdictions.

In the United States, engaging in the impermissible promotion of our products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to administrative, civil and criminal penalties, damages, monetary fines, disgorgement, individual imprisonment, exclusion from participation in Medicare, Medicaid and other federal healthcare programs, curtailment or restructuring of our operations and agreements that materially restrict the manner in which a company promotes or distributes drug products. These false claims statutes include, but are not limited to, the federal civil False Claims Act, which allows any individual to bring a lawsuit against an individual or entity, including a pharmaceutical or biopharmaceutical company on behalf of the federal government alleging the knowing submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment or approval by a federal program such as Medicare or Medicaid. These False Claims Act lawsuits against pharmaceutical and biopharmaceutical companies have increased significantly in number and breadth, leading to several substantial civil and criminal settlements regarding certain sales practices, including promoting off-label drug uses involving fines in excess of $1.0 billion. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations, and be excluded from participation in Medicare, Medicaid and other federal and state healthcare programs. If we, or any partner that we may engage, do not lawfully promote our approved products, we may become subject to such litigation, which have a material adverse effect on our business, financial condition and results of operations.

***Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial scope of their approved use, or result in significant negative consequences following any marketing approval.***

Undesirable side effects caused by our product candidates could cause the interruption, delay or halting of the trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other foreign regulatory authorities. In our Phase 2b clinical trial of entinostat in advanced HR+, HER2- breast cancer, the most significant adverse events were fatigue, gastrointestinal disturbances and hematologic toxicities, all of which occurred in higher numbers than in the placebo group. Results of the clinical trials may reveal a high and unacceptable severity and prevalence of side effects or other unexpected characteristics. In such event, the trials could be suspended or terminated, or the FDA or foreign regulatory authorities could deny approval of our product candidates for any or all targeted indications. Drug-related side effects could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects.

Additionally, if our product candidates receive marketing approval, and we or others later identify undesirable side effects, a number of potentially significant negative consequences could result, including:

- we may suspend marketing of, or withdraw or recall, the product;
- regulatory authorities may withdraw approvals;
- regulatory authorities may require additional warnings on the product labels;

- the FDA or other regulatory authorities may issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about the product;
- the FDA may require the establishment or modification of a REMS or foreign regulatory authorities may require the establishment or modification of a similar strategy that may, for instance, restrict distribution of the product and impose burdensome implementation requirements on us;
- regulatory authorities may require that we conduct post-marketing studies;
- we could be sued and held liable for harm caused to subjects or patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates for use in targeted indications or otherwise materially harm its commercial prospects, if approved, and could harm our business, results of operations and prospects.

***Our failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our product candidates outside the United States.***

In order to market and sell our product candidates in other jurisdictions, we must obtain separate marketing approvals for those jurisdictions and comply with their numerous and varying regulatory requirements. We may not obtain foreign regulatory approvals on a timely basis, or at all. 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 regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, product reimbursement approvals must be secured before regulatory authorities will approve the product for sale in that country. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. For example, based on scientific advice that we received from the European Medicines Agency in March 2014, the current Phase 3 clinical trial is likely to be insufficient to receive regulatory approval in Europe for entinostat to treat advanced HR+, HER2- breast cancer. Our failure to obtain approval of our product candidates by foreign regulatory authorities may negatively impact the commercial prospects of such product candidates and our business prospects could decline. Also, if regulatory approval for our product candidates is granted, it may be later withdrawn. If we fail to comply with the regulatory requirements in international jurisdictions and receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential for our product candidates will be harmed and our business may be adversely affected.

***We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.***

The pharmacologic treatment of NSCLC and melanoma patients has included chemotherapies and therapies targeting specific gene mutations. Over the past few years, immune checkpoint inhibitors have been approved for NSCLC and melanoma. Currently there are few approved combination immuno-oncology therapies although numerous drugs are undergoing active clinical investigation. We believe that if entinostat in combination with *Keytruda* were approved for the treatment of NSCLC or melanoma it would face competition from standard-of-care approaches and other investigational drugs being tested in combination with any of these approaches.

If entinostat in combination with exemestane were approved for treatment of advanced HR+, HER2- breast cancer, it could face competition from other therapies recently approved for use in combination with hormone therapy in this population, including *Ibrance*, *Kisqali*, *Afinitor*, *Verzenio*, and other therapies under FDA review such as alpelisib, or currently in Phase 3 clinical development.

Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Our competitors may be more successful than us in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective or more effectively marketed and sold than any drug we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available.

We believe that our ability to successfully compete will depend on, among other things:

- the efficacy and safety profile of our product candidates relative to marketed products and product candidates in development by third parties;
- the time it takes for our product candidates to complete clinical development and receive marketing approval;
- our ability to commercialize our product candidates if they receive regulatory approval;
- the price of our product candidates, including in comparison to branded or generic competitors;
- whether coverage and adequate levels of reimbursement are available under private and governmental health insurance plans, including Medicare;
- our ability to manufacture commercial quantities of our product candidates if they receive regulatory approval; and
- acceptance of entinostat in combination with exemestane, *Keytruda*, and other drugs by physicians and other healthcare providers.

Even if we obtain regulatory approval of our product candidates, the availability and price of our competitors' products could limit the demand and the price we are able to charge. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment, or if physicians switch to other new drug or biologic products or choose to reserve our drugs for use in limited circumstances.

***Adverse events in the field of immuno-oncology could damage public perception of our product candidates and negatively affect our business.***

The commercial success of our product candidates will depend in part on public acceptance of the use of cancer immunotherapies. Adverse events in clinical trials of our product candidates or in clinical trials of others developing similar products and the resulting publicity, as well as any other adverse events in the field of immuno-oncology that may occur in the future, could result in a decrease in demand for any products that we may develop. If public perception is influenced by claims that the use of cancer immunotherapies is unsafe, our product candidates may not be accepted by the general public or the medical community.

Future adverse events in immuno-oncology or the biopharmaceutical industry could also result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approvals of our products. Any increased scrutiny could delay or increase the costs of obtaining regulatory approval for our product candidates.

***Our employees, consultants and collaborators may engage in misconduct or other improper activities, including insider trading and non-compliance with regulatory standards and requirements.***

We are exposed to the risk that our employees, consultants, distributors, and collaborators may engage in fraudulent or illegal activity. Misconduct by these parties could include intentional, reckless or negligent conduct or disclosure of unauthorized activities to us that violates the regulations of the FDA and non-U.S. regulators, including those laws requiring the reporting of true, complete and accurate information to such regulators, manufacturing standards, healthcare fraud and abuse laws and regulations in the United States and abroad or laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry, including the sale of pharmaceuticals, are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. It is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws 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 result in the imposition of significant fines or other sanctions, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings and curtailment of operations, any of which could adversely affect our ability to operate our business and our results of operations. Whether or not we are successful in defending against such actions or investigations, we could incur substantial costs, including legal fees, and divert the attention of management in defending ourselves against any of these claims or investigations.

***We must attract and retain additional highly skilled employees in order to succeed.***

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel and we face significant competition for experienced personnel. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. The competition for qualified personnel in the pharmaceutical industry is intense and as a result, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel.

Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover and develop product candidates and our business will be limited.

***Even if we commercialize our product candidates, they or any other product candidates that we develop, may become subject to unfavorable pricing regulations or third-party coverage or reimbursement practices, which could harm our business.***

Our ability to successfully commercialize our existing product candidates, or any other product candidates that we develop, will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government healthcare programs, private health insurers, managed care plans and other organizations. Third-party payors determine which medications they will cover and establish reimbursement levels. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products.

We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Limitation on coverage and reimbursement may impact the demand for, or the price of, and our ability to successfully commercialize entinostat or any other product candidates that we develop.

There may be significant 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 foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States.

Private payors often follow decisions by the Centers for Medicare & Medicaid Services, or CMS, regarding coverage and reimbursement to a substantial degree. However, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have an adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

The regulations that govern marketing approvals, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. 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 product 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 may obtain marketing approval for our product candidates in a particular country, but be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues we generate from the sale of the product in that particular country. Adverse pricing limitations may hinder our ability to recoup our investment even if our product candidates obtain marketing approval.

There can be no assurance that our product candidates, if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication, that it will be considered cost effective by third-party payors, that coverage and an adequate level of reimbursement will be available, or that third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably.

***Current and future legislation may increase the difficulty and cost for us to commercialize our product candidates and affect the prices we may obtain.***

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidate for which we obtain marketing approval. For example, then President Obama signed into law the Affordable Care Act. Among other cost containment measures, the Affordable Care Act established an annual, nondeductible fee on any entity that manufactures or imports branded prescription drugs and biologic agents, a Medicare Part D coverage gap discount program, and a formula that increased the rebates a manufacturer must pay under the Medicaid Drug Rebate Program. Some of the provisions of the Affordable Care Act have yet to be implemented, while certain provisions have been subject to judicial and Congressional challenges, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the Affordable Care Act or

otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain fees mandated by the Affordable Care Act, 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, or the BBA, among other things, amended the Affordable Care Act, effective January 1, 2019, to increase from 50% to 70% 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". In July 2018, CMS published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under its risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by the U.S. Congress as part of the Tax Cuts and Jobs Act of 2017 Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care and our business. In addition, Congress may consider other legislation to repeal and replace elements of the Affordable Care Act.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, in August 2011, then President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not agree upon a targeted deficit reduction of at least $1.2 trillion for fiscal years 2012 through 2021, triggering the Affordable Care Act's automatic reduction to several government programs. This included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective as of 2013. Further legislation, including the BBA, has extended the 2% reduction to 2027. In January 2013, then President Obama signed into law 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.

Further, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains additional drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid and to eliminate cost. The Trump administration also released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019. While some of these and other-sharing for generic drugs for low-income patients. While proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly 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.

We expect that the Affordable Care Act, as well as other current or future healthcare reform measures may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. This could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

***Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of our product candidates.***

We face an inherent risk of product liability exposure related to the testing of our product candidates in human trials and will face an even greater risk if we commercially sell any products that we may develop. Product liability claims may be brought against us by subjects enrolled in our trials, patients, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against claims that our product candidates or other products that we may develop caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- withdrawal of trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial subjects or patients;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize any products that we may develop.

While we currently hold trial liability insurance coverage consistent with industry standards, this may not adequately cover all liabilities that we may incur. We also may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise in the future. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval for our product candidates, but we may be unable to obtain commercially reasonable product liability insurance. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business and financial condition.

***Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations as well as privacy and data security laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, exclusion from participation in government healthcare programs, curtailments or restrictions of our operations, administrative burdens and diminished profits and future earnings.***

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with physicians, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we conduct clinical research and market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, but are not limited to, the following:

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

- the federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- HIPAA also imposes obligations on certain covered entity health care providers, health plans and health care clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- 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 to report annually to the U.S. Department of Health and Human Services information related to "payments or other transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians (as defined above) 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 sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws that require manufactures to report pricing information regarding certain drugs; and foreign laws that govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and federal, state, and foreign laws that govern the privacy and security of other personal information, including federal and state consumer protection laws, state data security laws, and data breach notification laws (a data breach affecting sensitive personal information, including health information, could result in significant legal and financial exposure and reputational damages).

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 interpreting 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, disgorgement, individual imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any physician or other healthcare provider or entity with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

## Risks Related to Our Financial Position and Capital Needs

***We have incurred net losses since our inception and anticipate that we will continue to incur net losses for the foreseeable future.***

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval or be commercially viable. We are a clinical stage biopharmaceutical company with limited operating history. We have no products approved for commercial sale and have not generated any product revenues to date, and we continue to incur significant research and development and other expenses related to our ongoing operations and clinical development of entinostat. As a result, we are not and have never been profitable and have incurred losses in each period since our inception in 2005.

For the year ended December 31, 2018, we reported a net loss of $74.0 million; and as of December 31, 2018, we had an accumulated deficit of $439.4 million, which included non-cash charges for stock-based compensation, preferred stock accretion and extinguishment charges. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, our product candidates. We may also encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues, if any. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

***We currently have no source of product revenue and may never achieve or maintain profitability.***

Our ability to generate product revenue and become profitable depends upon our ability to successfully commercialize our product candidates. We do not anticipate generating revenue from the sale of our product candidates for the foreseeable future. Our ability to generate future product revenue also depends on a number of additional factors, including, but not limited to, our ability to:

- successfully complete the research and clinical development of, and receive regulatory approval for, our product candidates;
- launch, commercialize and achieve market acceptance of our product candidates, and if launched independently, successfully establish a sales, marketing and distribution infrastructure;
- continue to build a portfolio of product candidates through the acquisition or in-license of products, product candidates or technologies;
- initiate preclinical and clinical trials for any additional product candidates that we may pursue in the future;
- establish and maintain supplier and manufacturing relationships with third parties, and ensure adequate and legally compliant manufacturing of bulk drug substances and drug products to maintain that supply;
- obtain coverage and adequate product reimbursement from third-party payors, including government payors;
- establish, maintain, expand and protect our intellectual property rights; and
- attract, hire and retain additional qualified personnel.

In addition, because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of increased expenses, and if or when we will achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we decide to or are required by the FDA or foreign regulatory authorities to perform studies or trials in addition to those that we currently anticipate. Even if we complete the development and regulatory processes described above, we anticipate incurring significant costs associated with launching and commercializing our current product candidates and any other product candidates we may develop.

Even if we generate revenues from the sale of our product candidates, we may not become profitable and may need to obtain additional funding to continue operations or acquire additional products that will require additional funding to develop them. If we fail to become profitable or do not sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations or even shut down.

***We will require additional capital to finance our planned operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of, or obtain regulatory approval for our existing product candidates or develop new product candidates.***

Our operations have consumed substantial amounts of cash since our inception, primarily due to our research and development efforts. We expect our research and development expenses to increase substantially in connection with our ongoing and planned activities. We believe that our existing cash, cash equivalents and short-term investments will fund our projected operating expenses and capital expenditure requirements for at least the next 12 months. Unexpected circumstances may cause us to consume capital more rapidly than we currently anticipate. For example, we may discover that we need to conduct additional activities that exceed our current budget to achieve appropriate rates of patient enrollment, which would increase our development costs.

In any event, we will require additional capital to continue the development of, obtain regulatory approval for, and to commercialize our existing product candidates and any future product candidates. Any efforts to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we do not raise additional capital when required or on acceptable terms, we may need to:

- delay, scale back or discontinue the development or commercialization of our product candidates or cease operations altogether;
- seek strategic alliances for our existing product candidates on terms less favorable than might otherwise be available; or
- relinquish, or license on unfavorable terms, our rights to technologies or any future product candidates that we otherwise would seek to develop or commercialize ourselves.

If we need to conduct additional fundraising activities and we do not raise additional capital in sufficient amounts or on terms acceptable to us, we may be unable to pursue development and commercialization efforts, which will harm our business, operating results and prospects.

Our future funding requirements, both short- and long-term, will depend on many factors, including:

- the initiation, progress, timing, costs and results of clinical trials of our product candidates;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more trials than we currently expect;
- the cost to establish, maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights;
- market acceptance of our product candidates;
- the cost and timing of selecting, auditing and developing manufacturing capabilities, and potentially validating manufacturing sites for commercial-scale manufacturing;
- the cost and timing for obtaining pricing, and coverage and reimbursement by third-party payors, which may require additional trials to address pharmacoeconomic benefit;

- the cost of establishing sales, marketing and distribution capabilities for our product candidates if any candidate receives regulatory approval and we determine to commercialize it ourselves;
- the costs of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- the effect of competing technological and market developments; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems, as we grow our company.

If we cannot expand our operations or otherwise capitalize on our business opportunities because we cannot secure sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

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

We have incurred substantial losses during our history. We do not expect to become profitable in the near future, and we may never achieve profitability. Unused losses generally are available to be carried forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. We completed an analysis through December 31, 2017 and determined that on March 30, 2007 and August 21, 2015 ownership changes had occurred. We did not experience ownership changes since August 21, 2015 but we may also experience ownership changes in the future as a result of shifts in our stock ownership, some of which may be outside of our control. As a result, our ability to use our pre-change NOLs to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

***Comprehensive tax reform legislation could adversely affect our business and financial condition.***

On December 22, 2017, the Tax Cuts and Jobs Act of 2017, or the Tax Act, was signed into law. The Tax Act, among other things, contains significant changes to corporate taxation, including (i) reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, (ii) limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), (iii) limitation of the deduction for net operating losses to 80% of current year taxable income in respect of net operating losses generated during or after 2018 and elimination of net operating loss carrybacks, (iv) one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, (v) immediate deductions for certain new investments instead of deductions for depreciation expense over time, and (vi) modifying or repealing many business deductions and credits. Any federal net operating loss incurred in 2018 and in future years may now be carried forward indefinitely pursuant to the Tax Act. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. We will continue to examine the impact the Tax Act may have on our business.

## Risks Related to Intellectual Property

***If we are unable to obtain or protect intellectual property rights, we may not be able to compete effectively in our market.***

Our success depends in significant part on our and our licensors' and licensees' ability to establish, maintain and protect patents and other intellectual property rights and operate without infringing the intellectual property rights of others. We have filed patent applications both in the United States and in foreign jurisdictions to obtain patent rights to inventions we have discovered. We have also licensed from third parties rights to patent portfolios. Some of these licenses give us the right to prepare, file and prosecute patent applications and maintain and enforce patents we have licensed, and other licenses may not give us such rights.

The patent prosecution process is expensive and time-consuming, and we and our current or future licensors and licensees may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our licensors or licensees will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors or licensees fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors or licensees are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors' or licensees' patent rights are highly uncertain. Our and our licensors' or licensees' pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our licensors or licensees to narrow the scope of the claims of our or our licensors' or licensees' pending and future patent applications, which may limit the scope of patent protection that may be obtained. It is possible that third parties with products that are very similar to ours will circumvent our or our licensors' or licensees' patents by means of alternate designs or processes. We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patents. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidate, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidate or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around the claims of patents that we have had issued that cover our products. Our and our licensors' or licensees' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology.

Furthermore, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Entinostat composition of matter U.S. Patent RE39,754, which we licensed from Bayer, covers the chemical entity of entinostat and any crystalline or non-crystalline form of entinostat and expired in September 2017.

The portfolio we licensed from Bayer also includes U.S. Patent 7,973,166, or the ‘166 patent, which covers a crystalline polymorph of entinostat which is referred to as crystalline polymorph B, the crystalline polymorph used in the clinical development of entinostat. Many compounds can exist in different crystalline forms. A compound which in the solid state may exhibit multiple different crystalline forms is called polymorphic, and each crystalline form of the same chemical compound is termed a polymorph. A new crystalline form of a compound may arise, for example, due to a change in the chemical process or the introduction of an impurity. Such new crystalline forms may be patented. The ‘166 patent expires in 2029. On March 7, 2014, our licensor Bayer applied for reissue of the ‘166 patent. The reissue application seeks to add three inventors not originally listed on the ‘166 patent. The reissue application does not seek to amend the claims issued in the ‘166 patent. On April 28, 2015, the USPTO re-issued the ‘166 patent as U.S. patent RE45,499. RE45,499 reissued with the same claims originally issued in the ‘166 patent and the list of inventors on RE45,499 now lists the additional three inventors that were not included on the ‘166 patent. The ‘166 patent has now been surrendered in favor of RE45,499. RE45,499 has the same term as the initial term of the ‘166 patent, which expires in August 2029. After expiry of RE39,754, which occurred in September 2017, a competitor may develop a competing polymorphic form other than based on polymorph B, which could compete with polymorph B.

In spite of our efforts and efforts of our licensor, we may not be successful in defending the validity of the claims of the RE45,499 reissue patent or any of its foreign counterparts. If the claims of the ‘166 patent or any of its counterparts are found to be invalid by a competent court, we may not be able to effectively block entry of generic versions of our entinostat crystalline polymorph B candidate products into markets where the crystalline polymorph B patent claims are found to be invalid. Additionally, even if we submit an NDA before the expiration of U.S. Patent RE45,499 and are successful in obtaining an extension of the term of U.S. Patent RE45,499 based on FDA regulatory delays, such extension will only extend the term of RE45,499 for a few additional years (up to a maximum of five additional years for patent claims covering a new chemical entity).

The portfolio that we licensed from UCB includes patent applications with pending claims directed to the composition of matter of SNDX-6352 (a humanized, full-length IgG4 (kappa light chain) antibody with high affinity for the CSF-1R) as well as claims directed to methods of use of SNDX-6352. There is no guarantee that any patents will be granted based on the pending applications we licensed from UCB or even if one or more patents are granted that the claims issued in those patents would cover SNDX-6352 or methods of using SNDX-6352. Based on the priority date and filing date of the applications in the portfolio we licensed from UCB, we expect that a patent, if any, granted based on the currently pending applications would expire in 2034. The actual term of any patents granted based on the pending applications we licensed from UCB can only be determined after such patents are actually granted.

The portfolio that we licensed from Vitae Pharmaceuticals, a subsidiary of Allergan, includes patent applications with pending claims directed to inhibitors of the interaction of menin with MLL and MLL fusion proteins, pharmaceutical compositions containing the same, and their use in the treatment of cancer and other diseases mediated by the menin-MLL interaction. There is no guarantee that any patents will be granted based on the pending applications that we licensed from Allergan or even if one or more patents are granted that the claims issued in those patents would cover the desired lead compounds, compositions, and methods of use thereof. Based on the priority date and filing date of the applications in the portfolio that we licensed from Allergan, we expect that a patent, if any, granted based on the currently pending applications would expire in 2036. The actual term of any patents granted based on the pending applications that we licensed from Allergan can only be determined after such patents are actually granted.

***We may not be able to protect our intellectual property rights throughout the world.***

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

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us and our licensors to stop the infringement of our and our licensors' patents or marketing of competing products in violation of our and our licensors' proprietary rights generally. Proceedings to enforce our and our licensors' patent rights in foreign jurisdictions could result in substantial costs and divert our attention from other aspects of our business, could put our and our licensors' patents at risk of being invalidated or interpreted narrowly and our and our licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors. We or our licensors may not prevail in any lawsuits that we or our licensors initiate and the damages or other remedies awarded, if any, may not be commercially meaningful.

The requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval of a drug and its patent status. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for, and launch generic versions of our products. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our and our licensors' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

***If we breach our license agreement with Bayer related to entinostat or if the license agreement is otherwise terminated, we could lose the ability to continue the development and commercialization of entinostat.***

Our commercial success depends upon our ability to develop, manufacture, market and sell entinostat. In March 2007, we entered into a license, development and commercialization agreement, or the Bayer license agreement, with Bayer pursuant to which we obtained a worldwide, exclusive license to develop and commercialize entinostat and any other products containing the same active ingredient. The Bayer license agreement, as amended, permits us to use entinostat or other licensed products under the Bayer license agreement for the treatment of any human disease, and we are obligated to use commercially reasonable efforts to develop, manufacture and commercialize licensed products for all commercially reasonable indications.

We are obligated to pay Bayer up to approximately $50 million in the aggregate upon obtaining certain milestones in the development and marketing approval of entinostat, assuming that we pursue at least two different indications for entinostat or any other licensed product under the Bayer license agreement. We are also obligated to pay Bayer up to $100 million in aggregate sales milestones, and a tiered, single-digit royalty on net sales by us, our affiliates and sublicensees of entinostat and any other licensed products under the Bayer license agreement. We are obligated to pay Bayer these royalties on a country-by-country basis for the life of the relevant licensed patents covering such product or 15 years after the first commercial sale of such product in such country, whichever is longer. We cannot determine the date on which our royalty payment obligations to Bayer would expire because no commercial sales of entinostat have occurred and the last-to-expire relevant patent covering entinostat in a given country may change in the future.

The Bayer license agreement will remain in effect until the expiration of our royalty obligations under the agreement in all countries. Either party may terminate the Bayer license agreement in its entirety or with respect to certain countries in the event of an uncured material breach by the other party. Either party may terminate the Bayer license agreement if voluntary or involuntary bankruptcy proceedings are instituted against the other party, if the other party makes an assignment for the benefit of creditors, or upon the occurrence of other specific events relating to the insolvency or dissolution of the other party. Bayer may terminate the Bayer license agreement if we seek to revoke or challenge the validity of any patent licensed to us by Bayer under the Bayer license agreement or if we procure or assist a third party to take any such action.

If the Bayer license agreement is terminated, we would not be able to develop, manufacture, market or sell entinostat and would need to negotiate a new or reinstated agreement, which may not be available to us on equally favorable terms, or at all.

***If we breach the UCB license agreement related to SNDX-6352 or if the UCB license agreement is otherwise terminated, we could lose the ability to continue the development and commercialization of SNDX-6352.***

Our commercial success depends upon our ability to develop, manufacture, market and sell SNDX-6352. Subject to the achievement of certain milestone events, we may be required to pay UCB up to $119.5 million in one-time development and regulatory milestone payments over the term of the UCB license agreement. If we or any of our affiliates or sublicensees commercializes SNDX-6352, we will also be obligated to pay UCB low double-digit royalties on sales, subject to reduction in certain circumstances, as well as up to an aggregate of $250 million in potential one-time sales-based milestone payments based on achievement of certain annual sales thresholds. Under certain circumstances, we may be required to share a percentage of non-royalty income from sublicensees, subject to certain deductions, with UCB.

Either party may terminate the UCB license agreement in its entirety or with respect to certain countries in the event of an uncured material breach by the other party. Either party may terminate the UCB license agreement if voluntary or involuntary bankruptcy proceedings are instituted against the other party, if the other party makes an assignment for the benefit of creditors, or upon the occurrence of other specific events relating to the insolvency or dissolution of the other party. UCB may terminate the UCB license agreement if we seek to revoke or challenge the validity of any patent licensed to us by UCB under the UCB license agreement or if we procure or assist a third party to take any such action.

Unless terminated earlier in accordance with its terms, the UCB license agreement will continue on a country-by-country and product-by-product basis until the later of: (i) the expiration of all of the licensed patent rights in such country; (ii) the expiration of all regulatory exclusivity applicable to the product in such country; and (iii) 10 years from the date of the first commercial sale of the product in such country. We cannot determine the date on which our royalty payment obligations to UCB would expire because no commercial sales of SNDX-6352 have occurred and the last-to-expire relevant patent covering SNDX-6352 in a given country may change in the future.

If the UCB license agreement is terminated, we would not be able to develop, manufacture, market or sell SNDX-6352 and would need to negotiate a new or reinstated agreement, which may not be available to us on equally favorable terms, or at all.

***If we breach the license agreement related to SNDX-5613 or if the license agreement is otherwise terminated, we could lose the ability to continue the development and commercialization of SNDX-5613.***

Our commercial success depends upon our ability to develop, manufacture, market and sell SNDX-5613. Subject to the achievement of certain milestone events, we may be required to pay Vitae, a subsidiary of Allergan, up to $99 million in one-time development and regulatory milestone payments over the term of the Allergan license agreement. In the event that we or any of our affiliates or sublicensees commercializes SNDX-5613, we will also be obligated to pay Allergan low single to low double-digit royalties on sales, subject to reduction in certain circumstances, as well as up to an aggregate of $70 million in potential one-time sales-based milestone payments based on achievement of certain annual sales thresholds. Under certain circumstances, we may be required to share a percentage of non-royalty income from sublicensees, subject to certain deductions, with Allergan.

Either party may terminate the license agreement in its entirety or with respect to certain countries in the event of an uncured material breach by the other party. Either party may terminate the license agreement if voluntary or involuntary bankruptcy proceedings are instituted against the other party, if the other party makes an assignment for the benefit of creditors, or upon the occurrence of other specific events relating to the insolvency or dissolution of the other party. Allergan may terminate the license agreement if we seek to revoke or challenge the validity of any patent licensed to us by Allergan under the license agreement or if we procure or assist a third party to take any such action.

Unless terminated earlier in accordance with its terms, the license agreement will continue on a country-by-country and product-by-product basis until the later of: (i) the expiration of all of the licensed patent rights in such country; (ii) the expiration of all regulatory exclusivity applicable to the product in such country; and (iii) 10 years from the date of the first commercial sale of the product in such country. We cannot determine the date on which our royalty payment obligations to Allergan would expire because no commercial sales of SNDX-5613 have occurred and the last-to-expire relevant patent covering SNDX-5613 in a given country may change in the future.

If the license agreement is terminated, we would not be able to develop, manufacture, market or sell SNDX-5613 and would need to negotiate a new or reinstated agreement, which may not be available to us on equally favorable terms, or at all.

***Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.***

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve technological and legal complexity, and obtaining and enforcing biopharmaceutical patents is costly, time-consuming, and inherently uncertain. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our and our licensors' ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts, and the U.S. Patent and Trademark Office, or USPTO, the laws and regulations governing patents could change in unpredictable ways that may weaken our and our licensors' ability to obtain new patents or to enforce existing patents and patents we and our licensors or collaborators may obtain in the future. In view of recent developments in U.S. patent laws, in spite of our efforts and the efforts of our licensors, we may face difficulties in obtaining allowance of our biomarker based patient selection patent claims or if we are successful in obtaining allowance of our biomarker based patient selection claims, we or our licensor may be unsuccessful in defending the validity of such claims if challenged before a competent court.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the America Invents Act, was signed into law. The America Invents Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO recently developed new regulations and procedures to govern administration of the American Invents Act, and many of the substantive changes to patent law associated with the America Invents Act and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents, all of which could harm our business and financial condition.

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

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would harm our business.

***We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have an adverse effect on the success of our business and on our stock price.***

Third parties may infringe our or our licensors' patents or misappropriate or otherwise violate our or our licensors' intellectual property rights. In the future, we or our licensors may initiate legal proceedings to enforce or defend our or our licensors' intellectual property rights, to protect our or our licensors' trade secrets or to determine the validity or scope of intellectual property rights we own or control. Also, third parties may initiate legal proceedings against us or our licensors to challenge the validity or scope of intellectual property rights we own or control. The proceedings can be expensive and time-consuming and many of our or our licensors' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensors can. Accordingly, despite our or our licensors' efforts, we or our licensors may not be able to prevent third parties from infringing upon or misappropriating intellectual property rights we own or control, particularly in countries where the laws may not protect our rights as fully as in the United States. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, in an infringement proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our or our licensors' patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our or our licensors' patents at risk of being invalidated, held unenforceable or interpreted narrowly.

Third-party preissuance submission of prior art to the USPTO, or opposition, derivation, reexamination, *inter partes* review or interference proceedings, or other preissuance or post-grant proceedings in the United States or other jurisdictions provoked by third parties or brought by us or our licensors or collaborators may be necessary to determine the priority of inventions with respect to our or our licensors' patents or patent applications. An unfavorable outcome could require us or our licensors to cease using the related technology and commercializing our product candidates, or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us or our licensors a license on commercially reasonable terms or at all. Even if we or our licensors obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors. In addition, if the breadth or strength of protection provided by our or our licensors' patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Even if we successfully defend such litigation or proceeding, we may incur substantial costs and it may distract our management and other employees. We could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this process. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a downward effect on the price of shares of our common stock.

***Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights or we may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, the outcome of which would be uncertain and could have an adverse effect on the success of our business.***

Third parties may initiate legal proceedings against us or our licensors or collaborators alleging that we or our licensors or collaborators infringe their intellectual property rights or we or our licensors or collaborators may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, including in oppositions, interferences, reexaminations, *inter partes* reviews or derivation proceedings before the United States or other jurisdictions. These proceedings can be expensive and time-consuming and many of our or our licensors' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensors or collaborators can.

An unfavorable outcome could require us or our licensors or collaborators to cease using the related technology or developing or commercializing our product candidates, or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us or our licensors or collaborators a license on commercially reasonable terms or at all. Even if we or our licensors or collaborators obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors or collaborators. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business.

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

Many of our employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, for some of our in-licensed patents and patent applications, we do not have access to every patent assignments or employee agreements demonstrating that all inventors have assigned their rights to the inventions or related patents. As a result, we may be subject to claims of ownership by such inventors.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management.

***Our inability to protect our confidential information and trade secrets would harm our business and competitive position.***

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, third-party manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing or unwilling to protect trade secrets. If a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

***Significant disruptions of our information technology systems or data security incidents could result in significant financial, legal, regulatory, business and reputational harm to us.***

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, store, process and transmit large amounts of sensitive information, including intellectual property, proprietary business information, personal information and other confidential information. It is critical that we do so in a secure manner to maintain the confidentiality, integrity and availability of such sensitive information. We have also outsourced elements of our operations (including elements of our information technology infrastructure) to third parties, and as a result, we manage a number of third-party vendors who may or could have access to our computer networks, our confidential information or the confidential information of third parties that is in our possession. In addition, those third party vendors may in turn subcontract or outsource some of their responsibilities to other parties. While all information technology operations are inherently vulnerable to inadvertent or intentional security breaches, incidents, attacks and exposures, the accessibility and distributed nature of our information technology systems, and the sensitive information stored on those systems, make such systems potentially vulnerable to unintentional or malicious, internal and external attacks on our technology environment. Potential vulnerabilities can be exploited from inadvertent or intentional actions of our employees, third-party vendors, business partners, or by malicious third parties. Attacks of this nature are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives (including, but not limited to, industrial espionage) and expertise, including organized criminal groups, “hacktivists,” nation states and others. In addition to the extraction of sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. The prevalent use of mobile devices further increases the risk of data security incidents.

Significant disruptions of our, our third-party vendors' and/or business partners' information technology systems or other similar data security incidents could adversely affect our business operations and/or result in the loss, misappropriation and/or unauthorized access, use or disclosure of, or the prevention of access to, sensitive information, which could result in financial, legal, regulatory, business and reputational harm to us. In addition, information technology system disruptions, whether from attacks on our technology environment or from computer viruses, natural disasters, terrorism, war and telecommunication and electrical failures, could result in a material disruption of our development programs and our business operations. 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.

There is no way of knowing with certainty whether we have experienced any data security incidents that have not been discovered. While we have no reason to believe this to be the case, attackers have become very sophisticated in the ways that they conceal access to systems. Many companies that have been attacked are not aware that they have been attacked. Any event that leads to unauthorized access, use or disclosure of personal information, including but not limited to personal information regarding employees or clinical trial patients, could disrupt our business, harm our reputation, compel us to comply with applicable federal and/or state breach notification laws and foreign law equivalents, subject us to time consuming, distracting and expensive litigation, regulatory investigation and oversight, mandatory corrective action, require us to verify the correctness of database contents, or otherwise subject us to liability under laws, regulations and contractual obligations, including those that protect the privacy and security of personal information. This could result in increased costs to us, and result in significant legal and financial exposure and/or reputational harm. Any failure or perceived failure by us or our vendors or business partners to comply with our privacy, confidentiality or data security-related legal or other obligations to third parties, or any further security incidents or other inappropriate access events resulting in the unauthorized access, release or transfer of sensitive information, which could include personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation, or public statements against us by advocacy groups or others, and could cause third parties, including clinical sites, regulators or current and potential partners, to lose trust in us or we could be subject to claims by third parties that we have breached our privacy- or confidentiality-related obligations, which could materially and adversely affect our business and prospects. Moreover, data security incidents and other inappropriate access can be difficult to detect. Any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or security incidents.

## Risks Related to Ownership of Our Common Stock

***The market price of our stock may be volatile and you could lose all or part of your investment.***

The trading price of our common stock is highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors include:

- the success of competitive products or technologies;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated changes in our growth rate relative to our competitors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- results of trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to our product candidates or clinical development programs;

- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry, political and market conditions.

In addition, the stock market in general, and the Nasdaq Global Select Market and biopharmaceutical companies in particular, frequently experiences extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of such companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and negative impact on the market price of our common stock.

***We may sell additional equity or debt securities or enter into other arrangements to fund our operations, which may result in dilution to our stockholders and impose restrictions or limitations on our business.***

Until we can generate a sufficient amount of revenue from our products, if ever, we expect to finance future cash needs through public or private equity or debt offerings. In April 2017, we filed a shelf registration statement on Form S-3 (Registration No. 333-217172) that allows us to sell up to an aggregate of $200 million of our common stock, which includes up to $50.0 million designated in the prospectus supplement for an at-the-market offering program, or ATM program. As of December 31, 2018, $32.1 million of common stock remained available for sale under the at-the-market offering program. In the first quarter of 2019, through March 6, 2019, we sold 140,819 shares of common stock under the ATM program for net proceeds of approximately $0.9 million. As of March 6, 2019, we have $31.2 million of common stock available for sale under the ATM program. We may also seek additional funding through government or other third-party funding and other collaborations, strategic alliances and licensing arrangements. These financing activities may have an adverse impact on our stockholders' rights as well as on our operations, and such additional funding may not be available on reasonable terms, if at all. If we raise additional funds through the issuance of additional debt or equity securities, it may result in dilution to our existing stockholders and/or increased fixed payment obligations. Furthermore, these securities may have rights senior to those of our common stock and could contain covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, if we seek funds through arrangements with collaborative partners, these arrangements may require us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us. Any of these events could significantly harm our business, financial condition and prospects.

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

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If no or few securities or industry analysts continue coverage of us, the trading price for our stock could be negatively impacted. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our trials or operating results fail to meet the expectations of analysts, our stock price could decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

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

As of December 31, 2018, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially own approximately 60.8% of our outstanding voting stock and options. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

***We are an "emerging growth company" as defined in the JOBS Act and may avail ourselves of reduced disclosure requirements applicable to emerging growth companies, which could make our common stock less attractive to investors and adversely affect the market price of our common stock.***

For so long as we remain an "emerging growth company" as defined in the JOBS Act, we may take advantage of certain exemptions from various requirements applicable to public companies that are not "emerging growth companies" including:

- the provisions of Section 404(b) of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, requiring that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting;
- the "say on pay" provisions (requiring a non-binding stockholder vote to approve compensation of certain executive officers) and the "say on golden parachute" provisions (requiring a non-binding stockholder vote to approve golden parachute arrangements for certain executive officers in connection with mergers and certain other business combinations) of the Dodd-Frank Act and some of the disclosure requirements of the Dodd-Frank Act relating to compensation of our chief executive officer;
- the requirement to provide detailed compensation discussion and analysis in proxy statements and reports filed under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and instead provide a reduced level of disclosure concerning executive compensation; and
- any rules that the Public Company Accounting Oversight Board may adopt requiring mandatory audit firm rotation or a supplement to the auditor's report on the financial statements.

We may take advantage of these exemptions until we are no longer an "emerging growth company." We would cease to be an "emerging growth company" upon the earliest of: (i) the first fiscal year following the fifth anniversary of our IPO; (ii) the first fiscal year after our annual gross revenues are $1.07 billion or more; (iii) the date on which we have, during the previous three-year period, issued more than $1.0 billion in non-convertible debt securities; or (iv) as of the end of any fiscal year in which the market value of our common stock held by non-affiliates exceeded $700 million as of the end of the second quarter of that fiscal year.

We currently take advantage of some, but not all, of the reduced regulatory and reporting requirements that are available to us so long as we qualify as an "emerging growth company." For example, we have irrevocably elected not to take advantage of the extension of time to comply with new or revised financial accounting standards available under Section 102(b) of the JOBS Act. Our independent registered public accounting firm is not be required to provide an attestation report on the effectiveness of our internal control over financial reporting so long as we qualify as an "emerging growth company," which may increase the risk that material weaknesses or significant deficiencies in our internal control over financial reporting go undetected. Likewise, so long as we qualify as an "emerging growth company," we may elect not to provide you with certain information, including certain financial information and certain information regarding compensation of our executive officers, that we would otherwise have been required to provide in filings we make with the Securities and Exchange Commission, or SEC, which may make it more difficult for investors and securities analysts to evaluate our company. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile and may decline.

***We will continue to incur significant costs as a result of operating as a public company, and our management will devote substantial time to compliance initiatives.***

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company, and these expenses may increase even more after we are no longer an "emerging growth company." We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and the Nasdaq Global Select Market.

***Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.***

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 shares, could reduce the market price of our common stock.

Some of the holders of our securities have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act except for shares held by our affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

***We may be subject to securities litigation, which is expensive and could divert management attention.***

The market price of our common stock may be volatile, and in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

***If we fail to maintain an effective system of internal control over financial reporting in the future, we may not be able to accurately report our financial condition, results of operations or cash flows, which may adversely affect investor confidence in us and, as a result, the value of our common stock.***

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. Commencing after the filing of our initial annual report on Form 10-K, we will be required, under Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. Section 404 of the Sarbanes-Oxley Act also generally requires an attestation from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. However, for as long as we remain an emerging growth company as defined in the JOBS Act, we intend to take advantage of the exemption permitting us not to comply with the independent registered public accounting firm attestation requirement. Our compliance with Section 404 will require that we incur substantial expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge, and compile the system and process documentation necessary to perform the evaluation needed to comply with Section 404. We may not be able to complete our evaluation, testing and any required remediation in a timely fashion. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control

over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begin its Section 404 reviews, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the Nasdaq Global Select Market, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

***Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would benefit our stockholders and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, or remove our current management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, who are responsible for appointing the members of our management. Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. Under the DGCL, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other things, the board of directors has approved the transaction. Any provision of our amended and restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change of control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

## Item 1B. Unresolved Staff Comments

None.

## Item 2. Properties

Our headquarters is currently located in Waltham, Massachusetts, and consists of 12,207 square feet of leased office space under a lease that expires on March 1, 2022. We also have 4,039 square feet of leased office space in New York, New York, under a lease that expires on February 28, 2021. We believe that our existing facilities are sufficient for our needs for the foreseeable future. If we determine that additional or new facilities are needed in the future, we believe that sufficient options would be available to us on commercially reasonable terms.

## Item 3. Legal Proceedings

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

## Item 4. Mine Safety Disclosures

Not applicable.

## PART II

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

#### Market Information

Our common stock began trading on the Nasdaq Global Select Market on March 2, 2016, under the symbol "SNDX." Prior to that time, there was no public market for our common stock.

#### Holders of Record

As of March 6, 2019, we had approximately 26 holders of record of our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

#### Dividend Policy

We have never declared or paid any cash dividends on our common stock. We currently intend to retain future earnings to fund the development and growth of our business. We do not expect to pay any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial conditions, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

#### Use of Proceeds

In March 2016, we completed our initial public offering, or IPO, pursuant to a registration statement on Form S-1 (File No. 333-208861), which the SEC declared effective on March 2, 2016. In our IPO, we issued and sold 4,809,475 shares of common stock (inclusive of 409,475 shares of common stock sold by us pursuant to the partial exercise of an overallotment option granted to the underwriters in connection with the offering) at a public offering price of $12.00 per share. The aggregate net proceeds received by us from our IPO were $50.5 million, net of underwriting discounts and commissions and offering expenses payable by us. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10% or more of any class of our equity securities or to any other affiliates. The managing underwriters for our IPO were Morgan Stanley & Co. LLC, Citigroup Global Markets Inc., JPM Securities LLC, and Oppenheimer & Co. Inc.

There has been no material change in the use of proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on March 2, 2016. As of December 31, 2018, we have used all of the proceeds from the IPO.

**Item 6. Selected Financial Data**

*The following table sets forth our selected consolidated financial data. We derived the consolidated statement of operations data for the years ended December 31, 2018, 2017, and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017, from our audited consolidated financial statements, included elsewhere in this Annual Report on Form 10-K. The following selected consolidated statements of operations data for the years ended December 31, 2015 and 2014 and the selected consolidated balance sheet data as of December 31, 2016, 2015 and 2014 are derived from our audited consolidated financial statements not included in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of results to be expected for any period in the future. The selected consolidated financial data presented below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes thereto, included elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data in this section is not intended to replace our consolidated financial statements and the related notes thereto.*

**Consolidated Statement of Operations Data:**

| | Years Ended December 31, | | | | |
|---|---|---|---|---|---|
| *(In thousands, except share and per share data)* | 2018 | 2017 | 2016 | 2015 | 2014 |
| Revenue | $ 1,517 | $ 2,108 | $ 1,220 | $ 627 | $ — |
| Operating expenses: | | | | | |
| Research and development | 60,106 | 48,201 | 31,665 | 9,549 | 10,175 |
| General and administrative | 17,287 | 15,861 | 13,321 | 11,591 | 11,157 |
| Total operating expenses | 77,393 | 64,062 | 44,986 | 21,140 | 21,332 |
| Loss from operations | (75,876) | (61,954) | (43,766) | (20,513) | (21,332) |
| Interest income (expense) | 1,942 | 1,421 | 956 | (1,414) | (289) |
| Other expense | (27) | (269) | (1,662) | (2,192) | 1,793 |
| Net loss | $ (73,961) | $ (60,802) | $ (44,472) | $ (24,119) | $ (19,828) |
| Net loss attributable to common stockholders (1) | $ (73,961) | $ (60,802) | $ (47,070) | $ (103,845) | $ (26,357) |
| Net loss per share attributable to common stockholders--basic and diluted (1) | $ (2.92) | $ (2.90) | $ (3.22) | $ (1,519.27) | $ (453.02) |
| Weighted-average common shares outstanding--basic and diluted (1) | 25,371,511 | 20,997,211 | 14,619,716 | 68,352 | 58,181 |

**Consolidated Balance Sheet Data:**

| | December 31, | | | | |
|---|---|---|---|---|---|
| *(In thousands)* | 2018 | 2017 | 2016 | 2015 | 2014 |
| Cash, cash equivalents, short-term and long-term investments | $ 80,911 | $ 133,220 | $ 105,330 | $ 86,489 | $ 12,901 |
| Working capital (2) | 67,241 | 117,644 | 98,144 | 83,160 | 2,181 |
| Total assets (2) | 83,938 | 137,186 | 109,013 | 89,903 | 12,525 |
| Convertible preferred stock | — | — | — | 319,113 | 146,853 |
| Accumulated deficit (3) | (439,423) | (366,111) | (305,293) | (259,675) | (159,801) |
| Total stockholders' equity (deficit) | 53,047 | 104,319 | 84,139 | (252,415) | (152,569) |

(1) See Note 5 to our consolidated financial statements included elsewhere herein for an explanation of the method used to compute basic and diluted net loss and net loss per share and the weighted-average number of shares used in the computation of the per share amounts.

(2) Working capital and total assets for 2014 have been restated for the adoption of Accounting Standard Update 2015-03, *Interest-Imputation of Interest (Subtopic 835-30): Simplifying the Presentation of Debt Issuance Costs*. The impact of the adoption was an increase of $83,000 in working capital and a decrease of $291,000 in total assets.

(3) Accumulated deficit for 2018 includes the impact of the adoption of Accounting Standard Update 2014-09, *Revenue from Contracts with Customers (Topic 606)*. The impact on Accumulated deficit was an increase of $648,000.

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

*The following discussion and analysis should be read in conjunction with "Selected Financial Data" and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and analysis and other parts of this Annual Report on Form 10-K contain forward-looking statements based upon current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under "Risk Factors" and elsewhere in this Annual Report on Form 10-K. You should carefully read the "Risk Factors" section of this Annual Report on Form 10-K to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section entitled "Special Note Regarding Forward-Looking Statements."*

### Overview

We are a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies. We are developing our lead product candidate, entinostat, a once-weekly, oral, small molecule, Class I HDAC inhibitor, in combination with exemestane and several approved PD-1/PD-L1 antagonists. Our pipeline also includes SNDX-6352, a monoclonal antibody that blocks the colony stimulating factor 1, or CSF-1 receptor, as well as a portfolio of potent and selective inhibitors, including our lead candidate SNDX-5613, targeting the binding interaction of Menin with mixed lineage leukemia-rearranged, or MLLr, and acute myeloid leukemia, or AML, with a mutated nucleophosmin 1, or NPM1. We plan to continue to leverage the technical and business expertise of our management team and scientific collaborators to license, acquire and develop additional cancer therapies to expand our pipeline.

We have no products approved for commercial sale and have not generated any product revenues from product sales to date. We continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not and have never been profitable and have incurred losses in each period since our inception in 2005. For the years ended December 31, 2018, 2017, and 2016, we reported a net loss of $74.0 million, $60.8 million and $44.5 million, respectively. As of December 31, 2018, we had an accumulated deficit of $439.4 million, which included non-cash charges for stock-based compensation, preferred stock accretion and extinguishment charges. As of December 31, 2018, we had cash, cash equivalents and short-term investments of $80.9 million.

### Pipeline Updates

**Entinostat**

- We continue to anticipate the next interim overall survival (OS) analysis for E2112, our NCI-sponsored, ECOG-ACRIN led Phase 3 registration trial of entinostat plus exemestane in advanced hormone receptor positive, human epidermal growth factor receptor 2 negative (HR+, HER2-) breast cancer, in the second quarter of 2019. Additional interim analyses will be conducted by ECOG-ACRIN approximately every six months until either an OS benefit is observed, or the final target number of events occur. Any positive OS assessment would enable us to file for full regulatory approval. The E2112 trial design was informed by the Phase 2b ENCORE 301 trial, the results of which led to entinostat's Breakthrough Therapy designation in HR+, HER2- breast cancer, in which patients receiving the entinostat/exemestane combination demonstrated a statistically significant OS benefit.
- The Phase 2 portion of ENCORE 603, our randomized, double-blind, placebo-controlled trial of entinostat, our Class I selective HDAC inhibitor, in combination with Pfizer/Merck KGaA's PD-L1 inhibitor, *Bavencio*® (avelumab), in patients with heavily pretreated advanced epithelial ovarian cancer did not meet its primary endpoint of a statistically significant improvement in PFS for the combination regimen compared with *Bavencio* monotherapy. The Phase 2 trial randomized 126 patients to receive 10 mg/kg *Bavencio* every two weeks in combination with either 5 mg of entinostat (n=85) or placebo (n=41) once weekly.

- The Phase 2 portion of ENCORE 602, our randomized, double-blind, placebo-controlled trial of entinostat in combination with Genentech's PD-L1 inhibitor, *Tecentriq*® (atezolizumab), in patients with PD-1 naïve, previously treated triple negative breast cancer did not meet its primary endpoint of statistically significant improvement in PFS for the combination regimen versus *Tecentriq* monotherapy. The Phase 2 trial randomized 81 patients to receive 1200 mg *Tecentriq* every three weeks in combination with either 5 mg of entinostat (n=40) or placebo (n=41) once weekly.
- Data from the NSCLC and melanoma cohorts of the ENCORE 601 trial will each be featured during oral presentations at the American Association of Cancer Research (AACR) Meeting in March. This data will include our most recent insights into the potential mechanisms that allow entinostat to enhance the benefit of immune checkpoint therapy.
- Based on the activity observed to date, we have decided not to advance the ENCORE 601 cohort of patients with microsatellite stable colorectal cancer to the second stage of the trial.
- Due to strategic considerations, we have mutually agreed with Nektar Therapeutics to discontinue the clinical collaboration to evaluate the safety and efficacy of Nektar's NKTR-214, a CD122-biased agonist, in combination with entinostat.

**SNDX-5613**

- Preclinical data supporting our Menin-Mixed Lineage Leukemia (MLL) inhibitor program were presented during an oral session at the 60th American Society of Hematology (ASH) Annual Meeting in December 2018.
- We continue to expect to complete pre-investigational new drug (IND) studies and submit the IND filing to the U.S. Food and Drug Administration for our Menin inhibitor, SNDX-5613, in the second quarter of 2019, with the initiation of a Phase 1 clinical trial in a defined subset of acute leukemias patients expected to follow.

**SNDX-6352**

- We continue to anticipate initial results from the Phase 1 dose escalation trial of SNDX-6352, our anti-CSF-1R monoclonal antibody, in patients with chronic graft versus host disease (cGVHD) in the second half of the year. The objectives of this trial are to evaluate the safety and preliminary efficacy of SNDX-6352 in cGVHD and to identify a recommended Phase 2 dose and schedule.
- We continue to anticipate identifying a recommended Phase 2 dose and schedule for SNDX-6352 monotherapy and in combination with *Imfinzi*® (durvalumab), AstraZeneca's human monoclonal antibody directed against PD-L1 in the second quarter of 2019. The dose selections will be based on the results of the ongoing Phase 1/1b ascending dose trial evaluating the safety of SNDX-6352 alone or in combination with *Imfinzi*.

**Financial Overview**

***Revenue***

To date, we have not generated any product revenues. Our ability to generate revenue and become profitable depends upon our ability to obtain marketing approval of and successfully commercialize our product candidates. Our revenues for the years ended December 31, 2018 and 2017 have been solely derived from our license agreement with Kyowa Hakko Kirin Co., Ltd., or KHK, under which we granted KHK an exclusive license to develop and commercialize entinostat in Japan and Korea, or the KHK license agreement. In 2015, we received a $25.0 million upfront payment from KHK, inclusive of an equity investment. We allocated $17.3 million of the upfront payment to the license fee, and such fee is being recognized as revenue ratably over our expected performance period (currently expected to be through 2029). The balance of the upfront payment of $7.7 million was allocated to KHK's purchase of shares of our convertible preferred stock.

In October 2017, KHK enrolled the first Japanese patient into a local pivotal study of entinostat for the treatment of hormone receptor positive, human epidermal growth factor receptor 2 negative breast cancer. In accordance with the terms of the KHK License Agreement, in December 2017 we received a $5.0 million milestone payment from KHK for achievement of the development milestone.

***Research and Development***

Since our inception, we have primarily focused on our clinical development programs. Research and development expenses consist primarily of costs incurred for the development of our product candidates and include:

- expenses incurred under agreements related to our clinical trials, including the costs for investigative sites and contract research organizations, or CROs, that conduct our clinical trials;
- employee-related expenses associated with our research and development activities, including salaries, benefits, travel and non-cash stock-based compensation expenses;
- manufacturing process-development, clinical supplies and technology-transfer expenses;
- license fees and milestone payments under our license agreements;
- consulting fees paid to third parties;
- allocated facilities and overhead expenses; and
- costs associated with regulatory operations and regulatory compliance requirements.

Internal and external research and development costs are expensed as they are incurred. Cost-sharing amounts received by us are recorded as reductions to research and development expense. Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or other information provided to us by our vendors.

Research and development activities are central to our business model. Drug candidates in late stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of late-stage clinical trials. We plan to increase our research and development expenses for the foreseeable future as we continue to advance the development of our product candidates. The amount of research and development expenses allocated to external spending will continue to grow, while we expect our internal spending to grow at a slower and more controlled pace. From inception through December 31, 2018, we have incurred $211.7 million in research and development expenses.

It is difficult to determine, with certainty, the duration and completion costs of our current or future preclinical programs, clinical studies and clinical trials of our product candidates. The duration, costs and timing of clinical studies and clinical trials of our product candidates will depend on a variety of factors that include, but are not limited to, the following:

- per patient costs;
- the number of patients that participate;
- the number of sites;
- the countries in which the studies and trials are conducted;
- the length of time required to enroll eligible patients;
- the potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient monitoring;
- the efficacy and safety profile of the product candidates; and
- timing and receipt of any regulatory approvals.

In addition, the probability of success for each drug product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability. The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of our product candidates for the period, if any, in which material net cash inflows from these potential product candidates may commence. Clinical development timelines, the probability of success and development costs can differ materially from expectations.

***General and Administrative***

General and administrative expenses consist primarily of employee-related expenses, including salaries, benefits, non-cash stock-based compensation and travel expenses, for our employees in executive, finance, business development and support functions. Other general and administrative expenses include facility-related costs not otherwise allocated to research and development expenses and accounting, tax, legal and consulting services. We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our product candidates. Additionally, if and when we believe a regulatory approval of the first product candidate appears likely, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

***Interest Income (Expense), Net***

Interest income consists of interest income earned on our cash, cash equivalents, and short-term investment balances. Interest expense consists primarily of interest expense on capital leases.

***Recent Accounting Pronouncements***

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board, or FASB, or other standard setting bodies and adopted by us as of the specified effective date. Unless otherwise discussed in Note 3 to our audited consolidated financial statements included in this Annual Report on Form 10-K, we believe that the impact of recently issued standards that are not yet effective will not have a material impact on our financial position or results of operations upon adoption.

***Critical Accounting Policies and Use of Estimates***

Our management's discussion and analysis of financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities, revenues and expenses, and other financial information. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies.

While our significant accounting policies are more fully described in Note 3 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our consolidated financial statements and understanding and evaluating our reported financial results.

***Revenue from Contracts with Customers***

On January 1, 2018, we adopted Financial Accounting Standards Board Accounting Standards Codification Topic 606, Revenue from Contracts with Customers, or ASC 606 using the modified retrospective method applied to those contracts which were not completed as of January 1, 2018. The provisions of ASC 606 supersedes the revenue recognition requirements in Topic 605 "Revenue Recognition," and requires entities to recognize revenue when control of the promised goods or services is transferred to customers at an amount that reflects the consideration to which the entity expects to be entitled to in exchange for those goods or services. The adoption of ASC 606 requires us to provide expanded disclosures related to our contracts with customers but did not have a material impact on the Company's consolidated financial position, results of operations, equity or cash flows as of the adoption date or for the periods presented. See note 4 for additional information on the impact of ASC 606 on our consolidated financial statements.

For license fee revenues, we applied and may continue to apply significant judgment to our KHK Agreement. We evaluated whether our contractual obligations represented distinct performance obligations. Such evaluation required judgment since it was made from the customer's perspective. We determined that our performance obligations under the collaboration at contract inception were not distinct and represented a single performance obligation. The KHK agreement also includes variable consideration. We assess variable consideration at each reporting period as to whether it is not subject to significant future reversal and, therefore, should be included in the transaction price. For development milestones related to the KHK Agreement, the Company does not take a substantive role or control the research, development or commercialization of any products generated by KHK. Therefore, the Company is not able to reasonably estimate when, if at all, any development milestone payments may be payable to the Company. As such, the development milestone payments associated with the KHK Agreement involve a substantial degree of uncertainty and risk that they may never be received. Sales-based milestones and royalties will be recognized as royalty revenue in the period the related sale occurred.

***Accrued Research and Development Expenses***

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing contracts and vendor agreements, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to contract research organizations, or CROs, and investigative sites in connection with clinical studies and to vendors related to product manufacturing and development of clinical supplies.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows and expense recognition. Payments under some of these contracts depend on factors out of our control, such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period. To date, we have not experienced any significant adjustments to our estimates.

**Results of Operations**

***Comparison of the years ended December 31, 2018 and 2017:***

| *(in thousands)* | Years Ended December 31, 2018 | 2017 | Increase (Decrease) $ | % |
|---|---|---|---|---|
| Revenues: | | | | |
| License fees | $ 1,517 | $ 2,108 | $ (591) | (28)% |
| Total revenues | 1,517 | 2,108 | (591) | (28)% |
| Operating expenses: | | | | |
| Research and development | 60,106 | 48,201 | 11,905 | 25% |
| General and administrative | 17,287 | 15,861 | 1,426 | 9% |
| Total operating expenses | 77,393 | 64,062 | 13,331 | 21% |
| Loss from operations | (75,876) | (61,954) | 13,922 | 22% |
| Other income (expense): | | | | |
| Interest income (expense), net | 1,942 | 1,421 | 521 | 37% |
| Other (expense) income, net | (27) | (269) | 242 | 90% |
| Total other income (expense) | 1,915 | 1,152 | 763 | 66% |
| Net loss | $ (73,961) | $ (60,802) | $ 13,159 | 22% |

***License Fees***

For the year ended December 31, 2018, license fees decreased $0.6 million, or 28%, to $1.5 million compared to $2.1 million in the prior year. This decrease in license fees is primarily due to receipt of a $5.0 million milestone payment from KHK in 2017. We recognized $0.9 million in 2017 and $0.3 million in 2018 due to the ratable recognition over our expected performance period.

***Research and Development***

For the year ended December 31, 2018, our total research and development expenses increased $11.9 million, or 25%, to $60.1 million from $48.2 million for the prior year due to increases in clinical trial activities of $5.4 million, employee compensation expense of $4.4 million, legal and consultant expenses of $1.8 million, facility costs of $0.2 million and other expenses of $0.1 million. The increase in clinical trial activities was primarily due to increases in spending related to our CMC activities for SNDX-6352 of $7.9 million, activities related to our Menin program of $5.8 million, increased clinical activities for SNDX-6352 and the ENCORE studies, offset by decreases in spending to our clinical pharmacology trials and clinical activities for E2112. In 2017 we expensed a nonrefundable upfront payment of $5.0 million made to Allergan plc for the purchase of the Menin Assets. The increase in employee compensation of $4.4 million was due to increased salary expense of $3.7 million and increased bonus expense of $0.3 million due to increased headcount and non-cash charges related to stock-based compensation of $0.5 million, partially offset by reduced severance expenses of $0.1 million. The increase in legal and consulting expenses was primarily due to increased activities related to NDA preparation of $1.2 million, medical communication and patient advocacy of $0.5 million and other professional fees of $0.1 million. We expect our research and development expenses to fluctuate from quarter to quarter depending on the timing of clinical trial activities, clinical manufacturing and other development activities, however we anticipate the full year research and development expenses to decrease in 2019.

Research and development expenses consisted of the following:

| (in thousands) | Years Ended December 31, 2018 | 2017 | Increase (Decrease) $ | % |
|---|---|---|---|---|
| External research and development expenses | $ 44,545 | $ 37,398 | $ 7,147 | 19% |
| Internal research and development expenses | 15,561 | 10,803 | 4,758 | 44% |
| Total research and development expenses | $ 60,106 | $ 48,201 | $ 11,905 | 25% |

***General and Administrative***

For the year ended December 31, 2018, our total general and administrative expenses increased $1.4 million, or 9%, to $17.3 million, from $15.9 million for the prior year. The increase in general and administrative expenses was primarily due to increases in pre-commercialization work of $1.1 million and increases in employee compensation of $0.4 million. The increase in employee compensation of $0.4 million was due to increased headcount of $0.2 million and non-cash charges related to stock-based compensation of $0.2 million.

***Interest Income (Expense), Net***

For the year ended December 31, 2018, interest income (expense), net, increased $0.5 million from the prior year. This increase was primarily due to increased yield on our cash, cash equivalents and short-term and long-term investments, offset by a lower average cash and investment balance.

***Comparison of the years ended December 31, 2017 and 2016:***

| (in thousands) | Years Ended December 31, 2017 | 2016 | Increase (Decrease) $ | % |
|---|---|---|---|---|
| Revenues: | | | | |
| License fees | $ 2,108 | $ 1,220 | $ 888 | 73% |
| Total revenues | 2,108 | 1,220 | 888 | 73% |
| Operating expenses: | | | | |
| Research and development | 48,201 | 31,665 | 16,536 | 52% |
| General and administrative | 15,861 | 13,321 | 2,540 | 19% |
| Total operating expenses | 64,062 | 44,986 | 19,076 | 42% |
| Loss from operations | (61,954) | (43,766) | 18,188 | 42% |
| Other (expense) income: | | | | |
| Interest (expense) income, net | 1,421 | 956 | 465 | 49% |
| Change in fair value of common stock warrant liability | — | (1,703) | (1,703) | 100% |
| Other (expense) income, net | (269) | 41 | (310) | (756)% |
| Total other (expense) income | 1,152 | (706) | 1,858 | 263% |
| Net loss | $ (60,802) | $ (44,472) | $ 16,330 | 37% |

***License Fees***

For the year ended December 31, 2017, license fees increased $0.9 million, or 73%, to $2.1 million compared to $1.2 million in the prior year. In 2015, arrangement consideration of $17.3 million related to the KHK license agreement was allocated to the license unit of accounting and is being recognized as revenue ratably over our expected service period (currently expected to be through 2029), commencing on the date of the first delivery of the clinical trial materials, which occurred in June 2015. In October 2017, KHK enrolled the first Japanese patient into a local pivotal study of entinostat for the treatment of hormone receptor positive, human epidermal growth factor receptor 2 negative breast cancer. In accordance with the terms of the KHK License Agreement, in December 2017 we received a $5.0 million milestone payment from KHK for achievement of the development milestone. We determined that the milestone is not substantive as the achievement was dependent upon the counterparty. Therefore, during the fourth quarter of 2017, we recorded $0.9 million as license fee revenue and have deferred the remaining $4.1 million to be recognized over the remaining performance period coinciding with the license unit of accounting.

***Research and Development***

For the year ended December 31, 2017, our total research and development expenses increased $16.5 million, or 52%, to $48.2 million from $31.7 million for the prior year due to increases in clinical trial activities of $9.1 million, employee compensation expense of $3.6 million, legal and consultant expenses of $3.1 million, facility costs of $0.3 million and travel costs of $0.4 million. The increase in clinical trial activities was primarily due to increases in spending related to our Phase 1 clinical pharmacology trials, increased enrollment in ENCORE 601, costs related to SNDX-6352 trials, increased activities in ENCORE 602 and ENCORE 603, and CMC activities. In 2017 we expensed a nonrefundable upfront payment of $5.0 million to Allergan plc for the Menin Assets and in 2016 we expensed a nonrefundable upfront payment of $5.0 million related to the UCB License Agreement. The increase in employee compensation costs was primarily due to increased headcount. We expect our research and development expenses for the foreseeable future to increase as we continue to advance the development of our product candidates.

Research and development expenses consisted of the following:

| | Years Ended December 31, | | Increase (Decrease) | |
|---|---|---|---|---|
| *(in thousands)* | 2017 | 2016 | $ | % |
| External research and development expenses | $ 37,398 | $ 25,236 | $ 12,162 | 48% |
| Internal research and development expenses | 10,803 | 6,429 | 4,374 | 68% |
| Total research and development expenses | $ 48,201 | $ 31,665 | $ 16,536 | 52% |

***General and Administrative***

For the year ended December 31, 2017, our total general and administrative expenses increased $2.5 million, or 19%, to $15.9 million, from $13.3 million for the prior year. The increase in general and administrative expenses was primarily due to increases in employee compensation of $1.3 million, increases in pre-commercialization work of $0.7 million, professional fees of $0.5 million, directors' and officers' insurance and other costs related to being a public company of $0.2 million and facilities costs of $0.3 million. These increases were partially offset by decreases in legal expenses of $0.5 million primarily due to lower general and business development legal costs. The increase in employee compensation of $1.3 million was due to increased salary expense of $1.1 million due to increased headcount and non-cash charges related to stock-based compensation of $0.3 million offset in part by decrease in bonus expense of $0.1 million.

***Interest Income (Expense), Net***

For the year ended December 31, 2017, interest income (expense), net, increased $0.5 million from the prior year. The increase was primarily due to increased yield on our cash, cash equivalents, short-term and long-term investments and increase in our cash, cash equivalents, short-term and long-term investment balances which increased as a result of the $48.7 million of net proceeds from our follow on offering in May 2017 and $24.9 million of net proceeds from our direct stock placement with BVF in October 2017.

***Change in Fair Value of Common Stock Warrant Liability***

The change in fair value of common stock warrant liability for the year ended December 31, 2017 decreased $1.7 million. There was no common stock warrant liability outstanding during the year ended December 31, 2017. At each period end until the closing of our IPO, the fair value of the outstanding common stock warrant liability was re-measured; and the change in the fair value was recorded in other expense in the condensed consolidated statement of comprehensive loss. Upon the closing of our IPO, the antidilution provision of the warrant expired and the warrant liability was reclassified to additional paid-in capital. Just prior to the reclassification, the warrant was re-measured using current assumptions on that date, and the change in fair value was recorded in other expense.

**Liquidity and Capital Resources**

As of December 31, 2018, we had cash, cash equivalents and short-term investments totaling $80.9 million. Since our inception, our operations have been primarily financed by net proceeds from our IPO, our follow-on stock offering, sale of convertible preferred stock and convertible debt securities and proceeds from our license agreements. We believe that our existing cash, cash equivalents and short-term investments will fund our projected operating expenses and capital expenditure requirements for at least the next 12 months. In addition to our existing cash, cash equivalents and short-term investments, we are eligible to receive research and development funding and to earn milestone and other contingent payments for the achievement of defined collaboration objectives and certain development, regulatory and commercial milestones and royalty payments under our collaboration agreements. Our ability to earn these milestone and contingent payments and the timing of achieving these milestones is primarily dependent upon the outcome of our collaborators' research and development activities and is uncertain at this time.

In March 2016, we completed our IPO whereby we sold 4,809,475 shares of our common stock at the price of $12.00 per share, resulting in total net proceeds of $50.5 million, after deducting underwriting discounts and commissions and offering expenses.

In April 2017, we entered into a sales agreement with Cowen under which we may issue and sell shares of our common stock having aggregate sales proceeds of up to $50.0 million from time to time pursuant to the ATM Program. Cowen is not required to sell any specific amount but acts as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. Shares sold pursuant to the sales agreement will be sold pursuant to a shelf registration statement on Form S-3 (Registration No. 333-217172), which was declared effective on April 20, 2017. Our common stock will be sold at prevailing market prices at the time of the sale; and as a result, prices may vary. We will pay Cowen up to 3% of the gross proceeds from any common stock sold through the sales agreement. The proceeds from the offerings, if any, will be used for general corporate purposes, including expenditures for research and development of the Company's drug products. During the year ended December 31, 2018, the Company sold 2,114,169 shares of common stock, with net proceeds of $15.5 million. As of December 31, 2018, $32.1 million of common stock remained available for sale under the ATM program. In the first quarter of 2019, up to March 6, 2019, we have sold an additional 140,819 shares of our common stock with net proceeds of approximately $0.9 million. As of March 6, 2019, we have $31.2 million of common stock available for sale under the ATM program.

In May 2017, we completed a follow-on public offering whereby we sold 3,950,190 shares of our common stock at a price of $13.25 per share, resulting in total net proceeds of $48.7 million, net of underwriting discounts and commissions and estimated offering expenses.

In October 2017, we issued to BVF 2,021,018 shares of our common stock at a price of $12.37 per share. Net proceeds after deducting expenses were approximately $24.9 million.

***Future Funding Requirements***

Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research and development services, clinical costs, legal and other regulatory expenses and general overhead costs. We have based our estimates on assumptions that may prove to be incorrect, and we could use our capital resources sooner than we currently expect.

Additionally, the process of testing drug candidates in clinical trials is costly, and the timing of progress in these trials is uncertain. We cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or whether, or when, we may achieve profitability. Our future capital requirements will depend on many factors, including:

- the initiation, progress, timing, costs and results of clinical trials of our product candidates;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more trials than we currently expect;
- the cost to establish, maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights;
- market acceptance of our product candidates;
- the cost and timing of selecting, auditing and developing manufacturing capabilities, and potentially validating manufacturing sites for commercial-scale manufacturing;
- the cost and timing for obtaining pricing and reimbursement, which may require additional trials to address pharmacoeconomic benefit;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates if either candidate receives regulatory approval and we determine to commercialize it ourselves;
- the costs of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- the effect of competing technological and market developments; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems, as we grow our company.

We have no products approved for commercial sale and have not generated any product revenues from product sales to date. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and additional funding from license and collaboration arrangements. Except for any obligations of our collaborators to reimburse us for research and development expenses or to make milestone or royalty payments under our agreements with them, we will not have any committed external source of liquidity.

We have incurred losses and cumulative negative cash flows from operations since our inception. As of December 31, 2018, we had an accumulated deficit of $439.4 million. We anticipate that we will continue to incur significant losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase. As a result, we will need additional capital to fund our operations, which we may raise through a combination of the sale of equity, debt financings, or other sources, including potential collaborations. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or drug candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

***Cash Flows***

The following is a summary of cash flows:

| *(in thousands)* | Years Ended December 31, 2018 | 2017 | 2016 |
|---|---|---|---|
| Net cash used in operating activities | $ (68,531) | $ (47,371) | $ (35,157) |
| Net cash provided by (used in) investing activities | 51,398 | (17,072) | (18,283) |
| Net cash provided by financing activities | 15,729 | 75,722 | 54,202 |
| Net (decrease) increase in cash and cash equivalents | $ (1,404) | $ 11,279 | $ 762 |

***Net Cash Used in Operating Activities***

Net cash used in operating activities for the year ended December 31, 2018 was $68.5 million and primarily consisted of our net loss of $74.0 million adjusted for non-cash items including stock-based compensation of $6.2 million and a net decrease in operating assets and liabilities of $0.3 million. The significant items in the decrease in operating assets and liabilities include an increase in prepaid expenses and other assets of $1.0 million and a decrease in deferred revenue of $1.5 million partially offset by a decrease in accounts payable of $0.8 million and an increase in accrued expenses and other liabilities of $1.0 million.

Net cash used in operating activities for the year ended December 31, 2017 was $47.4 million and primarily consisted of our net loss of $60.8 million adjusted for non-cash items, including stock-based compensation of $5.5 million and a net increase in operating assets and liabilities of $7.7 million. The significant items in the increase in operating assets and liabilities include increases in accrued expenses and other liabilities of $5.3 and increase in deferred revenue of $2.9 million partially offset by an increase in prepaid expenses and other assets of $0.3 million and a decrease in account payable of $0.2 million.

Net cash used in operating activities for the year ended December 31, 2016 was $35.2 million and primarily consisted of our net loss of $38.1 million adjusted for non-cash items including stock-based compensation of $4.7 million and the change in fair value of warrants of $1.7 million and a net increase in operating assets and liabilities of $2.9 million. The significant items in the increase in operating assets and liabilities include an increase in prepaid expenses and other assets of $1.6 million and a decrease in deferred revenue of $1.2 million partially offset by increases in accounts payable of $0.9 million and accrued expenses and other liabilities of $4.8 million

***Net Cash Provided by (Used in) Investing Activities***

Net cash provided by investing activities for the year ended December 31, 2018 was $51.4 million and primarily due to the purchases of available-for-sale marketable securities of $78.8 million and property and equipment of $0.2 million offset by proceeds from the maturities of available-for-sale marketable securities of $130.4 million.

Net cash used in investing activities for the year ended December 31, 2017 was $17.0 million and was primarily due to the purchase of $152.3 million of available-for-sale marketable securities partially offset by $135.3 million in proceeds from the maturities of available-for-sale marketable securities and purchases of property and equipment of $0.1 million.

Net cash used in investing activities for the year ended December 31, 2016 was $18.4 million and was primarily due to the purchase of $158.3 million of available-for-sale marketable securities partially offset by $140.3 million in proceeds from the maturities of available-for-sale marketable securities, purchases of property and equipment of $0.3 million and an increase in restricted cash of $0.1 million.

***Net Cash Provided by Financing Activities***

Net cash provided by financing activities for the year ended December 31, 2018 was $15.7 million and was primarily due to the net proceeds from "at-the-market" offerings of $15.5 million and $0.2 million from stock option exercises and ESPP employee stock purchases.

Net cash provided by financing activities for the year ended December 31, 2017 was $75.7 million and was primarily due to the $48.7 million of net proceeds from our follow-on offering, $24.9 million in net proceeds from our direct stock placement with BVF, $1.7 million of net proceeds from our "at-the-market" offering and $0.4 million of proceeds from stock option exercises and ESPP employee stock purchases.

Net cash provided by financing activities for the year ended December 31, 2016 was $54.2 million and was primarily due to the $52.1 million of proceeds from our IPO, net of underwriting discounts and commissions of $4.0 million and other direct costs of $1.5 million, and $2.1 million of proceeds from stock option exercises.

***Contractual Obligations and Commitments***

The following table summarizes our significant contractual obligations as of December 31, 2018:

| *(in thousands)* | Total | Less than 1 Year | 1 to 3 Years | 3 to 5 Years | More than 5 Years |
|---|---|---|---|---|---|
| Operating leases for office space (1) | $ 1,604 | $ 566 | $ 979 | $ 59 | $ — |
| Operating lease for office equipment (2) | 7 | 3 | 4 | — | — |
| Capital lease for office equipment (3) | 13 | 4 | 8 | 1 | — |
| | $ 1,624 | $ 573 | $ 991 | $ 60 | $ — |

(1) In September 2016, we entered into a new five-year operating lease for office space in Waltham, Massachusetts, with a lease commencement date of March 1, 2017. We have the right to terminate the Waltham lease after three years as long as proper notice is given and a termination fee of $55,000 is paid on the lease termination date. The landlord also has the right to terminate the Waltham least after three years as long as proper notice is given. In December 2015, we entered into a 62-month building lease for office space in New York, New York, which commenced on January 1, 2016. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) In February 2016, we entered into a five-year non-cancelable operating lease for office equipment.

(3) In April 2018, we entered into a four-year non-cancelable lease for office equipment, which is accounted for as a capital lease. The leased asset is included in property, plant and equipment, at cost.

The contractual obligations table does not include any potential contingent payments upon the achievement by us of clinical, regulatory and commercial events, as applicable, or royalty payments we may be required to make under license or collaboration agreements we have entered into with various entities pursuant to which we have in-licensed certain intellectual property. See "Business—Collaborations," "Business—License Agreements" and "Business—In-Licensed Intellectual Property" for additional information. The table also excludes potential payments we may be required to make under manufacturing agreements as the timing of when these payments will actually be made is uncertain and the payments are contingent upon the initiation and completion of future activities.

**Net Operating Loss and Research and Development Tax Credit Carryforwards**

At December 31, 2018, we had federal and state tax net operating loss carryforwards of approximately $51.7 million and $27.9 million, respectively. The federal and state net operating loss carryforwards begin to expire at various dates starting in 2025. Any federal net operating loss incurred in 2018 and in future years may now be carried forward indefinitely pursuant to the Tax Cuts and Jobs Act of 2017. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. At December 31, 2018, we had available income tax credits of approximately $3.7 million, with $2.3 million attributable to Federal R&D Credits and $1.4 million attributable to state R&D Credits, which are available to reduce future income taxes, if any. These income tax credits begin to expire in 2021.

Utilization of the net operating losses and credits may be subject to a substantial annual limitation due to ownership change limitations provided by the Internal Revenue Code of 1986, as amended. The annual limitation may result in the expiration of our net operating losses and credits before we can use them. We have recorded a valuation allowance on all of our deferred tax assets, including our deferred tax assets related to our net operating loss and research and development tax credit carryforwards.

**Off-Balance Sheet Arrangements**

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

**Emerging Growth Company Status**

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- reduced disclosure about our executive compensation arrangements;
- no non-binding stockholder advisory votes on executive compensation or golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We have taken advantage of reduced reporting burdens in this Annual Report on Form 10-K. In particular, in this Annual Report on Form 10-K, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1.07 billion in annual revenues as of the end of any fiscal year, if we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC, or if we issue more than $1.0 billion of non- convertible debt over a three-year period. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

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

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of December 31, 2018, we had cash and cash equivalents of $33.8 million, consisting of overnight investments, interest-bearing money market funds and highly rated corporate bonds and short-term investments of $47.1 million, consisting of commercial paper and highly rated corporate bonds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our marketable securities without significantly increasing risk. We have established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity. Due to the short-term maturities of our cash equivalents and the low risk profile of our short-term investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents and short-term investments. We do not believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein.

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

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear in this Annual Report on Form 10-K beginning on page F-1.

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

None.

**Item 9A. Controls and Procedures**

**Management's Evaluation of our Disclosure Controls and Procedures**

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures. Based on that evaluation of our disclosure controls and procedures as of December 31, 2018, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act are 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 us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

**Management's Annual Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2018 based on the framework in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework). Based on the results of its evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2018.

**Attestation Report of the Registered Public Accounting Firm**

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

**Changes in Internal Control Over Financial Reporting**

There was no change in our internal control over financial reporting that occurred during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**Item 9B. Other Information**

None.

## PART III

### Item 10. Directors, Executive Officers, and Corporate Governance

The information required by this item is incorporated by reference to the information set forth in the sections titled “Information About Our Board of Directors,” “Executive Officers,” “The Board of Directors and Its Committees,” and “Section 16(a) Beneficial Ownership Reporting Compliance” in our 2019 Proxy Statement.

### Item 11. Executive Compensation

The information required by this item is incorporated by reference to the information set forth in the section titled “Executive Officer and Director Compensation” in our 2019 Proxy Statement.

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

The information required by this item is incorporated by reference to the information set forth in the section titled “Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters” in our 2019 Proxy Statement.

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

The information required by this item is incorporated by reference to the information set forth in the section titled “The Board of Directors and Its Committees – Board Independence” and “Certain Relationships and Related Party Transactions” in our 2019 Proxy Statement.

### Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to the information set forth in the section titled “Independent Registered Public Accounting Firm Fees” contained in Proposal 2 in our 2019 Proxy Statement.

## PART IV

**Item 15. Exhibits, Financial Statements and Schedules**

(a)(1) Financial Statements.

The response to this portion of Item 15 is set forth under Item 8 hereof.

(a)(2) Financial Statement Schedules.

All schedules have been omitted because they are not required or because the required information is given in the Consolidated Financial Statements or Notes thereto.

(a)(3) Exhibits.

| Exhibit No. | Description |
|---|---|
| 3.1 | Amended and Restated Certificate of Incorporation of the Company (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-37708), as filed with the SEC on March 8, 2016). |
| 3.2 | Amended and Restated Bylaws of the Company (incorporated herein by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-37708), as filed with the SEC on March 8, 2016). |
| 4.1 | Specimen Common Stock Certificate of the Company (incorporated herein by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1/A (File No. 333-208861), as filed with the SEC on February 20, 2016). |
| 4.2 | Form of Warrant to purchase Common Stock issued pursuant to the Warrant Agreement by and between the Company and Bayer Schering Pharma AG, dated as of March 26, 2007 (incorporated herein by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 4.3 | Form of Indenture, between the Registrant and one or more trustees to be named (incorporated herein by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-3 (File No. 333-217172), as filed with the SEC on April 6, 2017). |
| 4.4 | Form of Common Stock Warrant Agreement and Warrant Certificate (incorporated herein by reference to Exhibit 4.7 to the Company's Registration Statement on Form S-3 (File No. 333-217172), as filed with the SEC on April 6, 2017). |
| 4.5 | Form of Debt Securities Warrant Agreement and Warrant Certificate (incorporated herein by reference to Exhibit 4.9 to the Company's Registration Statement on Form S-3 (File No. 333-217172), as filed with the SEC on April 6, 2017). |
| 4.6 | Form of Preferred Stock Warrant Agreement and Warrant Certificate (incorporated herein by reference to Exhibit 4.8 to the Company's Registration Statement on Form S-3 (File No. 333-217172), as filed with the SEC on April 6, 2017). |
| 10.1 | Warrant Agreement by and between the company and Bayer Schering Pharma AG, dated as of March 26, 2007 (incorporated herein by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.2* | 2007 Stock Plan (incorporated herein by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.3* | 2007 Stock Plan Amendment, dated as of March 8, 2013 (incorporated herein by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |

| Exhibit No. | Description |
|---|---|
| 10.4* | 2007 Stock Plan Amendment, dated as of July 10, 2013 (incorporated herein by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.5* | 2007 Stock Plan Amendment, dated as of January 23, 2014 (incorporated herein by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.6* | 2007 Stock Plan Amendment, dated as of December 17, 2014 (incorporated herein by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.7* | 2007 Stock Plan Amendment, dated as of May 28, 2015 (incorporated herein by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.8* | 2007 Stock Plan Amendment, dated as of August 20, 2015 (incorporated herein by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.9* | Form of Incentive Stock Option Agreement under 2007 Stock Plan (incorporated herein by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.10* | Form of Non-Statutory Stock Option Agreement under 2007 Stock Plan (incorporated herein by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.11* | 2015 Omnibus Incentive Plan (incorporated herein by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-8 (File No. 333-210412), as filed with the SEC on March 25, 2016). |
| 10.12* | Form of Incentive Stock Option Agreement under 2015 Omnibus Incentive Plan (incorporated herein by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.13* | Form of Non-Qualified Option Agreement under 2015 Omnibus Incentive Plan (incorporated herein by reference to Exhibit 10.14 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.14* | 2015 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 4.16 to the Company's Registration Statement on Form S-8 (File No. 333-210412), as filed with the SEC on March 25, 2016). |
| 10.15* | Executive Employment Agreement by and between the company and Briggs W. Morrison, M.D., dated as of September 30, 2015 (incorporated herein by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.16* | Executive Employment Agreement by and between the company and Michael A. Metzger, dated as of September 30, 2015 (incorporated herein by reference to Exhibit 10.17 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.17* | Executive Employment Agreement by and between the Company and Michael L. Meyers, M.D., Ph.D., dated as of October 1, 2015 (incorporated herein by reference to Exhibit 10.18 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.18* | Executive Employment Agreement by and between the Company and Richard P. Shea, dated as of February 9, 2017 (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on August 10, 2017). |

| Exhibit No. | Description |
|---|---|
| 10.19* | Form of Indemnification Agreement by and between the company and each of its directors and officers (incorporated herein by reference to Exhibit 10.21 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.20† | License, Development and Commercialization Agreement by and between the company and Bayer Schering Pharma AG, dated as of March 26, 2007 (incorporated herein by reference to Exhibit 10.22 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.21† | First Amendment to the License, Development and Commercialization Agreement by and between the company and Bayer Pharma AG, dated as of October 13, 2012 (incorporated herein by reference to Exhibit 10.23 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.22 | Second Amendment to the License, Development and Commercialization Agreement by and between the company and Bayer Pharma AG, dated as of February 1, 2013 (incorporated herein by reference to Exhibit 10.24 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.23† | Third Amendment to the License, Development and Commercialization Agreement by and between the company and Bayer Pharma AG, dated as of October 9, 2013 (incorporated herein by reference to Exhibit 10.25 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.24† | Letter Agreement by and between the company and Bayer Pharma AG, dated as of September 18, 2014 (incorporated herein by reference to Exhibit 10.26 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.25† | Clinical Trial Agreement by and between the company and Eastern Cooperative Oncology Group, dated as of March 14, 2014 (incorporated herein by reference to Exhibit 10.27 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.26† | Amendment No. 1 to Clinical Trial Agreement by and between the company and ECOG-ACRIN Cancer Research Group, dated as of January 30, 2015 (incorporated herein by reference to Exhibit 10.28 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.27† | Amendment No. 2 to Clinical Trial Agreement by and between the company and ECOG-ACRIN Cancer Research Group, dated as of July 31, 2015 (incorporated herein by reference to Exhibit 10.37 to the Company's Registration Statement on Form S-1/A (File No. 333-208861), as filed with the SEC on February 22, 2016). |
| 10.28† | Amendment No. 3 to Clinical Trial Agreement by and between the Company and ECOG-ACRIN Cancer Research Group, dated as of April 20, 2016 (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on August 15, 2016). |
| 10.29† | Amendment No. 4 to Clinical Trial Agreement by and between the Company and ECOG-ACRIN Cancer Research Group, dated as of April 20, 2016 (incorporated herein by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on August 15, 2016). |
| 10.30† | Amendment No. 5 to Clinical Trial Agreement by and between the Company and ECOG-ACRIN Cancer Research Group, dated as of April 20, 2016 (incorporated herein by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on August 15, 2016). |
| 10.31† | Amendment No. 6 to Clinical Trial Agreement by and between the Company and ECOG-ACRIN Cancer Research Group, dated as of April 25, 2016 (incorporated herein by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on August 15, 2016). |

| Exhibit No. | Description |
|---|---|
| 10.32† | Amendment No. 7 to Clinical Trial Agreement by and between the Company and ECOG-ACRIN Cancer Research Group, dated January 9, 2017 (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on May 9, 2017). |
| 10.33† | Amendment No. 8 to Clinical Trial Agreement by and between the Company and ECOG-ACRIN Cancer Research Group, dated January 18, 2017 (incorporated herein by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on May 9, 2017). |
| 10.34† | Amendment No. 9 to Clinical Trial Agreement by and between the Company and ECOG-ACRIN Cancer Research Group, dated November 22, 2017 (incorporated herein by reference to Exhibit 10.34 to the Company's Annual Report on Form 10-K, as filed with the SEC on March 8, 2018). |
| 10.35† | Amendment No. 10 to Clinical Trial Agreement by and between the Company and ECOG-ACRIN Cancer Research Group, dated October 15, 2018. |
| 10.36† | Clinical Trial Collaboration and Supply Agreement by and between the company and MSD International GmbH, dated as of March 27, 2015 (incorporated herein by reference to Exhibit 10.32 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.37† | First Amendment to Clinical Trial Collaboration and Supply Agreement by and between the company and MSD International GmbH, dated as of August 13, 2015 (incorporated herein by reference to Exhibit 10.38 to the Company's Registration Statement on Form S-1/A (File No. 333-208861), as filed with the SEC on February 22, 2016). |
| 10.38† | Amendment #1 to Clinical Trial Collaboration and Supply Agreement by and between the Company, Merck Sharp & Dohme B.V., and MSD International GmbH, dated as of April 26, 2017 (incorporated herein by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on August 10, 2017). |
| 10.39† | License, Development and Commercialization Agreement by and between the company and Kyowa Hakko Kirin Co., Ltd., dated December 19, 2014 (incorporated herein by reference to Exhibit 10.33 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.40† | Side Letter by and between the company and Kyowa Hakko Kirin Co., Ltd., dated December 19, 2014 (incorporated herein by reference to Exhibit 10.34 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.41† | Amendment #1 to License, Development and Commercialization Agreement by and between the company and Kyowa Hakko Kirin Co., Ltd., dated September 18, 2015 (incorporated herein by reference to Exhibit 10.39 to the Company's Registration Statement on Form S-1/A (File No. 333-208861), as filed with the SEC on February 22, 2016). |
| 10.42† | Amendment #2 to License, Development and Commercialization Agreement by and between the company and Kyowa Hakko Kirin Co., Ltd., dated January 16, 2017 (incorporated herein by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on May 9, 2017). |
| 10.43† | Combination Study Collaboration Agreement by and between the company and Genentech, Inc. dated August 24, 2015 (incorporated herein by reference to Exhibit 10.35 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.44† | Clinical Trial Collaboration and Supply Agreement by and between the company, Pfizer Inc. and Ares Trading S.A., dated as of December 31, 2015 (incorporated herein by reference to Exhibit 10.36 to the Company's Registration Statement on Form S-1/A (File No. 333-208861), as filed with the SEC on January 11, 2016). |

| Exhibit No. | Description |
|---|---|
| 10.45† | License Agreement by and between the Company and UCB Biopharma Sprl, dated as of July 1, 2016 (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001- 37708), as filed with the SEC on October 7, 2016). |
| 10.46† | Side Agreement by and between the Company and UCB Biopharma Sprl, dated March 8, 2017 (incorporated herein by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on May 9, 2017). |
| 10.47 | Third Amended and Restated Investors' Rights Agreement by and among the company and the parties thereto, dated as of August 21, 2015 (incorporated herein by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 10.48† | License Agreement by and between the Company and Vitae Pharmaceuticals, Inc., dated as of October 13, 2017 (incorporated herein by reference to Exhibit 10.47 to the Company's Annual Report on Form 10-K, as filed with the SEC on March 8, 2018). |
| 10.49 | Purchase Agreement by and among the Company, Biotechnology Value Fund, L.P. and certain entities affiliated with BVF, dated as of October 17, 2017 (incorporated herein by reference to Exhibit 10.1 to the Company's Periodic Report on Form 8-K, as filed with the SEC on October 20, 2017). |
| 21.1 | Subsidiaries of the Registrant (incorporated herein by reference to Exhibit 21.1 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016). |
| 23.1 | Consent of Independent Registered Public Accounting Firm |
| 24.1 | Power of Attorney (included on the signature page to this report). |
| 31.1 | Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934. |
| 31.2 | Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934. |
| 32.1+ | Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rule 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |
| 101.INS | XBRL Instance Document. |
| 101.SCH | XBRL Taxonomy Extension Schema Document. |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase Document. |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase Document |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document. |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase Document. |

* Indicates a management contract or compensatory plan.

\+ Furnished herewith and not deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act.

† Confidential treatment has been granted for certain portions of this exhibit. These portions have been omitted and filed separately with the SEC.

**Item 16. Form 10-K Summary**

Not applicable.

## SIGNATURES

Pursuant to the requirements of Section 13 of 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.

**SYNDAX PHARMACEUTICALS, INC.**

Date: March 7, 2019

By: /s/ Briggs W. Morrison, M.D.
Briggs W. Morrison, M.D.
*Chief Executive Officer*

## POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Briggs W. Morrison, M.D. and Luke J. Albrecht, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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/ Briggs W. Morrison, M.D.<br>Briggs W. Morrison, M.D. | Chief Executive Officer and Director<br>(Principal Executive Officer) | March 7, 2019 |
| /s/ Richard P. Shea<br>Richard P. Shea | Chief Financial Officer and Treasurer<br>(Principal Financial Officer and<br>Principal Accounting Officer) | March 7, 2019 |
| /s/ Dennis G. Podlesak<br>Dennis G. Podlesak | Chairman of the Board of Directors | March 7, 2019 |
| /s/ Pierre Legault<br>Pierre Legault | Director | March 7, 2019 |
| /s/ Fabrice Egros, PharmD, Ph.D.<br>Fabrice Egros, PharmD, Ph.D. | Director | March 7, 2019 |
| /s/ Keith A. Katkin<br>Keith A. Katkin | Director | March 7, 2019 |
| /s/ Jennifer Jarrett<br>Jennifer Jarrett | Director | March 7, 2019 |
| /s/ William Meury<br>William Meury | Director | March 7, 2019 |

**Syndax Pharmaceuticals, Inc.**

**Index to Consolidated Financial Statements**

**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders of Syndax Pharmaceuticals, Inc.

**Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of Syndax Pharmaceuticals, Inc. and its subsidiaries (the “Company”) as of December 31, 2018 and 2017, and the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders’ equity (deficit), and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.

**Basis for Opinion**

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the 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 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 financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 7, 2019

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

**SYNDAX PHARMACEUTICALS, INC.**

**CONSOLIDATED BALANCE SHEETS**

*(In thousands, except share and per share data)*

| | December 31, 2018 | December 31, 2017 |
|---|---|---|
| **ASSETS** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 33,769 | $ 35,168 |
| Restricted cash | 101 | 106 |
| Short-term investments | 47,142 | 94,806 |
| Prepaid expenses and other current assets | 2,334 | 3,362 |
| Total current assets | 83,346 | 133,442 |
| Long-term investments | — | 3,246 |
| Property and equipment, net | 373 | 267 |
| Other assets | 219 | 231 |
| Total assets | $ 83,938 | $ 137,186 |
| **LIABILITIES AND STOCKHOLDERS' EQUITY** | | |
| Current liabilities: | | |
| Accounts payable | $ 1,439 | $ 2,232 |
| Accrued expenses and other current liabilities | 13,149 | 11,993 |
| Current portion of deferred revenue | 1,517 | 1,573 |
| Total current liabilities | 16,105 | 15,798 |
| Long-term liabilities: | | |
| Deferred revenue, less current portion | 14,650 | 16,759 |
| Other long-term liabilities | 136 | 310 |
| Total long-term liabilities | 14,786 | 17,069 |
| Total liabilities | 30,891 | 32,867 |
| Commitments (Note 14) | | |
| Stockholders' equity: | | |
| Preferred stock, $0.001 par value, 10,000,000 shares authorized; 0 shares outstanding at December 31, 2018 and December 31, 2017, respectively | — | — |
| Common stock, $0.0001 par value, 100,000,000 shares authorized; 24,835,951 and 24,390,033 shares outstanding at December 31, 2018 and December 31, 2017, respectively | 2 | 2 |
| Additional paid-in capital | 492,493 | 470,571 |
| Accumulated other comprehensive loss | (25) | (143) |
| Accumulated deficit | (439,423) | (366,111) |
| Total stockholders' equity | 53,047 | 104,319 |
| Total liabilities and stockholders' equity | $ 83,938 | $ 137,186 |

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

**SYNDAX PHARMACEUTICALS, INC.**

**CONSOLIDATED STATEMENTS OF OPERATIONS**

*(In thousands, except share and per share data)*

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Revenues: | | | |
| License fees | $ 1,517 | $ 2,108 | $ 1,220 |
| Total revenues | 1,517 | 2,108 | 1,220 |
| Operating expenses: | | | |
| Research and development | 60,106 | 48,201 | 31,665 |
| General and administrative | 17,287 | 15,861 | 13,321 |
| Total operating expenses | 77,393 | 64,062 | 44,986 |
| Loss from operations | (75,876) | (61,954) | (43,766) |
| Other income (expense): | | | |
| Interest income (expense), net | 1,942 | 1,421 | 956 |
| Change in fair value of common stock warrant liability | — | — | (1,703) |
| Other (expense) income, net | (27) | (269) | 41 |
| Total other income (expense) | 1,915 | 1,152 | (706) |
| Net loss | $ (73,961) | $ (60,802) | $ (44,472) |
| Net loss attributable to common stockholders | $ (73,961) | $ (60,802) | $ (47,070) |
| Net loss per share attributable to common stockholders—basic and diluted | $ (2.92) | $ (2.90) | $ (3.22) |
| Weighted-average common shares outstanding—basic and diluted | 25,371,511 | 20,997,211 | 14,619,716 |

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

**SYNDAX PHARMACEUTICALS, INC.**

**CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**

*(In thousands)*

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Net loss | $ (73,961) | $ (60,802) | $ (44,472) |
| Other comprehensive loss: | | | |
| Unrealized (losses) gains on marketable securities, net of tax | 118 | (199) | 28 |
| Comprehensive loss | $ (73,843) | $ (61,001) | $ (44,444) |

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

**SYNDAX PHARMACEUTICALS, INC.**

**CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)**

*(In thousands, except share and per share data)*

| | Convertible Preferred Stock $0.001 Par Value | | Series A Convertible Preferred Stock $0.001 Par Value | | Common Stock $0.0001 Par Value | | Additional Paid-In | Accumulated Other Comprehensive | Accumulated | Total Stockholders' Equity |
|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | Shares | Amount | Capital | Income (Loss) | Deficit | (Deficit) |
| BALANCE--January 1, 2016 | 12,732,466 | 319,113 | 700,435 | 7,231 | 85,440 | 1 | — | 28 | (259,675) | (252,415) |
| Accretion for convertible preferred stock dividends | — | 2,598 | — | — | — | — | (1,452) | — | (1,146) | (2,598) |
| Proceeds from initial public offering, net of offering costs of $7,186 | — | — | — | — | 4,809,475 | — | 50,527 | — | — | 50,527 |
| Conversion of preferred stock into common stock | (12,732,466) | (321,711) | (700,435) | (7,231) | 12,872,551 | 1 | 328,941 | — | — | 321,711 |
| Reclassification of common stock warrant liability | — | — | — | — | — | — | 4,551 | — | — | 4,551 |
| Exercise of stock options | — | — | — | — | 441,573 | — | 2,058 | — | — | 2,058 |
| Vesting of restricted stock | — | — | — | — | 6,142 | — | 42 | — | — | 42 |
| Stock-based compensation expense | — | — | — | — | — | — | 4,708 | — | — | 4,708 |
| Unrealized gain on short-term investments | — | — | — | — | — | — | — | 28 | — | 28 |
| Repurchase of fractional shares resulting from reverse stock splits | — | — | — | — | — | — | (1) | — | — | (1) |
| Net loss | — | — | — | — | — | — | — | — | (44,472) | (44,472) |
| Balance—December 31, 2016 | — | $ — | — | $ — | 18,215,181 | $ 2 | $ 389,374 | $ 56 | $ (305,293) | $ 84,139 |
| Proceeds from follow on offering, net of offering cost of $3,665 | — | — | — | — | 3,950,190 | — | 48,675 | — | — | 48,675 |
| Proceeds from exercise of stock options | — | — | — | — | 46,680 | — | 277 | — | — | 277 |
| Vesting of restricted stock | — | — | — | — | 8,543 | — | 59 | — | — | 59 |
| Stock-based compensation expense | — | — | — | — | — | — | 5,450 | — | — | 5,450 |
| Proceeds from "At-the-market" offering, net | — | — | — | — | 148,421 | — | 1,705 | — | — | 1,705 |
| Unrealized losses on short-term investments | — | — | — | — | — | — | — | (199) | — | (199) |
| Employee withholdings ESPP | — | — | — | — | — | — | 97 | — | — | 97 |
| Cumulative effect adjustment of adoption ASU 2016-09 | — | — | — | — | — | — | 16 | — | (16) | — |
| Proceeds from direct stock placement, net | — | — | — | — | 2,021,018 | — | 24,918 | — | — | 24,918 |
| Net loss | — | — | — | — | — | — | — | — | (60,802) | (60,802) |
| Balance—December 31, 2017 | — | $ — | — | $ — | 24,390,033 | $ 2 | $ 470,571 | $ (143) | $ (366,111) | $ 104,319 |
| Proceeds from "At-the-market" offering, net | — | — | — | — | 2,114,169 | — | 15,497 | — | — | 15,497 |
| Proceeds from exercise of stock options | — | — | — | — | 7,850 | — | 26 | — | — | 26 |
| Stock issuance due to warrant exercise, cashless | — | — | — | — | 299,215 | — | — | — | — | — |
| Stock purchase under ESPP | — | — | — | — | 24,684 | — | — | — | — | — |
| Stock-based compensation expense | — | — | — | — | — | — | 6,201 | — | — | 6,201 |
| Unrealized losses on short-term investments | — | — | — | — | — | — | — | 118 | — | 118 |
| Employee withholdings ESPP | — | — | — | — | — | — | 198 | — | — | 198 |
| Cumulative effect adjustment of adoption ASU 2014-09 | — | — | — | — | — | — | — | — | 649 | 649 |
| Retirement of common stock in exchange for common stock warrant | — | — | — | — | (2,000,000) | — | (16,780) | — | — | (16,780) |
| Issuance of common stock warrant in exchange for retirement of common stock | — | — | — | — | — | — | 16,780 | — | — | 16,780 |
| Net loss | — | — | — | — | — | — | — | — | (73,961) | (73,961) |
| Balance—December 31, 2018 | — | $ — | — | $ — | 24,835,951 | $ 2 | $ 492,493 | $ (25) | $ (439,423) | $ 53,047 |

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

**SYNDAX PHARMACEUTICALS, INC.**

**CONSOLIDATED STATEMENTS OF CASH FLOWS**

*(In thousands)*

| | Years Ended December 31, | | |
|---|---|---|---|
| | **2018** | **2017** | **2016** |
| **CASH FLOWS FROM OPERATING ACTIVITIES:** | | | |
| Net loss | $ (73,961) | $ (60,802) | $ (44,472) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Depreciation | 78 | 76 | 89 |
| Amortization and accretion of investments | (558) | 223 | (126) |
| Stock-based compensation | 6,201 | 5,450 | 4,708 |
| Change in fair value of warrants | — | — | 1,703 |
| Other | 11 | 8 | 25 |
| Changes in operating assets and liabilities: | | | |
| Prepaid expenses and other assets | 1,033 | (329) | (1,629) |
| Accounts payable | (792) | (194) | 923 |
| Deferred revenue | (1,517) | 2,892 | (1,220) |
| Accrued expenses and other liabilities | 974 | 5,305 | 4,842 |
| Net cash used in operating activities | (68,531) | (47,371) | (35,157) |
| **CASH FLOWS FROM INVESTING ACTIVITIES:** | | | |
| Purchases of property and equipment | (187) | (84) | (261) |
| Purchases of short-term investments | (78,844) | (152,263) | (158,319) |
| Proceeds from sales and maturities of short-term investments | 130,429 | 135,275 | 140,297 |
| Net cash provided by (used in) investing activities | 51,398 | (17,072) | (18,283) |
| **CASH FLOWS FROM FINANCING ACTIVITIES:** | | | |
| Proceeds from issuance of common stock in initial public offering, net | — | — | 52,148 |
| Proceeds from issuance of common stock in follow on public offering, net | — | 48,675 | — |
| Proceeds from issuance of common stock in at-the-market offering, net | 15,497 | 1,755 | — |
| Proceeds from issuance of common stock in direct placement offering, net | — | 24,918 | — |
| Proceeds from Employee Stock Purchase Plan | 198 | 97 | — |
| Proceeds from exercise of stock options | 26 | 277 | 2,058 |
| Other | 8 | — | (4) |
| Net cash provided by financing activities | 15,729 | 75,722 | 54,202 |
| NET (DECREASE) INCREASE IN CASH, CASH EQUIVALENTS AND RESTRICTED CASH | (1,404) | 11,279 | 762 |
| CASH, CASH EQUIVALENTS AND RESTRICTED CASH—beginning of year | 35,389 | 24,110 | 23,348 |
| CASH, CASH EQUIVALENTS AND RESTRICTED CASH—end of year | $ 33,985 | $ 35,389 | $ 24,110 |

Supplemental disclosures of cash flow information (Note 15).

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

**1. Nature of Business**

Syndax Pharmaceuticals, Inc. (the Company) is a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies. The Company is developing its lead product candidate, entinostat, a once-weekly, oral, small molecule, Class I HDAC inhibitor, in combination with exemestane and several approved PD-1/PD-L1 antagonists. The Company's pipeline also includes SNDX-6352, a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor, as well as SNDX-5613, a selective inhibitor targeting the binding interaction of Menin with the mixed lineage leukemia ("MLL") protein. The Company plans to continue to leverage the technical and business expertise of our management team and scientific collaborators to license, acquire and develop additional cancer therapies to expand our pipeline.

In March 2016, the Company completed its initial public offering ("IPO") whereby it sold 4,809,475 shares of common stock at the initial public offering price of $12.00 per share. The aggregate net proceeds received by the Company from the offering were $50.5 million, net of underwriting discounts and commissions and offering expenses.

In April 2017, the Company entered into a sales agreement with Cowen and Company, LLC ("Cowen") under which the Company may issue and sell shares of our common stock having aggregate sales proceeds of up to $50.0 million from time to time through Cowen, acting as agent, in a series of one or more at-the-market ("ATM program") equity offerings. Cowen is not required to sell any specific amount but acts as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. Shares sold pursuant to the sales agreement will be sold pursuant to a shelf registration statement, which became effective on April 20, 2017. Our common stock will be sold at prevailing market prices at the time of the sale; and as a result, prices may vary. We will pay Cowen up to 3% of the gross proceeds from any common stock sold through the sales agreement. Since inception of the ATM program in 2017, though March 6, 2019, the Company has sold 2,403,409 shares of common stock pursuant to the ATM program, at an average price of $7.82 per share for gross proceeds of $18.8 million, resulting in net proceeds of $18.2 million after deducting sales commissions and offering expenses. As of December 31, 2018, $32.1 million of common stock remained available for sale under the ATM program. In 2019, the Company sold 140,819 shares of common stock pursuant to the ATM program, with net proceeds of $0.9 million. As of March 6, 2019, $31.2 million of common stock remained available for sale under the ATM program.

In May 2017, the Company completed a follow-on public offering whereby the Company sold 3,950,190 shares of common stock at a price of $13.25 per share. The aggregate net proceeds received by the Company from the offering were approximately $48.7 million, net of underwriting discounts and commissions and estimated offering expenses payable by the Company.

On October 13, 2017, the Company entered into a license agreement with Vitae Pharmaceuticals, Inc., a subsidiary of Allergan plc ("Allergan"), under which Allergan granted to the Company a worldwide, sublicenseable, exclusive license to a portfolio of preclinical, orally-available, small molecule inhibitors of the interaction of Menin with the MLL protein (the "Menin Assets"). The Company made a nonrefundable upfront payment of $5.0 million to Allergan in the fourth quarter of 2017. The Company is developing the Menin Assets to potentially treat two genetically defined acute leukemias: (i) a genetically-defined subset of acute leukemias with chromosomal rearrangements in the MLL gene ("MLL-r") and (ii) acute myeloid leukemia ("AML") with a mutated nucleophosmin 1 ("NPM1").

On October 17, 2017, the Company entered into a purchase agreement with Biotech Value Fund, L.P. ("BVF") and certain entities affiliated with BVF (the "Purchase Agreement"). Pursuant to the Purchase Agreement, the Company issued directly to BVF in a registered direct offering (the "Offering"), 2,021,018 shares of the Company's common stock at a price of $12.37 per share, representing the closing price of the Company's shares on the Nasdaq Global Select Market on Friday, October 13, 2017. The net proceeds from the Offering, after deducting estimated expenses, were $24.9 million.

Since its inception, the Company has devoted its efforts principally to research and development and raising capital. The Company is subject to risks common to companies in the development stage, including, but not limited to, successful development of therapeutics, obtaining additional funding, protection of proprietary therapeutics, compliance with government regulations, fluctuations in operating results, dependence on key personnel and collaborative partners, and risks associated with industry changes. The Company's long-term success is dependent upon its ability to successfully develop and market its product candidates, expand its oncology drug pipeline, earn revenue, obtain additional capital when needed, and ultimately, achieve profitable operations. The Company anticipates that it will be several years before any of its product candidates is approved, if ever, and the Company begins to generate revenue from sales of such product candidates. Accordingly, management expects to incur substantial losses on the ongoing development of its product candidates and does not expect to achieve positive cash flow from operations for the foreseeable future, if ever. As a result, the Company will continue to require additional capital to move forward with its business plan. While certain amounts of this additional capital were raised in the past, there can be no assurance that funds necessary beyond these amounts will be available in amounts or on terms sufficient to ensure ongoing operations.

The Company's management believes that the cash, cash equivalents and short-term investments balances as of December 31, 2018 should enable the Company to maintain its planned operations for at least twelve months from the date these financial statements were issued. The Company's ability to fund all of its planned operations internally beyond that date, including the completion of its ongoing and planned clinical trial activities, may be substantially dependent upon whether the Company can obtain sufficient funding on terms acceptable to the Company. Proceeds from additional capital transactions would allow the Company to accelerate and/or expand its planned research and development activities. In the event that sufficient funds were not available, the Company may be required to delay or reduce expenditures to conserve cash, which could involve scaling back or curtailing development and general and administrative activities.

**2. Basis of Presentation**

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

In 2011, the Company established a wholly owned subsidiary in the United Kingdom. There have been no activities for this entity to date. In 2014, the Company established a wholly owned U.S. subsidiary, Syndax Securities Corporation. The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

**3. Summary of Significant Accounting Policies**

***Use of Estimates***

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of costs and expenses during the reporting period. The Company bases estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. The Company evaluates its estimates and assumptions on an ongoing basis. The Company's actual results may differ from these estimates under different assumptions or conditions.

***Cash Equivalents***

Cash equivalents include all highly liquid investments maturing within 90 days or less from the date of purchase. Cash equivalents include money market funds, corporate debt securities, U.S. government agency notes, and overnight deposits.

***Restricted Cash***

The Company classifies as restricted cash all cash pledged as collateral to secure long-term obligations and all cash whose use is otherwise limited by contractual provisions. Amounts are reported as non-current unless restrictions are expected to be released in the next 12 months.

***Short-Term and Long-Term Investments***

Short-term investments include marketable securities with maturities of less than one year or where management's intent is to use the investments to fund current operations or to make them available for current operations. Long-term investments include marketable securities with remaining maturities greater than one year or that are due after one year from the balance sheet date. All investments in marketable securities are classified as available-for-sale and are reported at fair value with unrealized gains and losses excluded from earnings and reported net of tax in accumulated other comprehensive income, which is a component of stockholders' equity (deficit). Unrealized losses that are determined to be other-than-temporary, based on current and expected market conditions, are recognized in earnings. Declines in fair value determined to be credit related are charged to earnings. The cost of marketable securities sold is determined by the specific identification method.

***Segment Reporting***

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions regarding resource allocation and assessing performance. The Company has one operating segment.

***Concentrations of Credit Risk***

Cash and cash equivalents, restricted cash, and short-term and long-term investments are financial instruments that potentially subject the Company to concentrations of credit risk. Substantially all of the Company's cash, cash equivalents, and short-term and long-term investments were deposited in accounts at two financial institutions, and at times, such deposits may exceed federally insured limits. The Company has not experienced any losses in such accounts, and 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 available-for-sale investments primarily consist of U.S. Treasury securities, U.S. government agency securities, corporate debt securities, certificates of deposit and overnight deposits and potentially subject the Company to concentrations of credit risk.

***Property and Equipment***

Property and equipment are recorded at cost. Depreciation is recorded using the straight-line method over the estimated useful lives of the assets (three to five years). Assets under capital leases are amortized over the shorter of their useful lives or lease term using the straight-line method. Major replacements and improvements are capitalized, while general repairs and maintenance are expensed as incurred.

***Impairment of Long-Lived Assets***

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows. If this comparison indicates that there is impairment, the amount of impairment is calculated as the difference between the carrying value and fair value. To date, no such impairments have been recognized.

***Revenue Recognition***

The Company adopted Accounting Standards Codification Rule 606 Revenue from Contracts with Customers (ASC 606), on January 1, 2018, using the modified retrospective method for all contracts not completed as of the date of adoption. The reported results for 2018 reflect the application of ASC 606 guidance while the reported

results for 2017 were prepared under the guidance of ASC 605, Revenue Recognition (ASC 605). For the Company's accounting policy for revenue recognition under ASC 605, refer to Item 8 of the Annual Report on Form 10-K for the year ended December 31, 2017. As of January 1, 2018, the Company had only one contract within the scope of ASC 606, a license agreement with Kyowa Hakko Kirin Co., Ltd. ("KHK"), under which the Company granted KHK an exclusive license to develop and commercialize entinostat in Japan and Korea (the "KHK License Agreement"). The KHK License Agreement is discussed further in Note 6.

The Company enters into license agreements for the development and commercialization of its product candidates. License agreements may include non-refundable upfront payments, contingent payments based on the occurrence of specified events under the Company's license arrangements, partial or complete reimbursement of research and development expenses, license fees and royalties on sales of entinostat if they are successfully approved and commercialized. The Company's performance obligations under the license agreements may include the transfer of intellectual property rights in the form of licenses, obligations to provide research and development services and related materials and participation on certain development and/or commercialization committees.

Revenue is recognized when, or as, performance obligations are satisfied, which occurs when control of the promised products or services is transferred to customers. Revenue is measured as the amount of consideration the Company expects to receive in exchange for transferring products or services to a customer ("transaction price"). To the extent that the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing the most likely amount method. Variable consideration is included in the transaction price if, in the Company's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Estimates of variable consideration and determination of whether to include estimated amounts in the transaction price are based largely on an assessment of the Company's anticipated performance and all information (historical, current and forecasted) that is reasonably available.

The Company assesses the promises to determine if they are distinct performance obligations. Once the performance obligations are determined, the transaction price is allocated based on a relative standalone selling price basis. Milestone payments and royalties are typically considered variable consideration at the outset of the contract and are recognized in the transaction price either upon occurrence or when the constraint of a probable reversal is no longer applicable.

Licenses of intellectual property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer 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. Arrangements containing licenses to the Company's intellectual property typically provide for a know-how transfer period. These arrangements may or may not also include rights to future updates of that intellectual property and related know-how. Revenues from non-refundable, up-front fees allocated to the licenses are recognized as the license is transferred to the customer and the customer is able to use and benefit from the license. This generally takes place over the related know-how transfer period, or if applicable, over the term of transfer of future updates to the intellectual property.

Development Milestone Payments: At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license fees and earnings in the period of adjustment. For development milestones related to the KHK Agreement, the Company does not take a substantive role or control the research, development or commercialization of any products generated by KHK. Therefore, the Company is not able to reasonably estimate when, if at all, any development milestone payments may be payable to the Company. As such, the development milestone payments associated with the KHK Agreement involve a substantial degree of uncertainty and risk that they may never be received.

Commercial Milestone Payments and Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of commercial sales, and the license is deemed to be the predominant item to which the royalties or commercial milestones relate, the Company will recognize revenue at the later of when the related sales occur or when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date no commercial milestone payments or royalties have been achieved.

When no performance obligations are required of the Company, or following the completion of the performance obligation period, such amounts are recognized as revenue upon transfer of control of the goods or services to the customer. Generally, all amounts received or due other than sales-based milestones and royalties are classified as license fees. Sales-based milestones and royalties will be recognized as royalty revenue at the later of when the related sales occur or when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Deferred revenue arises from amounts received in advance of the culmination of the earnings process and is recognized as revenue in future periods as performance obligations are satisfied. Deferred revenue expected to be recognized within the next twelve months is classified as a current liability. Upfront payment contract liabilities resulting from the Company’s license agreements do not represent a financing component as the payment is not financing the transfer of goods or services, and the technology underlying the licenses granted reflects research and development expenses already incurred by the Company.

***Research and Development***

Research and development costs are expensed as incurred. Research and development expenses include payroll and personnel expenses, consulting costs, external contract research and development expenses, and allocated overhead, including rent, equipment depreciation, and utilities. Research and development costs that are paid in advance of performance are capitalized as a prepaid expense and amortized over the service period as the services are provided. The Company expenses upfront license payments related to acquired technologies that have not yet reached technological feasibility and have no alternative future use.

In instances where the Company enters into cost-sharing arrangements, all research and development costs reimbursed by the collaborators are accounted for as reductions to research and development expense. During the year ended December 31, 2018, the Company incurred $4.7 million in external costs related to cost-sharing collaborations, of which $2.4 million has been recorded as a reduction to research and development expense. During the year ended December 31, 2017, the Company incurred $3.0 million in external costs related to cost-sharing collaborations, of which $1.4 million has been recorded as a reduction to research and development expense.

***Clinical Trial Costs***

Clinical trial costs are a component of research and development expenses. The Company accrues and expenses clinical trial activities performed by third parties based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or other information provided to us by our vendors.

***Income Taxes***

The Company records deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax bases of assets and liabilities and for loss and credit carryforwards using enacted tax rates expected to be in effect in the years in which the differences reverse. A valuation allowance is provided to reduce the net deferred tax assets to the amount that will more likely than not be realized. The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes.

***Guarantees and Indemnifications***

As permitted under Delaware law, the Company indemnifies its officers, directors, and employees for certain events or occurrences that happen by reason of the relationship with, or position held at, the Company. The Company has standard indemnification arrangements under office leases (as described in Note 14) that require it to indemnify the landlord against all costs, expenses, fines, suits, claims, demands, liabilities, and actions directly resulting from any breach, violation, or nonperformance of any covenant or condition of the Company's lease. Through December 31, 2018, the Company had not experienced any losses related to these indemnification obligations and no claims were outstanding. The Company does not expect significant claims related to these indemnification obligations, and consequently, concluded that the fair value of these obligations is negligible, and no related reserves were established.

***Stock-Based Compensation***

The Company accounts for all stock option awards granted to employees and non-employees using a fair value method. Stock-based compensation is measured at the grant date fair value of employee stock option grants and is recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis. Stock option awards to non-employees are subject to periodic revaluation over their vesting terms. The Company accounts for forfeitures as they occur.

***Convertible Preferred Stock***

Upon closing of the IPO, all of the outstanding shares of the Company's outstanding convertible preferred stock converted into shares of the common stock. Prior to the IPO, the Company had classified certain series of convertible preferred stock as temporary equity in the consolidated balance sheets due to certain change in control events that were outside of the Company's control, including liquidation, sale, or transfer of control of the Company, as holders of the convertible preferred stock could cause redemption of the shares in these situations. The carrying value of the convertible preferred stock was presented at its maximum redemption value. As of December 31, 2015, the Series A preferred stock had no liquidation preference and was presented in permanent equity.

***Recently Issued and Adopted Accounting Pronouncements***

In June 2018, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2018-07, *Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"). ASU 2018-07 is intended to simplify several aspects of the accounting for nonemployee share-based payment transactions by expanding the scope of Topic 718 to include share-based

payment transactions for acquiring goods and services from nonemployees. This ASU is effective for public reporting companies for interim and annual periods beginning after December 15, 2018, with early adoption permitted but no earlier than an entity's adoption date of Topic 606. The Company has evaluated the effect of the new guidance on the Company's consolidated financial statements and related disclosures and determined that the impact is not material.

In May 2017, the FASB issued ASU 2017-09, *Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"). ASU 2017-09 provides guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. An entity should account for the effects of a modification unless all of the following are met: (1) the fair value (or calculated value or intrinsic value, if such an alternative measurement method is used) of the modified award is the same as the fair value (or calculated value or intrinsic value, if such an alternative measurement method is used) of the original award immediately before the original award is modified. If the modification does not affect any of the inputs to the valuation technique that the entity uses to value the award, the entity is not required to estimate the value immediately before and after the modification; (2) the vesting conditions of the modified award are the same as the vesting conditions of the original award immediately before the original award is modified; (3) the classification of the modified award as an equity instrument or a liability instrument is the same as the classification of the original award immediately before the original award is modified. The Company adopted ASU 2017-09 on January 1, 2018, and it did not have a material impact on its consolidated balance sheet, consolidated statement of comprehensive loss or consolidated statement of cash flows. As part of the adoption of this guidance, the Company adopted a policy to account for the effects of a modification unless certain exclusions are met.

In November 2016, the FASB issued ASU 2016-18, "Statement of Cash Flows (Topic 230): Restricted Cash" ("ASU 2016-18"). ASU 2016-18 requires that restricted cash and restricted cash equivalents be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The statement of cash flows must also explain the change during the period in the total of cash, cash equivalents, and restricted cash or restricted cash equivalents. The Company adopted ASU 2016-18 on January 1, 2018, utilizing the retrospective transition method and it did not have a material impact on its consolidated statement of cash flows. As part of the adoption of this guidance, the Company included restricted cash with cash and cash equivalent in the consolidated statement of cash flows for the periods ending December 31, 2018, 2017 and 2016. The following table provides a reconciliation of the cash, cash equivalents and restricted cash balances as of December 31, 2018, 2017 and 2016, as shown below:

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | (In thousands) | | |
| Cash and cash equivalents | $ 33,769 | $ 35,168 | $ 23,844 |
| Restricted cash included in current and noncurrent assets | 216 | 221 | 266 |
| Cash, cash equivalents and restricted cash | $ 33,985 | $ 35,389 | $ 24,110 |

In February 2016, the FASB issued ASU 2016-02, "*Leases (Topic 842).*" Under ASU 2016-02, lessees will be required to recognize, for all leases of 12 months or more, a liability to make lease payments and a right-of-use asset representing the right to use the underlying asset for the lease term. Additionally, the guidance requires improved disclosures to help users of financial statements better understand the nature of an entity's leasing activities. The provisions of ASU 2016-02 are effective for annual reporting periods beginning after December 15, 2018; early adoption permitted. In July 2018, an amendment was made that allows companies the option of using the effective date of the new standard as the initial application date (at the beginning of the period in which it is adopted, rather than at the beginning of the earliest comparative period). The standard is effective for the Company on January 1, 2019. The Company has completed its assessment on the impact of the standard, including optional practical expedients and transition methods that the Company will elect upon adoption. The implementation plan included identifying the Company's lease population, assessing significant leases under the new guidance and identifying changes to processes and controls. The Company concluded that upon adoption of this standard there will not be a material impact to its consolidated balance sheet with expected recognition of right-of-use assets and liabilities between $1 million and $1.5 million. The Company will utilize the prospective approach of adopting this standard.

The Company has identified and implemented appropriate changes to its business processes and controls to support recognition and disclosure under this standard.

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-09"). The Company adopted ASU 2014-09 and its related amendments (collectively known as ASC 606) effective January 1, 2018 using the modified retrospective method. See Note 4 "Revenue from Contracts with Customers" for the required disclosures related to the impact of adopting this standard and a discussion of the Company's updated policies related to revenue recognition.

**4. Revenue from Contracts with Customers**

*Financial Statement Impact of Adopting ASC 606*

On January 1, 2018, the Company adopted ASC 606 applying the modified retrospective method, which only impacted the accounting for the KHK License Agreement. As a result of applying the modified retrospective method to adopt the new revenue guidance, the following adjustments were made to accounts on the consolidated balance sheet as of January 1, 2018:

| | As Reported at December 31, 2017 | Adjustments Due to ASC 606 | Balance at January 1, 2018 |
|---|---|---|---|
| **Liabilities and Stockholders' Equity** | | | |
| Current liabilities: | | | |
| Current portion of deferred revenue | 1,573 | (56) | 1,517 |
| Total current liabilities | 15,798 | (56) | 15,742 |
| Long-term liabilities: | | | |
| Deferred revenue, less current portion | 16,759 | (593) | 16,166 |
| Total long-term liabilities | 17,069 | (593) | 16,476 |
| Total liabilities | 32,867 | (649) | 32,218 |
| Stockholders' equity: | | | |
| Accumulated deficit | (366,111) | 649 | (365,462) |
| Total stockholders' equity | 104,319 | 649 | 104,968 |
| Total liabilities and stockholders' equity | $ 137,186 | — | $ 137,186 |

*Impact of New Revenue Guidance on Financial Statement Line Items*

Results for reporting periods beginning after January 1, 2018 were presented under ASC 606, while prior period amounts were not adjusted and reported under the accounting standards in effect for the prior periods. The following tables show the impact on the reported consolidated balance sheet for the year ended December 31, 2018, and the statements of operations and comprehensive loss for the year ended December 31, 2018, for pro-forma amounts had the previous guidance been in effect (in thousands):

| **Financial Statement Line Item *** | **Increase (Decrease)** |
|---|---|
| **Consolidated Statements of Operations and Comprehensive Loss** | **Year ended December 31, 2018** |
| License fee | (56) |
| Net loss | (56) |
| Comprehensive loss | (56) |

| **Consolidated Balance Sheet **** | **December 31, 2018** |
|---|---|
| Current portion of deferred revenue | (56) |
| Deferred revenue, less current portion | (537) |
| Accumulated deficit | 593 |

* Excludes line items that were not affected by the Company's adoption of ASC 606. The adoption had no impact to cash provided by or used in net operating, investing or financing activities in the Consolidated Statement of Cash Flows.

** Balance sheet line item amounts include the cumulative-effect adjustment recorded on December 31, 2017.

*Impact on KHK License Agreement Revenue*

Under ASC 606, the Company determined that the performance obligations associated with the KHK License Agreement include (i) the combined license, rights to access and use materials and data, and rights to additional intellectual property, and (ii) the clinical supply obligation. All other goods or services promised to KHK are immaterial in the context of the agreement. Under ASC 606, the identification of the clinical supply obligation as a distinct performance obligation separate and apart from the license performance obligation resulted in a change in the performance period. The start of the performance period under ASC 606 was determined to be the contract inception date, December 19, 2014, as opposed to the initial delivery of the clinical trial materials in June 2015. The clinical supply was identified as a separate performance obligation under ASC 606 as (i) the Company is not providing a significant service of integration whereby the clinical supply and other promises are inputs into a combined output, (ii) the clinical supply does not significantly modify or customize the other promises nor is it significantly modified or customized by them and (iii) the clinical supply is not highly interdependent or highly interrelated with the other promises in the agreement as KHK could choose not to purchase the clinical supply from the Company without significantly affecting the other promised goods or services. The Company further concluded that the clinical supply represented an immaterial performance obligation and therefore the entire $17.3 million allocated to the upfront payment was allocated to the combined license and will be recognized ratably over the performance period, representing contract inception though 2029. In 2017, KHK achieved a development milestone, and was required to pay the Company $5.0 million. The Company is recognizing the development milestone consideration over the performance period coinciding with the license to intellectual property. As the Company determined that its performance obligations associated with the KHK Agreement at contract inception were not distinct and represented a single performance obligation, and that the obligations for goods and services provided would be completed over the performance period of the agreement, any payments received by the Company from KHK, including the upfront payment and progress-dependent development and regulatory milestone payments, are recognized as revenue using a time-based proportional performance model over the contract term (December 2014 through 2029) of the collaboration, within license fees. To date no commercial milestone payments or royalties have been achieved.

Contract liabilities consisted of deferred revenue, as presented on the consolidated balance sheet, as of December 31, 2018. Deferred revenue related to the KHK License Agreement was $16.2 million as of December 31, 2018 and will be recognized over the remainder of the contract term. The Company recognized license fees revenue of $1.5 million during the year ended December 31, 2018 that was included in the deferred revenue balance as of January 1, 2018.

**5. Net Loss per Share Attributable to Common Stockholders**

Basic net loss attributable to common stockholders per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period. Because the Company has reported a net loss for the three years ended December 31, 2018, 2017, and 2016, diluted net loss per common share is the same as basic net loss per common share for those periods. The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company (in thousands, except per share data):

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| **Numerator--basic and diluted:** | | | |
| Net loss | $ (73,961) | $ (60,802) | $ (44,472) |
| Accretion of convertible preferred stock dividends | — | — | (2,598) |
| Net loss attributable to common stockholders--basic and diluted | $ (73,961) | $ (60,802) | $ (47,070) |
| Net loss per share—basic and diluted | $ (2.92) | $ (2.90) | $ (3.22) |
| **Denominator—basic and diluted:** | | | |
| Weighted-average common shares used to compute net loss per share—basic and diluted | 25,371,511 | 20,997,211 | 14,619,716 |

The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares outstanding because such securities have an antidilutive impact due to losses reported (in common stock equivalent shares):

| | December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Options to purchase common stock | 4,252,983 | 3,391,832 | 2,560,737 |
| Common stock warrant | — | 357,840 | 357,840 |
| Restricted stock subject to future vesting | — | — | 8,542 |

As discussed in Note 11, in June 2018, the Company signed an exchange agreement with an investor under which the investor exchanged 2,000,000 shares of common stock for 2,000,000 warrant shares. The warrants are exercisable into shares of common stock for $0.0001 per share. The shares of common stock into which the warrants may be exercised are considered outstanding for the purposes of computing earnings per share.

**6. Significant Agreements**

***Vitae Pharmaceuticals, Inc.***

In October 2017, the Company entered into a license agreement (the "Allergan License Agreement") with Vitae Pharmaceuticals, Inc., a subsidiary of Allergan ("Allergan"), under which Allergan granted the Company an exclusive, sublicensable, worldwide license to a portfolio of preclinical, orally available, small molecule inhibitors of the interaction of Menin with Mixed Lineage Leukemia ("MLL") protein (the "Menin Assets"). The Company made a nonrefundable upfront payment of $5.0 million to Allergan in the fourth quarter of 2017. Additionally, subject to the achievement of certain milestone events, the Company may be required to pay Allergan up to $99.0 million in one-time development and regulatory milestone payments over the term of the Allergan License Agreement. In the event that the Company or any of its affiliates or sublicensees commercializes the Menin Assets, the Company will also be obligated to pay Allergan low single to low double-digit royalties on sales, subject to reduction in certain circumstances, as well as up to an aggregate of $70.0 million in potential one-time, sales-based milestone payments based on achievement of certain annual sales thresholds. Under certain circumstances, the Company may be required to share a percentage of non-royalty income from sublicensees, subject to certain deductions, with Allergan. The Company is solely responsible for the development and commercialization of the Menin Assets. Each party may terminate the Allergan License Agreement for the other party's uncured material breach or insolvency; and the Company may terminate the Allergan License Agreement at will at any time upon advance written notice to Allergan. Allergan may terminate the Allergan License Agreement if the Company or any of its affiliates or sublicensees institutes a legal challenge to the validity, enforceability, or patentability of the licensed patent rights. Unless terminated earlier in accordance with its terms, the Allergan License Agreement will continue on a country-by-country and product-by-product basis until the later of: (i) the expiration of all of the licensed patent rights in such country; (ii) the expiration of all regulatory exclusivity applicable to the product in such country; and (iii) 10 years from the date of the first commercial sale of the product in such country.

As of the date of the Allergan License Agreement, the asset acquired had no alternative future use nor had it reached a stage of technological feasibility. As the processes or activities that were acquired along with the license do not constitute a "business," the transaction has been accounted for as an asset acquisition. As a result, in 2017, the upfront payment of $5.0 million was recorded as research and development expense in the consolidated statements of operations.

***UCB Biopharma Sprl***

In July 2016, the Company entered into a license agreement (the "UCB License Agreement") with UCB Biopharma Sprl ("UCB"), under which UCB granted to the Company a worldwide, sublicenseable, exclusive license to UCB6352, which the Company refers to as SNDX-6352, an IND-ready anti-CSF-1R monoclonal antibody. The Company made a nonrefundable upfront payment of $5.0 million to UCB in the third quarter of 2016. Additionally, subject to the achievement of certain milestone events, the Company may be required to pay UCB up to $119.5 million in one-time development and regulatory milestone payments over the term of the UCB License Agreement. In the event that the Company or any of its affiliates or sublicensees commercializes SNDX-6352, the Company will also be obligated to pay UCB low double-digit royalties on sales, subject to reduction in certain circumstances, as well as up to an aggregate of $250.0 million in potential one-time, sales-based milestone payments based on achievement of certain annual sales thresholds. Under certain circumstances, the Company may be required to share a percentage of non-royalty income from sublicensees, subject to certain deductions, with UCB. The Company will be solely responsible for the development and commercialization of SNDX-6352, except that UCB is performing a limited set of transitional chemistry, manufacturing and control tasks related to SNDX-6352. Each party may terminate the UCB License Agreement for the other party's uncured material breach or insolvency; and the Company may terminate the UCB License Agreement at will at any time upon advance written notice to UCB. UCB may terminate the UCB License Agreement if the Company or any of its affiliates or sublicensees institutes a legal challenge to the validity, enforceability, or patentability of the licensed patent rights. Unless terminated earlier in accordance with its terms, the UCB License Agreement will continue on a country-by-country and product-by-product basis until the later of: (i) the expiration of all of the licensed patent rights in such country; (ii) the expiration of all regulatory exclusivity applicable to the product in such country; and (iii) 10 years from the date of the first commercial sale of the product in such country.

As of the date of the UCB License Agreement, the asset acquired had no alternative future use nor had it reached a stage of technological feasibility. As the processes or activities that were acquired along with the license do not constitute a "business," the transaction has been accounted for as an asset acquisition. As a result, in 2016, the upfront payment of $5.0 million was recorded as research and development expense in the consolidated statements of operations.

***Kyowa Hakko Kirin Co., Ltd.***

On December 19, 2014 (the "Effective Date"), the Company entered into the KHK License Agreement, under which the Company granted KHK an exclusive license to develop and commercialize entinostat in Japan and Korea. Under the terms of the KHK License Agreement, the Company will be responsible for the manufacture and supply of the products during the development activities. In addition to the license and manufacturing obligations, the Company is obligated to provide KHK access to know-how and regulatory information the Company may develop over the life of the entinostat patent. Lastly, to the extent additional intellectual property is developed during the term of the agreement, KHK will receive the right to the intellectual property when and if available. KHK will conduct the development, regulatory approval filings, and commercialization activities of entinostat in Japan and Korea. KHK paid the Company $25.0 million upfront, which included a $7.5 million equity investment and a $17.5 million non-refundable cash payment. In addition, to the extent certain development and commercial milestones are achieved, KHK will be required to pay the Company up to $75.0 million in milestone payments over the term of the license agreement. The term of the agreement commenced on the Effective Date and, unless earlier terminated in accordance with the terms of the agreement, will continue on a country-by-country and product-by-product basis, until the later of: (i) the date all valid claims of the last effective patent among the Company's patents expires or is abandoned, withheld, or is otherwise invalidated in such country; and (ii) 15 years from the date of the first commercial sale of a product in the Japan or Korea.

The equity purchase and the up-front payment of the license fee were accounted for separately. The Company allocated the amount of consideration equal to the fair value of the shares on the Effective Date, which resulted in $7.7 million of proceeds allocated to the equity purchase and the remaining consideration of $17.3 million allocated to the up-front license fee.

In October 2017, the Company announced that KHK enrolled the first Japanese patient into a local pivotal study of entinostat for the treatment of hormone receptor positive, human epidermal growth factor receptor 2 negative breast cancer. In accordance with the terms of the agreement KHK paid the Company a $5.0 million milestone payment which the Company received in December 2017. Please refer to Note 4, Revenue from Contracts with Customers, for further discussion related to the accounting for the milestone.

In October 2016, the Company entered into a clinical trial co-funding agreement with KHK under which the Company expanded its clinical trial agreement with Eastern Cooperative Oncology Group (the "ECOG Agreement") to include enrollments from sites in Korea.

***Eastern Cooperative Oncology Group***

In March 2014, the Company entered into the "ECOG Agreement with Eastern Cooperative Oncology Group, a contracting entity for the Eastern Cooperative Oncology Group—American College of Radiology Imaging Network Cancer Research Group ("ECOG-ACRIN"), that describes the parties' obligations with respect to the NCI-sponsored pivotal Phase 3 clinical trial of entinostat. Under the terms of the ECOG Agreement, ECOG-ACRIN will perform this clinical trial in accordance with the clinical trial protocol and a mutually agreed scope of work. The Company will provide a fixed level of financial support for the clinical trial through an upfront payment of $0.7 million and a series of payments of up to $1.0 million each that are comprised of milestone payments through the completion of enrollment and time-based payments through the completion of patient monitoring post-enrollment. In addition, the Company is obligated to supply entinostat and placebo to ECOG-ACRIN for use in the clinical trial. From the second quarter of 2016 through the fourth quarter of 2018, the Company has entered into a number of amendments to the agreement to provide for additional study activities resulting in an increase of the contractual obligation of $5.1 million. As of December 31, 2018, the Company's aggregate payment obligations under this agreement were approximately $24.5 million; and as of December 31, 2018, the Company's remaining payment obligations are approximately $9.6 million over an estimated period of approximately three years.

Data and inventions from the Phase 3 clinical trial are owned by ECOG-ACRIN. The Company has access to the data generated in the clinical trial, both directly from ECOG-ACRIN under the ECOG Agreement as well as from the NCI. Additionally, ECOG-ACRIN has granted the Company a non-exclusive royalty-free license to any inventions or discoveries that are derived from entinostat as a result of its use during the clinical trial, along with a first right to negotiate an exclusive license to any of these inventions or discoveries. Either party may terminate the ECOG Agreement in the event of an uncured material breach by the other party or if the FDA or NCI withdraws the authorization to perform the clinical trial in the United States. The parties may jointly terminate the ECOG Agreement if the parties agree that safety-related issues support termination of the clinical trial.

The Company records the appropriate clinical trial expenses in its financial statements by matching those expenses with the period in which the services and efforts are expended. The Company accounts for these expenses according to the progress of the clinical trial as measured by patient enrollment and the timing of various aspects of the clinical trial. The Company determines accrual estimates through financial models, taking into account discussion with applicable personnel and ECOG-ACRIN as to the progress or state of consummation of the clinical trial or the services completed.

***Bayer Pharma AG (formerly known as Bayer Schering Pharma AG)***

In March 2007, the Company entered into a license agreement (the "Bayer Agreement") with Bayer Schering Pharma AG ("Bayer") for a worldwide, exclusive license to develop and commercialize entinostat and any other products containing the same active ingredient. Under the terms of the Bayer Agreement, the Company paid a nonrefundable up-front license fee of $2.0 million and is responsible for the development and marketing of entinostat. The Company recorded the $2.0 million license fee as research and development expense during the year ended December 31, 2007, as it had no alternative future use. The Company will pay Bayer royalties on a sliding scale based on net sales, if any, and make future milestone payments to Bayer of up to $150.0 million in the event that certain specified development and regulatory goals and sales levels are achieved. In June 2014, a development milestone was achieved, and the Company recorded $2.0 million of research and development expense, which has been fully paid.

In connection with the Bayer Agreement, the Company issued to Bayer a warrant to purchase the number of shares of the Company's common stock equal to 1.75% of the shares of common stock outstanding on a fully diluted basis as of the earlier of the date the warrant was exercised or the closing of the IPO. The warrant contained anti-dilution protection to maintain Bayer's potential ownership at 1.75% of the shares of common stock outstanding on a fully diluted basis, requiring that the actual number of shares of common stock issuable pursuant to the warrant be increased or decreased for any changes in the fully diluted shares of common stock outstanding. The warrant was exercisable at an exercise price of $1.54 per share and would have expired upon the earlier of the 10-year anniversary of the closing of the IPO or the date of the consummation of a disposition transaction. The warrant was classified as a long-term liability and recorded at fair value with the changes in the fair value recorded in other expense. The Company used the Black-Scholes option-pricing model to determine the fair value of the warrant. Upon the closing of the IPO, the anti-dilution protection for the warrant expired, resulting in the reclassification of the warrant liability to additional paid-in capital. The warrant was re-measured using current assumptions just prior to the reclassification. On March 1, 2018, Bayer notified the Company of its election to exercise the warrant utilizing the net exercise feature contained therein, resulting in the Company's issuance to Bayer of 299,215 shares of the Company's common stock for no net cash proceeds.

**7. Property and Equipment, net**

Property and equipment, net, consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Office and computer equipment | $ 38 | $ 68 |
| Furniture and fixtures | 134 | 134 |
| Equipment | 256 | 84 |
| Office equipment under capital lease | 13 | 13 |
| Leasehold improvements | 167 | 167 |
| Total property and equipment | 608 | 466 |
| Accumulated depreciation | (235) | (199) |
| Property and equipment, net | $ 373 | $ 267 |

**8. Fair Value Measurements**

The carrying amounts of cash and cash equivalents, restricted cash, accounts payable, and accrued expenses approximated their estimated fair values due to the short-term nature of these financial instruments. Fair value is defined 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. Valuation techniques used to measure fair value are performed in a manner to maximize the use of observable inputs and minimize the use of unobservable inputs. The accounting standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value, which are the following:

*Level 1*—Quoted prices in active markets that are accessible at the market date for identical unrestricted assets or liabilities.

*Level 2*—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs for which all significant inputs 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.

During the years presented, the Company has not changed the manner in which it values assets and liabilities that are measured at fair value using Level 3 inputs. The Company recognizes transfers between levels of the fair value hierarchy as of the end of the reporting period. There were no transfers within the hierarchy during the years ended December 31, 2018, 2017 and 2016.

A summary of the assets and liabilities carried at fair value in accordance with the hierarchy defined above is as follows (in thousands):

| | Total Carrying Value | Fair Value Measurements Using | | |
|---|---|---|---|---|
| | | Quoted Prices in Active Markets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
| **December 31, 2018** | | | | |
| Assets: | | | | |
| Cash equivalents | $ 33,769 | $ 29,270 | $ 4,499 | $ — |
| Short-term investments | 47,142 | — | 47,142 | — |
| Total assets | $ 80,911 | $ 29,270 | $ 51,641 | $ — |
| **December 31, 2017** | | | | |
| Assets: | | | | |
| Cash equivalents | $ 35,168 | $ 24,972 | $ 10,196 | $ — |
| Short-term investments | 94,806 | — | $ 94,806 | — |
| Long-term investments | 3,246 | — | 3,246 | — |
| Total assets | $ 133,220 | $ 24,972 | $ 108,248 | $ — |

Cash equivalents of $29.3 million as of December 31, 2018 and $25.0 million as of December 31, 2017 consisted of overnight investments and money market funds and are classified within Level 1 of the fair value hierarchy because they are valued using quoted market prices in active markets. Cash equivalents of $4.5 million as of December 31, 2018 and $10.2 million as of December 31, 2017 consisted of highly rated corporate bonds and commercial paper and are classified within Level 2 of the fair value hierarchy because pricing inputs are other than quoted prices in active markets, which are either directly or indirectly observable as of the reporting date; and fair value is determined through the use of models or other valuation methodologies.

Short-term investments of $47.1 million as of December 31, 2018 and $94.8 million as of December 31, 2017, and long-term investments of $3.2 million as of December 31, 2017 consisted of commercial paper and highly rated corporate bonds and are classified within Level 2 of the fair value hierarchy because pricing inputs are other than quoted prices in active markets, which are either directly or indirectly observable as of the reporting date; and fair value is determined through the use of models or other valuation methodologies.

The short-term and long-term investments are classified as available-for-sale securities. As of December 31, 2018, the remaining contractual maturities of the available-for-sale securities were less than 9 months, and the balance in the Company's accumulated other comprehensive income was comprised solely of activity related to the Company's available-for-sale securities. There were no realized gains or losses recognized on the sale or maturity of available-for-sale securities during the three years ended December 31, 2018. As a result, the Company did not reclassify any amounts out of accumulated other comprehensive income for the same periods. The Company has a limited number of available-for-sale securities in insignificant loss positions as of December 31, 2018, which the Company does not intend to sell and has concluded it will not be required to sell before recovery of the amortized cost for the investment at maturity. The following table summarizes the available-for-sale securities (in thousands):

| | Amortized Cost | Unrealized Gains | Unrealized Losses | Fair Value |
|---|---|---|---|---|
| **December 31, 2018** | | | | |
| Commercial paper | $ 22,619 | $ — | $ (15) | $ 22,604 |
| Corporate bonds | 29,047 | 2 | (12) | 29,037 |
| | $ 51,666 | $ 2 | $ (27) | $ 51,641 |
| **December 31, 2017** | | | | |
| Commercial paper | $ 36,567 | $ — | $ (40) | $ 36,527 |
| Corporate bonds | 71,824 | — | (103) | 71,721 |
| | $ 108,391 | $ — | $ (143) | $ 108,248 |

## 9. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Short-term deposits | $ 663 | $ 1,286 |
| Prepaid clinical supplies | 101 | 220 |
| Interest receivable on investments | 253 | 377 |
| Reimbursable costs | 797 | 1,029 |
| Prepaid insurance | 188 | 192 |
| Other | 332 | 258 |
| Total prepaid expenses and other current assets | $ 2,334 | $ 3,362 |

## 10. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Accrued professional fees | $ 484 | $ 265 |
| Accrued compensation and related costs | 2,804 | 2,393 |
| Accrued clinical costs | 9,726 | 9,177 |
| Other | 135 | 158 |
| Total accrued expenses | $ 13,149 | $ 11,993 |

## 11. Common Stock

In connection with the closing of the Company's IPO, the Company filed an amended and restated certificate of incorporation and adopted amended and restated bylaws; and pursuant to the amended and restated certificate of incorporation, the Company is authorized to issue 100,000,000 shares of common stock. The holders of each share of common stock are entitled to one vote per share held and are entitled to receive dividends, if and when declared

by the Board, and to share ratably in the Company's assets available for distribution to stockholders, in the event of liquidation.

On June 18, 2018, the Company signed an exchange agreement with Biotechnology Value Fund and certain affiliated funds ("BVF") under which BVF exchanged 2,000,000 shares of common stock for 2,000,000 warrant shares. The Company recorded the issuance of the warrants and the retirement of the common stock at fair value within additional paid-in capital. BVF can exercise the warrant shares at an exercise price per share equal to $0.0001 per share and the warrant shares expire 20 years from issuance. Per the terms of the warrant agreement, the outstanding warrants to purchase shares of common stock may not be exercised if the holder's ownership of the Company's common stock would exceed 9.99 percent following such exercise.

The Company has reserved for future issuance the following shares of common stock related to the potential warrant exercise, exercise of stock options, and the employee stock purchase plan:

| | December 31, 2018 |
|---|---|
| Common stock issuable under BVF warrant | 2,000,000 |
| Options to purchase common stock | 5,675,984 |
| Employee Stock Purchase Plan | 651,453 |
| Total | 8,327,437 |

**12. Stock-Based Compensation**

In September 2015, the Company's board of directors adopted its 2015 Omnibus Incentive Plan ("2015 Plan"), which was subsequently approved by its stockholders and became effective upon the closing of the IPO on March 8, 2016. The 2015 Plan replaced the 2007 Stock Plan ("2007 Plan") and allows for the granting of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock, unrestricted stock, stock units, dividend equivalent rights, performance awards, annual incentive awards, and other equity-based awards to the Company's executives and other employees, non-employee members of the board of directors, and consultants of the Company. Any options or awards outstanding under the Company's 2007 Plan remain outstanding and effective. Any shares of common stock related to awards outstanding under the 2007 Plan that thereafter terminate by expiration, forfeiture, cancellation or otherwise without the issuance of such shares will be added to, and included in, the 2015 Plan reserve amount. The Company initially reserved 1,750,000 shares of its common stock for the issuance of awards under the 2015 Plan. As of December 31, 2018, there were 1,423,001 shares available for issuance under the 2015 Plan.

The 2015 Plan provides that the number of shares reserved and available for issuance under the 2015 Plan will automatically increase each January 1, beginning on January 1, 2017, by 4% of the outstanding number of shares of common stock on the immediately preceding December 31 or such lesser number of shares as determined by the Company's board of directors. On January 1, 2019, the shares available for issuance under the 2015 Plan were increased to 2,416,439.

The Company recognized stock-based compensation expense related to the issuance of stock option awards to employees and non-employees and related to the Employee Stock Purchase Plan in the consolidated statements of operations as follows (in thousands):

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Research and development | $ 1,910 | $ 1,363 | $ 919 |
| General and administrative | 4,291 | 4,087 | 3,789 |
| Total | $ 6,201 | $ 5,450 | $ 4,708 |

***Stock Options***

As of December 31, 2018, there was $8.8 million of unrecognized compensation cost related to employee and non-employee unvested stock options granted under the 2007 and 2015 Plans, which is expected to be recognized

over a weighted-average remaining service period of 2.4 years. Stock compensation costs have not been capitalized by the Company.

Our stock-based awards are subject to either service or performance-based vesting conditions. Compensation expense related to awards to employees and directors with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Compensation expense related to awards to non-employees with service-based vesting conditions is recognized on the then-current fair value at each financial reporting date prior to the measurement date over the associated service period of the award, which is generally the vesting term, using the accelerated attribution method. Compensation expense related to awards to employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the straight-line method to the extent achievement of the performance condition is probable. To date, the Company has granted 60,000 options with performance conditions, none of which have vested as of December 31, 2018.

The fair value of each option award is estimated on the date of grant using the Black-Scholes option-pricing model with the weighted-average assumptions noted in the table below. Expected volatility for the Company's common stock was determined based on an average of the historical volatility of a peer group of similar public companies. The Company estimated the expected term of its employee stock options using the "simplified" method, whereby, the expected term equals the average of the vesting term and the original contractual term of the option. The contractual life of the option was used for the estimated life of the non-employee grants. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free interest rate for periods within the expected life of the option is based upon the U.S. Treasury yield curve in effect at the time of grant. The Company accounts for forfeitures when they occur. The grant date fair values of options issued to employees and non-employees were estimated using the Black-Scholes option-pricing model with the following assumptions:

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Expected term (in years) | 5.90 | 6.02 | 5.85 |
| Volatility rate | 76.28% | 73.86% | 71.40% |
| Risk-free interest rate | 2.69% | 2.02% | 1.41% |
| Expected dividend yield | 0.00% | 0.00% | 0.00% |

In determining the exercise prices for options granted, the Board has considered the fair value of the common stock as of each grant date. Prior to the Company's IPO, the fair value of the common stock underlying the stock options was determined by the Board at each award grant date based upon a variety of factors, including the results obtained from an independent third-party valuation, the Company's financial position and historical financial performance, the status of technological developments within the Company's products, the composition and ability of the current clinical and management team, an evaluation or benchmark of the Company's competition, the current business climate in the marketplace, the illiquid nature of the common stock, arm's-length sales of the Company's capital stock (including convertible preferred stock), the effect of the rights and preferences of the preferred stockholders, and the prospects of a liquidity event, among others.

A summary of employee and non-employee option activity under the Company's equity award plans is presented below (in thousands, except share data):

| | Number of Options | Weighted Average Exercise Price | Weighted Average Remaining Contractual Term (in years) | Aggregate Intrinsic Value |
|---|---|---|---|---|
| Outstanding—January 1, 2018 | 3,391,832 | $ 9.28 | 7.7 | $ 2,688 |
| Granted | 1,049,400 | $ 9.37 | | |
| Exercised | (7,850) | $ 3.33 | | |
| Canceled or forfeited | (180,399) | $ 11.31 | | |
| Outstanding—December 31, 2018 | 4,252,983 | $ 9.23 | 7.3 | $ 66 |
| Exercisable—December 31, 2018 | 2,794,957 | $ 8.92 | 6.6 | $ 66 |
| Options vested, exercisable or expected to vest—December 31, 2018 | 4,232,982 | $ 9.22 | 7.3 | $ 66 |

The weighted-average grant date fair value of options granted during the years ended December 31, 2018, 2017 and 2016, was $6.17, $6.68, and $7.94 per share, respectively. The fair value is being expensed over the vesting period of the options (usually three to four years) on a straight-line basis as the services are being provided.

There were 7,850 options exercised for the year ended December 31, 2018, resulting in total proceeds of $26,000; 46,680 options exercised for the year ended December 31, 2017, resulting in total proceeds of $0.3 million; and 441,573 options exercised for the year ended December 31, 2016, resulting in total proceeds of $2.1 million. The intrinsic value of options exercised during the years ended December 31, 2018, 2017 and 2016 was $0.1 million, $0.2 million, and $3.8 million, respectively. In accordance with the Company's policy, the shares were issued from a pool of shares reserved for issuance under the 2007 and 2015 Plans.

Upon the closing of the IPO in March 2016, the Company recorded $0.7 million of additional stock compensation expense related to certain options granted to two of the Company's executives.

***Employee Stock Purchase Plan***

In September 2015, the Company's Board adopted the Employee Stock Purchase Plan (the "ESPP"), which was subsequently approved by the Company's stockholders in February 2016 and became effective upon the closing of the IPO on March 8, 2016. The ESPP authorizes the initial issuance of up to a total of 250,000 shares of common stock to the Company's employees. The Company issued 24,684 shares during 2018. On January 1, 2019, the shares of common stock reserved for issuance under the ESPP was increased to 899,812. Under the terms of the ESPP, eligible employees can elect to acquire shares of the Company's common stock through periodic payroll deductions during a series of six month offering periods. Purchases under the ESPP are effected on the last business day of each offering period at a 15% discount to the lower of closing price on that day or the closing price on the first day of the offering period.

The ESPP is considered a compensatory plan with the related compensation cost expensed over the six-month offering period. In 2018 and 2017 the Company recorded stock-based compensation expense related to the ESPP of $132,000 and $42,000 respectively. There was zero expense for the year ended December 31, 2016.

***Employee Benefit Plan***

The Company has a Section 401(k) defined contribution savings plan for its employees. The plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pretax basis, subject to legal limitations. Company contributions to the plan may be made at the discretion of the Board. For the years ended December 31, 2018, 2017 and 2016, the Company made $126,000, $106,000 and $72,000 contributions to the plan, respectively.

**13. Income Taxes**

The Company has not recorded any net tax provision for the periods presented due to the losses incurred and the need for a full valuation allowance on deferred tax assets. The difference between the income tax expense at the U.S. federal statutory rate and the recorded provision is primarily due to the valuation allowance provided on all deferred tax assets. The Company's loss before income tax for the periods presented was generated entirely in the United States.

The significant components of the Company's deferred tax are as follows (in thousands):

| | Years Ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Deferred tax assets (liabilities): | | |
| Net operating loss carryforwards | $ 12,684 | $ 11,091 |
| Research and development credits | 3,443 | 2,380 |
| Capitalized start-up and research and development costs | 59,331 | 43,282 |
| Deferred revenue | 3,690 | 3,240 |
| Depreciation and amortization | (11,550) | (8,610) |
| Accruals | 630 | 534 |
| Other temporary differences | 3,423 | 2,530 |
| Deferred tax assets before valuation allowance | 71,651 | 54,447 |
| Valuation allowances | (71,651) | (54,447) |
| Net deferred tax assets | $ — | $ — |

The Company has provided a valuation allowance for the full amount of the net deferred tax assets as the realization of the deferred tax assets is not determined to be more likely than not. The valuation allowance decreased by $5.9 million in 2017, due to the decrease in the federal tax rate, and increased by $17.2 million in 2018 due to the increase in deferred tax assets, primarily due to net operating loss carryforwards and capitalized research and development costs.

As of December 31, 2018, the Company had approximately $51.7 million and $27.9 million in federal and state Net Operating Losses ("NOLs"), respectively, which begin to expire at various dates starting in 2025. As of December 31, 2018, the Company had federal and state research credits of $2.3 million and $1.4 million, respectively, which begin to expire in 2021.

The Tax Cuts and Jobs Act (the "Act") was enacted on December 22, 2017. The Act reduced the US federal corporate tax rate from 35% to 21%, required companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred and creates new taxes on certain foreign sourced earnings. The only impact of the Act was the remeasurement of the Company's deferred tax assets and liabilities, which was recorded in fiscal 2017 as a result of the reduction in U.S. corporate tax rates from 35% to 21%. The Company determined it had no accumulated unrepatriated foreign earnings, and therefore had recorded no liability for the repatriation transition tax. The Company has also completed its evaluation of and accounting for all other relevant changes resulting from the Act, and has determined that through December 31, 2018, these changes do not impact the Company's deferred tax assets. No changes have been made to the estimates recorded in fiscal 2017. For the years ended December 31, 2017 and December 31, 2018, the Company recognized no transition tax.

As a result of the Act, the Company re-measured certain deferred tax assets and liabilities based on the rates at which they are anticipated to reverse in the future, which is generally 21%. For the year end December 31, 2017, the provisional amount recorded related to the re-measurement of the deferred tax asset balance was a decrease of $28.8 million, with a corresponding reduction to the valuation allowance of $28.8 million for a net effect of $0.

Realization of future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the Internal Revenue Code provisions, certain substantial changes in the Company's ownership, including the sale of the Company or significant changes in

ownership due to sales of equity, may have limited, or may limit in the future, the amount of net operating loss carryforwards which could be used annually to offset future taxable income. The Company completed an analysis through December 31, 2017 and determined that on March 30, 2007 and August 21, 2015 ownership changes had occurred. The Company may also experience ownership changes in the future as a result of subsequent shifts in its stock ownership, some of which may be outside of the Company's control. As a result, the Company's ability to use its pre-change NOLs to offset U.S. federal taxable income may be subject to limitations, which could potentially result in an increased future tax liability. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

As of December 31, 2018, and 2017, the Company had uncertain tax positions of $0.2 million related to capitalized research and development costs and research and development credits, which reduce the deferred tax assets with a corresponding decrease to the valuation allowance. The Company has elected to recognize interest and penalties related to income tax matters as a component of income tax expense, of which no interest or penalties were recorded for the years ended December 31, 2018 and 2017. The Company expects none of the unrecognized tax benefits to decrease within the next 12 months related to expired statutes or settlement with the taxing authorities. Due to the Company's valuation allowance as of December 31, 2018, none of the Company's unrecognized tax benefits, if recognized, would affect the effective tax rate.

A reconciliation of the Company's unrecognized tax benefits is as follows (in thousands):

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Unrecognized tax benefit--beginning of year | $ 163 | $ 241 | $ 241 |
| Decreases related to prior period positions | — | (78) | — |
| Unrecognized tax benefit--end of year | $ 163 | $ 163 | $ 241 |

The Company files tax returns in the United States, Massachusetts, California, Pennsylvania, New Jersey and New York. All tax years since inception (October 11, 2005) remain open to examination by major tax jurisdictions to which the Company is subject, as carryforward attributes generated in years past may still be adjusted upon examination by the Internal Revenue Service or state tax authorities if they have or will be used in a future period. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years.

**14. Commitments**

***License Agreements***

NovaMedica—In August 2013, in connection with the third tranche of its Series B-1 financing, the Company entered into a Technology Transfer Agreement (the "Tech Transfer Agreement") with Domain Russia Investments Limited ("DRI"). Pursuant to the Tech Transfer Agreement, in exchange for nominal payment, the Company assigned to DRI certain patent applications and granted to DRI a license to develop and commercialize entinostat in certain Eastern European countries (the "Covered Territory"). The Company concurrently entered into a sublicense agreement with DRI (the "DRI Sublicense") and a sublicense agreement (the "NovaMedica Sublicense") with NovaMedica LLC ("NovaMedica"), which is jointly owned by Rusnano Medinvest LLC and DRI. Pursuant to the DRI Sublicense, the Company granted to DRI an exclusive sublicense to develop, manufacture and commercialize entinostat in the Russian Federation. Pursuant to the NovaMedica Sublicense, the Company granted to NovaMedica an exclusive sublicense to develop, manufacture and commercialize entinostat in the rest of the Covered Territory. Immediately thereafter, the Company, DRI and NovaMedica executed an assignment and assumption agreement, pursuant to which the assigned patents and all of DRI's rights and obligations under the Tech Transfer Agreement and the DRI Sublicense were transferred to NovaMedica. Under the Tech Transfer Agreement, in certain cases, the Company is required to assist NovaMedica, and NovaMedica is required to reimburse the Company for any out-of-pocket expenses incurred in providing this assistance, including travel-related expenses.

Eddingpharm—In April 2013, the Company entered into a License and Development Agreement (the "Eddingpharm License Agreement") and a Series B-1 purchase agreement (the "Eddingpharm Purchase Agreement") with Eddingpharm International Company Limited ("Eddingpharm"). Under the terms of the

Eddingpharm License Agreement, Eddingpharm, in exchange for rights to develop and commercialize entinostat in China and certain other Asian countries, purchased $5.0 million of Series B-1 and agreed to make certain contingent milestone and royalty payments based on revenue targets. In certain cases, the Company is required to assist Eddingpharm, and Eddingpharm is required to reimburse the Company for any out-of-pocket expenses incurred in providing this assistance, including reimbursement for person-hours above a certain cap.

***Lease Commitments***

In September 2016, the Company entered into a five-year operating lease for 12,207 square feet of office space in Waltham, Massachusetts, with a lease commencement date of March 1, 2017, and an option to extend the lease term once for an additional three years. The Company also has an option to cancel the lease after three years with the termination fee consisting of $55,000. The lease has monthly lease payments of $25,000 the first 12 months with annual rent escalations thereafter and provides a rent abatement of $0.2 million for the first year. The Company recorded the lease abatement as deferred rent and will amortize these amounts on a straight-line basis as a reduction of rent expense over the lease term. The Company paid the landlord a security deposit of $0.1 million in 2016, which will be returned without interest at the end of the lease. The Company recorded the security deposit as a long-term deposit on its consolidated balance sheet.

In December 2015, the Company entered into a 62-month operating lease for 4,039 square feet of space in New York, New York, which commenced on January 1, 2016. The lease has monthly lease payments of $18,000 the first 12 months with an annual rent escalation each year thereafter and provides a rent abatement of $18,000 per month for the first two months. The Company recorded the lease abatement as deferred rent and will amortize these amounts on a straight-line basis as a reduction of rent expense over the lease term. In accordance with the lease, in December 2015, the Company entered into a cash-collateralized irrevocable standby letter of credit in the amount of $0.1 million naming the landlord as beneficiary.

The Company also leases office equipment, which is accounted for as a capital lease and included in property and equipment at cost.

Future annual minimum lease payments as of December 31, 2018, are as follows (in thousands):

| | Operating Leases | Capital Lease Obligations |
|---|---|---|
| For the years ended December 31, | | |
| 2019 | 569 | $ 4 |
| 2020 | 588 | 4 |
| 2021 | 395 | 4 |
| 2022 | 59 | 1 |
| 2023 | — | — |
| 2024 and thereafter | — | — |
| Total minimum lease payments | $ 1,611 | 13 |
| Less amounts representing interest | | 2 |
| Present value of net minimum lease payments | | $ 11 |

Rent expense recognized under all operating leases, including additional rent charges for utilities, maintenance, and real estate taxes, is calculated on a straight-line basis and amounted to $0.8 million, $0.8 million and $0.4 million for the years ended December 31, 2018, 2017, and 2016, respectively.

**15. Supplemental Cash Flow Information**

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | | *(In thousands)* | |
| **Supplemental Disclosures of Cash Flow Information** | | | |
| Interest paid | $ — | $ — | $ 2 |
| **Supplemental Disclosures of Non-Cash Investing and Financing Activities:** | | | |
| Accretion of dividends on convertible preferred stock | $ — | $ — | $ 2,598 |
| Issuance costs included in accounts payable and accrued expenses | $ — | $ 50 | $ — |
| Vesting of restricted stock | $ — | $ 59 | $ 42 |
| Reclassification of common stock warrant liability to additional paid-in capital | $ — | $ — | $ 4,551 |
| Conversion of preferred stock to common stock upon closing of initial public offering | $ — | $ — | $ 328,941 |

**16. Related-Party Transactions**

In June 2015, the Company hired a Chief Executive Officer who was also appointed as a member of the Board. This individual is also a managing director at MPM Asset Management, LLC, which holds an investment in the Company's common stock.

**17. Quarterly financial information (unaudited)**

The following table contains quarterly financial information for 2018 and 2017. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

| | Three Months Ended 2018 | | | |
|---|---|---|---|---|
| *In thousands, except per share data* | March 31 | June 30 | September 30 | December 31 |
| License fees | $ 379 | $ 379 | $ 379 | $ 380 |
| Operating expenses: | | | | |
| Research and development | 15,339 | 14,851 | 14,095 | 15,821 |
| General and administrative | 4,791 | 4,479 | 4,125 | 3,892 |
| Total expenses | 20,130 | 19,330 | 18,220 | 19,713 |
| Loss from operations | (19,751) | (18,951) | (17,841) | (19,333) |
| Other income | 353 | 563 | 503 | 496 |
| Net loss | $ (19,398) | $ (18,388) | $ (17,338) | $ (18,837) |
| Net loss per share attributable to common stockholders—basic and diluted | $ (0.79) | $ (0.74) | $ (0.68) | $ (0.70) |
| Weighted-average shares--basic and diluted | 24,478,269 | 24,705,441 | 25,471,587 | 26,804,089 |

| | Three Months Ended 2017 | | | |
|---|---|---|---|---|
| *In thousands, except per share data* | March 31 | June 30 | September 30 | December 31 |
| License fees [1] | $ 305 | $ 305 | $ 305 | $ 1,193 |
| Operating expenses: | | | | |
| Research and development [2] | 9,552 | 9,862 | 12,188 | 16,599 |
| General and administrative | 3,930 | 4,285 | 3,563 | 4,083 |
| Total expenses | 13,482 | 14,147 | 15,751 | 20,682 |
| Loss from operations | (13,177) | (13,842) | (15,446) | (19,489) |
| Other income | 206 | 203 | 358 | 385 |
| Net loss | $ (12,971) | $ (13,639) | $ (15,088) | $ (19,104) |
| Net loss per share attributable to common stockholders—basic and diluted | $ (2.85) | $ (0.47) | $ (0.84) | $ (0.80) |
| Weighted-average shares--basic and diluted | 18,231,602 | 19,497,581 | 22,239,996 | 23,943,241 |

(1) License fees for the three months ended December 31, 2017 included $0.9 million for the partial recognition of the $5.0 million milestone received under the KHK License Agreement.

(2) Research and development expenses for three months ended December 31, 2017 included the $5.0 million upfront payment related to the Vitae License Agreement.

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

**Exhibit 10.35**

**AMENDMENT NO. 10 TO**
**CLINICAL TRIAL AGREEMENT**
**BETWEEN**
**ECOG-ACRIN CANCER RESEARCH GROUP**
**AND SYNDAX PHARMACEUTICALS, INC.**

This Amendment No. 10 to Clinical Trial Agreement (the "Amendment" or "Amendment 10") is entered into as of October 15, 2018 (the "Effective Date"), by and between ECOG-ACRIN Cancer Research Group, on behalf of itself and its member hospitals, institutions and physicians (the "Group," "ECOG" or "ECOG-ACRIN"), and Syndax Pharmaceuticals, Inc. ("Company" or "Syndax").

WITNESSETH:

WHEREAS, pursuant to the Clinical Trial Agreement dated March 14, 2014 between the parties ("Agreement"), the parties agreed to certain terms specified therein for research services related to Group's performance of the Study; and

WHEREAS, the parties agree to increase the support for the Study to offset the expenses of additional areas associated with [*] as set forth herein.

NOW, THEREFORE, the parties hereto, intending to be legally bound hereby, agree as follows:

A. The following is added to Section 1.G of the Agreement:

The Company will provide financial support to the Group in the amount of $177,121 to support the activities associated with [*] for the Study as set forth in Exhibit E. The maximum financial support for the Agreement is increased from $24,654,424 by $177,121 to $24,831,545.

B. Exhibit B of the Agreement is deleted in its entirety and replaced by Exhibit B attached hereto.

C. Exhibit F attached hereto is hereby added as Exhibit F of the Agreement thereto.

D. This Amendment constitutes the full understanding of the parties and a complete and exclusive statement of the terms of their agreement with respect to the subject matter described herein, and no terms, conditions, understanding, or agreement purporting to modify or vary the terms of this Amendment shall be binding unless made in writing and signed by the parties.

E. Except to the extent amended herein, all of the terms and conditions of the Agreement remain in full force and effect.

F. Capitalized terms herein that are not defined shall have the meaning ascribed to such terms in the Agreement.

G. This Amendment may be executed in one or more counterparts, each of which shall be deemed an original, but all of which shall be considered one and the same instrument.

IN WITNESS WHEREOF, the parties hereto have executed this Amendment, as of the Effective Date, by proper persons duly authorized.

| ECOG-ACRIN Cancer Research Group | Syndax Pharmaceuticals, Inc. |
|---|---|
| /s/ Donna Marinucci | /s/ Luke J. Albrecht |
| Name: Donna Marinucci | Name: Luke J. Albrecht |
| Title: Executive Director | Title: General Counsel |

**EXHIBIT B**

**E2112 Budget & Payment Schedule**

**A. Budget Details**

1. Budget – Excluding Amendments

The budget for this project is $19,406,948 which is itemized as follows:
[*]

2. Budget – Amendment 1

The budget for Amendment 1 is $1,200,000 which is itemized as follows:
[*]

3. Budget – Amendment 3

The budget for Amendment 3 ([*] Support) is $450,000 which is itemized as follows:
[*]

4. Budget – Amendment 4

The budget for Amendment 4 ([*]) is $7,908 which is itemized as follows:
[*]

5. Budget – Amendment 5

The budget for Amendment 5 is $30,121 which is itemized as follows:
[*]

Statistical services being provided through Amendment 5 is limited to [*] of [*] services plus [*] of Group [*].

6. Budget – Amendment 6

The budget for Amendment 6 is $287,438 which is itemized as follows:
[*]

7. Budget – Amendment 7

The budget for Amendment 7 is $484,091 which is itemized as follows:
[*]

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended

8. Budget – Amendment 8

The budget for Amendment 8 is $1,582,064 which is itemized as follows:
[*]

9. Budget – Amendment 9

[*]

10. Budget – Amendment 10

The budget for Amendment 10 is $177,121 which is to pay for [*] provided by [*].

11. Invoicing and Payments

Company will make payments within [*] of receipt of invoices from Group according to the Payment Schedule herein. Payments will be made to as set forth in Section 1.B of the Agreement as follows:

ECOG Research and Education Foundation, Inc.
Agent for ECOG-ACRIN Cancer Research Group
Attn: Donna Marinucci
1818 Market Street, Suite 3000
Philadelphia, PA 19103

Group will send invoices to the following address:

Jeannette Hasapidis
VP, Program Management
Syndax Pharmaceuticals, Inc.
35 Gatehouse Drive, Building D, 3rd Flr
Waltham, MA 02451

**B. Payment Schedule – Excluding Amendments**

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

**C. Payment Schedule – Amendment 1**

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

**D. Payment Schedule – Amendment 3 ([*])**

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

**E. Payment Schedule – Amendment 4**

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

**F. Payment Schedule – Amendment 5**

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

**G. Payment Schedule – Amendment 6**

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

**H. Payment Schedule – Amendment 7**

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

**I. Payment Schedule – Amendment 8**

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

**J. Payment Schedule – Amendment 9**

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

**K. Payment Schedule – Amendment 10**

Group will submit invoices to Company in accordance with the following Payment Schedule:
[*]

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended

**EXHIBIT F**
**E2112 Scope of Work – Amendment 10**

**Protocol Title:** A Randomized Phase III Trial of Endocrine Therapy plus Entinostat/Placebo in Patients with Hormone Receptor-Positive Advanced Breast Cancer

[*]

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended

**EXHIBIT 23.1**

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in Registration Statement Nos. 333-210412, 333-220172 and 333-226678 on Form S-8 and Registration Statement No. 333-217172 on Form S-3 of our report dated March 7, 2019, relating to the financial statements of Syndax Pharmaceuticals, Inc. appearing in this Annual Report on Form 10-K of Syndax Pharmaceuticals, Inc. for the year ended December 31, 2018.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 7, 2019

**Exhibit 31.1**

**CERTIFICATIONS**

I, Briggs W. Morrison, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Syndax Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 7, 2019

By: /s/ Briggs W. Morrison, M.D.
Briggs W. Morrison, M.D.
Chief Executive Officer
(Principal Executive Officer)

**Exhibit 31.2**

**CERTIFICATIONS**

I, Richard P. Shea, certify that:

1. I have reviewed this Annual Report on Form 10-K of Syndax Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 7, 2019

By: /s/ Richard P. Shea
Richard P. Shea
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

**Exhibit 32.1**

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,**
**AS ADOPTED PURSUANT TO**
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Syndax Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his or her knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 7, 2019

By /s/ Briggs W. Morrison, M.D.
Briggs W. Morrison, M.D.
Chief Executive Officer

Date: March 7, 2019

By /s/ Richard P. Shea
Richard P. Shea
Chief Financial Officer